



THE NATIONAL
WWII MUSEUM

“Thanks to Penicillin...He Will Come Home!”
The Challenge of Mass Production

A Lesson Plan from
The Education Department

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Thanks to Penicillin... He Will Come Home! The Challenge of Mass Production

World War II saw major advances in medical technology including the mass production of penicillin. On March 14, 1942, U.S. made-penicillin was used to successfully treat the first patient for septicemia, or blood poisoning. While that one treatment exhausted half of the available supply of penicillin in the entire U.S., the need for better techniques for rapidly producing penicillin on a large scale was necessary to treat soldiers fighting abroad. Scientists working around the clock manufactured 2.3 million doses of penicillin in preparation for the D-Day landings on June 6, 1944. Explore with your students the important role of antibiotics on human history and the collaborative effort to mass produce penicillin.

OBJECTIVES: Students will analyze historic images and interpret the meaning of print materials. After reading text, students will think critically about the challenges of mass production and recognize the role of collaboration in scientific undertakings. Students will analyze the speed at which bacteria reproduce and explore exponential growth patterns. By identifying the function of antibiotics on the structure and function of bacterial cells, students will recognize the impact of antibiotics on human health during the 20th century.

GRADE LEVEL: 7-12 with enrichment activities for advanced students

STANDARDS: NGSS HS-PS1-b, 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.

NGSS MS-LS1-c, Develop and use models to support explanations about the structure and function relationships in cells and specific parts of the cell.

CCSS.Math.Content.7.NS.A.3 – Solve real-world and mathematical problems involving the four operations with rational numbers.

CCSS.ELA-Literacy.RST Standard 2 - Determine the central ideas or conclusions of a text; provide an accurate summary of the text distinct from prior knowledge or opinions.

CCSS.ELA-Literacy.RH Standard 7 - Integrate visual information (e.g., in charts, graphs, photographs, videos, or maps) with other information in print and digital texts.

NCHS U.S. History Content Standard 3C (9-12) – Evaluate the impact [of World War II] on science, medicine, and technology, especially in nuclear physics, weaponry, synthetic fibers, and television.

TIME REQUIREMENT: One class period plus additional time for extension activities.

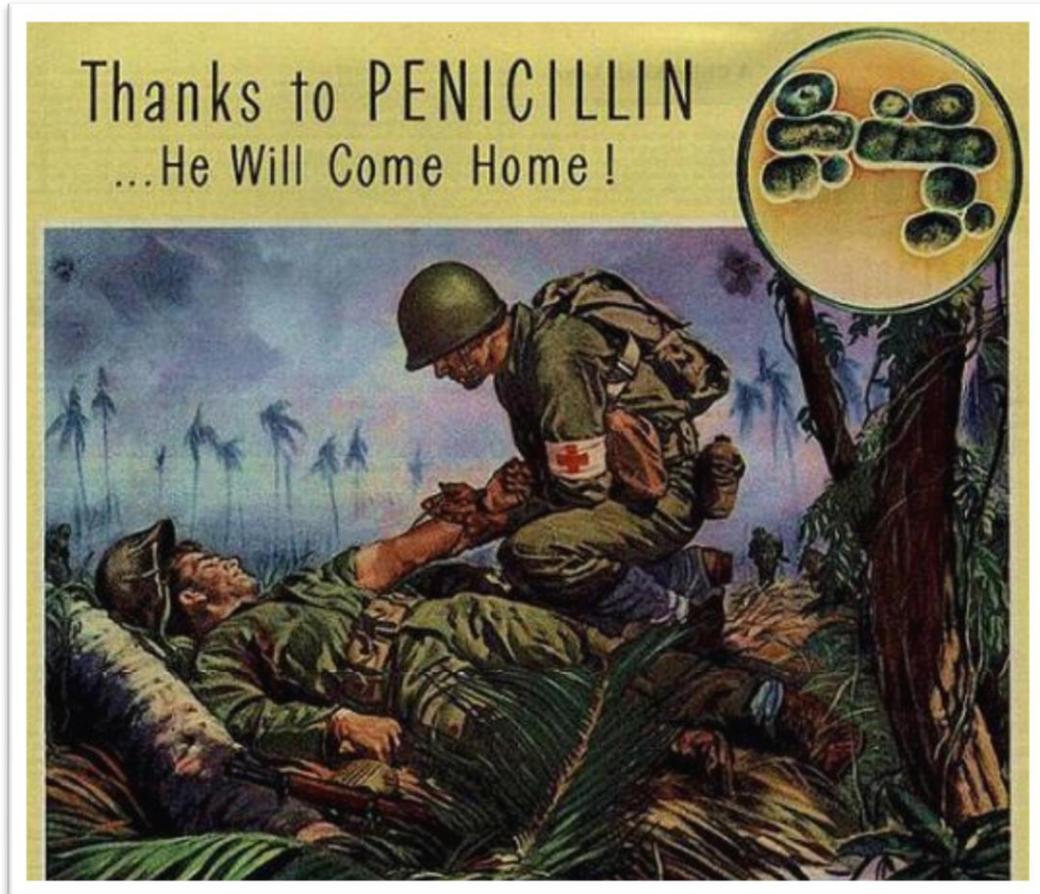
MATERIALS: Copies (paper or digital access) of Thanks to Penicillin: He Will Come Home, Fact Sheet: The Challenge of Mass Production, and the Student Activity Sheet.

Calculators

PRIOR KNOWLEDGE: This lesson fits nicely with any microbiology unit. Prior student knowledge about bacterial cell structure and reproduction is recommended. You may follow this lesson with more specific instruction on the variety of antibiotics available today, how antibiotics function to destroy bacteria and inhibit growth, antibiotic resistance, the differences between Gram-positive and Gram-negative bacteria species, and the uses of bacteria in food production and industry. Mathematics teachers might modify this lesson to simply explore exponential growth.

INTRODUCTION:

Show students the top portion of the advertisement, “Thanks to Penicillin...He Will Come Home!” Display on a video projector, overhead projector, or make copies for students to share. Use some or all of the questions to lead an introductory discussion about the history of the development of antibiotics and the effectiveness in treating bacterial infections. Hints are given after some questions in parentheses to help move the discussion forward.



Leading Discussion Questions:

- Take a look at this image. What is happening in the picture? (Hints for students: notice the smoke in the background; one man is laying down with the other holding his arm)
- Who are these men? (Notice their clothing and equipment, the cross on the man's arm)
- What time period is this? (Observe the style of uniform, the message at the top of the picture)
- Where is this? (Palm trees, tropical plants)
- Read the title, “Thanks to Penicillin...He Will Come Home!” Who is the intended audience? (This was printed in Life magazine in August 1944.)
- Have you heard of Penicillin before? If so, how is it used? (Have you ever taken amoxicillin or “the pink stuff?” Why did you take it?)
- What do you see within the circle in the top right-hand corner? (This is a picture taken from a microscope.)
- What are these cells doing? (Look carefully at the cell on the bottom left-hand side, it is pinching inward.)
- How does penicillin affect these cells? (Now is a good time to discuss the bacterial cell wall; penicillin stops the growth of the cell wall causing lysis.)

DIRECTIONS:

1. Reveal the entire advertisement. Have students read the text to meet the Common Core ELA Literacy Standard in History/Social Studies. Display on a video projector, overhead projector, or make copies for students to share.
2. Check for student understanding of the reading through formative assessment. Have students complete a one sentence summary of the reading, working individually. You might focus the students by asking them to describe the importance of penicillin to our victory in WWII. You may choose to collect student responses and/or have students share their answers with the class.
3. Distribute the Fact Sheet for students to read, meeting the Common Core ELA Literacy Standard in Science and Technical Subjects. You may choose for your students to read individually, as a small group, or as a class. Stop periodically to answer questions and clarify any terms from the reading.
4. Give the Student Activity Sheet to assess understanding of the reading. A calculator is recommended to complete the binary fission portion of the activity sheet.

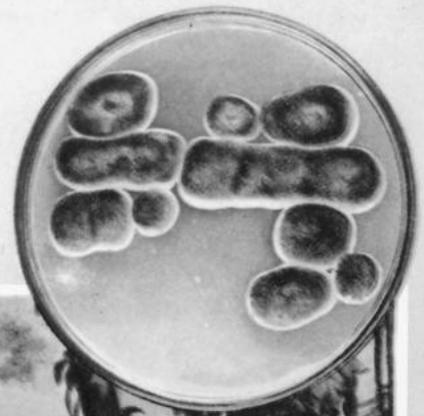
ASSESSMENT: Components for assessment include the student activity sheet, classroom discussion, and formative assessment.

ENRICHMENT: Graph exponential population growth on a linear or logarithmic scale (or both). Express population growth as an equation.

Discuss the mechanisms for and consequences of antibiotic resistance. Include the role of natural selection.

Research how drug manufacturing has changed with only one company making a specific drug. Students may explore the consequences, including drug shortages.

Thanks to PENICILLIN ...He Will Come Home!



FROM ORDINARY MOLD—

*the Greatest Healing
Agent of this War!*

On the gaudy, green-and-yellow mold above, called *Penicillium notatum* in the laboratory, grows the miraculous substance first discovered by Professor Alexander Fleming in 1928. Named penicillin by its discoverer, it is the most potent weapon ever developed against many of the deadliest infections known to man. Because research on molds was already a part of Schenley enterprise, Schenley Laboratories were well able to meet the problem of large-scale production of penicillin, when the great need for it arose.

When the thunderous battles of this war have subsided to pages of silent print in a history book, the greatest news event of World War II may well be the discovery and development — *not* of some vicious secret weapon that *destroys* — but of a weapon that *saves* lives. That weapon, of course, is penicillin.

Every day, penicillin is performing some unbelievable act of healing on some far battlefield. Thousands of men will return home who otherwise would not have had a chance. Better still, more and more of this precious drug is now available for civilian use... to save the lives of patients of every age.

A year ago, production of penicillin was difficult, costly. Today, due to specially-devised methods of mass-production, in use by Schenley Laboratories, Inc. and the 20 other firms designated by the government to make penicillin, it is available in ever-increasing quantity, at progressively lower cost.

Listen to "THE DOCTOR FIGHTS" starring RAYMOND MASSEY. Tuesday evenings,
C. B. S. See your paper for time and station.

SCHENLEY LABORATORIES, INC.

Lawrenceburg, Indiana

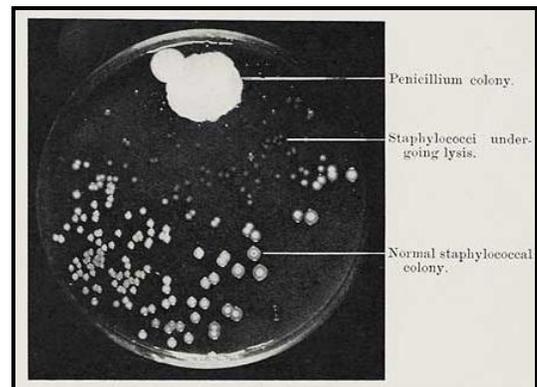
Producers of PENICILLIN-Schenley



Fact Sheet: The Challenge of Mass Production

Discovery

Sir Alexander Fleming discovered the bacteria-killing properties of penicillin while conducting research at St. Mary's Hospital in London in 1928. Upon returning to his disorganized lab from a weekend vacation, Fleming noticed that one of the Petri dishes was uncovered and a blue-green mold was growing inside. Rather than tossing the contaminated dish into the trash, he looked carefully and observed that the mold had killed bacteria growing nearby. Quite by accident Fleming had discovered penicillin, the antibiotic released by the mold of the genus *Penicillium*.



Alexander Fleming's original photograph of the contaminated dish.

Alexander Fleming was well acquainted with the treatment of bacterial infections after spending World War I as a captain in the British Medical Corps. He witnessed firsthand the lack of medicine to treat infections, with disease causing approximately one third of military deaths during the Great War. Despite its historical significance, Fleming's discovery of penicillin in 1928 brought little attention. The technology and funding needed to isolate and produce the antibiotic was unavailable at the time. Fleming, however, continued to grow the *Penicillium notatum* strain in his lab for twelve years, distributing it to scientists and saving the specimen for someone willing and able to transform the "mold juice" into a medicine suitable for human use.

Purification and Trials

Meanwhile, Australian scientist Howard Florey hired Ernst Chain to help with his microbiology research at Oxford University. Florey and Chain were interested in Alexander Fleming's work and in 1938, began studying the antibacterial properties of mold. Chain began by purifying and concentrating the penicillin "juice" through a complex and tiring process of freeze drying the product repeatedly. This slow and relatively inefficient process was improved upon by another researcher, Norman Heatley, who purified the penicillin by adjusting the acidity, or pH.

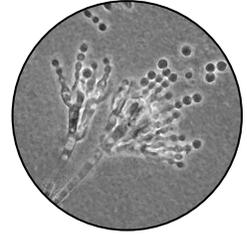


Norman Heatley working with *Penicillium* cultures.
Photograph William Dunn
School of Pathology, University of Oxford.

To their great excitement, Florey's team successfully cured infected mice with penicillin on May 25, 1940. Heatley oversaw the trials and recorded in his diary, "After supper with some friends, I returned to the lab and met the professor to give a final dose of penicillin to two of the mice. The 'controls' were looking very sick, but the two treated mice seemed very well. I stayed at the lab until 3:45am, by which time all four control animals were dead." Delirious with excitement, Heatley returned home early that morning, surprised to find that he had put his underpants on backwards in the dark! The usually mild-mannered Heatley noted in his journal, "It really looks as if penicillin may be of practical importance."

Mass Production

Florey and Chain's report about the mouse trials drew great interest from both scientific and military communities. World War II was well underway in Europe and the ability to combat disease and infection could mean the difference between victory and defeat. Because British facilities were manufacturing other drugs needed for the war effort in Europe, Florey and Heatley travelled to the U.S. in July of 1941 to continue research and seek help from the American pharmaceutical industry. They convinced four drug companies, Merck, E. R. Squibb & Sons, Charles Pfizer & Co., and Lederle Laboratories, to aid in the production of penicillin.



Penicillium notatum viewed with a microscope, 400x.

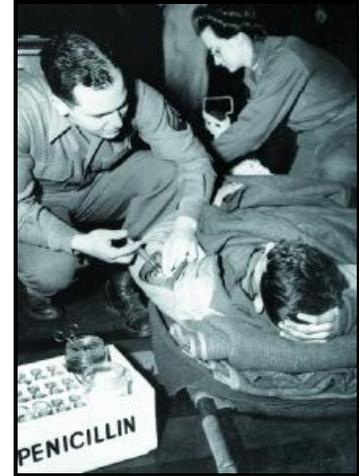


Penicillin production at pharmaceutical company, Eli Lilly.

Florey and Heatley ended up in Peoria, Illinois to work with researchers who had perfected the fermentation process necessary for growing penicillin. The researchers in Peoria used corn instead of glucose, or simple sugar, as the nutrient source, and the penicillin grew approximately 500 times more than it had in England! The team searched for more productive strains of *Penicillium notatum*, finding the best specimen growing on an over-ripe cantaloupe in a Peoria grocery store.

Meanwhile, penicillin was used to cure the first human bacterial infection, proving to researchers the vital importance of the drug to save lives. But, that one cure used up the entire supply of penicillin in the entire U.S! Following Japan's attack on Pearl Harbor on December 7, 1941, it was clear to scientists and military strategists that a combined effort was needed to produce the large amounts of penicillin needed to win the war. A total of 21 U.S. companies joined together, producing 2.3 million doses of penicillin in preparation of the D-Day invasion of Normandy. Penicillin quickly became known as the war's "miracle drug," curing infectious disease and saving millions of lives.

In 1945, Sir Alexander Fleming, Ernst Chain, Sir Howard Florey were awarded the Nobel Prize in Physiology or Medicine "for the discovery of penicillin and its curative effect in various infectious diseases." We have modern antibiotics today because scientists and drug companies worked together to solve a problem.



Medics using penicillin to combat infections in soldiers.

Thanks to Penicillin...He Will Come Home!
Student Activity Sheet

Directions: Read “Fact Sheet: The Mass Production of Penicillin.” Respond using complete sentences.

1. Louis Pasteur once said, “In the fields of observation chance favors only the prepared mind.” How does this statement, made in 1854, apply to Alexander Fleming’s discovery of penicillin?

2. Which organism produces penicillin? How does it affect bacteria cells?

3. What is an antibiotic? How do antibiotics help people?

4. Why didn’t Fleming make penicillin into a medicine himself?

5. How did Ernst Chain make the penicillin mixture stronger?

6. Describe the “controls” in Florey’s mouse experiment. How did Heatley know that the penicillin worked to cure the infection?

7. Why did Florey and Heatley go to the U.S. to produce more penicillin instead of staying in England?

8. List two changes made to the production process by the researchers in Peoria, Illinois.

9. Why did the U.S. become more interested in producing penicillin during 1942?

10. What role do you think penicillin played in winning the war?

*Bacteria reproduce through binary fission. One cell divides to become two cells, two cells divide to become four cells, and so forth. Infections occur when bacteria growth increases rapidly, releasing toxins and damaging healthy cells. These bacteria divide every 30 minutes. This is known as the **doubling time**: the time it takes for a population to double in size.*

Directions: As binary fission continues, fill in the blank portions of the chart. Then answer the questions using complete sentences.

Number of Cell Divisions	Number of Bacteria	Time
start	1	0 min
1	2	30 min
2	4	1 hour
3	8	1.5 hours
4	16	2 hours
5	36	2.5 hours
6	64	3 hours
7	128	3.5 hours
8		
9		
10	1024	5 hours
11		
12		
13	8192	6.5 hours
14		
15		
16	65536	8 hours
17		
18	262,144	9 hours
19		
20		
21		
22		

11. How long does it take for the population of bacteria to reach at least one million? ____ hours

12. Imagine that penicillin is given to treat the bacterial infection described by the chart above. Describe how you think the population size will change over time (increase, stay the same, decrease). Be specific and use numbers in your response.

Critical Thinking: In his Nobel Prize acceptance speech, Alexander Fleming predicted that penicillin might become less effective at killing bacteria over time. This is called antibiotic resistance, a major problem today. How do you think bacteria become resistant to antibiotics?

Thanks to Penicillin...He Will Come Home!

Student Activity Sheet Key

Directions: Read “Fact Sheet: The Mass Production of Penicillin.” Respond using complete sentences.

1. Louis Pasteur once said, “In the fields of observation chance favors only the prepared mind.” How does this statement, made in 1854, apply to Alexander Fleming’s discovery of penicillin?
Alexander Fleming could have easily thrown away the contaminated dish. Because he possessed knowledge and curiosity, Fleming identified the mold and the lack of bacteria growing nearby as unique. He hypothesized that the mold could be used to kill bacteria.
2. Which organism produces penicillin? How does it affect bacteria cells?
Penicillium notatum mold makes penicillin. It kills bacteria by stopping the cell wall from growing. As the inside of the cell grows, it presses against the cell wall causing the cell to burst and die (a process also called lysis).
3. What is an antibiotic? How do antibiotics help people?
Antibiotics kill bacteria or stop the bacteria from growing and reproducing. Antibiotics help people by curing bacterial infections that are possibly life-threatening without treatment.
4. Why didn’t Fleming make penicillin into a medicine himself?
He did not have the money or equipment required to make penicillin into a medicine for human use.
5. How did Ernst Chain make the penicillin mixture stronger?
He changed the pH or acidity of the penicillin making it more concentrated.
6. Describe the “controls” in Florey’s mouse experiment. How did Heatley know that the penicillin worked to cure the infection?
The two mice that did not receive penicillin made up the control group. These mice died. The mice that were treated with penicillin survived the infection. Without the control mice, Heatley could not conclude that the mice’s cure was due to the penicillin.
7. Why did Florey and Heatley go to the U.S. to produce more penicillin instead of staying in England?
British drug companies were busy making other drugs for the war effort in Europe. The U.S. had not yet entered into WWII, and the drug companies were able to help produce penicillin.
8. List two changes made to the production process by the researchers in Peoria, Illinois.
The nutrient source was changed from simple sugar to corn.
A new strain and faster growing of penicillin was found on a cantaloupe.
9. Why did the U.S. become more interested in producing penicillin during 1942?
The U.S. entered WWII following the attack on Pearl Harbor. The U.S. military needed penicillin to treat infectious disease on the front-lines.
10. What role do you think penicillin played in winning the war?
Answers will vary.

Bacteria reproduce through binary fission. One cell divides to become two cells, two cells divide to become four cells, and so forth. Infections occur when bacteria growth increases rapidly, releasing toxins and damaging healthy cells. These bacteria divide every 30 minutes. This is known as the **doubling time**: the time it takes for a population to double in size.

Directions: As binary fission continues, fill in the blank portions of the chart. Then answer the questions using complete sentences.

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7	128	3.5 hours
8	256	4 hours
9	512	4.5 hours
10	1024	5 hours
11	2048	5.5 hours
12	4096	6 hours
13	8192	6.5 hours
14	16384	7 hours
15	32768	7.5 hours
16	65536	8 hours
17	131,072	8.5 hours
18	262,144	9 hours
19	524,288	9.5 hours
20	1,048,576	10 hours
21	2,097,152	10.5 hours
22	4,194,304	11 hours

11. How long does it take for the population of bacteria to reach at least one million? 10 hours

12. Imagine that penicillin is given to treat the bacterial infection described by the chart above. Describe how you think the population size will change over time (increase, stay the same, decrease). Be specific and use numbers in your response.

Answers will vary. Population size will decrease over time.

Critical Thinking: In his Nobel Prize acceptance speech, Alexander Fleming predicted that penicillin might become less effective at killing bacteria over time. This is called antibiotic resistance, a major problem today. How do you think bacteria become resistant to antibiotics?

Bacteria with adaptations to resist antibiotics will survive and reproduce, passing those adaptations to offspring.