Unit 2, Lesson 4 – History of Vaccine 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 consider ethical considerations of 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. Through reading, students develop their understanding of science as a process of testing ideas, exploration and discovery, resulting in benefits and outcomes. For 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.

  o 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:**
  - Activity worksheets
  - Computer with Internet access
  - Relevant excerpts from *Vaccinated: One Man’s Quest to Defeat the World’s Deadliest Diseases*

**BACKGROUND FOR TEACHER**

Science is an evolving process, and its greatest discoveries and achievements often rely on the work of scientists who 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*. 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 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*. The 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 was a source of large quantities of the virus.
- To make hepatitis B vaccine, 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 the hepatitis B virus.
- Building on these findings, and realizing that hepatitis B virus was virtually impossible to grow in the lab, 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, with the emergence of the AIDS epidemic, 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.
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 class activities.
- Hepatitis B vaccine development is discussed in the documentary film, *Hilleman*. Students can watch the relevant section and take notes as a way of introducing the material for this lesson.

Resources

The following websites may help students to complete the lesson.

- Vaccine Education Center at The Children’s Hospital of Philadelphia: [http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-history](http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-history)
- Smithsonian National Museum of American History: [http://amhistory.si.edu/polio/virusvaccine/history.htm](http://amhistory.si.edu/polio/virusvaccine/history.htm)

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 Activity 1 in their worksheets.
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.
7. View the animation Attenuation: How Scientists Make Live Vaccines https://vimeo.com/198062653 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 Activity 2 worksheet, 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.
3. Students read pages 115 to 127 and 136 to 140 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 Worksheet.
5. Ask some check 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 suggested essay questions 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 On the Shoulders of Giants rubric as a guide to the correct responses on the worksheet.

2. Assess students for Activity 3 based on their completion of the A Tale of Two Vaccines Worksheet and their writing assignment.
Activity 2: On the Shoulders of Giants RUBRIC

The mumps vaccine was built on the science of others

In order for Dr. Hilleman to make the mumps vaccine, other discoveries had to precede his work. The *Eight Doors* chapter outlines the important discoveries that enabled development of the mumps vaccine.

<table>
<thead>
<tr>
<th>Chapter Section (Door)</th>
<th>Main Discovery</th>
<th>Date &amp; Place of Discovery</th>
<th>Contribution to Vaccine Research</th>
<th>Additional Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jenner (1)</td>
<td>Inoculated James Phipps with cowpox pus. Even two years later, Phipps was immune to smallpox.</td>
<td>1769, England</td>
<td>Proved the principle of vaccination as a way to provide immunity.</td>
<td>In 1768, 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.</td>
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<td>Pasteur (2)</td>
<td>Developed the first rabies vaccine</td>
<td>1885, Paris</td>
<td>Proved principle of using live, weakened virus as a vaccine</td>
<td>Used spinal cords of infected rabbits to create the vaccine. Spinal cords contain myelin protein, which can cause autoimmune disease.</td>
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<td>Beijerinck (3)</td>
<td>Identified what viruses were, where they reproduced, and how they caused disease</td>
<td>1898, Holland</td>
<td>Showed that viruses are smaller than bacteria, and could only reproduce in the living protoplasm of a cell.</td>
<td>Worked on plant viruses, and discovered the tobacco mosaic virus</td>
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<td>Carrel (4)</td>
<td>Showed that animal organs could be kept alive outside the body</td>
<td>1912, New York</td>
<td>Kept tissue cultured from a chicken embryo heart alive by feeding it nutrient broth every two days</td>
<td>The chicken heart tissue culture was kept alive for 20 years.</td>
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<td>Goodpasture (5)</td>
<td>Grew viruses in eggs</td>
<td>1930s, Nashville</td>
<td>Showed that virus could be easily grown</td>
<td>Made discovery while studying fowlpox. Injected the virus into the membrane surrounding the chick embryo.</td>
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<td>Theiler (6)</td>
<td>Showed that human viruses could be weakened by growing in animal cells</td>
<td>mid-1930s, New York</td>
<td>Demonstrated the basic method of weakening a human virus</td>
<td>Passed yellow fever from humans into mouse embryos and then into chicken embryos.</td>
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<td>Enders, Weller, and Robbins (7)</td>
<td>Developed cell cultures to grow animal and human</td>
<td>1940s, Boston</td>
<td>Used single layers of cells grown in a flask, allowing</td>
<td>This technique was also used to grow poliovirus for the polio vaccine.</td>
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<td></td>
<td>Viruses to be grown in various types of tissues.</td>
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<td>Salk (8)</td>
<td>Developed polio vaccine</td>
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<td>1954, Pittsburgh</td>
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<td>Showed that mass vaccination could alleviate widespread illness and suffering.</td>
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<td>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.</td>
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**Activity 3: Hepatitis B Vaccine – A Tale of Two Vaccines RUBRIC**

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<tr>
<th>Question</th>
<th>Hepatitis B vaccine derived from blood</th>
<th>Hepatitis B vaccine made using genetic engineering</th>
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<tr>
<td>What was the problem that Hilleman faced?</td>
<td>Source of antigen</td>
<td>Perception of safety in existing (blood-derived) vaccine</td>
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<td>What discoveries preceded the creation of the vaccine?</td>
<td>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.</td>
<td>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.</td>
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<tr>
<td>How did Hilleman discover a solution to the problem?</td>
<td>Killed potential pathogens by chemically treating blood plasma</td>
<td>Employing genetic engineering to make recombinant version of vaccine.</td>
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<tr>
<td>What was the reaction of society to the new discovery?</td>
<td>Concerns about safety of vaccine</td>
<td>Vaccine better accepted than previous version.</td>
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