Unit 2: Lesson 2 – Influenza and HIV

- **Lesson Questions:**
  - What steps are involved in viral infection and replication?
  - Why are some kinds of influenza virus more deadly than others?
  - How do flu viruses and HIV overcome immune system defenses?

- **Lesson objectives:**
  - Create a model of viral infection and replication.
  - Explain why some kinds of influenza virus are more deadly than others.
  - Describe how flu viruses and HIV overcome immune system defenses.

- **Overview:** In this lesson, students investigate the process of viral infection and replication. A hands-on activity provides a model for viral infection and replication, which is then applied to understand the concepts of genetic variation and genetic drift. Students use these concepts to explain why some kinds of influenza virus are more deadly than others. Students view a video describing the influenza pandemic of 1918, and analyze the video to explain how this flu strain overcame immune system defenses to become particularly deadly. Students investigate a model of the HIV life cycle to understand how HIV replicates.

- **Length:** Four to five 45-minute sessions.

- **Glossary terms:** AIDS, antigenic drift, antigenic shift, budding, epidemic, genotypes, hemagglutinin, HIV, messenger RNA, neuraminidase, pandemic, point mutation, reassortment, reverse transcription

- **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-LS4-2 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-LS4-4 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.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.B Make inferences and justify conclusions from sample surveys, experiments, and observational studies.

Materials:
- 4 highlighter pens colored red, green, blue and yellow.
- Tape or glue
- Scissors
- Paper clips
- 2 sheets copier paper
- Timer or stopwatch
- 4 envelopes for each group
BACKGROUND FOR TEACHER

This lesson focuses on the mechanisms by which viruses infect cells and replicate. The lesson also covers genetic processes by which viruses are able to circumvent immune system defenses. The hands-on activity models how a virus infects a cell and replicates. The aim of the activity is to demonstrate how the process of replication results in mistakes in viral genetic material leading to genetic variation. Since these mistakes can also alter viral proteins (antigens), this variation is called antigenic variation. Over time, mutations can accumulate, resulting in a genetic makeup quite different from the original RNA sequence. The small changes that occur regularly in the viral genome are called antigenic drift. If two different strains of influenza viruses replicate in the same cell, their can combine their genes may combine to form a new strain. This dramatic change in the viral genome is called antigenic shift. The resulting change in viral protein structure results in high levels of susceptibility among populations. Antigenic shift is the reason that influenza can cause pandemics.

Influenza Virus

Influenza viruses are classified based on their membrane glycoproteins, hemagglutinin (H) and neuraminidase (N). Numbers after these letters indicate a particular viral strain, such as H1N5 (the notorious “bird flu”) or H1N1 (“swine flu”).

Influenza viruses contain segmented, negative strand RNA in a capsid enclosed in an envelope. The RNA has eight genes for eleven proteins. When the gene base sequences change, surface proteins may change, leading to antigenic drift. These genetic changes enable a particular virus to repeatedly infect the same person, which is why we can get influenza one year even if we’ve had influenza or an influenza vaccine the previous year.

Influenza epidemics result when cases occur with higher than normal frequency. Seasonal patterns depend on the region and climate. In temperate regions, influenza season begins in late fall and extends into winter. During influenza (“flu”) season, between 5% and 20% of the U.S. population may be infected with influenza virus.

When a new influenza strain arises, the immune system may not recognize novel surface proteins, so almost everyone could be susceptible. This widespread susceptibility is the basis for pandemics. Such strains commonly arise when two different influenza viruses infect a single organism. For example, pigs can be infected by both human and bird influenza viruses. If both viruses infect the same cell their genes may rearrange to form a new influenza virus. If the new virus can infect humans and is easily transmitted between people, a pandemic can occur because almost everyone will be susceptible to the new virus.
Human Immunodeficiency Virus (HIV)

HIV targets immune system cells, primarily CD4+ T-lymphocytes. For this lesson, it is sufficient for students to understand that HIV directly infects the immune system’s cells. This strategy hinders the body’s ability to defend itself against the virus, as well as other routine infections.

The virus continues to change as it replicates in an individual. Therefore, antibodies against the original HIV particles will not neutralize later generations of viruses. The virus uses a host cell receptor called CD4 to recognize host cells and gain entry. Early during HIV infection, the immune system produces inflammatory cytokines. These activate more T cells, providing more targets for the virus to infect. Infected T cells are killed by enzymatic degradation (necrosis) or rupture of the plasma membrane (cytolysis). The HIV replication cycle includes the following steps:

1. Attachment of HIV particles to cells via CD4 receptors.
2. The virus membrane fuses with the cell membrane, allowing it to enter into a host cell, where viral RNA and reverse transcriptase are released into the cell.
3. Reverse transcription occurs in the cytoplasm making viral RNA into double-stranded DNA. Mistakes during reverse transcription are common, which can cause changes to the virus that is produced.
4. The viral DNA is transported into the nucleus and the integrase enzyme facilitates integration of viral DNA into the host cell’s DNA.
5. Integrated viral DNA is transcribed into messenger RNA during the cell’s metabolism. The mRNA is exported into the cytoplasm where it is translated into viral proteins.
6. The newly formed viral proteins are transported to the plasma membrane.
7. Virus particles form and begin budding from the cells. These newly released particles go on to infect additional cells.

GLOSSARY

The following glossary terms are required vocabulary for this lesson. It is not necessary for students to recall all the details, but students should be able to articulate how these relate to viral infection and replication.

AIDS – disease resulting from HIV infection

AIDS is the stage during which HIV has advanced to severely weaken the immune system. People at this stage of infection are at risk of opportunistic infections. Death from AIDS is commonly from these infections, not from the virus itself.
Antigenic drift – Accumulation of small genetic changes in a virus

Mutations in viral RNA accumulate so that antibodies resulting from prior viral exposure may no longer be protective. Influenza viruses are particularly good at employing antigenic drift as a means of maintaining a reservoir of susceptible people to infect.

Antigenic shift – Reassortment or recombination of viral genes resulting in dramatic changes in a virus

Major changes to viral structure can arise from antigenic shift, resulting in a virus that is not recognizable by antibodies resulting from previous infections. Antigenic shift is the primary mechanism by which influenza pandemics arise. Antigenic shift is relatively rare compared to antigenic drift.

Budding – process by which new viral particles are released from infected cells

Budding is one way in which viral particles (such as HIV) emerge from infected cells. The viral envelope incorporates part of the cell membrane as it forms a new viral particle.

Epidemic – high incidence of disease in a particular place and time

Genotypes – genetic differences among types of a pathogen

Different genotypes of a pathogen allow a diversity of surface antigens. For example, there are more than 84 known types of Streptococcus pneumoniae, which causes bacterial pneumonia. This variation means that antibodies against one genotype may not protect against other genotypes.

Hemagglutinin – surface glycoprotein on influenza viruses

Hemagglutinin is one of two surface proteins used to identify influenza viruses, being the “H” in strains such as H1N1. (See “neuraminidase”.)

HIV – human immunodeficiency virus

HIV is the virus responsible for AIDS. It is a retrovirus that infects the immune system’s helper T cells.

Messenger RNA – single-stranded nucleic acid created by transcription

All cells use messenger RNA (mRNA) to transcribe DNA into a form that can be used for protein synthesis. It is the type of RNA used to make viral proteins.
Neuraminidase – surface glycoprotein on influenza viruses

Neuraminidase is one of two used to identify influenza viruses, being the “N” in strains such as H1N1. (See “hemagglutinin”)

Pandemic – a worldwide epidemic

Pandemics may result when virtually an entire population is susceptible to an infection. The most severe pandemic in recent history was the 1918 Spanish flu pandemic, which killed at least 50 million people. A pandemic caused by the Black Death in Europe during the Middle Ages killed as many as 200 million people in less than ten years – up to half Europe’s population.

Point mutation – single base change to a gene

A point mutation is a change in a single base or nucleotide in RNA or DNA. Point mutations can result in no change to a protein or can totally change the protein structure. Point mutations may change the structure of the surface antigens to avoid recognition by the immune system. Point mutations can result in antigenic drift.

Reassortment – mixing of genetic material into new combinations

Reassortment is the process of swapping of genetic material between different viral genomes. The resulting virus has new characteristics that can allow it to infect previously immune individuals. Reassortment commonly occurs among influenza viruses because some strains can infect both humans and animals such as pigs and poultry. Scientists use reassortment as a method for developing vaccines.

Reverse transcription – process during which DNA is made from viral RNA

In normal transcription, DNA is copied to make RNA that is used to make protein. In reverse transcription, viral RNA is copied to make viral DNA.

NOTES

- The following websites may help students who need to review the basics of immune system function.
  - How Stuff Works: How Your Immune System Works
ENGAGE

1. Ask students to write down when they last had the flu, and then to write a short passage describing the symptoms, progress and treatment of the flu. (If a student has not had flu, he or she can write down their observations of someone else with the flu. They should not disclose the identity of anyone they know who has had flu.)
2. Students work in small groups to share their descriptions and develop a list of common symptoms.
3. Choose one or two individual students and ask if they or anyone they know has had flu shots. (They should not disclose the identity of anyone they know who has had flu shots.)
4. Choose another couple of students and ask if they remember having vaccinations for other diseases. (Most students should have received vaccinations for measles and whooping cough, or pertussis.)
5. Explain to students that they will learn why people need yearly “flu shots” whereas many other diseases require only one or a few vaccine doses.

EXPLORE 1

1. Students explore online sources and the interactive glossary to complete the vocabulary table in their worksheets.
2. Explain to students that their task is to determine how the influenza virus differs from other disease agents, and to explain why people need yearly flu vaccinations.
3. Propose a guiding question to students: Why are some illnesses prevented by single vaccinations, but repeated vaccinations are needed to prevent flu?
5. Working in small groups, students complete Activity 1 in their worksheets. The activity models the genetic processes underlying antigenic drift.
6. If time allows, students can complete the activity modified to demonstrate antigenic shift.
EXPLAIN 1

1. Depending on student’s understanding of the material, assign students to complete the Activity 1 questions either as a group or individually.
2. Working in groups, students develop an argument (hypothesize) why people need annual vaccinations against influenza. Ensure that the students’ hypotheses account for why only one or a few vaccine doses are needed for some illnesses. Their argument should include evidence to support their hypotheses.
3. Lead a class discussion on the groups’ hypotheses, including how well the activity modeled antigenic drift and antigenic shift.

EXPLORE 2

1. Students work in small groups to research the influenza pandemic of 1918. (See for example, https://www.cdc.gov/flu/pandemic-resources/.)
2. Each group creates a concept map to illustrate features of the pandemic including origin and spread, death toll, death rate, local impacts, prevention, treatment and scientific understanding of influenza.

EXPLAIN 2

1. Working individually, students complete the Activity 2 questions on their worksheets.
2. Lead a class discussion on the role of antigenic drift and antigenic shift in the development of the Spanish influenza virus responsible for the 1918 pandemic. Working individually students write a brief report on their investigation, including their answers to the guiding question.

ELABORATE

1. Refer students to Figure 3 in their worksheet supplement.
2. Explain to students that their task is to investigate the life cycle of HIV and to identify key steps allowing cell infection, replication and reinfection.
3. Propose a guiding question to students: What key steps in the HIV life cycle offer opportunities to prevent the life cycle continuing?
4. Working in small groups, students complete Activity 3 in their worksheets.
5. Each group chooses one of the six drug classes of HIV treatments and creates a poster to explain the parts of the HIV replication cycle that the therapy is attempting to combat.

EVALUATE

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

Activity 1: Antigenic Drift RUBRIC

1. The strip of paper represents a sequence of viral RNA bases.
2. This step represents infection of the cell by the virion. The virion injects its RNA sequence into the cell.
3. Answers may vary. In most cases, a mistake will have led to a change in the base sequence, and hence a change in the amino acid sequences. If students were particularly hasty, they may observe several differences between the first and last set of amino acids.
4. Answers may vary. Sample answer: Since the amino acid sequences in the later “Protein” strips of paper were different from the first amino acid sequence, the activity demonstrated antigenic variation.
5. Answers may vary. Sample answer: As the amino acid sequences in the “Protein” strips diverged over successive cycles, the observations do model antigenic drift. Lack of divergence would indicate an absence of antigenic drift.
6. Answers may vary. Sample answer: Antigenic shift occurs when two or more virus strains combine genetic material. This can happen when two different virus particles infect a cell at the same time. The changed genetic material presents a combination of viral surface antigens. We could modify the activity by requiring the “Cell” envelope to have specific sequences to prevent Agent Infection from putting yellow strips in the envelope. The activity would start with all the “Cell” sequences matching those on the initial yellow strip. Antigenic shift could be modeled by combining the sequence from another group’s yellow strips with our group’s yellow strips.

Activity 2 Causes and Consequences of an Influenza Pandemic RUBRIC

1. The 1918 influenza strain killed three times more people than were killed in action in World War 1.
2. An ordinary bird flu that had changed.
3. No one was immune because the strain was completely new and attacked a different part of the respiratory tract.
4. The genetic code was isolated from the tissue sample of a soldier killed in WW1.
5. Cells in the respiratory tract.
6. Hemagglutinin
7. Neuraminidase
8. The letters H and N stand for hemagglutinin and neuraminidase respectively. The numbers signify different combinations of antigens.
9. Researchers introduced two changes (mutations) that were found to have enabled the hemagglutinin protein to attach to human cells, making the strain lethal in the same way as the 1918 flu strain.
10. An epidemic is a higher than usual incidence of a disease in a particular geographic area. A pandemic is a widespread or worldwide epidemic.

Activity 3: The Life Cycle of the Human Immunodeficiency Virus RUBRIC

1. The CD4 receptor allows the HIV particle to recognize a host cell.
2. The fusion inhibitor drug could prevent infection by stopping the HIV envelope from fusing with the cell, and stopping HIV molecules entering the cell.
3. Reverse transcriptase converts the HIV RNA into DNA.
4. Integrase
5. The HIV DNA uses the host cell’s replication machinery to create long chains of HIV proteins.
6. During assembly, the HIV envelope fuses with the host cell membrane.
7. After it leaves the host cell, the HIV releases an enzyme called protease. This enzyme breaks up the long protein chains in the noninfectious virus. These smaller proteins then combine, forming the infectious HIV particle.