

Unit 2: Lesson 1 – Development of Disease

- **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 genetic 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
 - computer with internet access
 - blank index cards (50 per group of 11 players)
 - Marker pen
 - Six-sided dice
 - Decahedral dice (optional)

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

GLOSSARY

The following glossary terms are required vocabulary for this lesson. It is not necessary for students to recall all details, but students should be able to articulate how these play a role in the development of disease.

Adaptive immunity – Antigen-specific immune response

The response of the adaptive immune system gives rise to the host's adaptive immunity. The pathogen must now bypass immune defenses that specifically recognize and neutralize it. The pathogen circumvents adaptive immunity by maintaining a reservoir of susceptible targets.

Antigenic novelty – a pathogen not previously encountered by the immune system

When a pathogen is new to the immune system, it is capable of causing infection. In most cases, antigenic novelty is the result of the pathogen infecting someone whose immune system has not been exposed to the pathogen in the past. This is why babies tend to be more susceptible to many infections.

Antigenic variation – multiple versions of the surface proteins on a virus or bacteria that are different enough that they can each infect a single host.

Antigenic variation can be caused by spontaneous genetic changes (point mutations), genetic variety (programmed genetic rearrangements) or existence of various types of the same pathogen with different genes for their surface antigens (multiple genotypes).

Chronic infection – a pathogen remains in cells and replicates indefinitely

Continuous replication causes low levels of virus to be produced indefinitely resulting in chronic infection. Hepatitis B virus is an example of this type. Chronically infected individuals often have high quantities of virus in their blood so they may easily transmit the virus to others.

Latency – period after infection during which a virus remains in cells without replicating

Viruses in a latent phase do not replicate during the normal cell cycle. However, they may reactivate when the immune system is compromised. Symptoms may or may not appear during latency.

Herpes simplex virus, zoster virus which causes chickenpox and shingles, and Epstein-Barr virus, which infects B cells, are examples of viruses with latent phases.

Persistence – a pathogen remains in cells after initial infection

Persistence occurs when the initial infection is resolved, but the pathogen remains in cells of the body indefinitely. A latent viral infection is an example of persistence.

Programmed gene rearrangement – mechanism of a pathogen's genome allows it to regularly express different surface proteins

Programmed gene rearrangements during reproduction of pathogens cause variation in expression of surface molecules making it difficult for the immune system to recognize the different versions of the same pathogen. For example, trypanosomiasis ("sleeping sickness) genome contains about a thousand genes that can be variably expressed to make surface molecules. After the host makes antibodies for one set of molecules, the parasite changes its gene expression to make different surface molecules.

Resistance – means by which a pathogen avoids or counteracts the host immune system

Resistance occurs when the pathogen directly engages with the host's immune system by destroying or exploiting it for survival. Resistance may render part of the immune response ineffective or reduce the overall immune response. This is one of the mechanisms of survival employed by HIV, which hinders the typical immune response by infecting T cells.

NOTES

- Students will need a basic knowledge of the structure and function of the components of the immune system. Unit 1 of this package serves as the introduction to the immune system. If needed, review the structure and function of the immune system at these websites:
 - How Your Immune System Works, from How Stuff Works.com
<http://science.howstuffworks.com/life/human-biology/immune-system2.htm>
 - Immune system learning module, from the Vaccine Education Center at The Children's Hospital of Philadelphia
<http://vec.chop.edu/service/vaccine-education-center/related-information/vaccine-information-for-educators/immune-system-module.html>
- If needed, share the background information with students. The goal is to provide a broad picture of the causes of disease, which may not be accomplished just by completing lesson activities.

ENGAGE

1. Ask students to write down a list of video games they've played or movies 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. If needed guide students with a prompt question 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 for a show of hands if they have heard of a disease outbreak. Write the list of diseases on your whiteboard or overhead. Examples could include Ebola, measles, influenza or swine flu.
5. Students watch the animations, *How Does Hepatitis B Combat the Immune System?* <https://vimeo.com/198062885> and *A Virus Attacks a Cell* <https://vimeo.com/198062527>

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 interactive 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 *Unit 2 Overview*). 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. How do new pathogens result in natural selection on the host?
 - c. How does the immune response to pathogens result in natural selection?
4. Show students Figure 2, *Persistence*. 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 conduct Activity 1 in their worksheets.

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 conduct Activity 2 in their worksheets.
2. Students choose one of the diseases to research in more detail, and create a presentation to describe the development of the disease and the immune response.

EVALUATE

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

Activity 1: Development of Disease—Infection Simulation RUBRIC

Questions for Game Version 1

- 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.
- Answers will vary. However, the answer for successive rounds will be:
 - Round 2: no greater than 4
 - Round 3: no greater than 6
 - Round 4: no greater than 8
- The IM player did not lose any turns because all of the IM player's cards matched those of P players.
- 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.
- 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 $8/10 = 4/5$.
- 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

- 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.
- 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 the either throw. The probability of throwing the same number from 1 to 10 twice is $(1/10 \times 1/10)$ or $0.1 \times 0.1 = 0.01$. Therefore the probability that the P player card will not match the IM player's card in the two throws is $1 - 0.01 = 0.99$.
- 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 $\sim 7.6 \times 10^{-14}$.)

Questions for Game Version 3

1. 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, 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 $0.2 \times 0.2 = 0.04$.

Question for Game Version 4

1. 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 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.

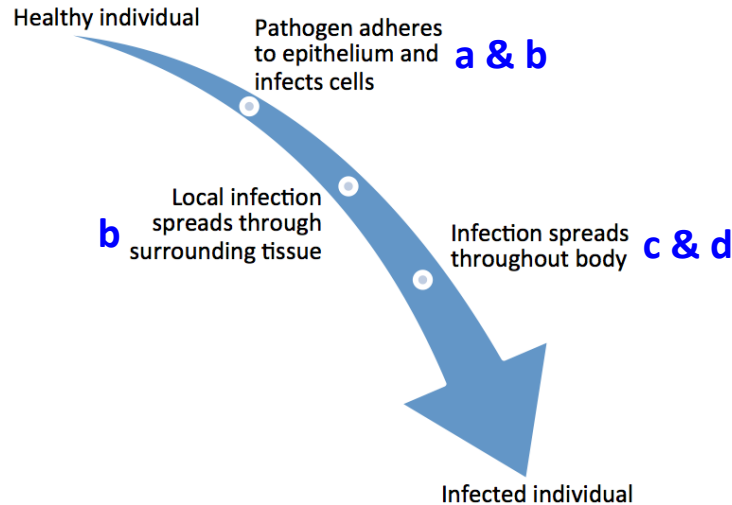
Persistence is represented in Game Version 2, since the P player has two cards, allowing the same card to be presented to the IM player twice. In this version, each player has two cards with the same letter. So the IM player will need two turns to neutralize each player. This is like the pathogen being 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 a dice means that even with a match, the IM player only has a 0.5 chance of neutralizing the P player. This is like a pathogen that is able to handicap the immune system.

Activity 2: Development of disease--The Infection Process: RUBRIC

Labeled diagram:



1. Key:

- a. Antigenic novelty
- b. Antigenic variation
- c. Persistence
- d. Resistance

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. If a pathogen cannot reproduce, it will cease to exist, which means that they must infect humans to survive.
3. Since the immune system has evolved to prevent infections, the pathogen has to evolve 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. <i>Streptococcus pneumoniae</i>	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. <i>Mycobacterium tuberculosis</i>	Resistance – infects macrophages
h. <i>Listeria monocytogenes</i>	Resistance – escapes phagosome to replicate in cytoplasm of macrophages
i. Human immunodeficiency virus (HIV)	Resistance – destroys CD4+ T cells Employs antigenic variation