Unit 2: Lesson 4 – Vaccine History and Research

LESSON QUESTIONS

- What are the key discoveries in the history of vaccine research?
- Who are the leading scientists in the history of vaccine research?
- What are the main ethical considerations of vaccine research?

LESSON OBJECTIVES

- Describe key discoveries in the history of vaccine research.
- Identify leading scientists in the history of vaccine research.
- Analyze ethical considerations of vaccine research.

OVERVIEW

In this lesson, students explore the history of vaccine research and explore ethical considerations related to vaccine research. In the first activity, students identify leading scientists in vaccine research and create a timeline highlighting their contributions. In the second activity, students read a historical account of vaccine research to develop their understanding of science as a process of testing ideas, exploration and discovery that results in benefits for society. In the third activity, students view a video and read an account of the development of hepatitis B vaccine. This reading provides background for students to analyze ethical questions related to vaccine development.

LENGTH

Two to three 45-minute sessions

GLOSSARY TERMS

cowpox, hepatitis B, mumps, polio, rabies, smallpox, tissue culture

STANDARDS

The Next Generation Science Standards for this unit reference the NGSS "Matrix of Connections to the Nature of Science."

- **Next Generation Science Standards**
  - Scientific Investigations Use a Variety of Methods
    - Science investigations use diverse methods and do not always use the same set of procedures to obtain data.
    - New technologies advance scientific knowledge.
    - Scientific investigations use a variety of methods, tools, and techniques to revise and produce new knowledge.

- Scientific Knowledge is Open to Revision in Light of New Evidence
  - Most scientific knowledge is quite durable but is, in principle, subject to change based on new evidence and/or reinterpretation of existing evidence.
- Science is a Way of Knowing
  - Science knowledge has a history that includes the refinement of, and changes to, theories, ideas, and beliefs over time.
- Science is a Human Endeavor
  - Scientific knowledge is a result of human endeavor, imagination, and creativity.
  - Individuals and teams from many nations and cultures have contributed to science and to advances in engineering.
  - Technological advances have influenced the progress of science and science has influenced advances in technology.
- Science Addresses Questions About the Natural and Material World
  - Science and technology may raise ethical issues for which science, by itself, does not provide answers and solutions.
  - Many decisions are not made using science alone, but rely on social and cultural contexts to resolve issues.

- **Common Core State Standards**
  - RH.11-12.1 Cite specific textual evidence to support analysis of primary and secondary sources, connecting insights gained from specific details to an understanding of the text as a whole.

  - RH.11-12.2 Determine the central ideas or information of a primary or secondary source; provide an accurate summary that makes clear the relationships among the key details and ideas.

  - RH.11-12.5 Analyze in detail how a complex primary source is structured, including how key sentences, paragraphs, and larger portions of the text contribute to the whole.

  - 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.

  - 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.11-12.1.A Introduce precise, knowledgeable claim(s), establish the significance of the claim(s), distinguish the claim(s) from alternate or

opposing claims, and create an organization that logically sequences the claim(s), counterclaims, reasons, and evidence.
    - 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.

MATERIALS

- Student worksheet
- Activity worksheets
- Computer with internet access
- For Timeline of Vaccine Research (Activity 1) each student group will need:
    - Poster paper, or other large sheet of paper and/or graphics software
    - Drawing instruments (if using poster paper).

BACKGROUND FOR TEACHER

Science is an evolving process, and its greatest achievements often build on discoveries that came before them. Vaccine science provides an opportunity to showcase how scientific knowledge builds on previous work. In his book, *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases*, Dr. Paul Offit illustrates this concept as it relates to the development of the mumps vaccine in the chapter titled *Eight Doors* (Chapter 3).

Mumps Vaccine
Mumps vaccine development is discussed in the documentary film, *HILLEMAN: A Perilous Quest to Save the World's Children*. Important points include:

- Mumps vaccine is a live, attenuated viral vaccine (see Lesson 3).
- Dr. Hilleman worked to develop a mumps vaccine in his laboratory at Merck Research Laboratories.
- A suitable candidate virus to make a vaccine must meet certain conditions:
    - The strain used needs to cause illness, but not severe illness. This is so the vaccine does not have severe side effects.
    - The virus also needs to grow well enough in lab conditions to make the large quantities necessary for commercial production.
- Researchers often have to test many different isolates of a virus before they find one that is a suitable vaccine candidate.
- Dr. Hilleman took throat swabs from his infected daughter to get a sample of the mumps virus.
- The virus Dr. Hilleman isolated from his daughter's throat proved to be a suitable candidate for the mumps vaccine. The isolate was grown repeatedly in the lab to be weakened and eventually ended up being the strain of mumps virus used to make the mumps vaccine given to children today. It is called the "Jeryl Lynn" strain after his daughter.

Hepatitis B Vaccine

Hepatitis B vaccine development is discussed in the documentary film, *HILLEMAN*. Important points include:

- Hepatitis B makes much more surface protein than it needs. Excess surface protein particles will soak up antibodies from the immune system making it more difficult for the immune system to overcome the infection.
- Blood from infected individuals is a source of large quantities of the virus.
- To make hepatitis B vaccine, Dr. Hilleman built on work by other researchers:
    - Baruch Blumberg identified Australia Antigen.
    - Alfred Prince proved that Australia antigen was, in fact, hepatitis B surface protein.
    - Saul Krugman showed that antibodies to the surface protein protected children from infection with hepatitis B virus.
- Building on these findings, and realizing that hepatitis B virus was virtually impossible to grow in the lab, Dr. Hilleman decided to use blood from infected individuals as the source of the surface protein.
- To ensure the safety of the vaccine, Dr. Hilleman treated the blood with a series of three chemicals to ensure that it did not contain any other infectious agents that could harm vaccine recipients.
- This version of the hepatitis B vaccine was licensed by the Food and Drug Administration (FDA) in 1981 and was on the market until 1986. However, the emergence of the AIDS epidemic and concerns about the use of blood from infected individuals as the source material led to underuse of the vaccine.
- Because science continued to evolve, a solution soon arose replacing the need to use human blood as a source of the antigen. Specifically, Herbert Boyer and Stanley Cohen discovered the field of genetic engineering by figuring out that:
    - Genes can be inserted into circular bacterial DNA, called plasmids.
    - When the plasmid is inserted back into a bacterial or yeast cell, the gene is expressed and the protein of interest is produced.
    - To make the new version of the vaccine, the gene for hepatitis B surface protein was inserted into a plasmid added to yeast cells. As the yeast cells reproduced, they produced the hepatitis B surface protein. This protein was purified and used as the vaccine.
    - On July 23, 1986, the FDA licensed the yeast-derived recombinant hepatitis B vaccine. The vaccine is still in use today.

TEACHER NOTES

Since this lesson involves several reading sessions, you may need to assign the required reading as homework and reserve class time to complete the activities.

Mumps and hepatitis B vaccine development is discussed in the documentary film, *HILLEMAN: A Perilous Quest to Save the World's Children*. The relevant film excerpts are included in the "lesson resources" section; however you may choose to show one or both of the clips as a way to introduce the material and alter the flow of the activities during the lesson.

When students complete online research, they may find variation in the years that a scientist made a discovery. This provides a useful opportunity to explain that science is a process of discovery. It typically occurs over a period of time, sometimes years. So when people write about it, they may choose a different moment in the process than another writer. For example, Salk worked on polio vaccine development from 1942 -1955. In 1952, the vaccine was found to be effective, and the definitive clinical trial was conducted in 1954. The vaccine first became available in 1955; therefore, different publications might indicate any of these different dates.

LESSON RESOURCES

- Lesson video and animations:
  - *HILLEMAN* film segment related to the development of the mumps vaccine (3:05) (https://vimeo.com/241593651)
  - *Attenuation: How Scientists Make Live Vaccines* (https://vimeo.com/227180098)
  - *HILLEMAN* film segment related to the development of the hepatitis B vaccine (10:47) (https://vimeo.com/255783696)
    - Film excerpt includes the animations *Using Genetic Engineering to Make Vaccines* (https://vimeo.com/227180912) and *How Does Hepatitis B Combat the Immune System?* (https://vimeo.com/227180367)

- Lesson glossary

- Reading passages:
  - Chapter 3 titled "Eight Doors" from *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases,* Paul A. Offit, M.D. © 2007 HarperCollins Publishers, Inc.
  - Chapter 8 titled "Blood" from *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases,* Paul A. Offit, M.D. © 2007 HarperCollins Publishers, Inc.

- Additional resources that may be helpful:
  - History of Vaccines Timeline, The College of Physicians of Philadelphia, http://www.historyofvaccines.org/timeline?timeline_categories[]=56
  - "A Forgotten Pioneer of Vaccines", *The New York Times,* http://www.nytimes.com/2013/05/07/health/maurice-hilleman-mmr-vaccines-forgotten-hero.html
  - Vaccine History, Vaccine Education Center at Children's Hospital of Philadelphia, http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-history
  - History of Vaccines, Smithsonian National Museum of American History, http://amhistory.si.edu/polio/virusvaccine/history.htm

- The history of vaccination, National Health Service (UK), http://www.nhs.uk/conditions/vaccinations/pages/the-history-of-vaccination.aspx

ENGAGE

1. Choose a student and ask the question, "What is the worst disease you can think of?" Ask another student the same question, and then for a show of hands if the class agrees with either response.
2. Ask students to write three things they know about how diseases are controlled or prevented. If needed, ask a guiding question such as "What developments enabled scientists make vaccines for some diseases such as the flu and hepatitis?"
3. Explain to students that vaccines now control many diseases that used to cause suffering and death, and that they will learn about the history of vaccine research.

EXPLORE

1. Explain to students that their task is to research the history of vaccines and to create a timeline based on the main discoveries and the researchers who made them.
2. Propose guiding questions to students:
    a. What are the key discoveries in the history of vaccine research?
    b. Who are leading scientists in the history of vaccine research?
3. Working in small groups, students complete Timeline of Vaccine Research (Activity 1)
4. Guide students to suitable resources to research the history of vaccines (see *Resources* for suggested websites).
5. Ensure the groups' timelines include all of the researchers in the worksheet and the dates of their significant discoveries.
6. Students view the section of the *HILLEMAN* film related to the development of the mumps vaccine (see Lesson Resources section).
7. View the animation *Attenuation: How Scientists Make Live Vaccines* (see Lesson Resources section) which describes the process of making a weakened live vaccine. If needed, review the definition of attenuation.
8. Students read Chapter 3 of *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases*, titled "Eight Doors". (If time is short, you will need to assign this chapter as homework reading before the lesson.)
9. Divide the class into eight groups. (Groups do not have to be equal size. If possible, ensure groups are a mix of accelerated and challenged students.)
10. Assign each group one of the "doors" to research.

EXPLAIN

1. Students complete the On the Shoulders of Giants (Activity 2) sheet, answering each question.
2. Each group briefly presents their findings to the class.

ELABORATE

1. Students view the *HILLEMAN* video section related to hepatitis B vaccine (see Lesson Resources section).
2. Students watch the animation, *Using Genetic Engineering to Make Vaccines* (see Lesson Resources section).
3. Students read an excerpt from the chapter titled "Blood" in *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases*. (If time is short, you will need to assign this chapter as homework reading before the lesson.)
4. As they review the resources, students complete the Hepatitis B Vaccine – A Tale of Two Vaccines (Activity 3) sheet.
5. Ask some questions to ensure students have a good grasp of the science related to each of the two types of hepatitis B vaccines.
6. Lead a class discussion or a debate on the ethics surrounding each method. Use the questions from Activity 3 to guide the discussion as necessary.
7. After the class discussion, students complete a writing assignment titled: Use of blood-derived hepatitis B vaccine—methods and ethics.

EVALUATE

1. Evaluate students based on their presentations on the book chapter they researched in Activity 2. Use the Activity 2 rubric as a guide to the correct responses.
2. Assess students for Activity 3 based on their completion of the Activity 3 questions and their writing assignment.

RUBRIC – Student Worksheet

Vocabulary table

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

RUBRIC – ACTIVITY 1: Timeline of Vaccine Research

Researcher	Significant Discovery	Year
Martinus Beijerinck	Identified viruses and determined they could cause disease in plants.	1898
Baruch Blumberg	Developed the idea that disease susceptibility is genetic and discovered Australia antigen.	1967
Herbert Boyer	Developed a technique in which an enzyme is used to cut plasmid DNA and insert a gene for a protein. As a cell with the plasmid reproduces, it works as a factory to produce the protein of interest.	1973
Alexis Carrel	Showed that animal organs could be kept alive outside the body.	1912
Stanley Cohen	Developed a technique in which an enzyme is used to cut plasmid DNA and insert a gene for a protein. As a cell with the plasmid reproduces, it works as a factory to produce the protein of interest.	1973
John F. Enders	One member of a Nobel prize-winning team that famously developed cell cultures to grow animal and human cells in the lab. This work allowed scientists around the world to complete experimental procedures more quickly and efficiently.	1940s
Ernest Goodpasture	Developed a technique to grow viruses in eggs.	1930s
Maurice Hilleman	A successful vaccinologist credited with developing 9 vaccines routinely used to protect children from infectious diseases. His success built on the scientific accomplishments of those who came before him.	1940s to 1980s
Edward Jenner	Created the first vaccine by scientifically testing a theory that exposure to cowpox could protect against smallpox.	1796
Saul Krugman	Discovered that heating blood containing hepatitis B would kill the virus while preserving its structure enough to allow for the production of effective antibodies if used as a vaccine; also distinguished hepatitis A and hepatitis B.	1950s and 1960s
Louis Pasteur	Developed the first rabies vaccine proving the principle of using live, weakened viruses as a vaccine.	1885
Alfred Prince	Figured out that Australia antigen was part of hepatitis B virus.	1968
Frederick Robbins	One member of a Nobel prize-winning team that famously developed cell cultures to grow animal and human cells in the lab. This work allowed scientists around the world to complete experimental procedures more quickly and efficiently.	1940s
Jonas Salk	Developed inactivated polio vaccine.	1955
Max Theiler	Showed that human viruses could be weakened by growing in animal cells.	mid-1930s
Thomas Weller	One member of a Nobel prize-winning team that famously developed cell cultures to grow animal and human cells in the lab. This work allowed scientists around the world to complete experimental procedures more quickly and efficiently.	1940s

RUBRIC – ACTIVITY 2: On the Shoulders of Giants

Chapter Section (Door)	Main Discovery	Date & Place of Discovery	Contribution to Vaccine Research	Additional Facts
Jenner (1)	Inoculated James Phipps with cowpox pus. Even two years later, Phipps was immune to smallpox.	1796, England	Proved the principle of vaccination as a way to provide immunity.	Jenner realized that milkmaids who got cowpox did not typically get sick with smallpox. People were vaccinated by an arm-to-arm technique. Pus from cowpox was passed from the arm of one volunteer to the next.
Pasteur (2)	Developed the first rabies vaccine.	1885, Paris	Proved principle of using live, weakened virus as a vaccine.	Used spinal cords of infected rabbits to create the vaccine. Spinal cords contain myelin protein, which can cause autoimmune disease.
Beijerinck (3)	Identified what viruses were, where they reproduced, and how they caused disease.	1898, Holland	Showed that viruses are smaller than bacteria, and could only reproduce in the living protoplasm of a cell.	Worked on plant viruses, and discovered the tobacco mosaic virus.
Carrel (4)	Showed that animal organs could be kept alive outside the body.	1912, New York	Kept tissue cultured from a chicken embryo heart alive by feeding it nutrient broth every two days.	By feeding the culture, the chicken heart tissue culture was kept alive for 20 years.
Goodpasture (5)	Grew viruses in eggs.	1930s, Nashville	Showed that virus could be easily grown.	Made discovery while studying fowlpox. Injected the virus into the membrane surrounding the chick embryo.
Theiler (6)	Showed that human viruses could be weakened by growing in animal cells.	mid-1930s, New York	Demonstrated the basic method of weakening a human virus.	Passed yellow fever from humans into mouse embryos and then into chicken embryos.

Enders, Weller, and Robbins (7)	Developed cell cultures to grow animal and human cells in the lab.	1940s, Boston	Used single layers of cells grown in a flask, allowing viruses to be grown in various types of tissues.	This technique was also used to grow poliovirus for the polio vaccine.
Salk (8)	Developed polio vaccine.	1954, Pittsburgh	Showed that mass vaccination could alleviate widespread illness and suffering.	Doctors injected four hundred thousand children with Salk's polio vaccine and two hundred thousand with a placebo. This remains the largest single test of a medical product.

RUBRIC - ACTIVITY 3: Hepatitis B Vaccine – A Tale of Two Vaccines

Question	**Hepatitis B vaccine derived from blood**	**Hepatitis B vaccine made using genetic engineering**
What was the problem Dr. Hilleman faced?	Source of antigen	Perception of safety in existing (blood-derived) vaccine
What discoveries preceded the creation of the vaccine?	Baruch Blumberg identified Australia Antigen. Alfred Prince proved that Australia antigen was, in fact, hepatitis B surface protein. Saul Krugman showed that antibodies to the surface protein protected children from infection with hepatitis B virus.	Herbert Boyer and Stanley Cohen discovered the field of genetic engineering by figuring out that: • Genes can be inserted into circular bacterial DNA, called plasmids. • When the plasmid is inserted back into the bacteria or yeast cell, the gene is expressed and the protein of interest is produced. To make the new version of the vaccine, hepatitis B surface protein was inserted into a plasmid and produced by yeast cells.
How did Dr. Hilleman discover a solution to the problem?	Killed potential pathogens by chemically treating blood plasma.	Employed genetic engineering to make recombinant version of vaccine.
What was the reaction of society to the new discovery?	Concerns about safety of vaccine.	Vaccine better accepted than previous version.