Unit 2: Lesson 1 – Development of Disease and Infection

LESSON QUESTIONS

- How do antigens and the immune system affect each other's evolution?
- What are key steps in the process of the development of infection and disease?

LESSON OBJECTIVES

- Define glossary terms related to the causes and development of infection and disease.
- Explain the roles of antigens and the immune system in the development of infection and disease.
- Describe key steps in the process of disease development.

OVERVIEW

In this lesson, students explore the origins of diseases, and particularly the pathogens that cause disease. Students explore glossary terms and read a passage about the causes and development of disease. In a hands-on activity, students simulate an attack on the immune system. Students analyze a model that shows steps of the infection process.

LENGTH

Two to three 45-minute sessions

GLOSSARY TERMS

adaptive immunity, antigenic novelty, antigenic variation, chronic infection, latency, persistence, programmed gene rearrangement, resistance

STANDARDS

- **Next Generation Science Standards**
    - HS-LS1-2.4.1 Models (e.g., physical, mathematical, computer models) can be used to simulate systems and interactions— including energy, matter, and information flows—within and between systems at different scales.
    - HS-LS4-1 Communicate scientific information that common ancestry and biological evolution are supported by multiple lines of empirical evidence.

- HS-LS4-2 Construct an explanation based on evidence that the process of evolution primarily results from four factors: (1) the potential for a species to increase in number, (2) the heritable genetic variation of individuals in a species due to mutation and sexual reproduction, (3) competition for limited resources, and (4) the proliferation of those organisms that are better able to survive and reproduce in the environment.

- HS-LS4-3 Apply concepts of statistics and probability to support explanations that organisms with an advantageous heritable trait tend to increase in proportion to organisms lacking this trait.

- HS-LS4-4 Construct an explanation based on evidence for how natural selection leads to adaptation of populations.

- **Common Core State Standards**

  - RST.11-12.3 Follow precisely a complex multistep procedure when carrying out experiments, taking measurements, or performing technical tasks; analyze the specific results based on explanations in the text.

  - RST.11-12.4 Determine the meaning of symbols, key terms, and other domain-specific words and phrases as they are used in a specific scientific or technical context.

  - RST.11-12.7 Integrate and evaluate multiple sources of information presented in diverse formats and media (e.g., quantitative data, video, multimedia) in order to address a question or solve a problem.

  - WHST.9-12.2 Write informative/explanatory texts, including the narration of historical events, scientific procedures/ experiments, or technical processes.

  - WHST.9-12.9 Draw evidence from informational texts to support analysis, reflection, and research.

  - WHST.9-12.5 Develop and strengthen writing as needed by planning, revising, editing, rewriting, or trying a new approach, focusing on addressing what is most significant for a specific purpose and audience.

  - WHST.11-12.6 Use technology, including the Internet, to produce, publish, and update individual or shared writing products in response to ongoing feedback, including new arguments or information.

- WHST.11-12.7 Conduct short as well as more sustained research projects to answer a question (including a self-generated question) or solve a problem; narrow or broaden the inquiry when appropriate; synthesize multiple sources on the subject, demonstrating understanding of the subject under investigation.

- HSS.IC.A Understand and evaluate random processes underlying statistical experiments.

- HSS.IC.B Make inferences and justify conclusions from sample surveys, experiments, and observational studies.

- HSS.ID.A Summarize, represent, and interpret data on a single count or measurement variable.

- HSS.CP.A Understand independence and conditional probability and use them to interpret data.

- HSS.CP.B Use the rules of probability to compute probabilities of compound events.

MATERIALS

- Student worksheet: https://vaccinemakers.org/sites/default/files/lessons/HS.student%20worksheet.unit2_.lesson1.FINAL_.pdf
- Each student group will need the items listed for Activity 1:
  - Activity sheet- Development of Disease Game (Activity 1) https://vaccinemakers.org/sites/default/files/lessons/HS.activity%201-Development%20of%20Disease%20Game.unit2_.lesson1.FINAL_.pdf
  - Blank index cards (50 per group of 11 players)
  - Marker pen
  - 2 six-sided dice or a decahedral die (optional)
- Activity sheet- The Infection Process (Activity 2) https://vaccinemakers.org/sites/default/files/lessons/HS.activity%202_The%20Infection%20Process.unit2_.lesson1_FINAL.pdf
- Computer with internet access

BACKGROUND FOR TEACHER

This lesson builds on the knowledge and understanding students acquire in Unit 1, which focuses on the function of the immune system. Students encounter new vocabulary that may be challenging. The key is to focus on processes rather than definitions. The main process covered in the lesson is how a pathogen's genetic strategy enables it to avoid or counter the immune system's response. Each of the vocabulary terms can be put into the context of this process. Likewise, the game activity focuses on the process of infection. From an evolutionary perspective, the pathogen and immune system are in a constant tug-of-war. Natural selection favors features that enable the pathogen to spread, increasing its reproductive success. On the other hand, immune defenses that prevent infection increase the survival chance of the host. If immune defenses cannot prevent access of the pathogen to body tissues and cells, the pathogen will cause an infection. There are four key steps in the development of infection.

Steps of infection process:

Step	Process	Infective Mechanisms	Protective Mechanisms
1	Attach to body	Pathogen attaches to body Cause infection or disease if in a compromised area of skin or mucous membranes	Chemical factors and phagocytes (especially lung)
2	Penetration of epithelium	Pathogen accesses internal tissues of the body	Wound healing, antibacterial proteins and peptides, phagocytes
3	Local tissue infection	Pathogen gains access to tissue cells	Complement proteins, natural killer cells, macrophages and other phagocytes, cytokines
4	Spreading	Pathogen spreads by lymphatic system or bloodstream to other organs and tissues	Phagocytes, antigen trapping, natural killer cells, adaptive immune system response

TEACHER NOTES

Students will need a basic knowledge of the structure and function of the components of the immune system. The Unit 1 lessons serve as an introduction to the immune system. If needed, review the structure and function of the immune system using the websites included in the Lesson Resources section under additional resources. The goal is to provide a broad picture of the causes of disease, which may not be accomplished just by completing lesson activities.

Especially pertinent to this lesson is the concept of pathogens adapting to overcome the immune system and the immune system adapting to prevent infection. The Unit 1 Lesson 2 Castle of the Body activity (Activity 1) includes a section where students explore ways to change the "pathogens" (balls or marbles) to help them gain entry into the "body" (shoebox), and also explore ways to fortify the box to discourage entrance. These observations can serve as scaffolding for the concept of how pathogens need to change to continue infecting people.

LESSON RESOURCES

- Lesson animations:
  - How Does Hepatitis B Combat the Immune System? https://vimeo.com/227180367
  - A Virus Attacks a Cell https://vimeo.com/227174435
- Lesson glossary: https://vaccinemakers.org/sites/default/files/resources/HS.student%20glossary.unit2_.lesson1_FINAL.pdf
- Reading passage, *The Eternal Arms Race: The Constant Battle between Pathogens and the Immune System*, https://vaccinemakers.org/sites/default/files/resources/HS.reading%20passage.unit2_.lesson1.FINAL_.pdf
- Student supplement diagrams sheet: https://vaccinemakers.org/sites/default/files/resources/HS.student%20diagram%20supplement.unit2_.lesson1.FINAL_.pdf

- Additional resources that may be helpful:
  - Comprehensive human immune system overview, VEC, https://www.chop.edu/vaccine-education-center/human-immune-system
  - Animation Expedition #1 – A Virus Attacks a Cell: How Does Infection Begin? https://vaccinemakers.org/news-events/animation-expedition-1-virus-attacks-cell-how-does-infection-begin
  - Animation Expedition #6 - How Hepatitis B Tries to Evade Our Immune System https://vaccinemakers.org/news-events/animation-expedition-6-how-hepatitis-b-tries-evade-our-immune-system
  - Video - "How does Natural Infection with Measles Suppress the Immune System?"https://www.youtube.com/watch?v=WHMYrCAkJ1A&list=PLUv9oht3hC6QXyTjllQVBIFqqASDOdnAa&index=7&t=1s
  - Video - "The Stages of Viral Infection," VEC, https://www.youtube.com/watch?v=EuCpagj2kMQ&list=PLUv9oht3hC6QXyTjllQVBIFqqASDOdnAa&index=4&t=13s
  - Trivia quizzes related to the lesson animations, Kahoot!, www.vaccinemakers.org/trivia

- Immune system information, with sections on immune system function and location, NIH, https://www.niaid.nih.gov/research/immune-systemoverview
- Basic information on immune system function, How Stuff Works.com, http://science.howstuffworks.com/life/human-biology/immunesystem2.htm

ENGAGE

1. Ask students to write down a list of video games they've played or movies/television shows they've watched about a worldwide or global outbreak of disease (e.g., Steven Soderbergh's *Contagion*).
2. Allow students to share their lists with neighbors. Students choose a favorite video game or movie from their shared lists.
3. Students write a brief passage to describe the degree of realism in the scenario depicted in their chosen game or video. Guide students as needed with a prompt such as "Do you think the game or video shows a situation that could actually happen? How is it similar or different from a real-life global outbreak of disease?"
4. Ask students to provide examples of disease outbreaks. Write the list of diseases on your whiteboard or overhead. Examples could include COVID-19, Ebola, measles, influenza or swine flu among others.
5. Students watch the animations, *How Does Hepatitis B Combat the Immune System*? and *A Virus Attacks a Cell*. If time allows, or to reinforce the concepts in the animations, students can complete the quizzes on *Kahoot!* related to these animations.
6. Explain to students that they will learn how pathogens overcome our immune defenses. Emphasize that for pathogens, infection means survival. On the other hand, for those infected, infection means disease or illness (and possibly death). These opposing forces of natural selection are the basis of the evolutionary "arms race" between pathogens and their hosts.

EXPLORE

1. Students explore online sources and the lesson glossary to complete the vocabulary table in their worksheets.
2. Students read the reading passage, *The Eternal Arms Race: The Constant Battle Between Pathogens and the Immune System*.
3. Show students Figure 1, *Pathogens and the Immune System* (see student supplement diagram sheet). Guide a brief class discussion on the evolutionary balance between pathogens and the immune system. If needed ask prompt questions, such as:
    a. How does the immune system deal with new types of pathogens?
    b. What do pathogens do to continue to survive?

   c. How do these responses contribute to natural selection?
4. Show students Figure 2, *Persistence* (see student supplement diagram sheet). Guide a brief class discussion on the four basic strategies pathogens use to overcome the immune system (persistence, antigenic novelty, antigenic variation and resistance).
5. Working in pairs or small groups, students engage in the Development of Disease Game (Activity 1) filling in the game supplement tables and completing the activity sheet questions.

EXPLAIN

1. Students write a simulated blog post or pop science magazine article explaining how infection and disease develop despite an immune response.
2. Students work in small groups to create a concept map of how infection and disease develop and the associated immune response.

ELABORATE

1. Working in pairs or small groups, students complete The Infection Process activity sheet (Activity 2).
2. Students choose one of the diseases to research in more detail and create a presentation to describe the infection process and the immune response.

EVALUATE

1. Assess students based on their presentations and completion of the activity questions.

RUBRIC: STUDENT WORKSHEET

Vocabulary table

- Refer to the lesson glossary for correct definitions of terms.

RUBRIC - ACTIVITY 1: Development of Disease Game

Questions for Game Version 1

1. How many turns (times the IM player called a number) did it take in Round 1 before the IM player lost the turn?

- Answers will vary. However, the answer will be no greater than 2, since the IM player has only 2 cards that will match those held by P players.

2. How many turns did it take in Round 2, 3 and 4 before the IM player lost the turn?

   - Answers will vary. However, the answer for successive rounds will be:
     a. Round 2: no greater than 4
     b. Round 3: no greater than 6
     c. Round 4: no greater than 8

3. What happened in Round 5 that was different from previous rounds? Explain.

   - The IM player did not lose any turns because all of the IM player's cards matched those of P players.

4. Is there a pattern in the number of turns taken in successive rounds before the IM player lost? Explain your answer.

   - The number of turns increases in successive rounds since the IM player has 2 more cards in each round that will match those held by P players, preventing the IM player from losing.

5. In Round 1, what is the probability that the IM player loses on the first turn? Explain your answer and show your calculation.

   - In Round 1, the IM player has two cards that could match a card presented by the P player. There are 10 different P player cards. Therefore, there is a 2 in 10 probability that the P player card will match the IM player's card in the first turn. Therefore, there is an 8 in 10 probability that the P player card will not match the IM player's card in the first turn, or 8/10 = 4/5.

6. In Round 5, what is the probability that the IM player loses on any given turn? Explain your answer.

   - In Round 5, all of the IM player's cards match those of P players. Therefore, there is zero chance that the IM player can lose on any turn, therefore P = 0.

Questions for Game Version 2

1. How many turns (times the IM player called a number) did it take in Round 1 before the IM player lost the turn?

- Answers will vary. However, the IM player has two lives, so can take two turns. The IM player can only win in the first two turns by throwing the same number twice.

2. In Round 1, what is the probability that the IM player loses after two throws? Explain your answer and show your calculation.

   - In Round 1, the IM player has two cards that could match a card presented by the P player. Since each P player has two cards, the IM player has to throw the same number twice. There is a 1 in 10 probability that the P player card will match the IM player's card in either throw. The probability of throwing the same number from 1 to 10 twice is (1/10 x 1/10) or 0.1 x 0.1 = 0.01. Therefore, the probability that the P player card will not match the IM player's card in the two throws is 1 – 0.01 = 0.99.

3. What can you conclude about the number of rounds it would take for the IM player's cards to match all the P player's cards?

   - Since there is a low probability of throwing the same two numbers consecutively in each round, a very large number of rounds would be needed for the IM player's cards to match all the P player's cards. (The probability of two matches for every two P player cards occurring in 20 consecutive turns is ~ 7.6 x 10-14.)

Questions for Game Version 3

1. How many turns (times the IM player called a number) did it take in Round 1 before the IM player lost the turn?

   - Answers will vary. As with Game Version 2, the IM player has two lives, so can take two turns. The IM player can only win in the first two turns by throwing the same number twice.

2. In Round 1, what is the probability that the IM player survives for two throws? Explain your answer and show your calculation.

   - In Round 1, the IM player has two cards that could match a P player card. Since the P players each have a different card, the IM player must throw 2 out of 10 numbers in each throw. Therefore, the IM player's probability of surviving one throw is 2/10 = 0.2, and of surviving 2 throws is 0.2 x 0.2 = 0.04.

Question for Game Version 4

1. In Round 1, what is the probability that the IM player loses on the first turn? Explain your answer and show your calculation.

    - In Round 1, the probability that the P player card will not match the IM player's card in the first turn is the same as in Game Version 1, 8/10 = 4/5 = 0.8. However, the IM player must throw a higher number than the P player to win. The chance of throwing a higher number is 0.5, so the probability of the IM player losing in either case is 0.8 + 0.5 = 0.9.

Activity 1 Summative Questions

1. How does this activity simulate active pathogens?

    - The P players simulate active pathogens. The P player presents their card with its letter, simulating the pathogen encountering the host.

2. What part of the activity represents the immune system recognizing the pathogen?

    - The matching of the letter on the IM player's card with the letter on the P player's card represents the immune system recognizing the pathogen.

3. How does this activity simulate the immune system neutralizing the pathogen?

    - When the letter on the IM player's card matches the letter on the P player's card, the IM player takes the P player's card.

4. Does this activity represent the adaptive or innate immune system? Explain your answer.

    - This activity represents the adaptive immune system because the letter on the P players' cards represents surface antigens. The letter on the IM player's cards represents antibodies that recognize the surface antigens. In each round, the IM player takes two more cards, enabling the IM player to recognize more kinds of pathogens, adapting to the pathogens.

5. How was antigenic novelty represented in the activity? Explain your answer.

    - The early rounds of each game represent antigenic novelty. In these rounds, the IM player does not have all cards with the correct letter to match (recognize) all the P players' cards. The new unrecognized cards reduce the probability that

the IM player will match the P players' cards. This is like the immune system being presented with pathogens that have new antigens on their surface.

6. How was antigenic variation represented in the activity? Explain your answer.

    - Antigenic variation is represented in Game Version 3 when the P players swap cards with other P players and can play with two cards, each having different letters. In this version, the P player has two different cards so if the letter on one card matches the IM player's card, they will still be able to play a new card in later rounds. Having two different cards increases the number of rounds that the IM player needs to match the P players' cards. This is like the immune system being presented with a pathogen that has different versions of antigens on their surface.

7. How was persistence represented in the activity? Explain your answer.

    - Persistence is represented in Game Version 2, since the P player has two cards, allowing the same card to be presented to the IM player twice. In this version, each player has two cards with the same letter. So, the IM player will need two turns to neutralize each player. This is like the pathogen being able to persist for longer in the host.

8. How was resistance represented in the activity? Explain your answer.

    - Resistance is represented in Game Version 4 when the P player has a chance to throw a higher number than the IM player, so the P player may not be removed the first time the letters match. In this version, the IM player does not automatically neutralize the P player in case of a match. Throwing the dice means that even with a match, the IM player only as a 0.5 chance of neutralizing the P player. This is like a pathogen that is able to handicap the immune system.

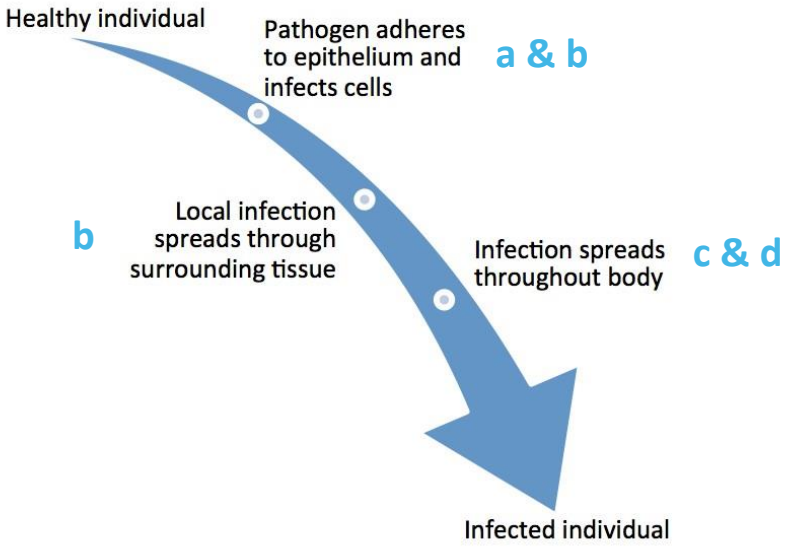
RUBRIC - ACTIVITY 2: The Infection Process

Activity 2 Questions

1. On the diagram of an infection arc, indicate where the pathogen may overcome the immune system response. You may use a letter more than once.
   Explain the placement of each letter.
    a. Antigenic novelty

b. Antigenic variation
c. Persistence
d. Resistance

- Labeled diagram:



- When the pathogen is new (a) or changes itself (b), it will be more likely to be able to enter the body. Antigenic variation (b) results in changes that may allow the infection to spread once it is in the body. Persistence (c) and resistance (d) are more likely later in infection because they make it more difficult for the body to rid the infection.

2. What happens to the pathogen if it cannot reproduce, and what are the consequences?

   - If a pathogen cannot reproduce, it will cease to exist, which means that it must infect humans to survive.

3. What process enables the pathogen to overcome the immune system?

   - Since the immune system has evolved to prevent infections, the pathogen has to evolve in ways to defeat the immune system. This leads to an ongoing evolutionary battle between infection by pathogens and the host's immune system.

4. Ensure students include the specific mechanism the pathogen has evolved to overcome the immune system:

a. *Streptococcus pneumoniae*	Antigenic variation – more than 84 antigenic types
b. African trypanosomes (sleeping sickness)	Antigenic variation – programmed genetic rearrangements. More than 1,000 different genes can rearrange to change surface proteins
c. Herpes simplex virus	Persistence (latency)
d. Varicella zoster virus (chickenpox)	Persistence (latency)
e. Epstein-Barr virus	Persistence (latency)
f. Hepatitis B virus	Persistence (chronic infection)
g. *Mycobacterium tuberculosis*	Resistance – infects macrophages
h. *Listeria monocytogenes*	Resistance – escapes phagosome to replicate in cytoplasm of macrophages
i. Human immunodeficiency virus (HIV)	Resistance – destroys CD4+ T cells Employs antigenic variation