

Pharmacology Curriculum



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Harbin is knowledgeable in a wide variety of pharmacology and therapeutic topics, including neuroscience, neurological disease, psychiatric disease, kidney disease, and oncology. He now works as a medical writer, assisting in the development of oncology clinical publications. In his free time, he loves to rock climb, play bass guitar, and solo travel across the U.S.

Curriculum Structure

The *Pharmacology Curriculum* comprises the following lessons. Approximate lesson times are included.

Lesson	Title	Approximate Time
One	Pharmacodynamics	60 minutes
Two	Pharmacokinetics	60 minutes
Three	Molecular Pharmacology	60 minutes
Four	Drug Development and Approval	60 minutes
Five	Autonomic Nervous System	60 minutes
Six	Central Nervous System	60 minutes
Seven	Anesthetics and Analgesics	60 minutes
Eight	Cardiovascular System	60 minutes
Nine	Renal System	60 minutes
Ten	Endocrine Systems	60 minutes
Eleven	Antimicrobials	60 minutes
Twelve	Cancer	60 minutes
	Total	12 hours

Lesson Structure

Each lesson begins with a Lesson Overview, Lesson Objectives, and a Lesson at a Glance table, which lists the lesson activities, materials required, suggested preparation steps, and approximate class time.

Lesson Sections

The actual lesson follows the overview, which will contain some of the sections described below. Most lessons are designed to be completed within 45-60 minutes.

FOCUS

Every lesson begins with a FOCUS activity intended to capture participants' attention. This may be in the form of a small or large class discussion, game, review of previous lesson information, or demonstration. During this activity, participants are introduced to the topic of the lesson.

LEARN

The LEARN activity in each lesson varies in its presentation mode. It may be a slide presentation, group activity, or demonstration.

REVIEW

The majority of lessons end with a REVIEW activity intended to briefly review the lesson's key messages or main points.

Lesson One – Pharmacodynamics

Lesson Overview

In this lesson, students learn the key concepts of pharmacodynamics, which describes the effects of a drug on the body. Students will learn common terms associated with pharmacodynamics and engage in hands-on activities to learn important principles in pharmacodynamics.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define six common terms in pharmacodynamics
- Describe the relationship between dose and drug response
- Draw a dose-response curve for a drug
- Define efficacy and potency and identify each on a dose-response curve

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• Smart device • Internet Access (https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm) • <i>Basic Pharmacodynamic Properties of a Drug</i> worksheet	1. Print/photocopy <i>Basic Pharmacodynamic Properties of a Drug</i> worksheet (one per participant). 2. Ensure students have a smart device with internet access and can access the website.	10 minutes
LEARN	• <i>Pharmacodynamics</i> slide presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of three whiteboard markers	1. Prepare the <i>Pharmacodynamics</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Pharmacodynamics Quiz</i> • <i>Pharmacodynamics Quiz – Answer Key</i>	1. Print/photocopy <i>Pharmacodynamics Quiz</i> (one per participant).	10 minutes

Lesson One – Pharmacodynamics

FOCUS: Basic Pharmacodynamic Properties of a Drug

10 minutes

Purpose:

To familiarize students with the basic pharmacodynamic properties of a prescription drug.

Materials:

- Smart device
- Internet access
 - <https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm>
- *Basic Pharmacodynamic Properties of a Drug* worksheet

Facilitation Steps:

1. Distribute the *Basic Pharmacodynamic Properties of a Drug* worksheets prior to or at the beginning of class.
2. Have students access the website above and fill in the table on their worksheet.
3. Have students share and compare their results with a peer.

Name: _____ Class: _____

Basic Pharmacodynamic Properties of a Drug

PURPOSE: To familiarize yourself with the basic pharmacodynamic properties of a prescription drug.

Select a prescription drug (<https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm>) and fill in the information in the table below:

Drug Name (see “Highlights of Prescribing Information” – write down the brand and generic name)	
Drug Class	
What does the drug treat? (see Section 1 “Indications and Usage” – Select one if there is more than one indication)	
Recommended Dose for Indication (see section 2 “Dosage and Administration”)	
What is the drug’s mechanism of action? (see section 12.1 “Mechanism of Action”)	

COMPARE what you found to a peer's findings.

Have you heard of the disease or drug class associated with your drug or your peer's? If so, where?

Are there any keywords that you have seen before?

What are the units of the dose? Are they similar or different compared to your peer?

Lesson One – Pharmacodynamics

LEARN: Pharmacodynamics Slide Presentation

40 minutes

Purpose:

To introduce the basic principles of pharmacodynamics and drug response

Materials:

- *Pharmacodynamics* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of three whiteboard markers

Facilitation Steps:

1. Distribute the whiteboard kits and tell students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Pharmacodynamics

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Pharmacodynamics
 - Mechanism of action
 - Ligand
 - Receptor
 - Agonist
 - Antagonist
- Describe the relationship between the amount of drug (dose) and drug response
- Draw a dose-response curve for a drug
- Define efficacy and potency and identify each on a dose-response curve

Slide 3: Pharmacodynamics

Pharmacodynamics can be defined as how a drug affects the body. Pharmacodynamics includes:

- Therapeutic effects
 - The desired effect of a drug
 - Example: Using opioids to relieve pain
- Adverse and toxic effects (side effects)
 - The undesired effects of a drug
 - Example: Constipation associated with opioid use
- Lethal effects
 - The unintended lethal effect of a drug
 - Example: Overdose on opioids

Slide 4: Mechanism of Action

The mechanism of action refers to the specific way a drug achieves its therapeutic effect. This includes the biological components and the manner of interaction of a drug with these components.

These components are the drug's "intended target."

The location of these components is the drug's "site of action."

A good drug will be specific to a target. This is because there are many things in the body that can be targeted. Side effects can occur if the drug is not specific to a target.

Slide 5: How Does a Drug Work to Affect the Body?

Most drugs will target proteins in the body called receptors. A receptor is a protein that binds a ligand and upon binding causes an effect in the body. A ligand is a molecule that binds to another, larger molecule.

Drugs act as ligands for receptors. There are also ligands within the body (endogenous ligands) that interact with receptors. Endogenous ligands often compete with drugs for occupation of a receptor. For example, opioids compete with endorphins for opioid receptors.

Slide 6: Agonism Versus Antagonism

An agonist is a drug that binds and activates the receptor or increases the effect of that receptor. An example of an agonist is an opioid binding to its receptor, which activates the receptor and relieves pain.

An antagonist is a drug that binds but does not activate the receptor and competes with any ligand that can also bind to the receptor. An example of an antagonist is Narcan (naloxone), which binds to the opioid receptor to prevent the action of the opioid and prevent opioid overdose.

Slide 7: How Do We Know the Amount of Drug to Give?

The amount of drug given to a person is known as the dose. In most cases, dose is measured by the raw amount of drug (milligrams (mg)) or based on an individual's weight (mg of drug per kilograms (kg) of weight – mg/kg).

Too small of a dose may not be enough to achieve a therapeutic response.

Too much of a dose could cause unintended effects such as toxicity or lethality.

Drug responses are determined by the amount of drug that reaches the site of action (i.e., receptor).

Slide 8: What Is a Drug Response?

Drug responses are measured after a drug is applied to a system. Responses can be measured in a variety of systems and levels including:

- A biological cell
 - Example: You measure the amount of energy the cell produces.
- A tissue or organ
 - Example: You measure the rate of heart contraction.
- An individual
 - Example: You measure perceived pain relief in a person.

Slide 9: Measuring Drug Response

Drug response is represented by the fraction $\frac{E}{E_{\max}}$, where E is the measured response and $E_{\max}$ is the maximal response.

A drug can cause anywhere between 0% and 100% of the maximal response.

Drug responses are determined by the amount of drug that reaches the site of action (i.e., receptor).

Slide 10: Visualizing Drug Response

Hands-On Activity:

- Have students draw the axes of the dose-response graph on their whiteboard.
- Give students several minutes to draw how the dose-response curve might look, starting at point of origin (bottom left) and ending at the top right of the graph
 - Will the graph be a line? A curve?
- Allow the students to discuss among peers

Slide 11: Visualizing Drug Response

This is called a dose-response curve. **Why does the curve look like this?**

Small amounts of drug produce a large response.

However, it is harder for those small amounts to produce a response when there is a large amount of drug already in the system.

Hands-on Activity:

- Have students draw the correct curve on their whiteboards

Slide 12: Visualizing Drug Response

Now, the graph has changed from a linear dose scale to a semi-logarithmic dose scale. That is, the drug response is plotted over the logarithm of dose ($\log[\text{Dose}]$) instead of dose.

Hands-On Activity:

- Have students draw this graph next to the first graph
- Give students several minutes to draw how the dose-response curve might look when plotting drug response over $\log[\text{Dose}]$, starting at point of origin (bottom left) and ending at the top right of the graph.
 - Will this graph be a line? A curve?
- Allow the students to discuss among peers.

Slide 13: Visualizing Drug Response

After plotting the drug response over $\log[\text{Dose}]$, the curve turns into a sideways S-shape.

Plotting dose-response in this semilogarithmic fashion allows us to better understand differences in drug response when higher doses are used.

Hands-on Activity:

- Have students draw the correct curve on their whiteboards.

Slide 14: Visualizing Drug Response

Why does the curve look like this?

This is a very typical biological phenomenon that is observed for most drugs.

Additionally, this curve can tell us valuable information about drug properties.

Hands-On Activity:

- Have students draw the correct curve on their whiteboards

Slide 15: Efficacy Versus Potency of a Drug

What is efficacy and potency of a drug?

Efficacy is the level of response that a drug can have. Efficacy is evaluated by measuring maximal response of a drug. Potency is the dose of a drug for a given level of response. Potency is evaluated by measuring the ED50, which is the effective dose that results in 50% of drug response.

How can we determine the efficacy or potency of a drug? A dose-response curve!

Slide 16: Efficacy and Potency on a Dose-Response Curve

Hands-On Activity:

- Have the students add the “50% response” tick on the y-axis
- Based on the definitions of this slide, have the students identify where efficacy and potency (ED50) can be found
 - Using a different color, draw a dashed line to locate efficacy
 - Think about the units of efficacy when drawing this line
 - Using a different color, draw a dashed line to locate potency
 - Think about the units of potency when drawing this line
 - Allow the students to discuss among peers.

Slide 17: Identify Efficacy and Potency on This Curve

Efficacy is evaluated by measuring the maximal response from a drug. Efficacy is described in units of drug response.

Potency is evaluated by measuring the dose of drug that gives a 50% response. Potency is described in units of drug dose.

Slide 18: New Drug – Same Efficacy, less Potent
Hands-On Activity:

- Now ask the students to utilize the magnets to make a curve for a drug that has the **same potency** but is **less effective**
 - Overlay the magnets with the curve that is drawn on the graph
- Allow the students to discuss among peers

Slide 19: Same Potency, Less Effective

The potency is the same because the concentration at which each drug produces 50% of the drug's maximal response is the same.

The blue curve is about 50% less effective than the red curve, although the potency is the same.

Slide 20: New Drug – Same Efficacy, Less Potent
Hands-On Activity:

- Now ask the students to use the magnets to make a curve for a drug that has the **same efficacy** but is **less potent** than the red curve
- Overlay the magnets with the curve that is drawn on the graph

Slide 21: Same Efficacy, Less Potent

The drug for the blue curve has the same efficacy as the red curve drug because they have similar maximal efficacies.

However, the blue curve drug is less potent because it takes more drug to achieve the same response as the red curve drug.

Lesson One – Pharmacodynamics

REVIEW: Pharmacodynamics Quiz

10 minutes

Purpose:

To review key concepts related to pharmacodynamics.

Materials:

- *Pharmacodynamics Quiz*
- *Pharmacodynamics Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Pharmacodynamics Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the answer key and have students self-check answers and correct any wrong answers.

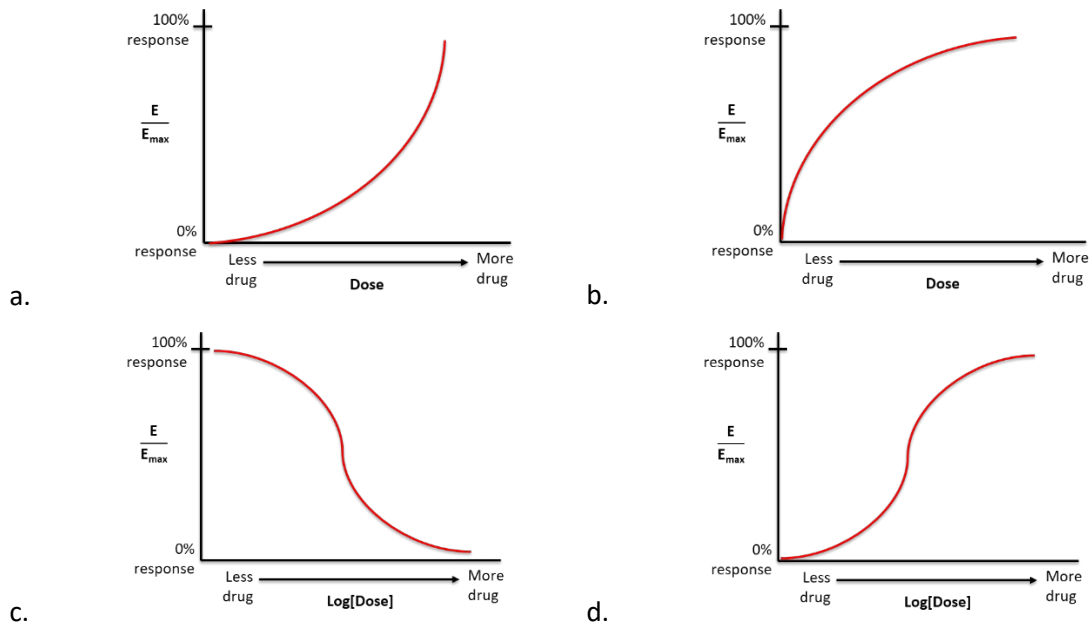
Name: _____ Class: _____

Pharmacodynamics Quiz

Instructions: Select the best answer to the following multiple-choice questions:

1. What phrase best describes pharmacodynamics?
 - a. The effect that the body has on the drug
 - b. How quickly the drug acts on the body
 - c. The effect that the drug has on the body
 - d. How quickly the body acts on the drug
2. A(n) _____ will bind and activate a receptor, while a(n) _____ will bind to a receptor without activating it and preventing other ligands from binding.
 - a. Antagonist; agonist
 - b. Agonist; antagonist
 - c. Ligand; drug
 - d. Drug; ligand
3. The _____ of a drug is the specific way a drug achieves its therapeutic effect.
 - a. Efficacy
 - b. Mechanism of action
 - c. Potency
 - d. Site of action
4. Which statement best describes the relationship between a drug and the response to a drug?
 - a. Drug responses are determined by the amount of drug that reaches the site of action
 - b. Drug responses are determined by the total amount of drug administered
 - c. Drug responses are determined by the amount of receptor, regardless of drug amount
 - d. Drug responses are determined by the amount of drug that leaves the body
5. Select all that apply. A _____ is a molecule that binds to a receptor and causes an effect in the body.
 - a. Dose
 - b. Ligand
 - c. Drug
 - d. Response

6. Select the graph that best represents a typical dose-response curve used by scientists and researchers.



7. The _____ of a drug describes the dose of a drug for a given response, and the _____ of a drug describes the level of response a drug can have.
- Agonism; antagonism
 - Efficacy; potency
 - Antagonism; agonism
 - Potency; efficacy

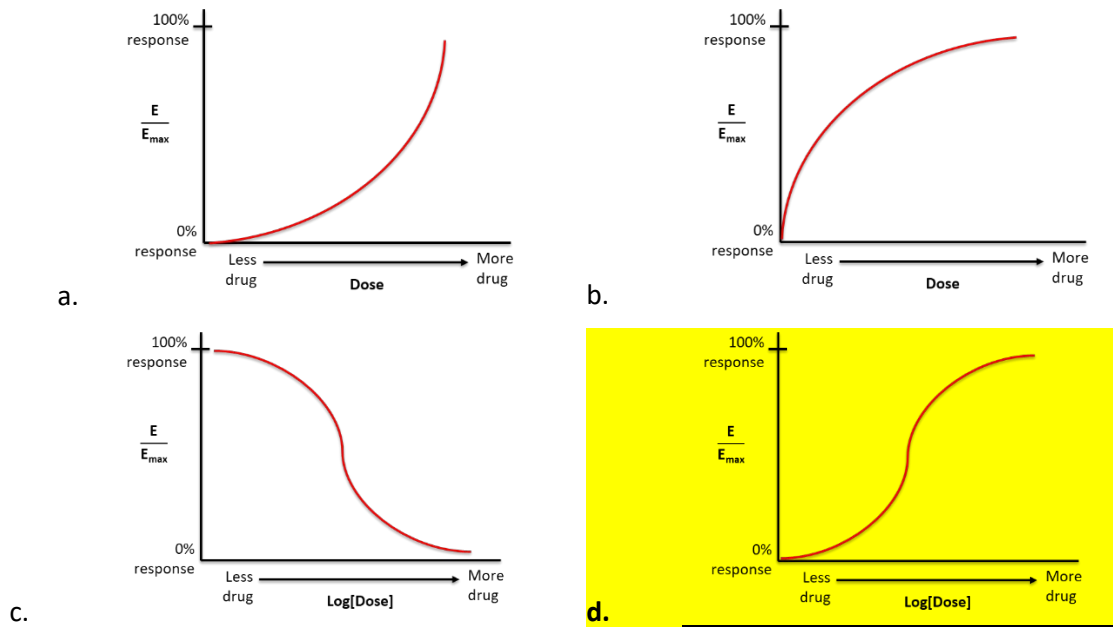
Name: _____ Class: _____

Pharmacodynamics Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice questions:

1. What phrase best describes pharmacodynamics?
 - a. The effect that the body has on the drug
 - b. How quickly the drug acts on the body
 - c. The effect that the drug has on the body**
 - d. How quickly the body acts on the drug
2. A(n) **agonist** will bind and activate a receptor, while a(n) **antagonist** will bind to a receptor without activating it and preventing other ligands from binding.
 - a. Antagonist; agonist
 - b. Agonist; antagonist**
 - c. Ligand; drug
 - d. Drug; ligand
3. The **mechanism of action** of a drug is the specific way a drug achieves its therapeutic effect.
 - a. Efficacy
 - b. Mechanism of action**
 - c. Potency
 - d. Site of action
4. Which statement best describes the relationship between a drug and the response to a drug?
 - a. Drug responses are determined by the amount of drug that reaches the site of action**
 - b. Drug responses are determined by the total amount of drug administered
 - c. Drug responses are determined by the amount of receptor, regardless of drug amount
 - d. Drug responses are determined by the amount of drug that leaves the body
5. Select all that apply. A **ligand** or **drug** is a molecule that binds to a receptor and causes an effect in the body.
 - a. Dose
 - b. Ligand**
 - c. Drug**
 - d. Response

6. Select the graph that best represents a typical dose-response curve used by scientists and researchers.



7. The **potency** of a drug describes the dose of a drug for a given response, and the **efficacy** of a drug describes the level of response a drug can have.
- Agonism; antagonism
 - Efficacy; potency
 - Antagonism; agonism
 - Potency; efficacy**

Sources

1. Alenghat, F. J., & Golan, D. E. (2004). Drug-Receptor Interactions. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (pp. 2-16). Wolters Kluwer.
2. Baca, Q. J., & Golan, D. E. (2004). Pharmacodynamics. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (pp. 17-26). Wolters Kluwer.

Lesson Two – Pharmacokinetics

Lesson Overview

In this lesson, students will learn the key concepts of pharmacokinetics, which describes the effects of the body on a drug. Students will learn common terms associated with pharmacokinetics, engage in hands-on activities to learn important principles in pharmacokinetics, and learn how to use a pharmacokinetic analysis.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define five common terms in pharmacokinetics
- Describe the four phases of pharmacokinetics
- Determine peak drug concentration, half-life, and bioavailability from a pharmacokinetic analysis
- Describe how bioavailability changes with different routes of administration

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• Smart device • Internet access (https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm) • <i>Basic Pharmacokinetic Properties of a Drug</i> worksheet	1. Print/photocopy <i>Basic Pharmacokinetic Properties of a Drug</i> worksheet (one per participant). 2. Ensure students have a smart device with internet access and can access the website.	10 minutes
LEARN	• <i>Pharmacokinetics</i> slide presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Pharmacokinetics</i> slide presentation	1. Prepare <i>Pharmacokinetics</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Pharmacokinetics Quiz</i> • <i>Pharmacokinetics Quiz – Answer Key</i>	1. Print/photocopy <i>Pharmacokinetics Quiz</i> (one per participant) and access the <i>Pharmacokinetics Quiz – Answer Key</i>.	10 minutes

Lesson Two – Pharmacokinetics

FOCUS: Basic Pharmacokinetic Properties of a Drug

10 minutes

Purpose:

To familiarize students with the basic pharmacokinetic properties of a prescription drug.

Materials:

- Smart device
- Internet access
(<https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm>)
- *Basic Pharmacokinetic Properties of a Drug* worksheet

Facilitation Steps:

1. Distribute the *Basic Pharmacokinetic Properties of a Drug* worksheets prior to or at the beginning of class.
2. Have students access <https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm> and fill the table on their worksheet.
3. Have students share and compare their results with a peer.

Name: _____ Class: _____

Basic Pharmacokinetic Properties of a Drug

PURPOSE: To familiarize yourself with the basic pharmacokinetic properties of a prescription drug.

Select a prescription drug (<https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm>) and fill in the information in the table below:

Drug Name (see “Highlights of Prescribing Information” – write down the brand and generic name)	
How is the drug administered? (look at what follows the drug name)	
See section 12.3 “Pharmacokinetics.” For a given dose of the drug, write down the following parameters:	
The area under the curve (AUC)	
The peak concentration of drug ($C_{\max}$)	
The half-life of drug ($t_{1/2}$)	
Does this section have a graph? If so, write down what is on each axis, including the units.	

COMPARE what you found to a peer's findings.

Do you and your peer have a drug that is administered in the same way or differently? Do you know what that administration method describes?

Compare the units of the pharmacokinetic parameters. Are they similar or different to your peer's?

If both of you have a graph, compare the two. Are there any obvious differences between the two? Look at the shape of the plotted data, the axes, and the units on the axes.

Lesson Two – Pharmacokinetics

LEARN: Pharmacokinetics Slide Presentation and Hands-On Activity

40 minutes

Purpose:

Introduce the key principles of pharmacokinetics and pharmacokinetic analysis.

Materials:

- *Pharmacokinetics* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for *Pharmacokinetics* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students that they should use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity precedes use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Pharmacokinetics

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Pharmacokinetics
 - Prodrug
 - Pharmacokinetic analysis
 - Half-life
 - Bioavailability
- Describe the four phases of pharmacokinetics

- Determine peak drug concentration, half-life, and bioavailability from a pharmacokinetic analysis
- Describe how bioavailability changes with different routes of administration

Slide 3: Pharmacokinetics

Pharmacokinetics is the effect that the body has on the drug. Remember, pharmacodynamics is the effect of the drug on the body.

Pharmacokinetics describes how the body interacts with and processes the drug once the drug is administered. Pharmacokinetics provides crucial information about:

- How much drug to administer
- How quickly the drug leaves the body and how often to administer the drug
- The route of drug administration

Slide 4: ADME – The 4 Phases of Pharmacokinetics

ADME is a simple way of understanding pharmacokinetics.

Each letter of ADME describes a phase of pharmacokinetics:

- Absorption
- Distribution
- Metabolism
- Excretion

The sum of these processes determines how effectively the drug enters the body, reaches the site of action, and leaves the body.

Slides 5-6: Absorption

Absorption describes how the drug enters the body and gets into the bloodstream.

Hands-On Activity:

- Have students attach the laminated activity to their whiteboard.
- Allow students several minutes to identify areas in the body where a drug could be absorbed. Mark these areas with green magnets.
- Students may identify the following: the mouth (oral or sublingual), in the gastrointestinal tract (from oral administration), in the nasal cavity (intranasal), in the muscle (intramuscular), directly into the blood (intravenous), or in the rectum (intrarectal)

A drug may enter the bloodstream by being absorbed in the mouth, gastrointestinal tract, nasal cavity, lungs, directly into the blood or muscle, or rectum.

The route of administration is important for how quickly and effectively a drug is absorbed.

Slide 7: Distribution

Distribution describes how the drug moves within the body towards its site of action once the drug enters the bloodstream.

Distribution is affected by the chemical properties of a drug and the patient's physiology. Some areas, like the brain, have barriers that prevent many drugs from penetrating it.

Drugs commonly bind to proteins in plasma (plasma-binding proteins). This binding can prolong the amount of time it takes for a drug to reach its target.

Slides 8-9: Metabolism

Metabolism describes how the drug is broken down by the body.

Hands-On Activity:

- Allow students several minutes to identify areas in the body where a drug could metabolize. Mark these areas with yellow magnets.
- Students may identify the following: liver, kidneys, lungs, blood, skin, and gastrointestinal tract

Metabolism occurs primarily in the liver, where many different enzymes readily metabolize drugs. Other areas include the kidneys, lungs, blood, and gastrointestinal tract.

Breaking down a drug typically inactivates them and facilitates their removal from the body.

Some drugs are activated by metabolism. Drugs that must be activated by metabolism are called prodrugs.

Slides 10-11: Excretion

Excretion describes how the drug is removed from the body.

Hands-On Activity:

- Allow students several minutes to identify areas in the body where a drug could be eliminated from the body. Mark these areas with white magnets.
- Students may identify the kidneys/urinary tract, liver and gastrointestinal tract (fecal excretion), lungs (exhalation), or skin (through sweat).

Most drugs are excreted in urine via the kidney. This process is called renal excretion. Other manners of excretion include feces, sweat, and exhalation.

Many drugs need to metabolize to facilitate their excretion.

Slides 12-14: Pharmacokinetic Analysis

A pharmacokinetic analysis is a study that analyzes the drug concentration in plasma over a given amount of time. Plasma is the component of blood

that does not include red blood cells, platelets, and other types of cells. Drug concentration is reported as the amount of drug (usually, micrograms (μg) or nanograms (ng)) per volume of plasma (milliliters (mL)).

A pharmacokinetic analysis monitors the concentration of drug in the body as the drug undergoes ADME.

This analysis is very helpful for determining:

- The route of administration
- The rate of drug administration

Now, we will explore a pharmacokinetic analysis in more depth.

Hands-On Activity:

- Have students remove the laminated overlay and the magnetic pins from the previous activity.
- Have students draw the axes from the slide and include units and tick marks for each axis.
- Allow students a few minutes to think about how this curve may look. Students may find it helpful to look back at the FOCUS activity for help.

This is a typical pharmacokinetic curve for most drugs, where the drug concentration rises quickly and falls slowly.

Hands-On Activity:

- If the students' curves do not look like this (a quick increase followed by a slower decrease with a definitive peak), have students correct their curve to one like this.

Slides 15-16: Pharmacokinetic Analysis

The peak concentration of the drug is abbreviated C_{max} .

Hands-On Activity:

- Have students draw a dot on their curve where they think the peak drug concentration is, label it " C_{max} ," and write the approximate value of C_{max} by the label.

The peak drug concentration (C_{max}) is located at the peak of this curve.

Hands-On Activity:

- If the students did not correctly identify " C_{max} " and/or correctly approximate the value, have them correct it on their graph.

Slides 17-18: Absorption Versus Elimination

The curve of a pharmacokinetic analysis can be split into two general phases: absorption and elimination.

Hands-On Activity:

- Have students draw a line on their curve where they think the absorption phase ends and the elimination phase begins. Label one side of the line with "Absorption" and the other side with "Elimination."

Initially, the drug is absorbed into the blood faster than it is eliminated.

When the drug reaches its peak concentration, the rate of elimination becomes faster than the rate of absorption. Then, the concentration of drug begins to decrease.

Drug elimination means the drug can no longer act on its target. Elimination involves the inactivation of a drug (metabolism) and/or the removal of a drug (excretion).

Hands-On Activity:

- If the students did not draw this line and/or label the line correctly, have them correct it on their graph.

Slides 19-20: Half-Life

Half-life ($t_{1/2}$) is defined as the time when the concentration of drug has been reduced to half of its peak (C_{max}).

Hands-On Activity:

- Have the students draw a dot on their curve where they think the half-life is located, label it as " $t_{1/2}$," and write the approximate value by the label.

Half-life ($t_{1/2}$) tells us how quickly the drug is eliminated from the body.

Remember, drug elimination means the drug can no longer act on its target. Elimination involves the inactivation of a drug (metabolism) and/or the removal of a drug (excretion).

Hands-On Activity:

- If the students did not correctly identify the half-life point on the curve and/or approximate the correct value, have them correct it on their graph.

Slide 21: Bioavailability

Bioavailability is defined as the extent to which the active form of the drug enters the blood.

Bioavailability is used to infer how much active drug reaches its site of action. It can be derived from the area under the curve in a pharmacokinetic analysis.

Slide 22: Bioavailability and Routes of Administration

The route of drug administration will affect the bioavailability of a drug. For example:

- Intravenous administration
 - The drug directly enters bloodstream.
 - Drugs administered this way are considered 100% bioavailable.

- Bioavailability for other routes of administration is expressed relative to intravenous administration.
- Oral administration
 - The drug is ingested and must be absorbed through gastrointestinal tract.
 - Drugs administered this way have widely variable bioavailability due to loss of the drug in the gastrointestinal tract.

Lesson Two – Pharmacokinetics

REVIEW: Pharmacokinetics Quiz

10 minutes

Purpose: To review key concepts related to pharmacokinetics and the learning objectives for the lesson.

Materials:

- *Pharmacokinetics Quiz*
- *Pharmacokinetics Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Pharmacokinetics Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Pharmacokinetics Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Pharmacokinetics Quiz

Instructions: Select the best answer to the following multiple-choice questions and matching questions.

1. What phrase best describes pharmacokinetics?
 - a. How quickly the drug acts on the body
 - b. The effect that the body has on the drug
 - c. How quickly the body acts on the drug
 - d. The effect that the drug has on the body

2. The _____ of a drug is the time when the concentration of drug is reduced to half of its peak (C_{max}), while the _____ of a drug refers to the extent which the active form of the drug enters the bloodstream.
 - a. Distribution; absorption
 - b. Half-life; bioavailability
 - c. Bioavailability; half-life
 - d. Absorption; distribution

3. Match the following ADME terms with their correct descriptions.

a. Absorption b. Distribution c. Metabolism d. Excretion	_____ How the drug moves within the body towards its site of action once it enters the bloodstream _____ How the drug is removed from the body _____ How the drug is broken down by the body _____ How the drug enters the body and gets into the bloodstream
--	---

4. Where in the body does drug metabolism primarily take place?
 - a. Kidneys
 - b. Liver
 - c. Gastrointestinal tract
 - d. Lungs

5. What is the primary way in which drugs are excreted from the body?
 - a. In feces via the gastrointestinal tract and liver
 - b. In sweat via the skin
 - c. Through exhalation via the lungs
 - d. In urine via the kidneys

6. Select all phrases that describe a pharmacokinetic analysis.
 - a. An analysis of the drug concentration in plasma over time
 - b. A way of determining bioavailability by calculating the area under the curve
 - c. A method of determining the half-life of a drug
 - d. An analysis that helps determine the route and rate of drug administration
7. What is a prodrug?
 - a. A drug that activates a receptor
 - b. A drug that is beneficial to a person
 - c. A drug that must be taken orally
 - d. A drug that must metabolize to become active
8. What is the bioavailability of a drug when it is administered intravenously (directly into the bloodstream)?
 - a. 100%
 - b. 90%
 - c. 50%
 - d. 0%

Name: _____ Class: _____

Pharmacokinetics Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice questions and matching questions.

1. What phrase best describes pharmacokinetics?
 - a. How quickly the drug acts on the body
 - b. The effect that the body has on the drug**
 - c. How quickly the body acts on the drug
 - d. The effect that the drug has on the body

2. The _____ of a drug is the time when the concentration of drug is reduced to half of its peak (C_{max}), while the _____ of a drug refers to the extent which the active form of the drug enters the bloodstream.
 - a. Distribution; absorption
 - b. Half-life; bioavailability**
 - c. Bioavailability; half-life
 - d. Absorption; distribution

3. Match the following ADME terms with their correct descriptions.

	b. How the drug moves within the body towards its site of action once it enters the bloodstream
a. Absorption	
b. Distribution	d. How the drug is removed from the body
c. Metabolism	c. How the drug is broken down by the body
d. Excretion	a. How the drug enters the body and gets into the bloodstream

4. Where in the body does drug metabolism primarily take place?
 - a. Kidneys
 - b. Liver**
 - c. Gastrointestinal tract
 - d. Lungs

5. What is the primary way in which drugs are excreted from the body?
 - a. In feces via the gastrointestinal tract and liver
 - b. In sweat via the skin
 - c. Through exhalation via the lungs
 - d. In urine via the kidneys**

6. Select all phrases that describe a pharmacokinetic analysis.
- a. **An analysis of the drug concentration in plasma over time**
 - b. **A way of determining bioavailability by calculating the area under the curve**
 - c. **A method of determining the half-life of a drug**
 - d. **An analysis that helps to determine the route and rate of drug administration**
7. What is a prodrug?
- a. A drug that activates a receptor
 - b. A drug that is beneficial to a person
 - c. A drug that must be taken orally
 - d. **A drug that must metabolize to become active**
8. What is the bioavailability of a drug when it is administered intravenously (directly into the bloodstream)?
- a. **100%**
 - b. 90%
 - c. 50%
 - d. 0%

Sources

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Lesson Three – Molecular Pharmacology

Lesson Overview

In this lesson, students will learn the key concepts of molecular pharmacology, which describes the cell signaling and the use of drugs to target components of cell signaling. Students will learn general concepts of cell signaling and use hands-on activities to learn how receptors work in the cell.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define five common terms in molecular pharmacology
- Describe cellular signaling and how pharmacology takes advantage of signaling
- List the four main receptor types that drugs target
- Describe how a drug interacts with each receptor type and causes a cellular effect

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Basic Components of a Cell</i> worksheet • <i>Basic Components of a Cell</i> – Answer Key	1. Print/photocopy <i>Basic Components of a Cell</i> worksheet (one per participant) and access the <i>Basic Components of a Cell</i> – Answer Key.	10 minutes
LEARN	• <i>Molecular Pharmacology</i> slide presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Molecular Pharmacology</i> slide presentation	1. Prepare <i>Molecular Pharmacology</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Molecular Pharmacology Quiz</i> • <i>Molecular Pharmacology Quiz</i> – Answer Key	1. Print/photocopy <i>Molecular Pharmacology Quiz</i> (one per participant) and access the <i>Molecular Pharmacology Quiz</i> – Answer Key.	10 minutes

Lesson Three – Molecular Pharmacology

FOCUS: Basic Components of a Cell

10 minutes

Purpose:

Review and familiarize yourself with the basic components of a cell.

Materials:

- *Basic Components of a Cell* worksheet
- *Basic Components of a Cell – Answer Key*

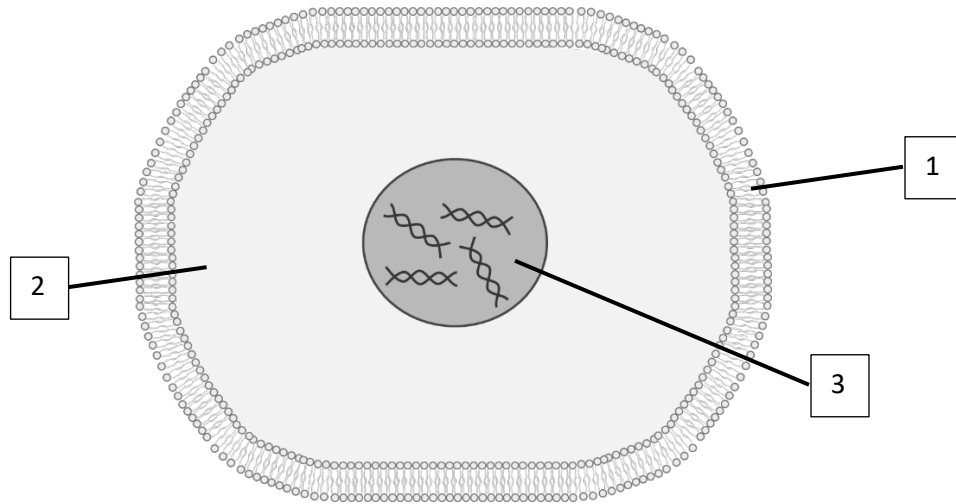
Facilitation Steps:

1. Distribute the *Basic Components of a Cell* worksheets prior to or at the beginning of class.
2. Have the *Basic Components of a Cell – Answer Key* available.
3. Have students answer the questions relating to the diagram of a cell on the worksheet. Allow students to discuss this with peers.
4. Use the *Basic Components of a Cell – Answer Key* to review answers with students. Ensure students understand these basic concepts as they will appear later in the lesson.

Name: _____ Class: _____

Basic Components of a Cell

PURPOSE: To review and familiarize yourself with the basic components of a cell.



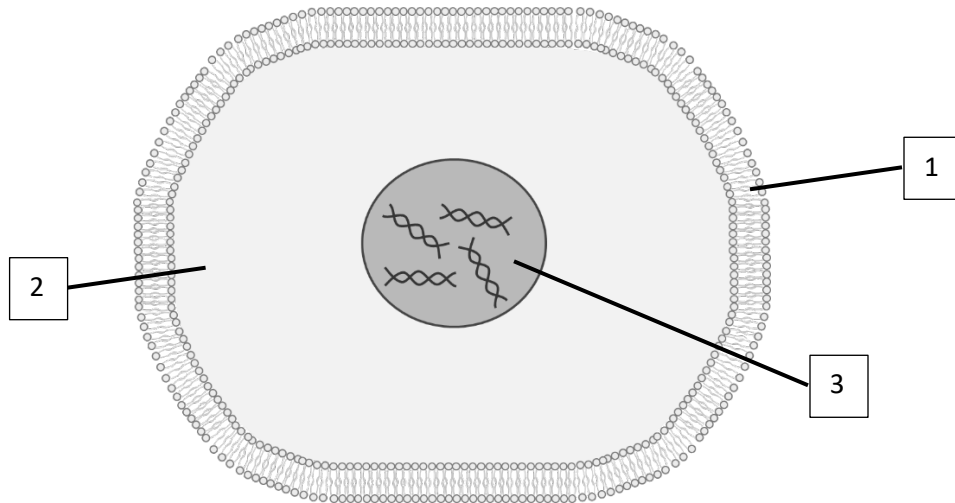
What is the name for 1, the layer on the outside of this cell? Write some things you know about this part of the cell, including key properties and its function in the cell.

What is the name for 2, the inside layer of this cell? Write some things you know about this part of the cell, including key properties and its function in the cell.

What is the name for 3, the organelle at the center of this cell? Write some things you know about this part of the cell, including key properties and its function in the cell.

Basic Components of a Cell – Answer Key

PURPOSE: To review and familiarize yourself with the basic components of a cell.



What is the name for 1, the layer on the outside of this cell? Write some things you know about this part of the cell, including key properties and its function in the cell.

Plasma membrane/Cell Membrane: This is a lipid bilayer that creates a barrier between the outside (extracellular space) and inside (intracellular space) of a cell. The plasma membrane is essential for gating molecules that are transported in and out of a cell. The plasma membrane also serves as a node for signals inside and outside of the cell.

What is the name for 2, the inside layer of this cell? Write some things you know about this part of the cell, including key properties and its function in the cell.

Cytosol/Cytoplasm: This is the intracellular space of a cell, which contains organelles and other molecules that help the cell function properly and survive. Organelles transport molecules between each other, and the cytoplasm acts as a medium for this transport. This is especially important between the plasma membrane and organelles.

What is the name for 3, the organelle at the center of this cell? Write some things you know about this part of the cell, including key properties and its function in the cell.

Nucleus: This is an organelle that contains the DNA of a cell. Here, genes located on DNA are transcribed into RNA, which can then be translated into protein. This process is called gene expression. The nucleus receives molecular signals from other parts of the cell, and these signals help regulate gene expression for the cell.

Lesson Three – Molecular Pharmacology

LEARN: Molecular Pharmacology Slide Presentation and Hands-On Activity

40 minutes

Purpose:

Introduce the key concepts of molecular pharmacology, cell signaling, and common drug targets.

Materials:

- *Molecular Pharmacology* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Molecular Pharmacology* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. The hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Molecular Pharmacology

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Cellular signaling
 - Signal transduction
 - Effector proteins
 - Secondary messengers
 - Enzyme
- Describe cellular signaling and how pharmacology takes advantage of signaling

- List the four main receptor types that drugs target
- Describe how a drug interacts with each receptor type and causes a cellular effect

Slide 3: Cell Signaling

Cell signaling is the process by which cells communicate with other cells or within a single cell.

Cells rely on molecular signals to mediate communication.

- You probably know of molecular signals, like hormones (e.g., estrogen) and neurotransmitters (e.g., dopamine)

Signal transduction is the process by which the signal is conveyed throughout the cell.

Slide 4: Essentials for Cell Signaling

Cell signaling requires the following components:

- **Molecular signals** to transmit the message
- **Receptors** that receive the signal
- **Effector proteins, secondary messengers, ions**, and other molecules that coordinate and mediate the consequences of the signal inside the cell
 - **Effector proteins** are proteins whose activity is either increased or decreased following receptor activation
 - **Secondary messengers** are released by effector proteins and relay the message to

molecules within the cell
(including other effector
proteins)

For cell signaling to function effectively, these components must be in the right **space** at the right **time** for the right **amount of time**.

Slide 5: Cell Signaling Dysfunction and Pharmacology

For cells and the body to function properly, cell signaling must be very precise and tightly coordinated.

If cell signaling is perturbed, disease can occur.

- For example, increased signaling that tells a cell to divide may lead to the development of cancer

Pharmacology takes advantage of cell signaling by developing drugs that target components of cell signaling that are dysfunctional.

- Generally, drugs treat disease by correcting dysfunction in a particular cell signaling pathway

Slide 6: Targeting Receptors

Most therapeutic strategies target a receptor on the plasma membrane because they do not need to permeate the cell.

- A drug that interacts with a cytosolic component must be able to permeate the cell

The type of drug used for a disease is based on the defect in cell signaling for that disease.

- If a disease results from under activation of receptor-dependent cell signaling, an agonist should be used to activate the receptor or increase its activity
- If a disease results from overactivation of receptor-dependent cell signaling, an antagonist should be used to inhibit the receptor or decrease its activity.

Slide 7: Types of Receptors

There four main receptor types are ion channels, G-protein coupled receptors (GPCRs), enzyme-linked receptors, and intracellular receptors.

Slide 8: Ion Channels

Ion channels are located on the plasma membrane.

Upon ligand binding, the opening of the channel will be affected.

- When the channel opens, ions flow into cytoplasm and/or out of the cell
- Common ions include calcium (Ca^{2+}), sodium (Na^+), potassium (K^+), and chloride (Cl^-)

Ions can trigger cellular responses or may cause changes to effector proteins.

As an example:

- Anti-seizure drugs, like phenobarbital, bind to GABA receptors, which are Cl^- channels
- Drug binding keeps the ion channel open for longer, which increases Cl^- flow into neurons and stops seizures

Slide 9: G-Protein Coupled Receptors (GPCRs)

GPCRs are located on the plasma membrane.

Upon ligand binding, the receptor activates a complex of G-proteins.

- Prior to binding, three G-proteins ($\text{G}\alpha$, $\text{G}\beta$, $\text{G}\gamma$) associate with the GPCR
- After binding, $\text{G}\alpha$ and $\text{G}\beta\gamma$ ($\text{G}\beta$ and $\text{G}\gamma$ are always coupled together) separate and interact with **effector proteins**
- G-proteins modulate the activity of effector proteins that release **secondary messengers (SM on graph)**

Most drugs act on GPCRs.

- As an example:

- Propranolol (heart failure medication) binds to and inhibits the β -adrenergic receptor (GPCR)
- After drug binding, G-protein signaling from receptor activation causes a cellular response that decreases the workload of the heart

Slide 10: Enzyme-Linked Receptors

Enzyme-linked receptors are on the plasma membrane and are linked to enzymes on the inside of the cell.

Upon ligand binding, the receptor causes activation of an enzyme.

- An enzyme catalyzes a biological process
- The receptor itself may contain an enzyme or may be connected to an enzyme in the cytoplasm
- Most enzyme-linked receptors cause protein phosphorylation
- This protein phosphorylation regulates the activity and function of effector proteins

The largest group of these receptors is tyrosine kinases.

- As an example:
 - HER2 is a receptor tyrosine kinase that can lead to breast cancer when overstimulated
 - Lapatinib treats breast cancer by inhibiting HER2.

Slide 11: Intracellular Receptors

Intracellular receptors are located inside the cell.

- A drug must permeate the plasma membrane to reach this target

A common intracellular receptor is a nuclear receptor.

- These are in the cytoplasm or nucleus
 - If the receptor is in the cytoplasm, ligand binding causes the receptor to move to the nucleus

- Ligand binding activates the receptor, which affects gene expression on DNA

Enzymes can also be intracellular receptors.

As an example:

- Prednisone is a steroid drug commonly used to alleviate inflammation in the body
- To alleviate inflammation, the drug binds to the glucocorticoid receptor (nuclear receptor) and alters gene expression

Slides 12-13: Ion Channel

Hands-On Activity:

- Have students attach the laminated overlay to their whiteboard.
- Have students place the green magnets where the drug will bind (green magnets represent the drug). Label the drug “extracellular” if it binds outside the cell and “intracellular” if it binds inside the cell.
- Have students place the yellow magnets where effector proteins will follow receptor activation (yellow magnets represent the protein). Draw arrows to indicate activation from one component to another.
- Have students place the white magnets where ions will flow (white magnets represent ions). Use arrows to indicate the direction of ions flowing.

Students’ responses should like the image in slide 13. The key concepts are:

- Drug binds to the receptor in an “extracellular” manner.
- Ions are inside and outside the cell. They can flow in a bidirectional manner when the drug binds to the receptor and opens the channel.
- Ions have cellular effects on their own or bind to effector proteins.

Slides 14-15: GCPR (G-Protein Coupled Receptor)

Hands-On Activity:

- Have students place the green magnets where the drug will bind (green magnets represent the drug). Label the drug “extracellular” if it binds outside the cell and “intracellular” if it binds inside the cell.
- Have students place the yellow magnets where effector proteins will follow receptor activation (yellow magnets represent the protein). Draw arrows to indicate activation of one component by another.
- Have students label the G-proteins, before and after receptor activation.
- Have students place the white magnets where secondary messengers are created (white magnets represent secondary messengers). Use arrows to connect proteins with the secondary messenger that was created by the protein.

Students’ responses should look like the image on slide 15. The key concepts are:

- Drug binds to the receptor in an “extracellular” manner.
- G-proteins are in a complex together with the receptor prior to drug binding.
- After drug binding, $G\alpha$ and $G\beta\gamma$ ($G\beta$ and $G\gamma$ are always coupled together) separate and interact with effector proteins.
- G-proteins modulate the activity of effector proteins that release secondary messengers (SM on graph).
- Effector proteins and secondary messengers produce a cellular response.

Slides 16-17: Enzyme-Linked Receptor

Hands-On Activity:

- Have students place the green magnets where the drug will bind (green magnets represent the drug). Label the drug “extracellular” if it binds outside the cell and “intracellular” if it binds inside the cell.
- Have students place the yellow magnets where effector proteins will follow receptor activation (yellow magnets represent the

protein). Draw arrows to indicate activation of one component by another.

- Have students place the white magnets where secondary messengers are created (white magnets represent secondary messengers). Use arrows to connect proteins with the secondary messenger that was created by the protein.

Students’ responses should look like the image on slide 17. The key concepts are:

- Drug binds to the receptor in an “extracellular” manner.
- Activation of receptor by the drug causes activation of the linked enzyme.
- The enzymes can interact with effector proteins.
- Although not labeled, these effector proteins could produce second messengers depending on the type of signaling.
- The effects of this signaling produces a cellular response.

Slides 18-19: Intracellular Receptor (Nuclear Receptor)

Hands-On Activity:

- Have students place the green magnets where the drug will bind (green magnets represent the drug). Label the drug “extracellular” if it binds outside the cell and “intracellular” if it binds inside the cell.
- Have students draw an arrow if a component moves in the cell.
- Have students draw an arrow between components if one component affects the other.

Students’ responses should look like the image on slide 19. The key concepts are:

- Drug binds to the receptor in an “intracellular” manner, either in the

cytoplasm or in the nucleus. Drug must pass through the membrane to do so.

- If the receptor is in the cytoplasm, drug binding will cause the receptor to move to the nucleus.
- Activated nuclear receptors will affect gene expression on DNA and produce a cellular response.

Lesson Three – Molecular Pharmacology

REVIEW: Molecular Pharmacology Quiz

10 minutes

Purpose:

Review key concepts related to molecular pharmacology and the learning objectives for the lesson.

Materials:

- *Molecular Pharmacology Quiz*
- *Molecular Pharmacology Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Molecular Pharmacology Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Molecular Pharmacology Quiz – Answer Key* and have students self-check answers, correcting any wrong answers.

Name: _____ Class: _____

Molecular Pharmacology Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. _____ is the process by which cells communicate with other cells or within a single cell, while _____ is the process by which the signal is conveyed throughout the cell.
 - a. Pharmacodynamics; pharmacokinetics
 - b. Signal transduction; cell signaling
 - c. Pharmacokinetics; pharmacodynamics
 - d. Cell signaling; signal transduction
2. Select all that apply. Which components participate in cell signaling?
 - a. Molecular signals
 - b. Receptors
 - c. Effector proteins
 - d. Secondary messengers
3. Select all that apply. Proper cell signaling requires its components to be in the right place at the right time for the right amount of time. What could occur if any of these components are dysfunctional?
 - a. Nothing because cells always have a backup plan
 - b. Disease may arise from dysfunction
 - c. Drugs may be used to correct the dysfunction if disease occurs
 - d. Drugs could not be used to correct the dysfunction even if disease occurs
4. Select all that apply. How can a drug target a receptor?
 - a. By binding to the receptor in the extracellular space
 - b. By binding to the receptor in the intracellular space
 - c. By activating the receptor when the receptor is under activated
 - d. By inhibiting the receptor when the receptor is overactivated
5. In cell signaling, the activity of a(n) _____ is increased or decreased following receptor activation, which alter the release of _____ that relay the message through the cell.
 - a. Effector protein; secondary messengers
 - b. Secondary messenger; effector proteins
 - c. Drug; enzymes
 - d. Enzymes; drugs

6. Match the following receptors with their correct descriptions.

- | | | |
|--|-----|--|
| | ___ | After activation, G-proteins separate and interact with effector proteins to release chemical messengers |
| a. Ion channel | | |
| b. G-protein coupled receptor (GPCR) | ___ | After activation, enzymes are activated and may interact with effector proteins |
| c. Enzyme-linked receptor | | |
| d. Intracellular receptor (nuclear receptor) | ___ | Drug permeates the cell to activate the receptor, which alters gene expression in the nucleus |
| | ___ | Receptor activation causes ions to flow through the channel |

7. What is an enzyme?

- a. A ligand that permeates the cell
- b. A molecule that relays a message
- c. A membrane that creates a barrier for the cell
- d. A protein that catalyzes a biological process

Name: _____ Class: _____

Molecular Pharmacology Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. _____ is the process by which cells communicate with other cells or within a single cell, while _____ is the process by which the signal is conveyed throughout the cell.
 - a. Pharmacodynamics; pharmacokinetics
 - b. Signal transduction; cell signaling
 - c. Pharmacokinetics; pharmacodynamics
 - d. **Cell signaling; signal transduction**
2. Select all that apply. Which components participate in cell signaling.
 - a. **Molecular signals**
 - b. **Receptors**
 - c. **Effector proteins**
 - d. **Secondary messengers**
3. Select all that apply. Proper cell signaling requires its components to be in the right place at the right time for the right amount of time. What could occur if any of these components are dysfunctional?
 - a. Nothing because cells always have a backup plan
 - b. **Disease may arise from dysfunction**
 - c. **Drugs may be used to correct the dysfunction if disease occurs**
 - d. Drugs could not be used to correct the dysfunction even if disease occurs
4. Select all that apply. How can a drug target a receptor to treat disease?
 - a. **By binding to the receptor in the extracellular space**
 - b. **By binding to the receptor in the intracellular space**
 - c. **By activating the receptor when the receptor is under activated**
 - d. **By inhibiting the receptor when the receptor is overactivated**
5. In cell signaling, the activity of a(n) _____ is increased or decreased following receptor activation, which alter the release of _____ that relay the message through the cell.
 - a. **Effector protein; secondary messengers**
 - b. Secondary messenger; effector proteins
 - c. Drug; enzymes
 - d. Enzymes; drugs

6. Match the following receptors with their correct descriptions.

- | | |
|--|--|
| a. Ion channel | b. After activation, G-proteins separate and interact with effector proteins to release chemical messengers |
| b. G-protein coupled receptor (GPCR) | c. After activation, enzymes are activated and may interact with effector proteins |
| c. Enzyme-linked receptor | d. Drug permeates the cell to activate the receptor, which alters gene expression in the nucleus |
| d. Intracellular receptor (nuclear receptor) | a. Receptor activation causes ions to flow through the channel |

7. What is an enzyme?

- a. A ligand that permeates the cell
- b. A molecule that relays a message
- c. A membrane that creates a barrier for the cell
- d. A protein that catalyzes a biological process**

Sources

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Lesson Four – Drug Development and Approval

Lesson Overview

In this lesson, students will learn the stages and key concepts of drug development and drug approval. Students will engage in a hands-on activity that will mimic the obstacles faced during drug development to assist in their learning.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define five common terms associated with drug development
- List and describe the stages of drug development and approval
- List the ethical principles that must be followed in clinical trials and the goal of clinical trials
- Describe the goals for each phase of clinical trials

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• Smart device • <i>Your Investigational Drug</i> worksheet • Internet access (https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm)	1. Print/photocopy <i>Your Investigational Drug</i> worksheet (one per participant).	10 minutes
LEARN	• <i>Drug Development and Approval</i> slide presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Drug Development and Approval</i> slide presentation	1. Prepare the <i>Drug Development and Approval</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Drug Development and Approval Quiz</i> • <i>Drug Development and Approval Quiz – Answer Key</i>	1. Print/photocopy <i>Drug Development and Approval Quiz</i> (one per participant) and access the <i>Drug Development and Approval Quiz – Answer Key</i> .	10 minutes

Lesson Four – Drug Development and Approval

FOCUS: Your Investigational Drug

10 minutes

Purpose:

Students create an imaginary drug that will be used throughout the lesson.

Materials:

- *Your Investigational Drug* worksheet
- Smart device
- Internet access
(<https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm>)

Facilitation Steps:

1. Distribute the *Your Investigational Drug* worksheets prior to or at the beginning of class.
2. Have students fill the table in the *Your Investigational Drug* worksheet.

Name: _____ Class: _____

Your Investigational Drug

Instructions: Create an imaginary drug that will be evaluated through the drug development process. Use the following website for inspiration: <https://dailymed.nlm.nih.gov/dailymed/browse-drug-classes.cfm>

Drug Name (generic or brand)	
What disease does the drug treat?	
How is the drug administered? (oral, intravenous, intranasal, intramuscular, sublingual, dermal)	
What type of receptor does the drug target? (ion channel, G-protein coupled receptor, enzyme-linked receptor, intracellular receptor)	

Lesson Four – Drug Development and Approval

LEARN: Drug Development and Approval Slide Presentation and Hands-On Activity

40 minutes

Purpose:

Students will have a foundation of the drug development and approval process, including practical and ethical hurdles encountered along the way.

Materials:

- *Drug Development and Approval* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Drug Development and Approval* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Drug Development and Approval

Slide 2: Learning Objectives

The learning objectives are:

- Define the following terms:
 - Preclinical and clinical
 - Biological assay
 - Hits and leads
 - Toxicology
 - Features of a clinical trial:
 - Blinded

- Placebo-controlled
- Randomized

- List and describe the stages of drug development and approval
- List the ethical principles that must be followed in clinical trials and the goal of clinical trials
- Describe the goals for each phase of clinical trials

Slides 3-4: Drug Development and Approval Process

Development and approval of a drug is costly, estimated to be over \$1 billion for each drug approved.

- Few drugs are approved for use and even fewer recoup costs

Hands-On Activity:

- Explain the rules of the game using the text above.
- Have students write their drug names from the FOCUS activity in the far-left column on their whiteboards.

Slide 5: Preclinical Development

Preclinical development refers to the experimental studies that take place prior to human studies (clinical studies).

An extensive amount of preclinical data must be collected to support testing of a drug in humans.

Preclinical studies include drug discovery, biological assay testing, and animal studies that assess the drug's effect in animal model of disease, pharmacokinetics, and toxicology.

Slide 6: Drug Discovery

Originally, drugs were derived from natural products (e.g., plants) known to alleviate illness.

- Most, if not all, cultures across history use natural products as medicine
- Based on this, scientists can reasonably hypothesize what types of natural products could treat disease

Now, it is more common for a drug target to be identified first based on biological studies.

- Then, a library of compounds is screened against the target to see if the drugs bind and cause an effect

Slide 7: Biological Assay Testing

A biological assay refers to the method of measuring a particular biological response (i.e., an effect on a drug target)

- Biological assays must be developed and optimized to screen drugs

“Hits” are those drugs that look promising following assay testing.

- Hits are optimized by chemists to make the drug more effective and potent in these assays

If the hit continues to look promising throughout optimization, then it becomes a “lead.”

Potential questions to ask the class based on prior lessons:

- Does this process relate more to evaluating the pharmacodynamics or pharmacokinetics of a drug?
- Which two graphs show an increase in drug efficacy?
- Which two graphs show an increase in drug potency?

Slides 8-9: Drug Development Scenarios

Hands-On Activity:

- Read each scenario aloud.
- Have students select a magnet with the color of their chosen scenario and place it on the row with their drug’s name in the “Drug Name” column. Use the white magnet for scenario three.
- All scenarios are successful. Have students move their magnets to the “Preclinical” column.

Slide 10: Animal Studies – Disease Modeling

Leads will be tested in animal models of disease.

It is critical that the animal model mimics human disease as closely as possible.

- Many drugs that are successful in animal models fail when they are used to treat disease in humans

Disease modeling in animals can be problematic, especially when the exact cause of disease is unknown.

- A drug target that alleviates disease in an animal may not be relevant to the disease in humans, especially if the disease is not natural to the animal.

All animal studies must be approved by an ethics review board to ensure they are performed in the most ethical manner possible.

Slide 11: Animal Studies – Pharmacokinetics

Leads are evaluated for their pharmacokinetic properties in animal studies, which include peak drug concentration (C_{max}), bioavailability (AUC), and drug half-life ($T_{1/2}$).

These studies provide insight into whether a drug will be safe and effective in human studies and answer questions like:

- Will the drug be found at levels effective to treat a disease?
- How much drug will be lost to ADME?
- How quickly will the drug be eliminated?

Slide 12: Animal Studies – Toxicology

Toxicology is the study of adverse effects of chemicals on living organisms.

Adverse effects include carcinogenicity (cancer), toxicity that affects development and reproduction, and toxicity that impairs organ function.

Animal toxicology studies provide a safety profile of the drug, which is the most important factor when considering human studies.

These studies evaluate adverse effects after a single dose and repeated doses of the drug.

- A goal of these studies is to determine the dose that produces minimal toxicity
- Typically, higher doses are more likely to have toxic effects

Slides 13-14: Drug Development Scenarios

Hands-On Activity:

- Read each scenario aloud.
- Have students select a magnet with the color of their chosen scenario and place it on the row with their drug's name in the "Preclinical" column. Use the white magnet for scenario three.
- Read the results of each scenario aloud.
- If a student's scenario was a **success**, have them move their magnet to the next column. If a student's scenario was a **failure**, have them remove their magnet from the board.

Slide 15: Clinical Trials

Clinical trials involve human subjects, which must follow these ethical principles:

- Respect for persons/informed consent
 - Patients make decisions in their best interest without coercion and give consent after being informed about the study
- Beneficence

- Evaluating benefits and mitigating risks, ensuring benefits outweigh risks

- Justice

- Selection of study participants is fair and equitable

The goal of a clinical trial is to establish the safety and efficacy of a drug for a given disease and patient population.

- To obtain a favorable result, clinical trials must be well-planned and very specific about the patients included/excluded, how a drug is given, and what responses are measured

There are many practical, regulatory, and ethical hurdles that can complicate or halt the clinical trial.

Slide 16: Phase I Trial

The goal of a phase I trial is to establish safety, tolerability, and pharmacokinetic properties of a drug in healthy human subjects (20 to 100 subjects).

These trials are usually nonblinded, meaning both patient and the researcher are aware of what is being administered.

Phase I is important for determining the drug dose and the frequency of dosing for subsequent trials.

- Dosing is gradually increased to determine the maximum dose that can be tolerated and shows limited toxicity

Slides 17-18: Drug Development Scenarios

Hands-On Activity:

- Read each scenario aloud.
- Have students select a magnet with the color of their chosen scenario and place it on the row with their drug's name in the "Phase I" column. Use the white magnet for scenario three.
- Read the results of each scenario aloud.
- If a student's scenario was a **success**, have them move their magnet to the next column. If a student's scenario was a

failure, have them remove their magnet from the board.

Slide 19: Phase II Trial

The goal of a Phase II trial is to establish the drug's efficacy in a smaller number of patients (up to several hundred) with the medical condition of interest.

These trials are usually placebo-controlled, which means the experimental group that receives the drug is compared to a control group that receives a placebo (something that should produce no therapeutic effect), and blinded, which means either the subject, researcher, or both are unaware of what is being administered.

Phase II trials usually involve multiple doses to determine dose-response and an optimal dose to be used for later trials.

Phase II also collects additional safety data.

Slides 20-21: Drug Development Scenarios

Hands-On Activity:

- Read each scenario aloud.
- Have students select a magnet with the color of their chosen scenario and place it on the row with their drug's name in the "Phase II" column. Use the white magnet for scenario three.
- Read the results of each scenario aloud.
- If a student's scenario was a **success**, have them move their magnet to the next column. If a student's scenario was a **failure**, have them remove their magnet from the board.

Slide 22: Phase III Trial

The goal of a pivotal phase III trial is to establish the efficacy of a drug in a large group of subjects with the medical condition of interest.

- These trials use several hundred to several thousand subjects

- These trials happen over multiple sites, and multiple phase III trials may be used to demonstrate a drug's efficacy

Phase III consists of randomized, controlled trials (RCTs). This means that subjects are randomly selected into groups, and the groups are balanced across many patient parameters (e.g., disease severity, age, sex). It also means that, with some exceptions, these trials are usually double-blinded and placebo-controlled.

These trials have a specified and validated endpoint (primary endpoint) that is used to determine the ultimate success of the trial. Common endpoints include survival rate or reduction of disease severity.

Slide 23: Drug Approval

In the United States, the Food and Drug Administration (FDA) oversees the drug approval process.

If Phase III results look promising, a New Drug Application (NDA) is submitted to the FDA demonstrating a drug's pharmacokinetics and pharmacodynamics, the clinical trial results, toxicology and safety, and many other components.

After thorough review of the NDA, the FDA will decide if the benefits of a drug outweigh the risks for the intended patient population. If so, the FDA approves the drug.

Slides 24-25: Drug Development Scenarios

Hands-On Activity:

- Read each scenario aloud.
- Have students select a magnet with the color of their chosen scenario and place it on the row with their drug's name in the "Phase III" column. Use the white magnet for scenario three.

- Read the results of each scenario aloud. If a student's scenario was a **success**, have them move their magnet to the next column. If a student's scenario was a **failure**, have them remove their magnet from the board.

Slide 26: Phase IV

Sometimes, the FDA will require Phase IV studies, or the pharmaceutical company will elect to perform a Phase IV study.

The goal of phase IV is to monitor the drug in the real world after the drug has been approved and marketed.

Most studies focus on safety monitoring of adverse events in the general population.

- Since clinical trials are so rigorously controlled and include a relatively small number of subjects, unexpected side effects may occur in the real world

Lesson Four – Drug Development and Approval

REVIEW: Drug Development and Approval Quiz

10 minutes

Purpose:

Review the goals and process of drug development and approval.

Materials:

- *Drug Development and Approval Quiz*
- *Drug Development and Approval Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Drug Development and Approval Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Drug Development and Approval Quiz – Answer Key* and have students self-check answers, correcting any wrong answers.

Name: _____ Class: _____

Drug Development and Approval Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. In drug development, _____ refers to experimental studies that include drug discovery and animal testing that takes prior to _____ in humans.
 - a. Pharmacokinetics; pharmacodynamics
 - b. Pharmacodynamics; pharmacokinetics
 - c. Preclinical development; clinical trials
 - d. Clinical trials; preclinical development

2. During drug discovery and biological assay testing, a _____ refers to a drug that looks promising following initial assay testing, while a _____ refers to a drug that continues to look promising throughout optimization.
 - a. Lead; hit
 - b. Agonist; antagonist
 - c. Antagonist; agonist
 - d. Hit; lead

3. Select all that apply. Animal studies evaluate a drug in which of the following ways?
 - a. A drug's ability to alleviate disease in an animal model of disease
 - b. A drug's pharmacokinetic properties, such as peak drug concentration, bioavailability, and half-life
 - c. A drug's safety profile by evaluating adverse effects in an animal
 - d. A drug's dose that produces minimal toxicity in an animal

4. Select all that apply. Which statement(s) describe a clinical trial?
 - a. It is very flexible and not very specific regarding which patients are included
 - b. The goal is to establish safety and efficacy of a drug for a given disease and patient population
 - c. It must follow ethical principles like respect for persons/informed consent, beneficence, and justice
 - d. There are many practical, regulatory, and ethical hurdles that can complicate or halt the trial

5. Match the following clinical trial phases with the correct goal.

- | | |
|--------------|---|
| | ___ To establish the drug's efficacy in a smaller number of patients with the medical condition of interest |
| a. Phase I | ___ To establish safety, tolerability, and pharmacokinetic properties of a drug in healthy human subjects |
| b. Phase II | |
| c. Phase III | ___ To monitor the drug in the real world after the drug has been approved and marketed |
| d. Phase IV | |
| | ___ To establish the efficacy of a drug in a large group of subjects with the medical condition of interest |

6. Select all that apply: Regarding their design, phase II and III clinical trials are usually

- a. Blinded, which means either the subject, researcher, or both (double-blind) are unaware of what is being administered
- b. Placebo-controlled, which means the experimental group that receives the drug is compared to a control group that receives a placebo
- c. Nonblinded, which means both the subject and researcher are aware of what is being administered
- d. Uncontrolled, which means there is no control group for comparison

Name: _____ Class: _____

Drug Development and Approval Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice questions and matching questions.

1. In drug development, _____ refers to experimental studies that include drug discovery and animal testing that takes place prior to _____ in humans.
 - a. Pharmacokinetics; pharmacodynamics
 - b. Pharmacodynamics; pharmacokinetics
 - c. Preclinical development; clinical trials**
 - d. Clinical trials; preclinical development
2. During drug discovery and biological assay testing, a **hit** refers to a drug that looks promising following initial assay testing, while a **lead** refers to a drug that continues to look promising throughout optimization.
 - a. Lead; hit
 - b. Agonist; antagonist
 - c. Antagonist; agonist
 - d. Hit; lead**
3. Select all that apply. Animal studies evaluate a drug in which of the following ways?
 - a. A drug's ability to alleviate disease in an animal model of disease**
 - b. A drug's pharmacokinetic properties, such as peak drug concentration, bioavailability, and half-life**
 - c. A drug's safety profile by evaluating adverse effects in an animal**
 - d. A drug's dose that produces minimal toxicity in an animal**
4. Select all that apply. Which statement(s) describe a clinical trial?
 - a. It is very flexible and not very specific regarding which patients are included
 - b. The goal is to establish safety and efficacy of a drug for a given disease and patient population**
 - c. It must follow ethical principles like respect for persons/informed consent, beneficence, and justice**
 - d. There are many practical, regulatory, and ethical hurdles that can complicate or halt the trial**

5. Match the following receptors with their correct descriptions.
- | | |
|--------------|---|
| | b. To establish the drug's efficacy in a smaller number of patients with the medical condition of interest |
| a. Phase I | a. To establish safety, tolerability, and pharmacokinetic properties of a drug in healthy human subjects |
| b. Phase II | |
| c. Phase III | d. To monitor the drug in the real world after the drug has been approved and marketed |
| d. Phase IV | |
| | c. To establish the efficacy of a drug in a large group of subjects with the medical condition of interest |
6. Select all that apply: Regarding their design, phase II and III clinical trials are usually
- a. Blinded, which means either the subject, researcher, or both (double-blind) are unaware of what is being administered**
 - b. Placebo-controlled, which means the experimental group that receives the drug is compared to a control group that receives a placebo**
 - c. Nonblinded, which means both the subject and researcher are aware of what is being administered
 - d. Uncontrolled, which means there is no control group for comparison

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Lesson Five – Autonomic Nervous System

Lesson Overview

In this lesson, students will learn the key features of the autonomic nervous system (ANS), how it regulates physiology, and ways that we use pharmacology to modify the ANS. Students will engage in hands-on activities that compare the sympathetic and parasympathetic divisions of the ANS.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define three common terms associated with the nervous system
- Describe the general features and order of the nervous system
- Compare the sympathetic and parasympathetic nervous systems
- Describe how drugs modify sympathetic or parasympathetic tone to treat medical conditions

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Fight-or-Flight Response</i> worksheet • <i>Fight-or-Flight Response – Answer Key</i>	1. Print/photocopy <i>Fight-or-Flight Response</i> worksheet (one per participant) and access the <i>Fight-or-Flight Response – Answer Key</i> .	10 minutes
LEARN	• <i>Autonomic Nervous System</i> slide presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Autonomic Nervous System</i> slide presentation	1. Prepare <i>Autonomic Nervous System</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Autonomic Nervous System Quiz</i> • <i>Autonomic Nervous System Quiz – Answer Key</i>	1. Print/photocopy <i>Autonomic Nervous System Quiz</i> (one per participant) and access the <i>Autonomic Nervous System Quiz – Answer Key</i> .	10 minutes

Lesson Five – Autonomic Nervous System

FOCUS: Fight-or-Flight Response

10 minutes

Purpose:

To introduce and relate an important phenomenon in autonomic nervous system function known as “fight or flight.”

Materials:

- *Fight-or-Flight Response* worksheet
- *Fight-or-Flight Response – Answer Key*

Facilitation Steps:

1. Distribute the *Fight-or-Flight Response* worksheets prior to or at the beginning of class.
2. Have the *Fight-or-Flight Response – Answer Key* page available.
3. Have students answer the questions on the *Fight-or-Flight Response* worksheet and have them discuss their answers with peers.

Name: _____

Class: _____

Fight-or-Flight Response

PURPOSE: To look back at a time when you have experienced or seen someone experience the phenomenon known as the fight-or-flight response and assess what you know about the fight-or-flight response.

The fight-or-flight response describes a survival phenomenon where a living organism is faced with a threat and must confront the threat (fight) or escape the threat (flight).

Describe a moment when you experienced or saw someone experience (maybe on TV/Internet) the fight-or-flight response and how it resolved. This can include psychological and physiological effects.

What part(s) of the body do you think is/are responsible for the fight-or-flight response?

What molecules have you heard of that are associated with the fight-or-flight response?

Fight-or-Flight Response – Answer Key

PURPOSE: To look back at a time when you have experienced or seen someone experience the phenomenon known as the fight-or-flight response and assess what you know about the fight-or-flight response.

The fight-or-flight response describes a survival phenomenon where a living organism is faced with a threat and must confront the threat (fight) or escape the threat (flight).

Describe a moment when you experienced or saw someone experience (maybe on TV/Internet) the fight-or-flight response and how it resolved. This can include psychological and physiological effects.

Answers vary

What part(s) of the body do you think is/are responsible for the fight-or-flight response?

The autonomic nervous system, which is part of the peripheral nervous system. The peripheral nervous system is the nerve cells and associated components outside the brain and spinal cord.

What molecules have you heard of that are associated with the fight-or-flight response?

Adrenaline/epinephrine, noradrenaline/norepinephrine, acetylcholine

Lesson Five – Autonomic Nervous System

LEARN: Autonomic Nervous System Slide Presentation

40 minutes

Purpose:

To develop an understanding of the autonomic nervous system and how pharmacology is used to modulate it to treat medical conditions.

Materials:

- *Autonomic Nervous System* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Autonomic Nervous System* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Autonomic Nervous System

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Neurons
 - Action potential
 - Neurotransmitter
- Describe the general features and order of the nervous system

- Compare the sympathetic and parasympathetic nervous systems including:
 - Physiological effects
 - Preganglionic and postganglionic neurons
 - Neurotransmitters and their receptor
- Describe how drugs modify sympathetic or parasympathetic tone to treat medical conditions

Slide 3: Features of a Nervous System

The nervous system is the master controller of the human body.

The defining feature of the nervous system is the use of nerve cells, called **neurons**, to transmit information.

- Neurons are excitable cells that fire **action potentials** when they are depolarized by the flow of ions
- Neurons transfer information during an action potential

Neurons are composed of:

- **Dendrites** that receive information
- **Cell body (soma)** that integrates information
- **Axons** that send information to neurons and other cells

Neurons transfer information between each other via neurotransmitters at the synapse during an action potential.

- A synapse is the bridge connecting two neurons

Slide 4: Order of the Nervous System

The brain and spinal cord make up the central nervous system (CNS).

The peripheral nervous system (PNS) is made up of neurons that connect the brain or spinal cord to the rest of the body.

- Sensory pathways provide information to the CNS
- The CNS responds by using motor pathways of the PNS

The motor response can be:

- Involuntary via the autonomic nervous system
- Voluntary via the somatic nervous system

Slide 5: Automatic Nervous System

The autonomic nervous system (ANS) exerts involuntary control of vital functions, such as:

- Heart rate and blood pressure control (cardiovascular)
- Breathing (respiratory)

The ANS causes **muscles** to relax or contract, **glands** to secrete hormones, and **organs** to stimulate metabolism.

The ANS is a two-neuron system composed of a:

- Preganglionic neuron (originates in the spinal cord or brainstem)
- Postganglionic neuron (terminates onto target tissues (e.g., muscles))
- Autonomic ganglion (synapse connecting the two neurons)

Slide 6: Sympathetic Versus Parasympathetic

The ANS is divided into two based on where each originates.

The **sympathetic nervous system** originates in the thoracic/lumbar region of the spinal cord (shown in

red). Activation of this system prompts a fight-or-flight response in the body.

The **parasympathetic nervous system** originates from the brainstem and the sacral region of the spinal cord (shown in green). Activation of this system prompts a rest-and-digest response in the body.

Slide 7: Physiology

Generally, sympathetic and parasympathetic actions have opposing effects. Most target tissues are controlled by both, so one will dominate over the other.

Activation of the sympathetic nervous system results in cardiovascular effects like increased blood pressure and heart rate, respiratory effects like bronchi relaxation that improves breathing, gastrointestinal effects that relax the GI and reduces digestion, metabolic effects that tell the body to consume sugars and fats for energy, and effects on eye function like pupil dilation.

Activation of the parasympathetic nervous system results in cardiovascular effects like decreased blood pressure and heart rate, respiratory effects like bronchi constriction that impairs breathing, gastrointestinal effects that constrict the GI and increases digestion, metabolic effects that tell the body to store fat and sugar, and effects on eye function like pupil constriction.

Slide 8: Dysfunction in the ANS

Many medical conditions can be treated by modifying the ANS, including:

- Hypertension (high blood pressure)
- Heart disease
- Asthma

Drugs modify the ANS by increasing or decreasing sympathetic or parasympathetic tone. Identifying the receptors and their endogenous ligands

(neurotransmitters) in the ANS is essential for knowing how to target the system with drugs.

Slide 9: Sympathetic and Parasympathetic Preganglionic Neurons

Both sympathetic and parasympathetic **preganglionic neurons** are cholinergic, which means they release **acetylcholine (ACh)**. In the autonomic ganglion, **ACh** released from the **preganglionic neuron** activates **nicotinic receptors** on the **postganglionic neuron**.

Hands-On Activity:

- Have students label the preganglionic neuron and autonomic ganglion diagrams on their whiteboards with information shown on the slide, using the diagram as a reference.
- Have students place green magnets on neurotransmitters and yellow magnets on receptors.

Slide 10: Nicotinic Receptors at Autonomic Ganglion

Nicotinic receptors are ion channels. Receptor activation causes positive ions to flow into the neuron, which depolarizes the neuron and causes an action potential.

Agonism of this receptor broadly activates all autonomic response. The net effect of activation causes an increase GI motility (cramps, vomiting), sweating, and salivation.

Antagonism of this receptor broadly inhibits autonomic response. The net effect of inhibition depends on the target tissue and if the dominant tone is sympathetic or parasympathetic.

Slide 11: Sympathetic and Parasympathetic Postganglionic Neurons

Sympathetic **postganglionic neurons** are adrenergic, which means they release **norepinephrine (NE)**. NE released from the

postganglionic neuron activates **adrenergic receptors** on the **target tissue**.

Parasympathetic **postganglionic neurons** are cholinergic, which means they release **acetylcholine (ACh)**. **ACh** released from the **postganglionic neuron** activates **muscarinic receptors** on the **postganglionic neuron**.

Hands-On Activity:

- Have students label the postganglionic neuron and target tissue diagrams on their whiteboards with information shown here, using the diagram below as a reference.
- Have students place green magnets on neurotransmitters and yellow magnets on receptors.

Slide 12: Adrenergic Receptors on Target Tissue
NE activates **adrenergic receptors** (GPCRs) on the postganglionic neuron to **increase sympathetic tone**. Drugs targeting adrenergic receptors increase or decrease sympathetic tone.

Adrenergic receptors are subtyped into α (α_1 , α_2) or β (β_1 , β_2) receptors. **Agonism of α_1 , β_1 , and β_2 receptors** on target tissue **increases sympathetic tone**. **Agonism of α_2 receptors decreases sympathetic tone** because these receptors provide negative feedback on the postganglionic neuron. **Antagonism** of these receptors **produces the opposite effect** on sympathetic tone

Slide 13: Muscarinic Receptors on Target Tissue
ACh activates **muscarinic receptors** (GPCRs) on the postganglionic neuron to **increase parasympathetic tone**. Drugs targeting muscarinic receptors increase or decrease parasympathetic tone.

Increase parasympathetic tone by agonism of muscarinic receptors. **Decrease parasympathetic tone** by antagonism of muscarinic receptors

Slides 14-15: ANS Tic-Tac-Toe

Hands-On Activity:

- Have students pair off and have each pair draw a 3 x 3 bingo board on their whiteboard.
- Have students write a number (1-9) in each box on the board. The numbers should be randomly distributed.
- Have students choose either X's or O's.

Each number will be paired with a drug that affects the ANS. Students will receive a description of each drug. On a student's turn (X's or O's), they will decide which receptor (nicotinic, adrenergic, or muscarinic) the drug targets based on the description given and what they know about the ANS.

On the student's turn, they must select a magnet of the same color as the receptor and place it on the number on your board.

- For example: For drug #3, they choose nicotinic. They select the yellow magnet and place it on #3 on their board.

If their choice was correct, they draw an X or O on that spot on the board. If their choice was wrong, have the other student draw an X or O.

Slides 16-17: Albuterol | 3 | X's

Hands-On Activity:

- Read the description of the drug.
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 17 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student can draw their symbol on that spot.

Slides 18-19: Bethanechol | 7 | O's

Hands-On Activity:

- Read the description of the drug.

- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 19 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 20-21: Phenylephrine | 1 | X's

Hands-On Activity:

- Read the description of the drug.
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 21 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 22-23: Atropine | 5 | X's

Hands-On Activity:

- Read the description of the drug.
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 23 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 24-25: Trimethaphan | 4 | O's

Hands-On Activity:

- Read the description of the drug.
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 25 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 26-27: Ipratropium | 2 | O's

Hands-On Activity:

- Read the description of the drug.
 - Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
 - Move on to slide 27 to reveal the answer.
 - Read the answer.
 - If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
 - Move on to slide 33 to reveal the answer.
 - Read the answer.
 - If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 28-29: Metoprolol | 9 | X's

Hands-On Activity:

- Read the description of the drug.
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 29 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 30-31: Methscopolamine | 6 | O's

Hands-On Activity:

- Read the description of the drug.
- Give students a minute to select a receptor and place the magnet of the receptor color on the tic-tac-toe board.
- Move on to slide 31 to reveal the answer.
- Read the answer.
- If the student was correct, have them draw their symbol (X or O) on that spot on the board. If they were wrong, the other student

Slides 32-33: Clonidine | 8 | X's

Hands-On Activity:

- Read the description of the drug.

Lesson Five – Autonomic Nervous System

REVIEW: Autonomic Nervous System Quiz

10 minutes

Purpose:

To review key concepts related to the autonomic nervous system and the learning objectives for the lesson.

Materials:

- *Autonomic Nervous System Quiz*
- *Autonomic Nervous System Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Autonomic Nervous System Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Autonomic Nervous System Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Autonomic Nervous System Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Match the following features of a nervous system with their correct descriptions:

_____	A molecule used to transfer information between two neurons
a. Neuron	_____
b. Action potential	The bridge that connects two neurons
c. Synapse	_____
d. Neurotransmitter	An excitable cell that transfers information

	An event that happens when a neuron is depolarized

2. The _____ exerts involuntary control of vital functions (like heart rate and breathing) and consists of _____ neuron(s) that connect(s) the spinal cord/brainstem to target tissues.
 - a. Somatic nervous system; 2
 - b. Autonomic nervous system; 2
 - c. Somatic nervous system; 1
 - d. Autonomic nervous system; 1

3. Select all that apply. What statements best describe the parasympathetic nervous system?
 - a. It is a division of the autonomic nervous system
 - b. Both preganglionic and postganglionic neurons release acetylcholine (ACh)
 - c. Activation prompts a fight-or-flight response
 - d. Responses on the target tissue are mediated by the adrenergic receptor

4. Select all that apply. What statements best describe the sympathetic nervous system?
 - a. It is a division of the somatic nervous system
 - b. Activation prompts a fight-or-flight response
 - c. Responses on the target tissue are mediated by muscarinic receptors
 - d. Preganglionic neurons release acetylcholine (ACh), while postganglionic neurons release norepinephrine (NE)

5. Select all that apply. What kind of drugs increase sympathetic tone?
 - a. Agonists of muscarinic receptors
 - b. Antagonists of muscarinic receptors
 - c. Agonists of adrenergic receptors (but not α_2)
 - d. Antagonists of adrenergic receptors (but not α_2)

6. Select all that apply. What kind of drugs decrease parasympathetic tone?
 - a. Antagonists of muscarinic receptors
 - b. Agonists of muscarinic receptors
 - c. Antagonists of adrenergic receptors (but not α_2)
 - d. Agonists of adrenergic receptors (but not α_2)

Name: _____ Class: _____

Autonomic Nervous System Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

- Match the following features of a nervous system with their correct descriptions:

a. Neuron	d. A molecule used to transfer information between two neurons
b. Action potential	c. The bridge that connects two neurons
c. Synapse	a. An excitable cell that transfers information
d. Neurotransmitter	b. An event that happens when a neuron is depolarized
- The _____ exerts involuntary control of vital functions (like heart rate and breathing) and consists of _____ neuron(s) that connect(s) the spinal cord/brainstem to target tissues.
 - Somatic nervous system; 2
 - b. Autonomic nervous system; 2**
 - Somatic nervous system; 1
 - Autonomic nervous system; 1
- Select all that apply. What statements best describe the parasympathetic nervous system?
 - a. It is a division of the autonomic nervous system**
 - b. Both preganglionic and postganglionic neurons release acetylcholine (ACh)**
 - Activation prompts a fight-or-flight response
 - Responses on the target tissue are mediated by the adrenergic receptor
- Select all that apply. What statements best describe the sympathetic nervous system?
 - It is a division of the somatic nervous system
 - b. Activation prompts a fight-or-flight response**
 - Responses on the target tissue are mediated by muscarinic receptors
 - d. Preganglionic neurons release acetylcholine (ACh), while postganglionic neurons release norepinephrine (NE)**

5. Select all that apply. What kind of drugs increase sympathetic tone?
- a. Agonists of muscarinic receptors
 - b. Antagonists of muscarinic receptors**
 - c. Agonists of adrenergic receptors (but not α_2)**
 - d. Antagonists of adrenergic receptors (but not α_2)
6. Select all that apply. What kind of drugs decrease parasympathetic tone?
- a. Antagonists of muscarinic receptors**
 - b. Agonists of muscarinic receptors
 - c. Antagonists of adrenergic receptors (but not α_2)
 - d. Agonists of adrenergic receptors (but not α_2)**

Sources

1. Atri, A., Chang, M. S., & Strichartz, G. R. (2004). Cholinergic Pharmacology. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 127-149). Wolters Kluwer.
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3. Gera, N., Armstrong, E. J., & Golan, D. E. (2004). Adrenergic Pharmacology. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 150-166). Wolters Kluwer.

Lesson Six – Central Nervous System

Lesson Overview

In this lesson, students will learn the key features of the central nervous system (CNS), the key features of neurotransmission, and ways that we use pharmacology to act on neurotransmitter systems. Students will engage in hands-on activities enhance understanding of CNS pharmacology.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define five common terms associated with the nervous system
- Describe how an action potential results in neurotransmission
- List the major neurotransmitters of the CNS and describe their importance in CNS function
- Understand how drugs act on neurotransmitter systems to treat CNS disorders

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Using Your Brain</i> worksheet • <i>Using Your Brain</i> – Answer Key	1. Print/photocopy <i>Using Your Brain</i> worksheet (one per participant) and access the <i>Using Your Brain</i> – Answer Key.	10 minutes
LEARN	• <i>Central Nervous System</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Central Nervous System</i> slide presentation	1. Prepare <i>Central Nervous System</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Central Nervous System Quiz</i> • <i>Central Nervous System Quiz</i> – Answer Key	1. Print/photocopy <i>Central Nervous System Quiz</i> (one per participant) and <i>Central Nervous System Quiz</i> – Answer Key.	10 minutes

Lesson Six – Central Nervous System

FOCUS: Using Your Brain

10 minutes

Purpose:

To assess students' knowledge about regions of the brain, neurotransmitters, and drugs that act on the brain.

Materials:

- *Using Your Brain* worksheet
- *Using Your Brain – Answer Key*

Facilitation Steps:

1. Distribute the *Using Your Brain* worksheets prior to or at the beginning of class.
2. Have the *Using Your Brain – Answer Key* available.
3. Have students answer the questions on the *Using Your Brain* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Using Your Brain

PURPOSE: To assess your knowledge about regions of the brain, neurotransmitters, and drugs that act on the brain.

1. List some regions of the brain. Do you know their primary function? If so, write them down.
2. Do you know of any neurotransmitters? If so, write them down. What do you associate with each neurotransmitter? A mental state? A disorder?
3. Do you know of any drugs that act on the brain? If so, write them down. Do you know what disorder or disease they treat? Or what effect they have on the mental state?

Using Your Brain – Answer Key

PURPOSE: To assess your knowledge about regions of the brain, neurotransmitters, and drugs that act on the brain.

4. List some regions of the brain. Do you know their primary function? If so, write them down.

Amygdala: Important for fear responses

Hippocampus: Important for learning and memory

Frontal cortex: Important for decision-making

Thalamus: The integration center of the brain

Hypothalamus: Important for maintaining homeostasis in the body (regulates feeding, drinking, etc.)

5. Do you know of any neurotransmitters? If so, write them down. What do you associate with each neurotransmitter? A mental state? A disorder?

Dopamine: Reward or pleasure

Serotonin: Associated with depression and mood disorders

Norepinephrine: Important for attention and arousal

GABA: Important for sleep and consciousness

6. Do you know of any drugs that act on the brain? If so, write them down. Do you know what disorder or disease they treat? Or what effect they have on the mental state?

SSRIs: Act on the serotonin system to treat depression and other mood disorders

Illicit drugs, like cannabis and LSD: Alters perception and consciousness

Caffeine: Keeps you alert, focused, and awake

Lesson Six – Central Nervous System

LEARN: Central Nervous System Slide Presentation

40 minutes

Purpose:

To develop an understanding of the central nervous system, its neurotransmitters and receptors, and how drugs target the CNS to treat CNS disorders.

Materials:

- *Central Nervous System* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Central Nervous System* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Central Nervous System

Slide 2: Learning Objectives

- Define the following:
 - Glia
 - Blood brain barrier (BBB)
 - Neurotransmission
 - Ionotropic receptors
 - Metabotropic receptors
- Describe how an action potential results in neurotransmission
- List the major neurotransmitters of the CNS and describe their importance in CNS function

- Understand how drugs act on neurotransmitter systems to treat CNS disorders

Slide 3: The Central Nervous System (CNS)

The central nervous system (CNS) is the master decision maker in the body. It receives information from the environment, integrates that information, and responds accordingly to promote survival of the organism. The CNS is made up of the brain and the spinal cord.

Slide 4: Cells of the CNS

The CNS is composed of several cell types. These include neurons that transmit information throughout the body via electrical impulses and chemical neurotransmitters. These also include **glia** (the “glue of the CNS”), which include astrocytes, microglia, and oligodendrocytes that support CNS function.

Slide 5: Blood Brain Barrier (BBB)

The **BBB** prevents toxic chemicals, drugs, and pathogens from entering the brain from the blood. The BBB regulates what enters and exits the brain. Impairment of the BBB is a common feature in many neurological diseases. Penetrating the BBB is a common issue in drug design. Many drugs can’t cross it.

Slide 6: Action Potential

The flow of ions through channels makes a neuron more electrically positive (depolarized) or more electrically negative (polarized). Neurotransmitters directly or indirectly cause depolarization/polarization.

Neurons fire an action potential once a threshold of depolarization is reached. An action potential is an all-or-nothing wave of depolarization (peak) followed by rapid repolarization (trough).

Slide 7: Neurotransmission

Neurotransmission occurs at the synapse when the presynaptic neuron fires an action potential and releases neurotransmitters.

On the postsynaptic neuron, neurotransmitters bind to:

- **Ionotropic receptors**, which are ion channels that allow flow of ions and cause depolarization or polarization
- **Metabotropic receptors**, which are GPCRs or other receptors that tune the ionotropic response via cell signaling

Neurotransmitters and drugs may excite neurons (increase action potential firing) or inhibit neurons (decrease action potential firing).

Slides 8-10: Glutamate

Glutamate is the primary **excitatory** neurotransmitter of the CNS and can activate **ionotropic** or **metabotropic** receptors to excite a neuron. Excessive glutamate may induce neuronal death in neurological disease, like Alzheimer's disease, and stroke. Alterations in glutamate neurotransmission are also found to promote seizures in epilepsy.

Hands-On Activity:

- Read the description of the drug on the slide.
- Give students a minute to think about how the drug will alter the receptor and neuron.
- Have students use their whiteboards according to the directions on the slide.
- On slide 10, read the answer below the description of the drug and ensure students understand why the answer is correct.

Slides 11-13: γ -Aminobutyric Acid (GABA)

GABA is the primary **inhibitory** neurotransmitter of the CNS and can activate **ionotropic** or **metabotropic** receptors to inhibit a neuron. Drugs that modify GABA and its receptors are used to treat epilepsy, anxiety, and insomnia. These drugs can sedate and anesthetize patient for surgery as well.

Hands-On Activity:

- Read the description of the drug on the slide.
- Give students a minute to think about how the drug will alter the receptor and neuron.
- Have students use their whiteboards according to the directions on the slide.
- On slide 13, read the answer below the description of the drug and ensure students understand why the answer is correct.

Slides 14-16: Norepinephrine (NE)

Norepinephrine is important for arousal, attention, and sleep-wake cycles and activates **metabotropic** receptors to tweak excitatory/inhibitory signals.

Norepinephrine is implicated in anxiety, pain, and mood disorders. Drugs that target the norepinephrine system will:

- Act specifically on norepinephrine receptors
- Alter the levels of norepinephrine at the synapse, which broadly affects norepinephrine signaling

Hands-On Activity:

- Read the description of the drug on the slide.
- Give students a minute to think about how the drug will alter the receptor and neuron.
- Have students use their whiteboards according to the directions on the slide.
- On slide 16, read the answer below the description of the drug and ensure students understand why the answer is correct.

Slides 17-19: Serotonin (5-HT)

Serotonin is important for regulating sleep-wake cycles, mood, and pain perception and activates **ionotropic** and **metabotropic** receptors to tweak excitatory/inhibitory signals. Serotonin is implicated in mood and pain disorders.

Drugs that target the serotonin system will:

- Act specifically on serotonin receptors
- Alter the levels of serotonin at the synapse, which broadly affects serotonin signaling

Hands-On Activity:

- Read the description of the drug on the slide.
- Give students a minute to think about how the drug will alter the receptor and neuron.
- Have students use their whiteboards according to the directions on the slide.
- On slide 19, read the answer below the description of the drug and ensure students understand why the answer is correct.

Slides 20-22: Dopamine (DA)

Dopamine is important for regulating movement, emotion, and reward and activates **metabotropic** receptors to tweak excitatory/inhibitory signals. Dopamine is implicated in disorders affecting movement (Parkinson's disease) and drug abuse.

Drugs that target the dopamine system will:

- Act specifically on dopamine receptors
- Alter the levels of dopamine at the synapse, which broadly affects dopamine signaling

Hands-On Activity:

- Read the description of the drug on the slide.
- Give students a minute to think about how the drug will alter the receptor and neuron.
- Have students use their whiteboards according to the directions on the slide.
- On slide 22, read the answer below the description of the drug and ensure students understand why the answer is correct.

Slides 23-25: Acetylcholine (Ach)

Acetylcholine is important for regulating sleep-wake cycles, memory, and arousal and activates **metabotropic** and **ionotropic** receptors to tweak excitatory/inhibitory signals. Acetylcholine is implicated in neurodegenerative disorders that impair cognition (e.g., memory).

Drugs that target the acetylcholine system will:

- Act specifically on acetylcholine receptors
- Alter the levels of acetylcholine at the synapse, which broadly affects acetylcholine signaling

Hands-On Activity:

- Read the description of the drug on the slide.
- Give students a minute to think about how the drug will alter the receptor and neuron.
- Have students use their whiteboards according to the directions on the slide.
- On slide 25, read the answer below the description of the drug and ensure students understand why the answer is correct.

Lesson Six – Central Nervous System

REVIEW: Central Nervous System Quiz

10 minutes

Purpose:

To review key concepts related to the central nervous system and the learning objectives for the lesson.

Materials:

- *Central Nervous System Quiz*
- *Central Nervous System Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Central Nervous System Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Central Nervous System Quiz – Answer Key* and have students self-check answers, correcting any wrong answers.

Name: _____ Class: _____

Central Nervous System Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. The CNS consists of _____ that transmit information and _____ that are the “glue” of the CNS that support its function.
 - a. Neurons; glia
 - b. Glia; neurons
 - c. The brain; spinal cords
 - d. The spinal cord; brains

2. Select all that apply. Which statement(s) describe(s) neurotransmission and action potentials?
 - a. A neuron fires an action potential after it reaches a threshold of depolarization
 - b. Drugs are released by the presynaptic neuron
 - c. Neurotransmitters bind to ionotropic and metabotropic receptors on the postsynaptic neuron
 - d. Drugs and neurotransmitters can excite or inhibit the postsynaptic neuron

3. A(n) _____ receptor is a GPCR or other receptor that tunes the response from _____ receptors, which cause depolarization or polarization of neurons via the flow of ions.
 - a. Glutamate; GABA
 - b. GABA; glutamate
 - c. Ionotropic; metabotropic
 - d. Metabotropic; ionotropic

4. Select all that apply. Which statement(s) describe(s) a drug’s potential action in the CNS?
 - a. A drug elevates levels of neurotransmitters in the synapse
 - b. A drug may antagonize a receptor for a neurotransmitter to increase receptor activation
 - c. A drug may agonize a receptor for a neurotransmitter to decrease receptor activation
 - d. Drugs can interact with metabotropic and ionotropic receptors to alter neuronal firing

5. Match the following neurotransmitters to their correct descriptions:

- | | |
|-------------------|---|
| | ___ Important for sleep-wake cycles and mood; commonly targeted to treat mood disorders (like depression) |
| a. Glutamate | ___ Important for arousal and attention; implicated in anxiety and pain disorders |
| b. GABA | ___ The primary excitatory neurotransmitter of the CNS |
| c. Norepinephrine | ___ Important for movement, emotion, and award; targeted to treat movement disorders (like Parkinson's disease) |
| d. Serotonin | ___ Important for memory and arousal; targeted in neurodegenerative diseases (like Alzheimer's disease) |
| e. Dopamine | ___ The primary inhibitory neurotransmitter of the CNS |
| f. Acetylcholine | |

Name: _____ Class: _____

Central Nervous System Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. The CNS consists of _____ that transmit information and _____ that are the “glue” of the CNS that support its function.
a. Neurons; glia
b. Glia; neurons
c. The brain; spinal cords
d. The spinal cord; brains
2. Select all that apply. Which statement(s) describe(s) neurotransmission and action potentials?
a. A neuron fires an action potential after it reaches a threshold of depolarization
b. Drugs are released by the presynaptic neuron
c. Neurotransmitters bind to ionotropic and metabotropic receptors on the postsynaptic neuron
d. Drugs and neurotransmitters can excite or inhibit the postsynaptic neuron
3. A(n) _____ receptor is a GPCR or other receptor that tunes the response from _____ receptors, which cause depolarization or polarization of neurons via the flow of ions.
a. Glutamate; GABA
b. GABA; glutamate
c. Ionotropic; metabotropic
d. Metabotropic; ionotropic
4. Select all that apply. Which statement(s) describe a drug’s potential action in the CNS?
a. A drug elevates levels of neurotransmitters in the synapse
b. A drug may antagonize a receptor for a neurotransmitter to increase receptor activation
c. A drug may agonize a receptor for a neurotransmitter to decrease receptor activation
d. Drugs can interact with metabotropic and ionotropic receptors to alter neuronal firing

5. Match the following neurotransmitters to their correct descriptions:

- | | |
|-------------------|--|
| | d. Important for sleep-wake cycles and mood; commonly targeted to treat mood disorders like depression |
| a. Glutamate | c. Important for arousal and attention; implicated in anxiety and pain disorders |
| b. GABA | a. The primary excitatory neurotransmitter of the CNS |
| c. Norepinephrine | e. Important for movement, emotion, and reward; targeted to treat movement disorders like Parkinson's disease |
| d. Serotonin | f. Important for memory and arousal and targeted in neurodegenerative diseases like Alzheimer's disease |
| e. Dopamine | b. The primary inhibitory neurotransmitter of the CNS |
| f. Acetylcholine | |

Sources

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Lesson Seven – Anesthesia and Analgesia

Lesson Overview

In this lesson, students will learn the properties of anesthetics and analgesics, how pain is sensed in the body, and how anesthetics and analgesics cause their effects. Students will engage in a hands-on activity to learn about common anesthetics and analgesics.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define four common terms associated anesthetics and analgesics
- Compare local and general anesthetics and their targets
- Describe nociception and how it's mediated through ascending and descending pathways
- List common analgesics and describe how they alleviate pain

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Anesthesia and Analgesia</i> worksheet	1. Print/photocopy <i>Anesthesia and Analgesia</i> worksheet (one per participant) and access the <i>Anesthesia and Analgesia – Answer Key</i>.	10 minutes
LEARN	• <i>Anesthesia and Analgesia</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Anesthesia and Analgesia</i> slide presentation	1. Prepare <i>Anesthesia and Analgesia</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Anesthesia and Analgesia Quiz</i> • <i>Anesthesia and Analgesia Quiz – Answer Key</i>	1. Print/photocopy <i>Anesthesia and Analgesia Quiz</i> (one per participant) and <i>Anesthesia and Analgesia Quiz – Answer Key</i>.	10 minutes

Lesson Seven – Anesthesia and Analgesia

FOCUS: Anesthesia and Analgesia

10 minutes

Purpose:

To assess students' understanding of anesthesia, analgesia, and the differences between the two.

Materials:

- *Anesthesia and Analgesia* worksheet

Facilitation Steps:

1. Distribute *Anesthesia and Analgesia* worksheets prior to or at the beginning of class.
2. Have students answer the questions on the *Anesthesia and Analgesia* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Anesthesia and Analgesia

PURPOSE: To assess your understanding of anesthesia, analgesia, and the differences between the two.

1. Analgesic drugs are used to relieve pain in the body without loss of consciousness. Have you ever needed analgesia? If so, when did you require it?
2. What medication(s) did you use to relieve your pain? What other medications do you know of that relieve pain?
3. Anesthetics are used to temporarily cause unconsciousness for medical purposes. Have you ever required anesthesia? If so, when did you require it?
4. Do you know of any drugs used to cause anesthesia? If so, list a few.

Lesson Seven – Anesthesia and Analgesia

LEARN: Anesthesia and Analgesia Slide Presentation

40 minutes

Purpose:

Help participants develop an understanding of anesthesia, analgesia, and common drugs that induce each.

Materials:

- *Anesthesia and Analgesia* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Anesthesia and Analgesia* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Anesthesia and Analgesia

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Anesthesia
 - Analgesia
 - Nociception
 - Nociceptors
- Compare local and general anesthetics and their targets

- Describe nociception and how it is mediated through ascending and descending pathways
- List common analgesics and describe how they alleviate pain

Slide 3: Analgesia Versus Anesthesia

Anesthesia is a loss of sensation, which may include a loss of consciousness. Anesthetic drugs will temporarily reduce all sensations (including pain) as well as motor and autonomic functions.

Analgesia is the inability to feel pain, which can be induced by medication. Analgesic drugs specifically target pain and no other sensations.

Drugs that cause anesthesia and analgesia may target the central (CNS), peripheral nervous system (PNS), and/or periphery (rest of the body).

Slide 4: Local Anesthetics

Local anesthetics are applied locally to the area of interest to disrupt neurotransmission there. They prevent all action potential firing in local neurons to prevent signaling to and from the area of application. These are commonly used in medical procedures to prevent pain and other sensations. Lidocaine is used a local anesthetic to numb your mouth at the dentist.

Slide 5: General Anesthetics

General anesthetics induce a temporary but reversible loss of consciousness for surgery. Other features of general anesthetics may include amnesia (loss of memory), temporary paralysis, and analgesia.

To induce loss of consciousness, general anesthetics act on the sleep center of the brain. However, it is still unknown exactly how these drugs cause the loss of consciousness.

General anesthetics can be inhaled or intravenously injected. Isoflurane and nitrous oxide (laughing gas) are common inhaled anesthetics. Benzodiazepines and propofol are common injected anesthetics.

Slide 6: Targets of General Anesthetics

General anesthetics act on ionotropic receptors to decrease neuronal excitation or increase neuronal inhibition.

GABA_A receptors are inhibitory ionotropic receptors. They are chloride (Cl⁻) ion channels that open upon **GABA** binding, which inhibit the neuron. Anesthetics potentiate ion channel function (more ion flow) and increase inhibition.

NMDA receptors are excitatory ionotropic receptors. They are sodium (Na⁺) and calcium (Ca²⁺) ion channels that open upon **glutamate** binding, which excite the neuron. Anesthetics inhibit the receptor (less ion flow) and decrease excitation.

Slide 7: Nociception

Nociception is the perception of a painful stimulus. Painful stimuli can be thermal, mechanical, or chemical. Pain stimuli are detected by sensory neurons in the PNS with pain-sensitive receptors called **nociceptors**:

- Thermal stimuli are detected by heat- or cold-sensitive ion channels, like when you touch a hot stove.
- Mechanical stimuli are detected by mechano-sensitive ion channel, like when you are pricked with a needle.
- Chemical stimuli are molecules associated with inflammation and tissue damage that

are detected by ionotropic or metabotropic receptors. This happens when you feel aches from inflammation caused by an infection.

There are two pathways that mediate nociception between the PNS and CNS.

Slide 8: Detection of Pain in the Nervous System
The **ascending pathway** mediates the detection of pain stimulus. Nociceptors sense painful stimuli in the PNS. The painful sensation is relayed through the spinal cord and different parts of the brain (medulla/pons). The pain signal ends in the cortex of the brain. The cortex perceives the painful sensation and emotion associated with the pain.

Slide 9: Modulation of Pain in the Nervous System
The **descending pathway** modulates pain sensation. The CNS modulates the intensity of the painful sensation, starting at the cortex. This happens in other parts of the brain (midbrain, medulla/pons) and the spinal cord. Molecules, like endorphins and serotonin, are released in this path to decrease the intensity of pain.

Slide 10: Pain Disorders

Chronic pain disorders can occur following neurological injury or persistent inflammation. In these disorders, the pain pathway becomes sensitized, where stimuli that did not cause pain now produces a painful sensation.

Chronic pain disorders include migraine (frequent and persistent headaches) and neuropathic pain (persistent pain in the periphery, usually following nerve damage). Compared to acute pain, treating chronic pain can be very challenging.

Slide 11: Opioids

The **opioid receptor** is a G-protein coupled receptor (GPCR) and consists of three subtypes: μ (mu), κ (kappa), and δ (delta). The body contains endogenous opioids (e.g., endorphins) that activate these receptors to modulate pain among other functions.

Opioid receptor agonists are analgesics that decrease nociception and alleviate acute pain very effectively. Agonists include morphine, buprenorphine, and fentanyl.

μ-opioid receptor agonists are most effective for pain relief but have the most abuse/overdose potential. μ-opioid antagonists like naloxone (Narcan) reverse the effects of opioids and prevent opioid overdose.

Slide 12: Opioid Side Effects and Abuse

However, opioid receptors are located throughout the body and are not specific to the pain pathway or elsewhere in the nervous system.

Among other side effects, opioids can cause constipation (decreased GI motility), respiratory depression (which is a common cause for opioid overdose), and euphoria (sense of contentment, happiness).

Opioids have a high abuse potential, so they are not recommended for chronic pain. Tolerance is quickly developed toward opioids, which creates a need for higher doses or more potent opioids. Opioid receptors are important for reinforcing behavior that leads to a reward. Opioids “hijack” this reward system in the brain.

Slide 13: NSAIDs and Acetaminophen

Non-steroidal anti-inflammatory drugs (NSAIDs) are very common analgesics for acute and chronic pain. This includes ibuprofen (Advil) and naproxen (Aleve®).

NSAIDs reduce the synthesis of prostaglandins, which promote inflammation throughout the body. NSAIDs inhibit the cyclooxygenase enzymes COX-1 and COX-2 to reduce inflammation where it occurs, which alleviates pain.

Acetaminophen (Tylenol®) is also used as analgesic, but it is not certain exactly how it does this. It is believed that acetaminophen and its metabolites act in the CNS with effects on COX in addition to other targets.

Slide 14: Anesthetic or Analgesic?

Hands-On Activity:

- Have students attach the overlay to their magnetic boards and read the table. Ensure they understand what is to be placed in each column of the table.
- Give students 5-10 minutes to read over the descriptions on slide 15.
- Have students use the magnets to indicate if the drug is an anesthetic or analgesic, and briefly describe its mechanism of action.
- Students may use the example at the top of the slide to assist them.
- The answers are as shown on slide 16. Review each answer and ensure students understand why each answer is correct.

Answers:

Diclofenac | analgesic | COX (Cyclooxygenase) enzyme – inhibitor – inhibits the enzyme to reduce prostaglandin synthesis and inflammation, which decreases nociception

Ketamine | anesthetic | NMDA Receptor (ionotropic glutamate receptor) – antagonist – decreases NMDAR activation, inhibits neuronal excitation by decreasing positive sodium/calcium ion flow

Benzocaine | anesthetic | Neuron action potential – prevents neuronal action potential from transmitting sensory information from the periphery where it is applied

Methadone | analgesic | mu-opioid receptor – agonist – decreases nociception in the pain pathway via GPCR activation in neurons

Midazolam | anesthetic | GABA(A) (ionotropic GABA receptor) – agonist (or potentiator) – increases GABAR function, which enhances neuronal inhibition by increasing negative chloride ion flow

Lesson Seven – Anesthetics and Analgesics

REVIEW: Anesthetics and Analgesics

10 minutes

Purpose:

Students review key concepts related to anesthetics and analgesics and the learning objectives for the lesson.

Materials:

- *Anesthetics and Analgesics Quiz*
- *Anesthetics and Analgesics Quiz* – Answer Key

Facilitation Steps:

1. Distribute the *Anesthetics and Analgesics Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Anesthetics and Analgesics Quiz* – Answer Key and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Anesthetics and Analgesics Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. _____ is the inability to feel pain, whereas _____ is the loss of sensation, which includes pain in addition to other sensations.
 - a. Anesthesia; analgesia
 - b. Analgesia; anesthesia
 - c. Nociception; hyperalgesia
 - d. Hyperalgesia; nociception
2. _____ prevent action potential firing in neurons where the drug is applied to prevent signaling to and from the area of application.
 - a. Opioid agonists
 - b. General anesthetics
 - c. Opioid antagonists
 - d. Local anesthetics
3. Select all that apply. What are some features of general anesthetics?
 - a. They induce a loss of consciousness
 - b. They induce analgesia
 - c. They are usually inhaled or intravenously injected
 - d. They target opioid receptors
4. Select all that apply. Which correctly describes the effect of a general anesthetic on its target?
 - a. Inhibits excitatory, ionotropic NMDA receptors (NMDAR) to decrease neuronal excitation
 - b. Potentiates excitatory, ionotropic NMDA receptors (NMDAR) to increase neuronal excitation
 - c. Inhibits inhibitory, ionotropic GABA_A receptors (GABA_AR) to decrease neuronal inhibition
 - d. Potentiates inhibitory, ionotropic GABA_A receptors (GABA_AR) to increase neuronal inhibition
5. Pain stimuli are detected by _____ on sensory neurons in the PNS and is the initial step for _____, which is the perception of painful stimuli.
 - a. Opioid receptors; nociception
 - b. Glutamate receptors; analgesia
 - c. Nociceptors; nociception
 - d. GABA receptors; analgesia

6. The _____ pathway is responsible for detecting a painful stimulus and relaying it through the spinal cord and brain to create a painful sensation, while the _____ pathway modulates the intensity of the painful sensation.
- Ascending; descending
 - Descending; ascending
 - Peripheral; central
 - Central; peripheral
7. Match the following drug or class of drugs with their descriptions:
- | | |
|---|--|
| a. μ -opioid receptor agonist | _____ Acts preferentially in the CNS on cyclooxygenase (COX) and other targets to induce analgesia |
| b. Non-steroidal anti-inflammatory drug (NSAID) | _____ Relieves pain but produces side effects, can result in overdose, and has a high abuse potential |
| c. μ -opioid receptor antagonist | _____ Acts on cyclooxygenases enzymes COX-1 and COX-2 to reduce prostaglandin synthesis and inflammation |
| d. Acetaminophen (Tylenol®) | _____ Reverses the actions of opioids, especially during overdose |

Name: _____ Class: _____

Anesthetics and Analgesics Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. _____ is the inability to feel pain, whereas _____ is the loss of sensation, which includes pain in addition to other sensations.
 - a. Anesthesia; analgesia
 - b. Analgesia; anesthesia**
 - c. Nociception; hyperalgesia
 - d. Hyperalgesia; nociception
2. _____ prevent action potential firing in neurons where the drug is applied to prevent signaling to and from the area of application.
 - a. Opioid agonists
 - b. General anesthetics
 - c. Opioid antagonists
 - d. Local anesthetics**
3. Select all that apply. What are some features of general anesthetics?
 - a. They induce a loss of consciousness**
 - b. They induce analgesia**
 - c. They are usually inhaled or intravenously injected**
 - d. They target opioid receptors
4. Select all that apply. Which correctly describes the effect of a general anesthetic on its target?
 - a. Inhibits excitatory, ionotropic NMDA receptors (NMDAR) to decrease neuronal excitation**
 - b. Potentiates excitatory, ionotropic NMDA receptors (NMDAR) to increase neuronal excitation
 - c. Inhibits inhibitory, ionotropic GABA_A receptors (GABA_AR) to decrease neuronal inhibition
 - d. Potentiates inhibitory, ionotropic GABA_A receptors (GABA_AR) to increase neuronal inhibition**
5. Pain stimuli are detected by _____ on sensory neurons in the PNS and is the initial step for _____, which is the perception of painful stimuli.
 - a. Opioid receptors; nociception
 - b. Glutamate receptors; analgesia
 - c. Nociceptors; nociception**
 - d. GABA receptors; analgesia

6. The _____ pathway is responsible for detecting a painful stimulus and relaying it through the spinal cord and brain to create a painful sensation, while the _____ pathway modulates the intensity of the painful sensation.

a. Ascending; descending

b. Descending; ascending

c. Peripheral; central

d. Central; peripheral

7. Match the following drug or class of drugs with their descriptions:

a. μ -opioid receptor agonist

d. Acts preferentially in the CNS on cyclooxygenase (COX) and other targets to induce analgesia

b. Non-steroidal anti-inflammatory drug (NSAID)

a. Relieves pain but produces side effects, can result in overdose, and has a high abuse potential

c. μ -opioid receptor antagonist

b. Acts on cyclooxygenases enzymes COX-1 and COX-2 to reduce prostaglandin synthesis and inflammation

d. Acetaminophen (Tylenol®)

c. Reverses the actions of opioids, especially during overdose

Sources

1. Baca, Q. J., Schulman, J. M., & Strichartz, G. R. (2004). Local Anesthetic Pharmacology. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 167-182). Wolters Kluwer.
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3. Martin, P. R., & Patel, S. (2004). Pharmacology of Drugs of Abuse. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 308-334). Wolters Kluwer.
4. Wouden, J., & Miller, K. W. (2004). General Anesthetic Pharmacology. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 265-286). Wolters Kluwer.

Lesson Eight – Cardiovascular System

Lesson Overview

In this lesson, students will learn the essential function of the cardiovascular system, issues that arise during cardiovascular disease, and common treatments for cardiovascular disease. Students will engage in a hands-on activity to understand how different drug classes alleviate cardiovascular disease.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define five common terms associated with the cardiovascular system
- Explain the function of the cardiovascular system and list its components
- Describe cardiac output, vascular resistance, and how each affects blood pressure
- Describe how cholesterol, low-density lipoprotein (LDL), and the LDL receptor contribute to atherosclerosis
- Identify common drugs that treat cardiovascular disease

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Cardiovascular System Function and Disease</i> worksheet • <i>Cardiovascular System Function and Disease</i> – Answer Key	1. Print/photocopy <i>Cardiovascular System Function and Disease</i> worksheet (one per participant) and access the <i>Cardiovascular System Function and Disease</i> – Answer Key.	10 minutes
LEARN	• <i>Cardiovascular System</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Cardiovascular System</i> slide presentation	1. Prepare the <i>Cardiovascular System</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Cardiovascular System Quiz</i> • <i>Cardiovascular System Quiz</i> – Answer Key	1. Print/photocopy <i>Cardiovascular System Quiz</i> (one per participant) and access the <i>Cardiovascular System Quiz</i> – Answer Key.	10 minutes

Lesson Eight – Cardiovascular System

FOCUS: Cardiovascular System Function and Disease

10 minutes

Purpose:

Assess students' understanding of the cardiovascular system and diseases that affect its function.

Materials:

- *Cardiovascular System Function and Disease* worksheet
- *Cardiovascular System Function and Disease* – Answer Key

Facilitation Steps:

1. Distribute the *Cardiovascular System Function and Disease* worksheets prior to or at the beginning of class.
2. Have the *Cardiovascular System Function and Disease* – Answer Key available.
3. Have students answer the questions on the *Cardiovascular System Function and Disease* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Cardiovascular System Function and Disease

PURPOSE: Assess your understanding of the cardiovascular system and diseases that affect its function.

1. In your own words, what does the cardiovascular system do?
2. Do you know of any components that are part of the cardiovascular system? If so, list them and briefly describe what each does.
3. Do you know of any cardiovascular diseases? If so, list them. Think of diseases that involve the heart, blood or blood pressure, or veins or arteries.

Cardiovascular System Function and Disease – Answer Key

PURPOSE: Assess your understanding of the cardiovascular system and diseases that affect its function.

1. In your own words, what does the cardiovascular system do?

The cardiovascular system pumps blood throughout the body. Blood contains oxygen and nutrients that organs need. Oxygen comes from the lungs, so the blood cycles between the lungs (which oxygenates the blood) and the organs (which deoxygenate the blood).

2. Do you know of any components that are part of the cardiovascular system? If so, list them and briefly describe what each does.

Heart – Pumps blood

Lungs – Oxygenates blood

Blood vessels, like arteries and veins – Give blood a path through the body

Nervous system – Regulates cardiovascular function

3. Do you know of any cardiovascular diseases? If so, list them. Think of diseases that involve the heart, blood or blood pressure, or veins or arteries.

Heart – heart disease, heart attacks, heart failure

Blood – High cholesterol, high blood pressure, blood clots

Lesson Eight – Cardiovascular System

LEARN: Cardiovascular System Slide Presentation

40 minutes

Purpose:

Students develop an understanding of the cardiovascular system, how it is impaired in cardiovascular disease, and how common cardiovascular disease treatments work.

Materials:

- *Cardiovascular System* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Cardiovascular System* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Cardiovascular System

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Cardiomyocyte
 - Cardiac output
 - Vascular resistance
 - Arteriole tone
 - Atherosclerosis

- Explain the function of the cardiovascular system and list its components.
- Describe cardiac output, vascular resistance, and how each affects blood pressure.
- Describe how cholesterol, low-density lipoprotein (LDL), and the LDL receptor contribute to atherosclerosis.
- Identify common drugs that treat CV disease.

Slide 3: Cardiovascular System

The cardiovascular (CV) system circulates blood throughout the body to:

- Transport oxygen, nutrients, and wastes
- Distribute hormones
- Dissipate body heat

CV disease is the most common cause of death worldwide. This includes:

- Hypertension (high blood pressure)
- Atherosclerosis (buildup of fatty plaques in arteries)
- Heart failure and heart attacks
- Stroke (loss of blood flow to brain)

Slide 4: Components of the CV System

The main components of the CV system are:

- **Blood**, which carries oxygen, nutrients, wastes
- **Heart**, which pumps blood
- **Lungs**, which oxygenates the blood
- **Blood vessels** that consist of:
 - **Veins and venules** that carry deoxygenated blood (blue) to heart

- **Arteries and arterioles** that carry oxygenated blood (red) away from heart
- **Capillaries** that exchange water, oxygen, wastes, and nutrients with organ tissues

The nervous system provides electrical impulse to maintain CV function.

Slide 5: Cycle of CV System

The general cycle of the CV system is:

- 1) The left heart pumps oxygenated blood through arteries to organs.
- 2) Arteries and arterioles narrow into small capillaries, where blood exchanges water, oxygen, and nutrients with organ tissue.
- 3) Deoxygenated blood from capillaries moves into venules and veins towards the right heart.
- 4) The right heart pumps deoxygenated blood to the lungs, where it is oxygenated.
- 5) The oxygenated blood is returned to the left heart, where the cycle repeats.

Slide 6: CV Disease and Treatment

Dysfunction in the **heart**, **arteries** and **arterioles**, and **nervous system** are common mediators of CV disease. CV drugs usually target receptors and other molecules in these components. Many drugs used to treat CV disease modify the autonomic nervous system that consists of sympathetic and parasympathetic divisions.

Slide 7: Heart

The heart is a pump consisting of mechanical and electrical components. **Mechanical components** contract the heart and pump blood. **Electrical components** control the rhythm of the contraction.

The synchrony of mechanical (contraction) and electrical (rhythm) components is essential for heart function.

Slide 8: Contraction and Rhythm

Cardiomyocytes are the heart muscle cells that mediate the **contraction** of the heart. Like neurons, cardiomyocytes depolarize and fire action potentials. Cardiac action potentials cause heart contraction.

Electrical nodes and signaling from the nervous system initiate cardiac action potentials and control the **rhythm** of contraction. Contraction and rhythm dictate **cardiac output**. **Cardiac output (CO)** is the volume of blood that is pumped from the heart per minute.

Slide 9: Cardiac Output (CO)

CO naturally varies given the needs of the body and is affected by:

- Heart rate (rhythm): **Faster heart rate** = $\uparrow \text{CO}$
- Force of heart contraction: **More force** = $\uparrow \text{CO}$

Heart rate and force of contraction are modified by the autonomic nervous system. Parasympathetic (green) activation slows heart rate with no effect on force. Sympathetic activation (red) increases heart rate and force.

Slide 10: Diseases of the Heart

Disruption of heart rhythm is called arrhythmia. Arrhythmia occurs when cardiac action potentials are abnormal and can lead to more serious issues like heart attack and heart failure.

Disruption of contraction occurs during heart attack and heart failure, which can be caused by cardiomyocytes being damaged or dead. Cardiomyocyte dysfunction and death can occur when the coronary artery in heart is blocked and impairs blood flow to cardiomyocytes.

Slide 11: Medication for the Heart

NE released from sympathetic neurons activate β_1 -adrenergic receptor ($\beta_1\text{AR}$) in cardiomyocytes.

β_1 AR activation causes an increase in heart rate and contraction force.

Beta (β)-blockers antagonize β_1 -adrenergic receptor in cardiomyocytes, which decrease the ($\downarrow$) sympathetic effects on the heart.

Therefore, beta blockers **decrease ($\downarrow$) HR and restore normal cardiac rhythm in arrhythmia**, while also **decreasing ($\downarrow$) force of heart contraction and relieving stress on cardiomyocytes in heart attack and heart failure**.

Hands-On Activity:

- Give students a minute or two to fill in the “Diseases treated,” “Effect on heart rate,” and “Effect on force of heart contraction” columns of the “Beta blockers” row on the table of their whiteboard.
- In the “Disease treated” column, have students list disease(s) treated by the drug.
- In the “Effect on heart rate” and “Effect on force of heart contraction” columns, have students use a “ $\uparrow$ ” to indicate an increase, a “ $\downarrow$ ” to indicate a decrease, and a “-” to indicate no effect of the drug.

Slide 12: Hands-On Activity

Ensure students filled in the table correctly.

Slides 13-14: Blood Pressure (BP)

BP is dependent on two factors: **CO** and **vascular resistance**. Vascular resistance arises primarily from arterioles and their tone. **Arterioles** are small branches of arteries that control blood flowing into organ tissue. Arterioles contain smooth muscle that contracts, and the extent of contraction is referred to as **arteriole tone**.

BP is affected by arteriole tone. BP increases when arterioles constrict, which is known as vasoconstriction. BP decreases when arterioles dilate, which is known as vasodilation.

Vascular resistance is modified by the autonomic nervous system, which acts on arteriole smooth muscle. Sympathetic activation is mediated by **NE, which activates α_1 -adrenergic receptors (α_1 AR)**. This causes arteriole vasoconstriction and increases BP. Parasympathetic activation causes arteriole vasodilation and decreases BP.

Activation of α_2 -adrenergic receptors (α_2 AR) receptors decreases sympathetic tone across entire body.

Slide 15: Hypertension Treatment

Hypertension (high blood pressure) is an extremely common effect of underlying CV disease. Lowering blood pressure is crucial for managing CV disease.

Treatment options that lower blood pressure aim to decrease cardiac output (CO) or decrease vascular resistance:

- Decrease cardiac output (CO)
 - **Beta blockers:** $\downarrow$ sympathetic effects on heart $\rightarrow \downarrow$ **HR and Force** $\rightarrow \downarrow$ **CO**
 - **α_2 -adrenergic agonists:** $\downarrow$ sympathetic tone $\rightarrow \downarrow$ **HR and Force** $\rightarrow \downarrow$ **CO**
- Decrease vascular resistance
 - **α_1 -adrenergic antagonists:** $\downarrow$ sympathetic effects on arteriole tone $\rightarrow$ **vasodilation**
 - **α_2 -adrenergic agonists:** $\downarrow$ sympathetic tone $\rightarrow$ **vasodilation**

Hands-On Activity:

- Have students fill in all but the last column of the “Beta-blockers,” “ α_1 -adrenergic antagonists,” and “ α_2 -adrenergic agonists” rows on the table of their whiteboard.
- In the “Disease treated” column, have students list disease(s) treated by the drug.
- In the “Effect on heart rate” and “Effect on force of heart contraction” columns, have students use a “ $\uparrow$ ” to indicate an increase, a “ $\downarrow$ ” to indicate a decrease, and a “-” to indicate no effect.
- In the “Effect on arteriole tone” column, have students write “vasodilation,” “vasoconstriction,” or “-” to indicate no effect.

Slide 16: Hands-On Activity

Ensure students filled in the table correctly.

Slide 17: Lipids and Lipoproteins

Lipids are fatty, insoluble molecules that are used for cell structure (membranes), energy, and synthesis of hormones and bile acid. Cholesterol is a common type of lipid.

Lipids are transported in the blood by proteins called **lipoproteins**. Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) are common lipoproteins measured in routine blood work. LDL transports cholesterol through the body.

LDL receptors (LDLR) in the liver remove LDL from the blood.

Slide 18: Atherosclerosis

Atherosclerosis occurs when LDL carrying cholesterol is deposited into arterial walls, causing buildup of fatty plaques that impair blood flow.

High levels of blood cholesterol and LDL increase the risk of atherosclerosis and CV disease. High levels of HDL lower risk of atherosclerosis and CV disease.

Increasing the amount of LDLR in the liver is the desired effect of most treatments. **Decreasing cholesterol synthesis** in the liver **increases LDLR**. **More LDLR in liver results in less LDL in the blood.**

Slide 19: Atherosclerosis Treatment

Statins are the most common treatment for atherosclerosis. **Statins inhibit cholesterol synthesis**. This inhibition increases LDLR in liver, which removes LDL from the blood. Removal of LDL helps prevent plaque formation and blockages in arteries.

Statins are used to prevent blockages in the coronary artery of the heart in patients who have a heart attack or heart failure.

Hands-On Activity:

- Have students fill in the “Statins” row and the last column “Does it reduce artery blockage?” on the table of their whiteboard.
- In the “Disease treated” column, have students list disease(s) treated by the drug.
- In the “Effect on heart rate” and “Effect on force of heart contraction” columns, have students use a “ $\uparrow$ ” to indicate an increase, a “ $\downarrow$ ” to indicate a decrease, and a “-” to indicate no effect.
- In the “Effect on arteriole tone” column, have students write “vasodilation,” “vasoconstriction,” or “-” to indicate no effect.
- In the “Does it reduce artery blockage?” column, have students indicate “Yes” or “No.”

Slides 20-21: Hands-On Activity

Ensure students filled in the table correctly (shown on slide 20).

Read the instructions (slide 21) aloud, and ensure they understand what is asked.

Slides 22-23: Scenario 1

Hands-On Activity:

- Read the scenario aloud.
- Give students several minutes to place arrows and magnets in the correct positions on their whiteboards.
- Read the answers on slide 23 aloud and ensure students understand why the answers are correct.

Slides 24-25: Scenario 2

Hands-On Activity:

- Read the scenario aloud.
- Give students several minutes to place arrows and magnets in the correct positions on their whiteboards.
- Read the answers on slide 25 aloud and ensure students understand why the answers are correct.

Slides 26-27: Scenario 3

Hands-On Activity:

- Read the scenario aloud.
- Give students several minutes to place arrows and magnets in the correct positions on their whiteboards.
- Read the answers on slide 25 aloud and ensure students understand why the answers are correct.

Lesson Eight – Cardiovascular System

REVIEW: Cardiovascular System Quiz

10 minutes

Purpose:

To review key concepts related to the cardiovascular system and the learning objectives for the lesson.

Materials:

- *Cardiovascular System Quiz*
- *Cardiovascular System Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Cardiovascular System Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Cardiovascular System Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Cardiovascular System Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Select all that apply. What best describes the primary function(s) of the cardiovascular system?
 - a. Dissipate body heat
 - b. Distribute hormones
 - c. Metabolize drugs
 - d. Transport oxygen, nutrients, and wastes

2. Match the following components of the cardiovascular system with their description.

_____ The pump of the system	
a. Blood	_____ Carries deoxygenated blood
b. Heart	
c. Lungs	_____ Exchanges oxygen, nutrients, and water with organ tissue
d. Veins and venules	_____ The fluid of the system
e. Arteries and arterioles	_____ Oxygenates the blood
f. Capillaries	_____ Carries oxygenated blood

3. Select all that apply. What is a cardiomyocyte?
 - a. A heart muscle cell that contracts the heart
 - b. An arteriole cell that contracts in response to the nervous system
 - c. A lipoprotein that carries cholesterol
 - d. An excitable cell that fires action potentials

4. Blood pressure is determined by _____, which is affected by heart rate and the force of heart contraction, and _____, which is affected by arteriole tone and artery blockages.
 - a. Vascular resistance; cardiac output
 - b. Cardiac output; vascular resistance
 - c. Lipid levels; lipoprotein levels
 - d. Lipoprotein levels; lipid levels

5. Atherosclerosis occurs when fatty plaques build up and deposit into the walls of arteries. Fatty plaques are made up of _____ containing cholesterol, which are removed by the _____ receptor.
 - a. Low-density lipoprotein; high-density lipoprotein
 - b. High-density lipoprotein; low-density lipoprotein
 - c. Low-density lipoprotein; low-density lipoprotein
 - d. High-density lipoprotein; high-density lipoprotein

6. Activation of the _____ nervous system causes vasodilation and decreases heart rate and force of heart contraction, while activation of _____ has the opposite effect.
- Peripheral; central
 - Central; peripheral
 - Sympathetic; parasympathetic
 - Parasympathetic; sympathetic
7. Match the following drug class with their descriptions:
- | | |
|---------------------------------------|---|
| | _____ Decreases heart rate and force of contraction to decrease cardiac output and treat heart problems |
| a. Beta blockers | _____ Inhibits cholesterol synthesis to enhance the removal of low-density lipoprotein (LDL) from the blood |
| b. α_2 -adrenergic agonists | |
| c. α_1 -adrenergic antagonists | _____ Decreases sympathetic effects on arteriole smooth muscle to cause vasodilation and lower blood pressure |
| d. Statins | _____ Decreases sympathetic tone throughout the body to lower blood pressure |

Name: _____ Class: _____

Cardiovascular System Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Select all that apply. What best describes the primary function(s) of the cardiovascular system?
a. Dissipate body heat
b. Distribute hormones
c. Metabolize drugs
d. Transport oxygen, nutrients, and wastes
2. Match the following components of the cardiovascular system with their description.

a. Blood	b. The pump of the system
b. Heart	d. Carries deoxygenated blood
c. Lungs	f. Exchanges oxygen, nutrients, and water with organ tissue
d. Veins and venules	a. The fluid of the system
e. Arteries and arterioles	c. Oxygenates the blood
f. Capillaries	e. Carries oxygenated blood
3. Select all that apply. What is a cardiomyocyte?
a. A heart muscle cell that contracts the heart
b. An arteriole cell that contracts in response to the nervous system
c. A lipoprotein that carries cholesterol
d. An excitable cell that fires action potentials
4. Blood pressure is determined by _____, which is affected by heart rate and the force of heart contraction, and _____, which is affected by arteriole tone and artery blockages.
a. Vascular resistance; cardiac output
b. Cardiac output; vascular resistance
c. Lipid levels; lipoprotein levels
d. Lipoprotein levels; lipid levels
5. Atherosclerosis occurs when fatty plaques build up and deposit into the walls of arteries. Fatty plaques are made up of _____ containing cholesterol, which are removed by the _____ receptor.
a. Low-density lipoprotein; high-density lipoprotein
b. High-density lipoprotein; low-density lipoprotein
c. Low-density lipoprotein; low-density lipoprotein
d. High-density lipoprotein; high-density lipoprotein

6. Activation of the _____ nervous system causes vasodilation and decreases heart rate and force of heart contraction, while activation of _____ has the opposite effect.
- a. Peripheral; central
 - b. Central; peripheral
 - c. Sympathetic; parasympathetic
 - d. Parasympathetic; sympathetic**
7. Match the following drug class with their descriptions:
- | | |
|---------------------------------------|---|
| | a. Decreases heart rate and force of contraction to decrease cardiac output and treat heart problems |
| a. Beta blockers | d. Inhibits cholesterol synthesis to enhance the removal of low-density lipoprotein (LDL) from the blood |
| b. α_2 -adrenergic agonists | |
| c. α_1 -adrenergic antagonists | c. Decreases sympathetic effects on arteriole smooth muscle to cause vasodilation and lower blood pressure |
| d. Statins | b. Decreases sympathetic tone throughout the body to lower blood pressure |

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Lesson Nine – Renal System

Lesson Overview

In this lesson, students will learn the primary functions of the renal system, how kidneys regulate blood volume and blood pressure, and common drugs that act on the kidney. Students will engage in a hands-on activity to deepen their understanding of the renin-angiotensin-aldosterone system (RAAS).

Lesson Objectives

After completing this lesson, participants will be able to:

- Define four common terms associated the renal system
- List the functions of the kidney
- Describe how the nephron removes waste and forms urine
- Explain how diuretics work to remove fluid from the body
- Describe how the renin-angiotensin-aldosterone system (RAAS) and RAAS inhibitors regulate blood volume, vascular resistance, and blood pressure

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Renal System Function and Disease</i> worksheet • <i>Renal System Function and Disease – Answer Key</i>	1. Print/photocopy the <i>Renal System Function and Disease</i> worksheet (one per participant) and access the <i>Renal System Function and Disease – Answer Key</i> .	10 minutes
LEARN	• <i>Renal System</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Renal System</i> slide presentation	1. Prepare the <i>Renal System</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Renal System Quiz</i> • <i>Renal System Quiz – Answer Key</i>	1. Print/photocopy the <i>Renal System Quiz</i> (one per participant) and <i>Renal System Quiz – Answer Key</i> .	10 minutes

Lesson Nine – Renal System

FOCUS: Renal Function and Disease

10 minutes

Purpose:

Assess students' understanding of the renal system and diseases that affect its function.

Materials:

- *Renal System Function and Disease* worksheet
- *Renal System Function and Disease – Answer Key*

Facilitation Steps:

1. Distribute *Renal System Function and Disease* worksheets prior to or at the beginning of class.
2. Have the *Renal System Function and Disease – Answer Key* available.
3. Have students answer the questions on the *Renal System Function and Disease* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Renal System Function and Disease

PURPOSE: Assess your understanding of the renal system and diseases and drugs that affect it.

1. In your own words, what is the function of the kidneys?
2. Do you know what a diuretic does? Hint: It's as if your bladder fills up too quickly...
3. If your kidneys fail, how would your life change? What are some possible effects of kidney failure?

Renal System Function and Disease – Answer Key

PURPOSE: Assess your understanding of the renal system and diseases and drugs that affect it.

1. In your own words, what is the function of the kidneys?

The kidneys remove waste from the body. They also create urine. These processes help balance fluid and electrolytes in the body.

2. Do you know what a diuretic does? Hint: It's as if your bladder fills up too quickly...

A diuretic makes you urinate more. This is because a diuretic increases urine formation.

3. If your kidneys fail, how would your life change? What are some possible effects of kidney failure?

You would not be able to filter waste properly, which can be fatal. Blood pressure would be altered, and cardiovascular diseases could occur. You would eventually need to have dialysis treatment (artificial removal of waste) and a kidney transplant.

Lesson Nine – Renal System

LEARN: Renal System Slide Presentation

40 minutes

Purpose:

Students develop an understanding of the renal system, how it functions to remove waste and balance blood volume and pressure, and the drugs that act on kidneys,

- Describe how the renin-angiotensin-aldosterone system (RAAS) and RAAS inhibitors regulate blood volume, vascular resistance, and blood pressure

Materials:

- *Renal* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Renal System* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Renal System

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Nephron
 - Transporter
 - Diuresis
 - Hormone
- List the functions of the kidney
- Describe how the nephron removes waste and forms urine
- Explain how diuretics work on to remove fluid from the body

Slide 3: Renal (Kidney) Function

The kidneys perform vital functions for the body.

Renal (another word for kidney) functions include:

- Filtration of waste from blood and excretion of waste through urine formation
- Balancing fluid and electrolyte levels in the body
- Regulation of blood pressure
- Synthesis and secretion of hormones

The renal system and cardiovascular system are closely related. Dysfunction in one usually causes dysfunction in the other and vice versa.

Slide 4: Waste Removal

Unfiltered blood enters the kidney. The kidney filters the blood. Filtered blood goes back into the blood stream. Urine and waste collect in the bladder prior to elimination from the body.

Slide 5: Renal Anatomy

The functional unit of the kidney is called the **nephron**. Nephrons remove wastes through the creation of urine. Waste includes toxic byproducts of metabolism, including drug metabolites. Dysfunction of the nephron can impair the elimination of drugs and their metabolites.

Nephrons consists of two basic parts:

- Renal corpuscle
- Renal tubule

Slide 6: Urine Formation - Filtration

Step 1 of urine formation is filtration, which occurs in the renal corpuscle. During filtration, waste is filtered from blood in glomerulus into glomerular capsule. Glomerular filtrate is created and enters renal tubule from the capsule.

The glomerular filtration rate (GFR) is a common way of evaluating kidney function. Diminished GFR is a sign of kidney disease or failure.

Slide 7: Urine Formation – Absorption

Step 2 is reabsorption, which occurs in the renal tubule. During reabsorption, water, electrolytes (ions), and other molecules are recovered from filtrate and returned to the blood.

Transporters mediate reabsorption. Transporters are proteins that exchange ions, water, and other molecules between barriers. Transporters are essential for urine formation and maintaining the balance of water and electrolytes in the body.

Slide 8: Urine Formation – Secretion

Step 3 is secretion, which also occurs in the renal tubule. During secretion, metabolites and other wastes that could not be filtered are secreted into blood.

Transporters also mediate secretion. Transporters exchange ions and water to facilitate secretion of waste.

Slide 9: Fluid and Electrolyte Balance

The body must regulate the volume of fluid in the blood. Increases in blood volume will increase cardiac output (CO) and blood pressure (BP). Decreases in blood volume will decrease CO and BP, which could impair blood flow to organs.

The body also regulates the levels of electrolytes (ions). Remember, ions are important for many cellular functions like action potentials. Too much or too little of one or more electrolytes can cause serious medical complications.

Slide 10: Diuretics

The nephron maintains the balance of fluid and electrolytes during urine formation.

Diuresis is the act of increasing urine volume.

Diuretics act on the nephron to increase urination.

Diuretics target transporters in the renal tubule.

Most diuretics will inhibit the absorption of sodium ions (Na^+) into the blood.

This increases Na^+ excretion in the urine. Because water follows ions (like Na^+), more water will also be excreted in the urine. The net effect is less fluid in the body.

Slide 11: Treatment with Diuretics

Diuretics are commonly used to treat:

- Hypertension, which is high blood pressure
- Edema, which is the buildup of fluid in body

They are also used to balance electrolyte levels in medical conditions that alter these levels. Some diuretics can decrease calcium (Ca^{2+}) levels if they are too high (hypercalcemia). Other diuretics can increase potassium (K^+) levels if they are too low (hypokalemia).

Slide 12: Adrenal Gland

The adrenal gland sits on top of the kidney. During sympathetic activation, the adrenal gland secretes **norepinephrine** (NE) and **epinephrine** (EPI) into the blood.

In the blood, NE and EPI act as **hormones** and mediate the long-term effects of the sympathetic nervous system. **Hormones** are molecules secreted into the blood that travel over long distances and cause long-lasting changes on the body.

Slide 13: Neurohormonal Systems

Kidneys regulate blood volume and pressure through hormones and the nervous system (neurohormonal control). The nervous system receives feedback from the body about blood volume and pressure.

In response, the nervous system causes certain organs to secrete hormones and enzymes into the blood. The combination of hormones, enzymes, and receptors causes a change in blood volume and pressure.

The renin-angiotensin-aldosterone system (RAAS) is a neurohormonal system. Activation of RAAS ultimately increases blood pressure.

Slides 14-21: RAAS

In the RAAS, the liver constantly secretes angiotensinogen into the blood.

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

When blood pressure drops or the sympathetic nervous system is activated, the kidneys secrete an enzyme called renin. Renin converts angiotensinogen to angiotensin I.

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

Lung tissue secretes the angiotensin converting enzyme (ACE). ACE converts angiotensin I to angiotensin II.

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

Angiotensin II activates angiotensin receptors (AT1R).

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

Angiotensin II activation of angiotensin receptors (AT1R) causes increased Na⁺/water reabsorption in kidneys, which increases blood volume.

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

Angiotensin II activation of angiotensin receptors (AT1R) also causes the release of aldosterone from adrenal gland, which increases Na⁺/water reabsorption in kidneys and increases blood volume.

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

Finally, angiotensin II activation of angiotensin receptors (AT1R) causes increased vasoconstriction in arterioles, which increases vascular resistance.

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

RAAS activation increases both blood volume and vascular resistance, which causes an increase blood pressure (BP).

Hands-On Activity:

- Have students fill in the information on their whiteboards as you present the following information about the renin-angiotensin-aldosterone system (RAAS).

Slide 22: RAAS Inhibitors

RAAS inhibitors are widely used for treatment of hypertension. There are three primary classes of RAAS inhibitors:

- Renin inhibitors that prevent conversion of angiotensinogen to angiotensin I
- ACE inhibitors that prevent conversion of angiotensin I to angiotensin II
- AT1R receptor antagonists that prevent receptor activation by angiotensin II

All lower blood pressure by decreasing blood volume and vascular resistance.

Slide 23: Hands-On Activity

Read the instructions to students and ensure they understand them.

Slides 24-25: Scenario 1

Hands-On Activity:

- Read the scenario to students and give them a couple of minutes to answer on their whiteboards.
- Read the answers to students and ensure they understand them.

Slide 26-27: Scenario 2

Hands-On Activity:

- Read the scenario to students and give them a couple of minutes to answer on their whiteboards.
- Read the answers to students and ensure they understand them.

Slide 28-29: Scenario 3

Hands-On Activity:

- Read the scenario to students and give them a couple of minutes to answer on their whiteboards.
- Read the answers to the students and ensure they understand them.

Lesson Nine – Renal System

REVIEW: Renal System Quiz

10 minutes

Purpose:

Review key concepts related to the renal system and the learning objectives for the lesson.

Materials:

- *Renal System Quiz*
- *Renal System Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Renal System Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Renal System Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Renal System Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Select all that apply. What are functions of the kidney?
 - a. Filters waste from the blood
 - b. Excretes waste through feces
 - c. Regulates blood pressure
 - d. Synthesizes and secretes hormones

2. Match the following terms to the correct description.

	___ A molecule that acts over long distances and has long-lasting effects
a. Nephron	___ The effect of increasing urine formation
b. Transporter	___ The functional unit of the kidney
c. Diuresis	___ A protein that exchanges ions, water, and other molecules across barriers
d. Hormone	

3. Match the steps of urine formation to the correct description.

	___ Waste is removed from the blood in the glomerulus and collected in the glomerular filtrate
a. Filtration	___ Remaining waste is removed from the blood in the renal tubule
b. Reabsorption	___ Water, electrolytes, and other molecules are recovered from the filtrate
c. Secretion	

4. Most diuretics will act on _____ in the renal tubule of the nephron to inhibit reabsorption of Na^+ and water. Diuretics _____ blood volume, which decreases cardiac output and blood pressure.
 - a. Receptors; decrease
 - b. Transporters; decrease
 - c. Receptors; increase
 - d. Transporters; increase

5. Match the following renin-angiotensin-aldosterone system (RAAS) components with their descriptions:

a. Angiotensinogen	___ Is secreted from lung tissue and converts angiotensin I to angiotensin II
b. Renin	___ Is secreted from the adrenal gland and increases Na ⁺ /water reabsorption
c. Angiotensin converting enzyme (ACE)	___ Is secreted by the liver and converted to angiotensin I
d. Angiotensin receptor (AT1R)	___ Is activated by angiotensin II
e. Aldosterone	___ Is secreted from kidneys and converts angiotensinogen to angiotensin I

6. Select all that apply. Which of the following drugs will decrease both Na⁺/water reabsorption and vasoconstriction to treat high blood pressure (hypertension)?
- a. Diuretics
 - b. Renin inhibitors
 - c. ACE inhibitors
 - d. AT1R antagonists

Name: _____ Class: _____

Renal System Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Select all that apply. What are functions of the kidney?

- a. Filters waste from the blood**
- b. Excretes waste through feces
- c. Regulates blood pressure**
- d. Synthesizes and secretes hormones**

2. Match the following terms to the correct description.

- | | |
|----------------|---|
| a. Nephron | d. A molecule that acts over long distances and has long-lasting effects |
| b. Transporter | c. The effect of increasing urine formation |
| c. Diuresis | a. The functional unit of the kidney |
| d. Hormone | b. A protein that exchanges ions, water, and other molecules across barriers |

3. Match the steps of urine formation to the correct description.

- | | |
|-----------------|--|
| a. Filtration | a. Waste is removed from the blood in the glomerulus and collected in the glomerular filtrate |
| b. Reabsorption | c. Remaining waste is removed from the blood in the renal tubule |
| c. Secretion | b. Water, electrolytes, and other molecules are recovered from the filtrate |

4. Most diuretics will act on _____ in the renal tubule of the nephron to inhibit reabsorption of Na^+ and water. Diuretics _____ blood volume, which decreases cardiac output and blood pressure.

- a. Receptors; decrease
- b. Transporters; decrease**
- c. Receptors; increase
- d. Transporters; increase

5. Match the following renin-angiotensin-aldosterone system (RAAS) components with their descriptions:

- | | |
|--|--|
| a. Angiotensinogen | c. Is secreted from lung tissue and converts angiotensin I to angiotensin II |
| b. Renin | e. Is secreted from the adrenal gland and increases Na^+ /water reabsorption |
| c. Angiotensin converting enzyme (ACE) | a. Is secreted by the liver and converted to angiotensin I |
| d. Angiotensin receptor (AT1R) | d. Is activated by angiotensin II |
| e. Aldosterone | b. Is secreted from kidneys and converts angiotensinogen to angiotensin I |

6. Select all that apply. Which of the following drugs will decrease both Na^+ /water reabsorption and vasoconstriction to treat high blood pressure (hypertension)?

- a. Diuretics
- b. Renin inhibitors**
- c. ACE inhibitors**
- d. AT1R antagonists**

Sources

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Lesson Ten – Endocrine Systems

Lesson Overview

In this lesson, students will learn the key features of endocrine system, and how the hypothalamus and pituitary glands form endocrine axes. Students will engage in a hands-on activity to deepen understanding of important endocrine axes and how their dysfunction causes disease and is treated.

Lesson Objectives

After completing this lesson, participants will be able to:

- List the key features of endocrine systems
- Describe how the hypothalamus and pituitary glands work to form endocrine axes
- List the hormones, target organs, receptors, and physiological effects from the following endocrine axes:
 - Hypothalamic pituitary adrenal (HPA) axis
 - Hypothalamic pituitary growth hormone axis
 - Hypothalamic pituitary gonadal (HPG) axis
- Understand how drugs can treat endocrine disease

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Hormones in the Real World</i> worksheet • <i>Hormones in the Real World</i> – Answer Key	1. Print/photocopy <i>Hormones in the Real World</i> worksheet (one per participant) and access the <i>Hormones in the Real World</i> – Answer Key.	10 minutes
LEARN	• <i>Endocrine Systems</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Endocrine Systems</i> slide presentation	1. Prepare the <i>Endocrine Systems</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Endocrine Systems Quiz</i> • <i>Endocrine Systems Quiz</i> – Answer Key	1. Print/photocopy <i>Endocrine Systems Quiz</i> (one per participant) and access the <i>Endocrine Systems Quiz</i> – Answer Key.	10 minutes

Lesson Ten – Endocrine Systems

FOCUS: Hormones in the Real World

10 minutes

Purpose:

Assess students' understanding of hormones and common uses of them.

Materials:

- *Hormones in the Real World* worksheet
- *Hormones in the Real World* – Answer Key

Facilitation Steps:

1. Distribute *Hormones in the Real World* worksheets prior to or at the beginning of class.
2. Have the *Hormones in the Real World* – Answer Key available.
3. Have students answer the questions on the *Hormones in the Real World* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Hormones in the Real World

PURPOSE: Assess your understanding of hormones and common uses of them.

1. In your own words, what is a hormone and how does it affect you?
2. Some athletes illegally use hormones to enhance their performance. What are these called? Do you know why they are called this?
3. What is female birth control and what are its effects? Do you know what hormones are involved?

Hormones in the Real World – Answer Key

PURPOSE: Assess your understanding of hormones and common uses of them.

4. In your own words, what is a hormone and how does it affect you?

A hormone is a molecule that is secreted into the blood. Hormones can make you feel irritable or emotional. Hormones are important for growth and development.

5. Some athletes illegally use hormones to enhance their performance. What are these called? Do you know why they are called this?

These are commonly referred to as “steroids” or “anabolic steroids.” They are called this because they mimic the effects of hormones that are derived from steroid molecules.

6. What is female birth control and what are its effects? Do you know what hormones are involved?

Birth control is used to prevent pregnancy. Female birth control consists of estrogens and progestins that prevent ovulation.

Lesson Ten – Endocrine Systems

LEARN: Endocrine Systems Slide Presentation

40 minutes

Purpose:

To develop an understanding of endocrine systems, the involvement of the hypothalamus and pituitary glands, and endocrine diseases and treatments.

Materials:

- *Endocrine Systems* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Endocrine Systems* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Endocrine Systems

Slide 2: Learning Objectives

The learning objectives are:

- List the key features of endocrine systems
- Describe how the hypothalamus and pituitary glands work to form endocrine axes
- List the hormones, target organs, receptors, and physiological effects from the following endocrine axes:
 - Hypothalamic-pituitary-adrenal (HPA) axis

- Hypothalamic-pituitary-growth-hormone axis
- Hypothalamic-pituitary-gonadal (HPG) axis

- Understand how drugs can treat endocrine diseases

Slide 3: Endocrine Systems

Endocrine systems use hormones that are secreted into the bloodstream and travel long-distances to affect target organs. Endocrine systems are slow to respond, often cause widespread effects in body, and act over long periods of time. Endocrine systems regulate many physiological responses including bone, muscle, and tissue growth, metabolism and energy storage, and reproduction.

Slide 4: Key Features of Endocrine Systems

There are three key features of every endocrine system:

- 1) Hormone-secreting cells are cells that respond to signals that tell them when to secrete hormones. Signals typically oscillate in fixed patterns or align with your sleep cycle.
- 2) Hormone-responsive cells are cells that contain hormone receptors that can cause the release of other hormones or produce a cellular response.
- 3) Negative feedback loops (-) occur when the hormone or the effect of the hormone decreases hormone secretion to tone down endocrine activity.

Slide 5: Hypothalamus and Pituitary

The hypothalamus and pituitary gland along with the target organ(s) make up the endocrine axes. The **hypothalamus** is a structure of the brain that integrates physiological signals (e.g., thirst, hunger,

sleep). In response to signals, it secretes hormones into the blood to initiate endocrine signaling.

The **pituitary gland** is located below the hypothalamus and responds to the hormones secreted by the hypothalamus. It secretes hormones of its own, which travel through the blood to target organs.

Hormones secreted by target organs cause effects on physiology and provide negative feedback to the hypothalamus and pituitary gland.

Slide 6: Hypothalamic-Pituitary (HP) Endocrine Axis

There are multiple hypothalamic-pituitary (HP) endocrine axes in the body. We will only discuss a few here. Each is defined by the hormones released, the target organs, and the physiological effects that are produced.

Many common diseases arise from dysfunction of HP axes. Dysfunction can be caused by:

- Deficiency or excess of hormone production or secretion
- Problems with negative feedback

Typically, treating endocrine diseases requires either:

- Replacement therapy or receptor agonists if a patient is hormone deficient
- Receptor antagonists if a patient is producing excessive amounts of hormones

Slides 7-9: Hypothalamic-Pituitary-Adrenal (HPA) Axis

The **adrenal glands** along with the hypothalamus and the pituitary gland make up the **HPA axis**.

Hypothalamus

Corticotropin-releasing hormone (CRH) is secreted from hypothalamus, and its secretion varies with sleep cycle and can increase with stress.

Pituitary Gland

CRH activates receptors on the pituitary gland. This causes secretion of adrenocorticotrophic hormone (ACTH) into the blood.

Adrenal Glands

ACTH stimulates synthesis and secretion of cortisol in the adrenal glands. Cortisol inhibits CRH and ACTH secretion.

Hands-On Activity:

- Have students place magnets to represent the hormones secreted from each area: hypothalamus (green magnet), pituitary gland (yellow magnet), and target organ (white magnet).
- Have students label each hormone and draw a blue arrow to where the hormone stimulates secretion and a red arrow where the hormone inhibits secretion.
- Have students correct any mistakes and ensure they understand why the answers on slide 9 are correct.

Slide 10: Physiology and Pharmacology of HPA Axis

Cortisol activates the glucocorticoid receptor (GR) throughout the body. Major effects of cortisol activation include:

- Breakdown of sugar and fat storage for energy consumption
- Inhibition of inflammation and immune response

Glucocorticoid receptor agonists (e.g., prednisone) are widely used for two primary reasons:

- Replacement therapy for patients with adrenal insufficiency (i.e., produce too little cortisol)
- Used as anti-inflammatory for those with autoimmune disorders

Hands-On Activity:

- Have students fill in the table on their whiteboards.

Slides 11-13: Hypothalamic-Pituitary-Growth-Hormone Axis

The **liver** along with the hypothalamus and the pituitary gland make up the **growth hormone axis**.

Hypothalamus

Growth hormone-releasing hormone (GHRH) is secreted from hypothalamus. Somatostatin is also secreted from here.

Pituitary Gland

GHRH on the pituitary gland causes secretion of growth hormone (GH) into the blood. Somatostatin inhibits secretion of GH.

Liver

In the liver, GH causes secretion of insulin-like growth factor (IGF-1). IGF-1 inhibits GH secretion from the pituitary gland.

Hands-On Activity:

- Have students place magnets to represent the hormones secreted from each area: hypothalamus (green magnet), pituitary gland (yellow magnet), and target organ (white magnet).
- Have students label each hormone and draw a blue arrow to where the hormone stimulates secretion and a red arrow where the hormone inhibits secretion.
- Have students correct any mistakes and ensure they understand why these answers are correct.

Slide 14: Physiology and Pharmacology of GH Axis

GH and IGF-1 promote growth throughout the body in multiple tissues. GH and IGF-1 stimulate protein synthesis, sugar storage, and fat metabolism. This is especially important during development but is problematic if it doesn't stop afterwards.

Synthetic human growth hormone can be used as replacement therapy for GH/IGF-1 deficiency. It is also used illicitly in professional sports ("anabolic steroids").

For excess GH:

- GH receptor antagonists can reduce GH effects across tissues.
- Somatostatin receptor agonists inhibit GH release.

Hands-On Activity:

- Have students fill in the table on their whiteboards.

Slides 15-18: Hypothalamic-Pituitary-Gonadal (HPG) Axis

The **gonadal tissue** along with the hypothalamus and the pituitary gland make up the **HPG axis**.

Hypothalamus

Gonadotropin-releasing hormone (GnRH) is secreted from hypothalamus. Pulsating release activates the HPG axis, while continuous release inhibits the HPG axis.

Pituitary Gland

GnRH activates receptors on the pituitary gland, which causes secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

Testes (male)

In men, LH and FSH stimulate synthesis of testosterone in the testes. Testosterone inhibits secretion of LH and FSH.

Ovaries (female)

In women, LH and FSH stimulate synthesis of estrogens and progestins in the ovaries. Estrogen may either inhibit or stimulate LH/FSH secretion.

Hands-On Activity:

- Have students place magnets to represent the hormones secreted from each area: hypothalamus (green magnet), pituitary gland (yellow magnet), and target organ (white magnet).
- Have students label each hormone and draw a blue arrow to where the hormone stimulates secretion and a red arrow where the hormone inhibits secretion.

- Have students correct any mistakes and ensure they understand why these answers are correct.

Slide 19: Physiology and Pharmacology of the Male

Testosterone is essential for development of the male reproductive system and sperm production. Testosterone causes muscle and bone growth, deepening of voice, and libido during male puberty. Testosterone activates the androgen receptor to mediate its effects.

Androgen receptor agonists are used to treat male hormone deficiency and used illicitly in professional sports. Androgen receptor antagonists are used to inhibit the androgen receptor and treat hormone-dependent prostate cancer.

Hands-On Activity:

- Have students fill in the table on their whiteboards.

Slide 21: Physiology and Pharmacology of the Female HPG and Axis

Estrogens and progestins mediate the development of the female reproductive system during female puberty. Estrogens and progestins activate estrogen and progesterone receptors, respectively.

The balance of LH/FSH and estrogen/progestin secretion coordinate the female menstrual cycle. Estrogen/progestin effects are dependent on the phase of the menstrual cycle.

Different formulations of estrogens and progestins are commonly used as contraceptives (“birth control”). Inhibitors of the enzyme that synthesizes estrogen are used to treat breast cancer, such as ER (estrogen-receptor)-positive breast cancer.

Hands-On Activity:

- Have students fill in the table on their whiteboards.

Slides 21-23: Diagnosis and Treatment

Hands-On Activity:

- Have students remove all magnets from their boards.
- Read the instructions for the students and ensure they understand.
- Read the example on slide 22.
- Ensure students understand the example and what they are expected to do for each scenario.
- Read the scenario on slide 23 and give students a minute or two to complete the activity.

Slide 24: Scenario 1 Answer

Hands-On Activity:

- Read the answer and ensure students understand it.

Slide 25: Diagnosis and Treatment

Hands-On Activity:

- Read the scenario and give students a minute or two to complete the activity.

Slide 26: Scenario 2 Answer

Hands-On Activity:

- Read the answer and ensure students understand it.

Slide 27: Diagnosis and Treatment

Hands-On Activity:

- Read the scenario and give students a minute or two to complete the activity.

Slide 28: Scenario 3 Answer

Hands-On Activity:

- Read the answer and ensure students understand it.

Lesson Ten – Endocrine Systems

REVIEW: Endocrine Systems

10 minutes

Purpose:

Review key concepts related to the endocrine systems and the learning objectives for the lesson.

Materials:

- *Endocrine Systems Quiz*
- *Endocrine Systems Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Endocrine Systems Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Endocrine Systems Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Endocrine Systems Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Select all that apply. What are the key features of the endocrine systems?
 - a. Negative feedback loops
 - b. Hormone-secreting cells
 - c. Hormone-responsive cells
 - d. Fast signaling over short distances

2. The _____ secretes hormones that travel to the _____, which secrete hormones that travel through the blood to target organs.
 - a. Pituitary gland; hypothalamus
 - b. Hypothalamus; pituitary gland
 - c. Liver; adrenal glands
 - d. Adrenal glands; liver

3. Select all that apply. Which statement(s) describe the actions of a hormone?
 - a. It can inhibit the secretion of hormones to negatively regulate endocrine function
 - b. It can cause effects on growth, reproduction, and metabolism
 - c. It mediates physiological effects through receptor activation
 - d. Its effects may last long durations of time

4. Match the following endocrine axes with their physiological function:

a. HPA axis	_____	Regulates the development of male and female reproductive systems
b. Growth hormone axis	_____	Regulates energy metabolism, inflammation, and immune response
c. HPG axis	_____	Regulates the developmental growth of the body

5. Match the following target organs with the hormones they secrete.

- | | |
|-------------------|--|
| a. Liver | ___ Testosterone |
| b. Adrenal glands | ___ Insulin-like growth factor 1 (IGF-1) |
| c. Testes | ___ Estrogen |
| d. Ovaries | ___ Cortisol |

6. Hormone excess can be treated with _____, while hormone deficiency can be treated with _____.

- Hormone receptor antagonists; hormone receptor agonists
- Hormone receptor agonists; hormone receptor antagonists
- Neurotransmitter receptor agonists; neurotransmitter receptor antagonists
- Neurotransmitter receptor antagonists; neurotransmitter receptor agonists

Name: _____ Class: _____

Endocrine Systems Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. Select all that apply. What are the key features of the endocrine system?
 - a. Negative feedback loops**
 - b. Hormone-secreting cells**
 - c. Hormone-responsive cells**
 - d. Fast signaling over short distances

2. The _____ secretes hormones that travel to the _____, which secrete hormones that travel through the blood to target organs.
 - a. Pituitary gland; hypothalamus
 - b. Hypothalamus; pituitary gland**
 - c. Liver; adrenal glands
 - d. Adrenal glands; liver

3. Select all that apply. Which statement(s) describe the actions of a hormone?
 - a. It can inhibit the secretion of hormones to negatively regulate endocrine function**
 - b. It can cause effects on growth, reproduction, and metabolism**
 - c. It mediates physiological effects through receptor activation**
 - d. Its effects may last long durations of time**

4. Match the following endocrine axes with their physiological function:

a. HPA axis b. Growth hormone axis c. HPG axis	c. Regulates the development of male and female reproductive systems a. Regulates energy metabolism, inflammation, and immune response b. Regulates the developmental growth of the body
--	---

5. Match the following target organs with the hormones they secrete.

- | | |
|-------------------|--|
| a. Liver | c. Testosterone |
| b. Adrenal glands | a. Insulin-like growth factor 1 (IGF-1) |
| c. Testes | d. Estrogen |
| d. Ovaries | b. Cortisol |

6. Hormone excess can be treated with _____, while hormone deficiency can be treated with _____.

- a. Hormone receptor antagonists; hormone receptor agonists**
- b. Hormone receptor agonists; hormone receptor antagonists
- c. Neurotransmitter receptor agonists; neurotransmitter receptor antagonists
- d. Neurotransmitter receptor antagonists; neurotransmitter receptor agonists

Sources

1. Armstrong, E. J., & Barbieri, R. L. (2004). Pharmacology of Reproduction. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 561-579). Wolters Kluwer.
2. Garg, R., & Adler, G. K. (2004). Pharmacology of the Adrenal Cortex. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 524-540). Wolters Kluwer.
3. Vaidya, A. (2004). Pharmacology of the Hypothalamus and Pituitary Gland. In D. E. Golan, E. J. Armstrong, & A. W. Armstrong (Eds.), *Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy* (4th ed., pp. 498-513). Wolters Kluwer.

Lesson Eleven – Antimicrobials

Lesson Overview

In this lesson, students will learn about different types of antimicrobials, including those that act against bacteria (antibiotics), fungi (antifungals), and viruses (antivirals). Students will engage in a hands-on activity to deepen their understanding of how each type of antimicrobial works to treat infectious disease.

Lesson Objectives

After completing this lesson, participants will be able to:

- Explain how antimicrobials distinguish between the pathogen and host to treat infectious disease
- Describe the central dogma of biology
- List and describe common antimicrobials for each type of pathogen:
 - Bacteria (antibiotics)
 - Fungi (antifungals)
 - Viruses (antivirals)

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Microbes and You</i> worksheet • <i>Microbes and You</i> – Answer Key	1. Print/photocopy the <i>Microbes and You</i> worksheet (one per participant) and access the <i>Microbes and You</i> – Answer Key.	10 minutes
LEARN	• <i>Antimicrobial</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Antimicrobials</i> slide presentation	1. Prepare the <i>Antimicrobials</i> slide presentation for viewing. 2. Distribute the whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Antimicrobial Quiz</i> • <i>Antimicrobial Quiz</i> – Answer Key	1. Print/photocopy the <i>Antimicrobial Quiz</i> (one per participant) and access the <i>Antimicrobial Quiz</i> – Answer Key.	10 minutes

Lesson Eleven – Antimicrobials

FOCUS: Microbes and You

10 minutes

Purpose:

Assess students' understanding of infections, pathogens, and common drugs that treat infectious disease.

Materials:

- *Microbes and You* worksheet
- *Microbes and You* – Answer Key

Facilitation Steps:

1. Distribute the *Microbes and You* worksheets prior to or at the beginning of class.
2. Have the *Microbes and You* – Answer Key available.
3. Have students answer the questions on the *Microbes and You* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Microbes and You

PURPOSE: Assess your understanding of infections and common drugs that treat them.

1. How often do you get sick with an infection? Are you susceptible to some infections over others? If so, what are common infections that you have to deal with?
2. What kind of infections do you know are associated with bacteria? Fungi? Viruses? Try to write one of each.
3. What medications have you received for your infection?

Microbes and You – Answer Key

PURPOSE: Assess your understanding of infections and common drugs that treat them.

4. How often do you get sick with an infection? Are you susceptible to some infections over others? If so, what are common infections that you have to deal with?

Answers vary

5. What kind of infections do you know are associated with bacteria? Fungi? Viruses? Try to write one of each.

Bacteria – strep throat, staph infection,

Fungi – ringworm, athlete's foot, yeast infections

Viruses – COVID, flu, HIV

6. What medications have you received for your infection?

Answers vary

Lesson Eleven – Antimicrobials

LEARN: Antimicrobials Slide Presentation

40 minutes

Purpose:

Develop an understanding of infectious disease, the different types of antimicrobials, and how each works to treat infection.

Materials:

- *Antimicrobials* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Antimicrobials* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Antimicrobials

Slide 2: Learning Objectives

- Explain how antimicrobials distinguish between the pathogen and host to treat infectious disease
- Describe the central dogma of biology
- List and describe common antimicrobials for each type of pathogen:
 - Bacteria (antibiotics)
 - Fungi (antifungals)
 - Viruses (antivirals)

Slide 3: Infectious Disease

Infectious diseases are caused by a variety of microbes. Microbes are microscopic unicellular or multicellular organisms. Pathogenic microbes infect host organisms to aid in their survival but at the expense of the host. Pathogenic microbes include bacteria, fungi, and viruses. Antimicrobials are drugs that inhibit microbial growth or kill microbes.

Slide 4: Antimicrobials

The strategy with antimicrobial treatment is to inhibit the growth of or kill the pathogen without harming the host. There are three broad types of targets for antimicrobials:

- **Unique targets** are those found only in the pathogen.
- **Selective targets** are those found in both the host and pathogen, but the pathogen target is specific enough to the pathogen that the drug interferes little or not at all with the host target.
- **Common targets** are those found in both the host and pathogen, but the target is more important for pathogen survival than host survival. However, the drug will likely interfere with the host target as well.

Instead of receptors, most antimicrobials target and inhibit enzymes that are essential for pathogen function.

Slide 5: Biology's Central Dogma

DNA is **replicated** by DNA polymerase during cell division, allowing the genome to be passed to the new cells. Biology's central dogma states:

- **DNA** is transcribed to **RNA** by an RNA polymerase in a process called **transcription**

- RNA contains the instructions for making proteins
- **RNA** is read and used by ribosomes to synthesize **protein** in a process called **translation**

Antimicrobials may target components of replication, transcription, or translation.

Slide 6: Bacteria and Antibiotics

Bacteria cause many diseases such as strep throat (*Streptococcus pyogenes*) and peptic ulcers (*Helicobacter pylori*). **Antibiotics** are used to treat bacterial infections. Because of the few similarities with humans, bacteria contain many unique targets for antibiotics.

Hands-On Activity:

- During the bacteria and antibiotics section, have students label the “Bacteria” diagram with the discussed drug classes (look for bold text “inhibitors” or “antibiotics”).
- Students should write the name or abbreviated name of each drug class with an arrow or line pointing to the component that the drug inhibits. Students may want to add a brief description of what a drug class does.

Slide 7: Cell Wall Inhibitors

A unique target of bacteria is their cell walls. Cell walls are necessary for bacterial survival and do not exist in humans. **Peptidoglycan** is a major component of cell walls. It is elongated through a process called polymerization, which forms the peptidoglycan layer. **Inhibitors of peptidoglycan polymerization** disrupt elongation and kill bacteria.

Peptidoglycan chains are crosslinked by transpeptidases to strengthen the cell wall. **β -lactam antibiotics** inhibit transpeptidase enzymes, which disrupt peptidoglycan crosslinking and kill bacteria.

Slide 8: Gram Positive (+) Versus (-) Bacteria

Gram+ bacteria have a thick, exposed cell wall, while Gram- bacteria have a thin cell wall that is squeezed between two membranes. Cell wall inhibitors tend to be more effective toward Gram+ bacteria as it is easier to access the peptidoglycan layer in the cell wall. However, these inhibitors can also kill Gram- bacteria if they can permeate through the membrane and into the cell wall.

Carbapenems are **β -lactam antibiotics** that act on both Gram+ and Gram- bacteria.

Slide 9: Folic Acid Inhibitors

Folic acid is a vitamin that is used to synthesize nucleic acids (DNA and RNA) and amino acids (protein) among other things. While humans take up folic acid from our diets, bacteria must synthesize their own. Folic acid inhibitors block synthesis in Gram+/- bacteria.

DHPS (dihydropteroate synthase) and **DHFR** (dihydrofolate reductase) are enzymes used in the bacterial folic acid synthesis. **DHPS inhibitors** and **DHFR inhibitors** are used to inhibit folic acid synthesis in bacteria. DHPS is only found in bacteria, while DHFR is found in both humans and bacteria. Drugs have been developed to selectively inhibit bacterial DHPS.

Slide 10: Inhibitors of Replication, Transcription, and Translation

Topoisomerases are enzymes that break, relax, and seal DNA strands during replication.

Topoisomerase inhibitors make the DNA unreadable, which prevents replication and transcription and kills bacteria. Bacteria have their own forms of the enzyme.

Bacteria contain their own form of **RNA polymerase** to transcribe DNA. **RNA polymerase inhibitors** bind to bacterial RNA polymerase to inhibit transcription.

Ribosomes are composed of two subunits that read RNA and make peptides/proteins. Bacteria contain their own form of ribosome subunits. **Ribosome inhibitors** stall translation by binding and inhibiting one of the ribosome subunits.

Slides 11-12: Unique, Selective, or Common Hands-On Activity:

- Have students check their diagram and correct it.
- Then, have students follow the instructions by placing magnets on drug classes based on the type of target: unique (green), selective (yellow), and common (white).
- Have students check their magnet placements and ensure they understand why each magnet was placed where it was.

Slide 13: Fungi and Antifungals

Fungi can be the cause of infectious disease. Athlete's foot, vaginal yeast infections, and ringworm are examples of fungal infections.

Fungal infections are treated with antifungals. Because humans are more similar to fungi than bacteria, they share similar drug targets. However, there are some unique features of fungi that can be targeted.

Hands-On Activity:

- During the fungi and antifungal section, have students label the "Fungi" diagram with the discussed drug classes (look for bold text "inhibitors" or "antibiotics").
- Students should write the name or abbreviated name of each drug class with an arrow or line pointing to the component that the drug inhibits. Students may want to add a brief description of what a drug class does.

Slide 14: Fungal Membrane Synthesis and Stability
While humans use cholesterol-derived molecules for plasma membrane synthesis, fungi use another molecule called **ergosterol**. Several antifungals inhibit enzymes in the ergosterol biosynthetic pathway

Ergosterol synthesis inhibitors inhibit enzymes that interfere with plasma membrane synthesis. One enzyme is unique to fungi, while another is common to humans and fungi.

Some drugs destabilize the fungal cell membrane by binding to ergosterol in the membrane. **Polyenes** bind to ergosterol and poke holes in the membrane, which causes the cellular contents to leak and kills the fungal cell. Polyenes are selective for ergosterol over cholesterol.

Slide 15: Fungal Cell Wall

Fungal cells also have cell walls. These walls are made up of sugars that polymerize and crosslink in chains (similar to peptidoglycan in bacteria).

Echinocandins inhibit the synthesis of one of the sugars in the chain. Echinocandins disrupt cell wall integrity, which causes fungal cell death.

Slide 16: Inhibition of Nucleic Acid Synthesis

Another approach is to inhibit nucleic acid synthesis in fungal cells. Fungal cells contain a transporter for molecules that are like nucleic acids. This transporter is unique to fungi. The drug flucytosine uses this transporter to enter the cell.

Flucytosine is modified in the cell and prevents DNA replication, causing fungal cell division to stall growth. Flucytosine is commonly used with other antifungals to treat infections.

Slides 17-18: Unique, Selective, or Common Hands-On Activity:

- Have students check their diagram and correct it.
- Then, have students follow the instructions by placing magnets on drug classes based on the type of target: unique (green), selective (yellow), and common (white).
- Have students check their magnet placements and ensure they understand why each magnet was placed where it was.

Slide 19: Viruses and Antivirals

Viruses are non-cellular organisms that causes many diseases including influenza (flu), HIV/AIDS, and hepatitis B. Viruses exist as virions: Small particles that consist of a capsid and genetic information (DNA or RNA) contained within the capsid.

Viruses must infect a host and use host machinery to synthesize proteins. These proteins are unique to the virus and its life cycle. Antivirals target these proteins and their associated pathways to treat infection.

Hands-On Activity:

- During the viruses and antivirals section, have students label the “Virus” diagram with the discussed drug classes (look for bold text “inhibitors” or “antibiotics”).
- Students should write the name or abbreviated name of each drug class with an arrow or line pointing to the component that the drug inhibits. Students may want to add a brief description of what a drug class does.

Slide 20: 1. Attachment, Entry, and Uncoating

A virus attaches to the cell surface via receptors and other proteins. The virus enters the cell by fusing with the host cell membrane. **Viral attachment/entry inhibitors** bind to receptors/proteins on the host cell or virus to prevent entry. Inhibitors may act on common targets (host components), selective, or unique targets (viral components).

The virus capsid is uncoated and releases the viral genome into the cell. The genome may be DNA or RNA.

Slide 21: 2. Gene Expression

Viral genes are expressed through transcription and translation to create the viral parts needed for replication. Retroviruses (e.g., HIV) carry RNA and use a reverse transcriptase enzyme to convert RNA to DNA (opposite of transcription). Reverse transcriptase inhibitors are used for these viruses that require the enzyme for gene expression and replication. Reverse transcriptase is a DNA polymerase but is different enough to be selectively targeted by antivirals.

Slide 22: 3. Genome Replication

Some viruses use their own DNA or RNA polymerases to replicate their genome. Viral DNA/RNA polymerases are different enough from human polymerases to be targeted by antivirals.

DNA or RNA polymerase inhibitors inhibit viral DNA or RNA polymerases to prevent replication. Many DNA/RNA polymerase inhibitors look like nucleic acids. However, they are chemically modified in the cell, which stalls replication when they are incorporated into DNA or RNA.

Slide 23: 4. Assembly and Maturation

The components of the virus (protein capsid and genome) assemble. However, most viruses cannot be infectious until the virion matures. Maturation describes the processing of virion particles by enzymes. This is usually accomplished by proteases (enzymes that cleave protein).

Several important HIV drugs are **protease inhibitors** that disrupt HIV maturation. Many proteases exist in humans, but some proteases are unique to viruses or different enough from human proteases to selectively target.

Slide 24: 5. Viral Release

Finally, the virion particles are released from the host cell. Depending on the virus, this may cause the host cell to rupture and die. **Viral release inhibitors** prevent the release of infectious virions from leaving the cell.

Several antivirals treat influenza (flu) by inhibiting the viral-specific enzyme that is necessary for viral release. A form of this enzyme is also found in humans, but there is little effect of antivirals on the human target.

Slides 25-26: Unique, Selective, or Common

Hands-On Activity:

- Have students check their diagram and correct it.
- Then, have students follow the instructions by placing magnets on drug classes based on the type of target: unique (green), selective (yellow), and common (white).
- Have students check their magnet placements and ensure they understand why each magnet was placed where it was.

Lesson Eleven – Antimicrobials

REVIEW: Antimicrobials

10 minutes

Purpose:

Review key concepts related to the antimicrobials and the learning objectives for the lesson.

Materials:

- *Antimicrobials Quiz*
- *Antimicrobials Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Antimicrobials Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Antimicrobials Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Antimicrobials Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. What are antimicrobials?
 - a. Drugs that kill or inhibit the growth of bacteria
 - b. Drugs that kill or inhibit the growth of viruses
 - c. Drugs that kill or inhibit the growth of fungi
 - d. Drugs that kill or inhibit the growth of any microbe

2. Select all that apply. Which statements describe antimicrobial action on the pathogen?
 - a. Antimicrobials may target a target common to host and pathogen as long as the target is more important for pathogen survival than host survival
 - b. Antimicrobials may target a target unique to a pathogen
 - c. Antimicrobials target receptors rather than enzymes
 - d. Antimicrobials may selectively target a component of the pathogen that is different enough than the form found in the host

3. Match the following central dogma principles of biology with their descriptions:

a. Replication	_____ Ribosomes synthesize peptides and proteins by reading RNA
b. Transcription	_____ DNA is converted to RNA by RNA polymerase
c. Translation	_____ DNA is copied during cell division by DNA polymerase

4. Select all that apply. What class(es) of drug act(s) on bacterial cell walls?
 - a. DHPS and DHFR inhibitors
 - b. Topoisomerase inhibitors
 - c. Inhibitors of peptidoglycan polymerization
 - d. β -lactam antibiotics

5. What molecule is specific to fungal cell membranes and targeted by inhibitors of its synthesis and polyenes?
- a. Cholesterol
 - b. Ergosterol
 - c. Sugars
 - d. Lipids
6. Match the antivirals with their description.
- | | |
|--------------------------------------|--|
| a. Viral attachment/entry inhibitors | ___ Block the maturation of the virion particles |
| b. Reverse transcriptase inhibitors | ___ Inhibit gene transcription of RNA retroviruses |
| c. DNA/RNA polymerase inhibitors | ___ Prevent the virus from exiting the host cell |
| d. Protease inhibitors | ___ Prevent the virus from entering the host cell |
| e. Viral release inhibitors | ___ Block viral genome replication |

Name: _____ Class: _____

Antimicrobials Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. What are antimicrobials?
 - a. Drugs that kill or inhibit the growth of bacteria
 - b. Drugs that kill or inhibit the growth of viruses
 - c. Drugs that kill or inhibit the growth of fungi
 - d. Drugs that kill or inhibit the growth of any microbe**

2. Select all that apply. Which statements describe antimicrobial action on the pathogen?
 - a. Antimicrobials may target a target common to host and pathogen as long as the target is more important for pathogen survival than host survival**
 - b. Antimicrobials may target a target unique to a pathogen**
 - c. Antimicrobials target receptors rather than enzymes
 - d. Antimicrobials may selectively target a component of the pathogen that is different enough than the form found in the host**

3. Match the following central dogma principles of biology with their descriptions:

a. Replication	c. Ribosomes synthesize peptides and proteins by reading RNA
b. Transcription	b. DNA is converted to RNA by RNA polymerase
c. Translation	a. DNA is copied during cell division by DNA polymerase

4. Select all that apply. What class(es) of drug act(s) on bacterial cell walls?
 - a. DHPS and DHFR inhibitors
 - b. Topoisomerase inhibitors
 - c. Inhibitors of peptidoglycan polymerization**
 - d. β -lactam antibiotics**

5. What molecule is specific to fungal cell membranes and is targeted by inhibitors of its synthesis and polyenes?
- a. Cholesterol
 - b. Ergosterol**
 - c. Sugars
 - d. Lipids
6. Match the antivirals with their description.
- | | |
|--------------------------------------|--|
| a. Viral attachment/entry inhibitors | d. Block the maturation of the virion particles |
| b. Reverse transcriptase inhibitors | b. Inhibit gene transcription of RNA retroviruses |
| c. DNA/RNA polymerase inhibitors | e. Prevent the virus from exiting the host cell |
| d. Protease inhibitors | a. Prevent the virus from entering the host cell |
| e. Viral release inhibitors | c. Block viral genome replication |

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Lesson Twelve – Cancer

Lesson Overview

In this lesson, students will learn about cancer, how cancer forms through carcinogenesis, and common treatments for cancer. Students will engage in a hands-on activity that will deepen their understanding of targeted therapies in cancer.

Lesson Objectives

After completing this lesson, participants will be able to:

- Define three common terms in cancer
- List and describe the stages of carcinogenesis
- Describe how cytotoxic drugs work for chemotherapy
- List common hallmarks of cancer and describe how targeted therapies exploit these hallmarks

Lesson at a Glance

Activity	Materials	Preparation	Approximate Class Time
FOCUS	• <i>Cancer</i> worksheet • <i>Cancer</i> – Answer Key	1. Print/photocopy the <i>Cancer</i> worksheet (one per participant).	10 minutes
LEARN	• <i>Cancer</i> presentation • Whiteboard kit • Magnetic whiteboard • Magnets • Wiping cloth • Set of 3 whiteboard markers • Laminated overlay for the <i>Cancer</i> slide presentation	1. Prepare the <i>Cancer</i> slide presentation for viewing. 2. Distribute whiteboard kits and ensure all kit components are included.	40 minutes
REVIEW	• <i>Cancer Quiz</i> • <i>Cancer Quiz</i> – Answer Key	1. Print/photocopy the <i>Cancer Quiz</i> (one per participant) and <i>Cancer Quiz</i> – Answer Key.	10 minutes

Lesson Twelve – Cancer

FOCUS: Cancer

10 minutes

Purpose:

Assess students' understanding of cancer and common therapies for cancer.

Materials:

- *Cancer* worksheet
- *Cancer* – Answer Key

Facilitation Steps:

1. Distribute *Cancer* worksheets prior to or at the beginning of class.
2. Have the *Cancer* – Answer Key available.
3. Have students answer the questions on the *Cancer* worksheet and discuss their answers with peers.

Name: _____ Class: _____

Cancer

PURPOSE: Assess your understanding of cancers and common therapies for cancer.

1. In your own words, describe cancer. What are some key features that you associate with cancer?
2. What is a carcinogen? How do carcinogens work?
3. Do you know someone who has or had cancer? If so, what kind of treatment did they receive? If not, what are some treatments you associate with cancer?

Cancer – Answer Key

PURPOSE: Assess your understanding of cancers and common therapies for cancer.

4. In your own words, describe cancer. What are some key features that you associate with cancer?

Cancer is an awful disease that usually appears randomly and can be hard to treat. Cancer is what happens when cells grow uncontrollably and form a tumor. DNA is usually affected to cause cancer.

5. What is a carcinogen? How do carcinogens work?

A carcinogen is a substance that can cause cancer. They damage or mutate DNA, which causes cancer.

6. Do you know someone who has or had cancer? If so, what kind of treatment did they receive? If not, what are some treatments you associate with cancer?

Answers vary

Lesson Twelve – Cancer

LEARN: Cancer Slide Presentation

40 minutes

Purpose:

Develop an understanding of cancer, the steps of developing cancer, and common treatments and targets of cancer.

Materials:

- *Cancer* slide presentation
- Whiteboard kit
 - Magnetic whiteboard
 - Magnets
 - Wiping cloth
 - Set of 3 whiteboard markers
 - Laminated overlay for the *Cancer* slide presentation

Facilitation Steps:

1. Distribute the whiteboard kits and inform students to use them when instructed.
2. Share the following information as you show the slide presentation. A hands-on activity will precede use of the whiteboard kits for an in-class activity. Use the subsequent information to instruct students during the activity.

Slide 1: Cancer

Slide 2: Learning Objectives

The learning objectives are:

- Define the following:
 - Cancer
 - Carcinogen
 - Mutagen
- List and describe the stages of carcinogenesis
- Describe how cytotoxic drugs work for chemotherapy
- List common hallmarks of cancer and describe how targeted therapies exploit these hallmarks

Slide 3: Cancer

Cancer is a disease characterized by the rapid and uncontrollable growth and spread of abnormal cells in the body. Cancer can form in any tissue with dividing cells.

Carcinogenesis is the process of developing cancer and eventually a malignant tumor. A malignant tumor is capable of spreading to other parts of the body. Metastasis describes the process of tumor spread to a part of the body where it did not originate.

Cancer can be difficult to treat because tumors are made up of genetically and functionally different cells (heterogeneity). Drugs that work on some cancer cells may not work for others, allowing the resistant cells to grow.

Slide 4: Carcinogens

Carcinogens are agents that promote the formation of cancer. Carcinogens that mutate and/or damage DNA to cause cancer are known as **mutagens**.

Chemical agents like those found in cigarettes are known to mutate and damage DNA. Physical agents like radiation from the Sun also mutate and damage DNA to make cells cancerous. Some viruses like HPV alter your DNA to cause cancer. However, other events that do not mutate DNA are also important for carcinogenesis.

Slide 5: Cancer Treatment

Cancer treatment is dependent on the type of cancer and the extent of tumor progression.

Common treatments include:

- Surgical removal of the tumor
- Radiation therapy is that is applied to the location of the tumor to kill cells in that area
- Chemotherapy

Chemotherapy uses **cytotoxic** drugs that kill cancer cells and typically in conjunction with surgery and/or radiation. Cytotoxic drugs act on dividing cells. Cytotoxic drugs work best on tumors that grow rapidly. These drugs also kill normally dividing cells, which can be very toxic to the patient.

Slide 6: Cytotoxic Drugs

Cytotoxic drugs are frequently used despite toxicity in patients. Cytotoxic drugs can inhibit DNA replication. This includes **DNA alkylating agents** (e.g., cyclophosphamide and cisplatin) that bind to and crosslink DNA strands, which prevents DNA replication, and **antibiotics** (e.g., doxorubicin) that are used to inhibit topoisomerases and other enzymes to prevent DNA replication.

Cytotoxic drugs also inhibit mitosis (cell division).

Mitotic inhibitors (e.g., paclitaxel) are used to bind and prevent mitotic spindles from dividing the cell.

Slides 7-9: Stages of Carcinogenesis

Carcinogenesis happens in three basic steps. The first step is initiation. During initiation, a normal cell acquires genetic mutations spontaneously during the cell cycle or from exposure with a carcinogen (“initiated cell”). Genetic mutations are commonly found in genes that regulate cell growth, DNA repair, and cell death and survival.

The second step is promotion. Promotion occurs when the initiated cell begins to proliferate (i.e., divide), which is enhanced by many factors.

Factors that promote proliferation are generally not mutagenic and occur repeatedly over time. These include:

- Enhancement of receptor-mediated signaling that enhances proliferation
- Alterations in gene expression that enhance proliferation and inhibit cell death
- Changes in the cell that allow it to evade the immune system

The result of promotion is a rapidly dividing clump of preneoplastic cells that appear before tumor formation.

The last step is progression and malignancy. Progression occurs when preneoplastic cells compete with each other for survival, causing tumor (neoplasm) formation.

Cells within the tumor pick up different genetic mutations to compete, which makes the tumor more heterogeneous. The tendency to mutate is known as genome instability, which increases as a tumor becomes more malignant. Increasing heterogeneity makes diagnosis and treatment of the tumor more difficult.

Slide 10: Targeted Therapies

Targeted therapies act on specific mechanisms known to mediate aspects of carcinogenesis. This is opposed to traditional chemotherapy with cytotoxic agents that broadly kill dividing cells.

There are many hallmarks of cancer that are being exploited in cancer drug development. A few key hallmarks and associated treatments targeting them will be discussed.

Slide 11: Sustained Proliferation

Sustained proliferation refers to cancer's ability to continuously grow and divide. Cancer cells sustain proliferation by altering the cellular signals that tell the cell to grow and divide. This may include:

- Secreting hormones and growth factors to stimulate cell growth and division in the tumor
- Elevating levels of receptors and other signaling components that receive and mediate these signals

Example: Breast cancer tumors may increase estrogen and estrogen receptor levels to grow. Tamoxifen is used to treat estrogen receptor (ER+) tumors.

Slide 12: Evading Growth Suppressors

Evading growth suppressors refers to decreasing activation of signals and pathways that prevent cell proliferation. In normal cells, tumor suppressor genes are expressed to stop cell proliferation. Cancer cells evade growth via mutation or decreased expression of tumor suppressor genes.

Example: The tumor suppressor gene p53 is mutated in many cases of cancer, allowing cells to proliferate more easily. The drug arsenic trioxide rescues p53 function, enabling tumor suppression.

Slide 13: Resisting Cell Death

Cancer cells resist death by modifying pathways that would normally tell the cell to die. In apoptotic cell death pathway, proapoptotic proteins promote cell death, while antiapoptotic proteins promote cell survival.

Mutation or altered gene expression of pathway components can prevent cell death in a tumor. Some cancer drugs stimulate apoptosis and other cell death pathways in cancer cells.

Example: The Bcl-2 protein is antiapoptotic. Venetoclax is a Bcl-2 inhibitor that stimulates apoptotic cell death in certain types of leukemia.

Slide 14: Evading Immune Response

Evading immune response refers to the ability of tumor cells to avoid immune detection and prevent the immune system from killing them. T cells of the immune system check cells to see if they are pathogenic.

T cells look for antigens expressed on the tumor cell's surface at immune checkpoints. If the antigen binds to the T cell receptor at the checkpoint, the T cell "turns on" to kill the cell. T cells express other receptors that "turn off" the cell when the receptor is bound.

For example, the PD-1 receptor bound to its PD-L1 ligand "turns off" a T cell. **Immune checkpoint inhibitors** antagonize these and similar receptors to promote T cell destruction of tumor cells.

Slide 15: Inducing Angiogenesis

Inducing angiogenesis refers to the tumor's ability to turn on a "switch" that causes blood vessels to sprout towards the tumor. Angiogenesis is the formation of new blood vessels.

Because of its rapid growth, a tumor requires a constant supply of oxygen and nutrients. To meet the demand, cancer cells secrete factors to recruit cells that promote blood vessel sprouting towards the tumor.

Example: Vascular endothelial growth factor (VEGF) is secreted from tumors and activates VEGF receptors to cause angiogenesis. Bevacizumab is an **angiogenesis inhibitor** that binds to the VEGF receptor to prevent angiogenesis.

Slide 16: Invasion and Metastasis

Invasion and metastasis refer to cancer cells invading blood vessels and other tissues to form tumors in other areas of the body (metastasis). Tumor invasion and metastasis is responsible for a large proportion of mortality in cancer patients.

Cancer cells transform into a type of cell (mesenchymal-like cells) that is more mobile and can more easily migrate and invade other tissues and blood vessels. Drugs are being developed to specifically inhibit invasion and metastasis in tumors.

Slide 17: Hands-On Activity

Read the instructions on the slide.

Slides 18-19: Scenario 1

Hands-On Activity:

- Read the scenario to students and give them a minute or so to place their magnets.
- Read the answers to students and ensure they understand why each answer is correct.
- Have students move their magnets to the box if correct or remove them from the board if incorrect.

Slides 20-21: Scenario 2

Hands-On Activity:

- Read the scenario to students and give them a minute or so to place their magnets.
- Read the answers to students and ensure they understand why each answer is correct.
- Have students move their magnets to the box if correct or remove them from the board if incorrect.

Slides 22-23: Scenario 3

Hands-On Activity:

- Read the scenario to students and give them a minute or so to place their magnets.
- Read the answers to students and ensure they understand why each answer is correct.
- Have students move their magnets to the box if correct or remove them from the board if incorrect.

Lesson Twelve – Cancer

REVIEW: Cancer

10 minutes

Purpose:

Review key concepts related to cancer and the learning objectives for the lesson.

Materials:

- *Cancer Quiz*
- *Cancer Quiz – Answer Key*

Facilitation Steps:

1. Distribute the *Cancer Quiz*.
2. Give students several minutes to take the quiz.
3. Review answers with the *Cancer Quiz – Answer Key* and have students self-check answers and correct any wrong answers.

Name: _____ Class: _____

Cancer Quiz

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. A _____ is an agent that mutates or damages DNA, whereas a _____ is an agent that can cause cancer.
 - a. Carcinogen; mutagen
 - b. Mutagen; carcinogen
 - c. Chemical; toxin
 - d. Toxin; chemical

2. Select all that apply. Which statements describe cytotoxic drugs used in chemotherapy?
 - a. They may inhibit mitosis to kill dividing cells
 - b. They may be antibiotics that inhibit DNA replication
 - c. They may specifically target cancer cells
 - d. They may cause DNA to crosslink to inhibit DNA replication

3. Match the following stages of carcinogenesis with their descriptions:

a. Initiation	_____	A normal cell acquires genetic mutations
b. Promotion	_____	Cells form a tumor while acquiring more genetic mutations
c. Progression and Malignancy	_____	Cells proliferate using factors that are not mutagenic

4. Match the cancer hallmarks with strategies to target them.

a. Sustained proliferation	_____	Reactivating tumor suppressor genes
b. Evading growth suppressors	_____	Immune checkpoint inhibitors for T cells
c. Resisting cell death	_____	Inhibiting receptors promote blood vessel formation
d. Evading immune response	_____	Inhibiting receptors that enhance cell growth/division
e. Inducing angiogenesis	_____	Prevent cells from transforming and migrating from the tumor
f. Invasion and metastasis	_____	Stimulating antiapoptotic proteins

Name: _____ Class: _____

Cancer Quiz – Answer Key

Instructions: Select the best answer to the following multiple-choice and matching questions.

1. A _____ is an agent that mutates or damages DNA, whereas a _____ is an agent that can cause cancer.
 - a. Carcinogen; mutagen
 - b. Mutagen; carcinogen**
 - c. Chemical; toxin
 - d. Toxin; chemical

2. Select all that apply. Which statements describe cytotoxic drugs used in chemotherapy?
 - a. They may inhibit mitosis to kill dividing cells**
 - b. They may be antibiotics that inhibit DNA replication**
 - c. They may specifically target cancer cells
 - d. They may cause DNA to crosslink to inhibit DNA replication**

3. Match the following stages of carcinogenesis with their descriptions:

a. Initiation	a. A normal cell acquires genetic mutations
b. Promotion	c. Cells form a tumor while acquiring more genetic mutations
c. Progression and malignancy	b. Cells proliferate using factors that are not mutagenic

4. Match the cancer hallmarks with strategies to target them.

a. Sustained proliferation	b. Reactivating tumor suppressor genes
b. Evading growth suppressors	d. Immune checkpoint inhibitors for T cells
c. Resisting cell death	e. Inhibiting receptors promote blood vessel formation
d. Evading immune response	a. Inhibiting receptors that enhance cell growth/division
e. Inducing angiogenesis	f. Prevent cells from transforming and migrating from the tumor
f. Invasion and metastasis	c. Stimulating antiapoptotic proteins

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