

Unit 2: Lesson 4 – Vaccine History and Research

LESSON QUESTIONS

- What are some key discoveries in the history of vaccine research?
- Who are some 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 activity provides background for students to analyze ethical questions related to vaccine development.

LENGTH

Two to four 45-minute sessions

GLOSSARY TERMS

COVID-19, cowpox, eradication, hepatitis B, human papillomavirus (HPV), lipid nanoparticle, meningitis, mRNA, mumps, polio, rabies, smallpox, tissue culture, valency, variolation, virulence

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
<https://vaccinemakers.org/sites/default/files/lessons/HS.student%20worksheet.unit2.lesson4.Final.pdf>
- Computer with internet access
- For Activity 1, each group will need:
 - Timeline of Vaccine Research worksheet
<https://vaccinemakers.org/sites/default/files/lessons/HS.activity1-Timeline%20of%20Vaccine%20Research.unit2.lesson4.FINAL.pdf>
 - Poster paper, or other large sheet of paper and/or graphics software
 - Drawing instruments (if using poster paper).
- For Activity 2, each group will need:
 - On the Shoulders of Giants worksheet
<https://vaccinemakers.org/sites/default/files/lessons/HS.activity2-On%20the%20Shoulders%20of%20Giants.unit2.lesson4.FINAL.pdf>
- For Activity 3, each group will need:
 - Hep B-a Tale of 2 Vaccines worksheet
<https://vaccinemakers.org/sites/default/files/lessons/HS.activity3-Hep%20B-a%20Tale%20of%202%20Vaccines.unit2.lesson4.FINAL.pdf>

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 live, attenuated viral 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 tested many isolates that were too virulent. Then, when his own daughter happened to contract mumps, he took throat swabs from her to get another 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.
- Dr. Hilleman used his mumps, measles, and rubella vaccines to create the first viral combination vaccine, although this version's rubella vaccine was grown in animal cells and was prone to some negative side effects.
- Dr. Hilleman later worked with Dr. Stanley Plotkin to combine his safer rubella vaccine with the "Jeryl Lynn" mumps vaccine and Dr. Hilleman's measles vaccine to create the MMR combination vaccine that we use today.

Hepatitis B Vaccine

Hepatitis B vaccine development is discussed in the documentary film, *HILLEMAN: A Perilous Quest to Save the World's Children*. 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 and its surface protein.
- To make hepatitis B vaccine, Dr. Hilleman built on work by other researchers:
 - Baruch Blumberg identified a protein in the blood of some people that he called 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 of surface protein led to underuse of the vaccine.
- Because science continues 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.

COVID-19 vaccines

Examples of COVID-19 vaccine technology is explained in the VMP animations *How COVID-19 Viral Vector Vaccines Work* and *How COVID-19 mRNA Vaccines Work*.

Important points include:

- COVID-19 vaccines are primarily mRNA or protein subunit vaccines (See Lesson 3).
- Both of these vaccine types are designed to deliver information about the COVID-19 surface proteins to dendritic cells, immune cells that consume and present antigens to other immune cells that start the immune response.
- The fastest vaccine development in history, the first COVID-19 vaccines were developed within 12 months. This was accomplished due to multiple factors, including:
 - Vaccine developers built on decades of prior research into mRNA and viral vector delivery methods as well as the prior SARS-CoV and MERS-CoV epidemics.
 - The USFDA employed a special process called an Emergency Use Authorization (EUA) that allows for accelerated vaccine production during public health emergencies if there is a viable vaccine candidate. COVID-19 vaccines were developed under the federal program Operation Warp Speed (OWS) that prioritized having all research focus on the development of a vaccine and provided government financial support in order to remove the financial risk of vaccine development.
 - Scientists and regulators postponed work on vaccine candidates for other pathogens and maintained a careful balance of speed and safety to ensure that the process was expedited without cutting corners.

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 excerpts from the documentary film, *HILLEMAN: A Perilous Quest to Save the World's Children*. COVID-19 vaccine technology is covered in the VMP animations, *How COVID-19 Viral Vector Vaccines Work* and *How COVID-19 mRNA Vaccines Work*. The relevant materials are included in the “Lesson Resources” however, you may choose to show any of the videos 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 the dates of any of these different milestones.

LESSON RESOURCES

- Lesson videos and animations:
 - Video - *HILLEMAN* film segment related to the development of the mumps vaccine (3:05), VMP, <https://vimeo.com/241593651>
 - Animation - *Attenuation: How Scientists Make Live Vaccines*, VMP, <https://vimeo.com/227180098>
 - Animation - *How COVID-19 Viral Vector Vaccines Work*, VMP, <https://vimeo.com/618385339>
 - Animation - *How COVID-19 mRNA Vaccines Work*, VMP, <https://vimeo.com/579667076>
 - Video - *HILLEMAN* film segment related to the development of the hepatitis B vaccine (10:47), VMP, <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>)
 - Video - *Stanley Plotkin: Pioneering the use of fetal cells to make rubella vaccine* (19:57), VMP, <https://vimeo.com/339593360>
- Lesson glossary
https://vaccinemakers.org/sites/default/files/resources/HS.student%20glossary.unit2_lesson4.Final_.pdf
- Lesson readings and resources:
 - PDF - 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.

https://vaccinemakers.org/sites/default/files/resources/HS.reading%20passage-Eight%20Doors.unit2_lesson4.FINAL.pdf

- PDF - 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.
https://vaccinemakers.org/sites/default/files/resources/HS.reading%20passage-Blood.unit2_lesson4.FINAL.pdf
- Webpage - Vaccine History, VEC, <https://www.chop.edu/vaccine-education-center/science-history/vaccine-history>
- Webpage - History of Vaccines Timeline, The College of Physicians of Philadelphia, <https://historyofvaccines.org/history/vaccine-timeline/timeline>
- Webpage - Vaccines and Immunizations: History, Timeline, and Invention, Encyclopedia Britannica, <https://www.britannica.com/explore/vaccines-immunization-history-timeline>
- Website - Vax Pack Hero, VEC, <https://www.vaxpackhero.com/vaccine-heroes/>
- Article - “mRNA Technology: Four Decades in the Making,” Unbiased Science, <https://theunbiasedscipod.substack.com/p/mrna-technology-four-decades-in-the>
- Webpage - Decades in the Making: mRNA COVID-19 Vaccines, NIAID, <https://www.niaid.nih.gov/diseases-conditions/decades-making-mrna-covid-19-vaccines>
- Webpage - Vaccine History: Vaccine Availability Timeline, VEC, <https://www.chop.edu/vaccine-education-center/science-history/vaccine-history/vaccine-availability-timeline>
- Article - The Long History of mRNA Vaccines, Johns Hopkins Bloomberg School of Public Health, <https://publichealth.jhu.edu/2021/the-long-history-of-mrna-vaccines>
- Webpage - World-changing mRNA vaccines, Penn Medicine, <https://www.pennmedicine.org/about/pioneering-the-future-of-medicine/mrna>
- PDF – History of HPV Vaccination, St. Jude Children’s Research Hospital, <https://sjr-redesign.stjude.org/content/dam/research-redesign/centers-initiatives/hpv-cancer-prevention-program/hpv-advocacy-campaign/history-hpv-vaccination.pdf>
- Video – European Inventor Award Ian Frazer, Jain Zhou, European Patent Office, <https://www.epo.org/en/news-events/european-inventor-award/meet-the-finalists/ian-frazer-jian-zhou>
- Webpage – The HPV Vaccine, National Cancer Institute Center for Cancer Research, <https://ccr.cancer.gov/news/landmarks/article/hpv-vaccine>
- Article – Lasker Prize Goes to HPV Vaccine Developers, History of Vaccines, <https://historyofvaccines.org/blog/lasker-prizer-goes-to-hpv-vaccine-developers>

- Webpage – Harald zur Hausen Facts, The Nobel Prize, <https://www.nobelprize.org/prizes/medicine/2008/hausen/facts/>
- Article – Katalin Karikó and Drew Weissman: 2023 Nobel Prize in Medicine, University of Pennsylvania Almanac, <https://almanac.upenn.edu/articles/katalin-kariko-and-drew-weissman-2023-nobel-prize-in-medicine>
- Webpage – Paul Berg Facts, The Nobel Prize, <https://www.nobelprize.org/prizes/chemistry/1980/berg/facts/>
- Webpage – Stanley Plotkin, Hilleman Film, <https://hillemanfilm.com/resources/other-scientist-stories/stanley-plotkin>
- Webpage - Nobel Prize in Physiology or Medicine 1912, <https://www.nobelprize.org/prizes/medicine/1912/summary/>
- Webpage – Reassessment of Carrel’s Immortal Tissue Culture Experiments, Arizona State University Center for Biology and Society, <https://embryo.asu.edu/pages/reassessment-carrels-immortal-tissue-culture-experiments>
- Webpage – Hayflick Limit, Science Direct, <https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/hayflick-limit>
- Article – That Record-breaking Sprint to Create a COVID-19 Vaccine, NIH Intramural Research Program, <https://irp.nih.gov/catalyst/29/5/that-record-breaking-sprint-to-create-a-covid-19-vaccine>
- Additional resources that may be helpful:
 - Article - “A Forgotten Pioneer of Vaccines,” *The New York Times*, https://www.nytimes.com/2013/05/07/health/maurice-hilleman-mmr-vaccines-forgotten-hero.html?unlocked_article_code=1.nE8.ANvU.TUoFnmNk719-&smid=url-share
 - Webpage - A Brief History of Vaccines, WHO, <https://www.who.int/news-room/spotlight/history-of-vaccination/a-brief-history-of-vaccination>
 - Article - A Closer Look – Beyond Vaccines: Promise and Progress in mRNA Technology, Hilleman Film, <https://hillemanfilm.com/news/closer-look-beyond-vaccines-promise-and-progress-mrna-technology>
 - Animation - *Pennsylvania: At the forefront in the prevention of infectious diseases*, VMP, <https://vimeo.com/931151654>
 - Animation Expedition #7 - Genetic Engineering and Vaccines, VMP, <https://vaccinemakers.org/news-events/animation-expedition-7-genetic-engineering-and-vaccines>
 - Article - Animation Expedition #8 – Viral Attenuation: One Way of Making Vaccines, VMP, <https://vaccinemakers.org/news-events/animation-expedition-8-viral-attenuation-one-way-making-vaccines>
 - Article - Spotlight on: A Tour of Penn’s Institute for RNA Innovation, VMP, <https://vaccinemakers.org/news-events/spotlight-tour-penns-institute-rna-innovation>

- Video - How are Vaccines Tested Before They Can Be Given to Kids?, The Children's Hospital of Philadelphia,
<https://www.youtube.com/watch?v=Z2OWPIu7CqI&list=PLUv9oht3hC6TTY-k6FbWQDWS-aR-KGRGZ&index=5&t=9s>
- Webpage - Global Immunization: Worldwide Disease Incidence, VEC,
<https://www.chop.edu/vaccine-education-center/science-history/global-immunization/diseases-and-vaccines-world-view>
- Video - Marion Gruber: Preparedness Is Prevention, VMP,
<https://vimeo.com/835999515>

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 to make vaccines for some diseases such as influenza and polio?"
3. Explain to students that when vaccines were introduced for a disease, the instance of the disease became greatly diminished, and that in this lesson they will learn about the history of vaccine research and when new vaccines were introduced.
4. Students view these lesson videos listed in the Lesson Resources:
 - The Animation *Attenuation: How Scientists Make Live Vaccines* which describes the process of making a weakened live vaccine.
 - The section of *HILLEMANN* related to the development of the mumps vaccine.
 - The two animations about how COVID-19 vaccines work, which describe how these vaccines work without using whole viruses.

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 some key discoveries in the history of vaccine research?
 - b. Who are some leading scientists in the history of vaccine research?
3. 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.)
4. Guide students to suitable resources to research the history of vaccines and vaccine scientists in the Lesson Resources.
5. Working in small groups, students complete Timeline of Vaccine Research activity (Activity 1).
6. Ensure the groups' timelines include all the researchers in the worksheet and the dates of their significant discoveries.

EXPLAIN

1. Discuss as a class how past achievements provide the structure for future discoveries.
2. Divide the class into groups and assign a researcher (or multiple researchers) to each group from the list in Activity 2. (If possible, ensure groups are a mix of accelerated and challenged students.)
3. Students complete the On the Shoulders of Giants (Activity 2) sheet, answering each question for their researcher.
4. 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 research 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.

EXTENSION 1 (Optional)

1. As a class, discuss additional examples of vaccines that have been improved and why. Reference the table on page 11 for examples of modern vaccine improvements.

Disease	Vaccine improvements
Anthrax	Dose reduction. Modern anthrax vaccines can be effective in 2 doses rather than 3, providing faster protection.
COVID-19	Keeping up with changes. The COVID-19 virus changes quickly and, thanks to mRNA technology that allows for rapid adjustments to existing vaccine formulas, modern COVID-19 vaccines have been updated to protect against the newest variants.
Dengue	Safety and access. Modern dengue vaccines can be given to a broader population regardless of previous infection, unlike the prior vaccine that could cause severe infection if the recipient had not already been exposed to dengue.
HPV	Multivalent cancer protection. Modern HPV vaccines are 9-valent, meaning they protect against 9 types of HPV. These include the seven that pose the highest risk for cancer as well as the two types that most often cause genital warts. Previous HPV vaccines protected against 4 types. Although the highest-risk types are now protected against by the vaccine, work continues to tackle the remaining types of HPV in future vaccines.
Meningococcal	Multivalent protection. Modern meningococcal vaccines can protect against 5 different strains of meningococcal disease. Previous meningococcal vaccines were tetravalent, meaning they only protected against 4 strains.
Measles, Mumps, Rubella, (Varicella)	Combined protection. Unlike a multivalent vaccine that contains different strains of the same pathogen, combination vaccines like the measles, mumps & rubella vaccine (MMR) protect against multiple different types of disease. Today, an MMRV vaccine is available that also adds protection against varicella (chickenpox).
Pneumococcal	Multivalent protection. Modern pneumococcal vaccines can protect against more than 20 different types of pneumococcal disease. The first pneumococcal vaccine was tetravalent, meaning it only protected against 4 types.
Rotavirus	Safety. Modern rotavirus vaccines use more advanced, safer and stable processes, eliminating a known safety issue of the prior vaccine.
Rubella	Safety and effectiveness. The original rubella vaccine was grown in animal cells and limited by the risk of side effects and relatively low immune response. The modern rubella vaccine is grown in human diploid cells, providing a safe, sterile environment that ensures no contamination from other viruses and a cell culture that the virus naturally performs well in to make attenuation easier and improve immune response. Another benefit is that cryo-freezing allows the same cell line to be used almost indefinitely for future vaccine production without the need to take new tissue samples.

EXTENSION 2 (Optional)

1. Students watch the short film, *Stanley Plotkin: Pioneering the use of fetal cells to make rubella vaccine*.
2. As in Activity 3, discuss or debate methods and ethics of the rubella vaccine.
3. If time allows, instruct students to complete a writing assignment titled: Use of fetal cell-derived rubella vaccine—methods and ethics.

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 Contribution	Year
Martinus Beijerinck	Identified viruses and determined they could cause disease in plants.	1898
Paul Berg	Discovered viral vectors by combining DNA from a bacterium and a virus. This discovery opened the door to a renaissance of new vaccine development including vaccines for Hepatitis B, COVID-19, Influenza, HPV, and Ebola.	1972
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
Kizzmekia Corbett and Barney Graham	Developed the first vaccine for COVID-19 using mRNA technology.	2020
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

Researcher	Significant Contribution	Year
Ian Frazer and Jian Zhou	Discovered virus-like particles (VLPs) that would later be used in some recombinant vaccines, including the HPV vaccine.	1990
Ernest Goodpasture	Developed a technique to grow viruses in eggs.	1930s
Harald zur Hausen	Demonstrated that human papillomaviruses (HPV) cause most cervical cancer.	1980s
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
Katalin Karikó and Drew Weissman	Modified mRNA nucleosides to prevent its recognition by the immune system, solving the problem of inflammation caused by mRNA and allowing the technology to be used in vaccines.	2005
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
Douglas Lowy and John Schiller	Developed the first vaccine for HPV using improved VLP (virus-like particle) technology.	2006
Louis Pasteur	Developed the first rabies vaccine proving the principle of using live, weakened viruses as a vaccine.	1885
Stanley Plotkin	One member of a team that developed the first rubella vaccine grown in human fetal diploid cells. The use of human diploid cells as a medium ensured a sterile environment for the virus to grow, made cold-adapted attenuation more effective, produced a better immune response with fewer side effects, and ensured a nearly endless supply for future vaccine production and scaling without needing to harvest more tissue.	1964
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

Researcher	Significant Contribution	Year
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

Scientist	Main Discovery	Date & Place of Discovery	Contribution to Vaccine Research	Additional Facts
Jenner	Inoculated James Phipps with cowpox pus. Even two years later, Phipps was immune to smallpox.	1796, Berkeley, 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	Developed the first rabies vaccine.	1885, Paris, France	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	Identified what viruses were, where they reproduced, and how they caused disease.	1898, Delft, 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	Showed that animal cells could be kept alive outside the body.	1912, New York, New York	Kept tissue cultured from a chicken embryo heart alive by feeding it nutrient broth made of chicken embryo extract. Although it's true that animal cells can be kept alive outside the body, Carrel's assertion that he kept "a chicken	Carrel's theory of cellular immortality was later disproven by Leonard Hayflick, but his work on sewing blood vessels together and cell preservation laid the groundwork for modern organ transplants and cold preservation.

Scientist	Main Discovery	Date & Place of Discovery	Contribution to Vaccine Research	Additional Facts
Carrel, cont.			heart” alive for twenty years is suspect. It is now believed that rather than perpetually maintaining the original cells, Carrel unknowingly replaced them with new cells included in the broth.	
Hayflick & Moorhead	Showed that cells can only divide a finite number of times, called the Hayflick Limit.	1961, Philadelphia, Pennsylvania	The Hayflick Limit is used along with cryo-freezing to maintain tissue cell lines used in the production of vaccines, like the rubella vaccine.	Illustrates a process known today as cellular senescence. Hayflick’s lab cultivated the WI-38 cell line, named after the Wistar Institute, for use in vaccine research.
Goodpasture	Grew viruses in eggs.	1930s, Nashville, Tennessee	Showed that viruses could be easily grown.	Made discovery while studying fowlpox. Injected the virus into the membrane surrounding the chick embryo.
Theiler	Showed that human viruses could be weakened by growing in animal cells.	mid-1930s, New York, 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	Developed cell cultures to grow animal and human cells in the lab.	1940s, Boston, Massachusetts	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, which allowed development of the polio vaccine to accelerate.
Salk	Developed inactivated polio vaccine.	1954, Pittsburgh, Pennsylvania	Showed that mass vaccination could alleviate widespread illness and suffering.	Doctors injected four hundred thousand children with Salk’s inactivated polio vaccine and two hundred thousand with a placebo. This remains the largest single test of a medical product.
Karikó and Weissman	Modified mRNA to evade the body’s immune response.	2005, Philadelphia, Pennsylvania	Solved the problem of mRNA being destroyed by inflammatory response before it could cause target protein expression in cells.	This discovery, along with using lipid nanoparticles as a delivery system, was instrumental to the development of COVID-19 vaccines.

Scientist	Main Discovery	Date & Place of Discovery	Contribution to Vaccine Research	Additional Facts
zur Hausen	Demonstrated that human papilloma-viruses (HPV) cause most cervical cancer.	1983-1984, Heidelberg, Germany	Brought critical awareness to HPV and set the foundation for HPV vaccines.	Modern HPV vaccines are highly effective, and countries that have implemented high HPV vaccination and testing, Scotland and Australia, are already approaching the elimination of cervical cancer.
Frazer and Zhou	Created the first non-infectious VLPs (virus-like particles) that teach the immune system to fight HPV.	1991, Queensland, Australia	VLPs are used in other recombinant vaccines.	This discovery was a proof-of-concept and a major step forward, but the actual particle created was assembled from a non-ideal strain and did not produce the necessary immune response.
Lowy and Schiller	Building on the work of Drs. Frazer & Zhao, used an HPV strain that, thanks to a single different amino acid, was able to correctly assemble LVPs.	2006, Bethesda, Maryland	Created the first vaccine for human papillomavirus.	The first HPV vaccine protected against two cancer-causing strains and two wart-causing strains.
Berg	Combined bacterial and viral DNA in the first example of a viral vector.	1972, Stanford, California	Provided the foundation for modern viral vector and recombinant vaccines.	Recombinant vaccine technology later allowed Dr. Maurice Hilleman to pivot away from a blood plasma-based Hepatitis B vaccine to a recombinant Hepatitis B vaccine that was better received by the public.

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 risks 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 without risk from virus.
What was the reaction of society to the new discovery?	Concerns about safety of vaccine.	Better acceptance of the vaccine.