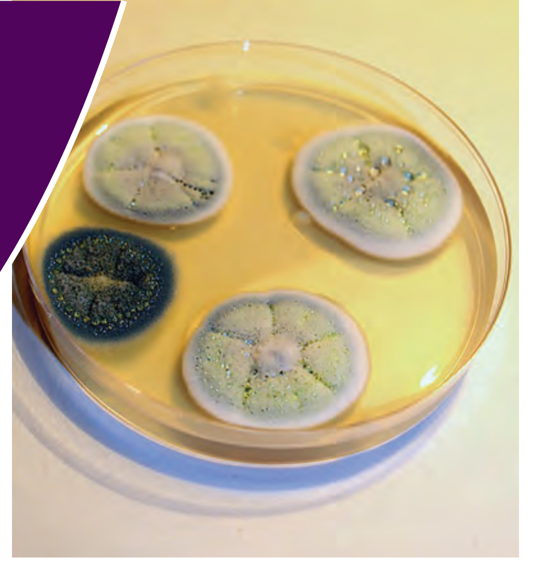
FEATURE ARTICLE

Using the Discovery of Penicillin Resistance to Teach Nature of Science & Natural Selection



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Abstract

The discovery of and research into penicillin resistance by Sir Edward Abraham and Sir Ernst Chain can be used to teach the concept of natural selection and also multiple nature of science (NOS) objectives associated with Next Generation Science Standards, such as "scientific knowledge is based on empirical evidence" and "science is a human endeavor." After a brief history of Abraham and Chain's work, we share a detailed multiday lesson plan and rationale for use in an eighth-grade in-person life science classroom. The instructional strategies discussed include analysis of excerpts of Abraham and Chain's published work through a case study jigsaw using an explicit and reflective approach to teaching NOS. The explicit approach used here is the direct instruction of NOS concepts, while the reflective approach allows students to think about and reflect on what they are learning. Instruction includes close reading, direct instruction, small and large group discussions, and writing. Students are asked to create a scavenger hunt map at the end of the multiday lesson and are assessed with an online five-question pre- and post-assessment.

Keywords: *nature of science, natural selection, lesson plan, middle school.*

○ Introduction

Science teachers recognize the importance of helping students appreciate issues associated with the nature of science (NOS), which, broadly construed, refers to not only the tools and products of science, but also human aspects of the process of science and the nature and limitation of scientific claims (McComas, 2015). NOS is indeed central to our understanding of what it means to be scientifically literate. When a student is said to be scientifically literate, we mean they have a sufficient understanding of both science content and the nature of science to make intelligent and informed decisions with regard to any issue that involves science and technology. For instance, a scientifically literate person is someone who has enough of an understanding of contagious diseases and the role vaccines play in protecting people to appreciate both why they should get vaccinated, and also why in the midst of a new pandemic, guidance regarding the use of masks, social distancing, etc. might change as more is learned about the cause of the disease and how it is spread. There are great resources on NOS available for use by teachers and students (e.g., https://undsci.berkeley.edu/article/scienceflowchart, and https://www.biointeractive.org/classroom-resources/how-science-works). But determining precisely how to teach NOS remains an intimidating task.

> *[T]he observations of antibiotic resistance documented through Abraham and Chain's 1940 letter to Nature (Abraham & Chain, 1988) provide a great opportunity to teach NOS learning objectives in addition to previewing concepts related to natural selection.*

When we recognize that issues associated with NOS are generalizations about the process of science, then the importance of reflecting on examples of the practice of science, both present and past, becomes apparent. This being said, as much as the truism "the best way to learn science is to do science" might seem relevant, it should be recognized that there are constraints on the insights one can gain from reflecting on one's own scientific research when it comes to NOS. For instance, a scientist may lack the objectivity needed to appreciate how their research is affected by cultural biases. The significance of a particular bit of research may only become clear decades or even centuries after the work has been done. Examples drawn from the history of science do not necessarily suffer from these limitations. We have the "historical distance" to appreciate general features of the process of science that might not be as readily apparent in the moment (Allchin, 2013).

In this article we share how the story of the discovery of and research into penicillin resistance can be used to address learning objectives for both NOS and natural selection content, based on Next Generation Science Standards (NGSS), through various instructional strategies. The NGSS matrix for NOS states: "Scientific knowledge is based on empirical evidence"

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and "Science is a human endeavor" (NGSS Lead States, 2013). The importance of teaching NOS in the middle school classroom is supported by NGSS: "The integration of scientific and engineering practices, disciplinary core ideas, and crosscutting concepts sets the stage for teaching and learning about the nature of science" (NGSS Lead States, 2013, p. 2). Additionally, this unit plan can serve as a precursor to prompt students' thinking about natural selection. Natural selection is a topic supported by NGSS, as indicated in the Disciplinary Core Idea LS4-B, Natural Selection (NGSS Lead States, 2015) and in *A Framework for K-12 Science Education*. Therefore, the observations of antibiotic resistance documented through Abraham and Chain's 1940 letter to *Nature* (Abraham & Chain, 1988) provide a great opportunity to teach NOS learning objectives in addition to previewing concepts related to natural selection.

The discovery of penicillin resistance is often miscredited solely to Alexander Fleming (1881–1955). According to this story, he returned to his laboratory at St. Mary's Hospital in London, England, after a holiday, only to discover that his petri dishes of staphylococci were contaminated and the bacteria's growth was inhibited (Lobanovska & Pilla, 2017). Fleming concluded that mold, specifically a species of *Penicillium*, was what had caused the lysis of staphylococcus colonies on his petri dishes (Fleming, 2001 [1929]). The traditional telling of this story excludes an important aspect of science—that science is nonlinear. Fleming's discovery did not directly lead to the use of penicillin as an antibiotic in a linear manner. Rather, multiple individuals were researching how to use penicillin as an antibiotic at the same time. Additional scientific research and discovery by others had to occur (Allchin, 2013). In this case, the concept of science being nonlinear refers to multiple individuals working on the antibiotic potential of penicillin at the same time, which was based upon Fleming's findings. The traditional story neglects the important role played by Sirs Edward Abraham (1913–1999) and Ernst Chain (1906–1979), at the Sir William Dunn School of Pathology at Oxford University, in isolating and purifying penicillin (Lobanovska & Pilla, 2017). The result of their work was that antibiotic resistance was actually first observed and recorded in a 1940 letter to *Nature* (Abraham & Chain, 1988). After briefly reviewing the history behind this episode, we share one approach for how best to use it to teach natural selection and also several issues associated with the nature of science.

History: Abraham & Chain's Discovery of Penicillin Resistance

Ernst Chain was a member of the team led by Howard Florey at Oxford University that studied penicillin as one of several antibacterial agents (Allchin, 2013; Lobanovska & Pilla, 2017). Along with Howard Florey (1898–1968), Chain recognized that penicillin might be useful medicinally by 1939. Together, the team cultured the mold *Penicillium* to obtain an adequate supply of the fungus for further study of its antibacterial properties (Lobanovska & Pilla, 2017). Edward Abraham, a biochemist, removed impurities within penicillin (The Alexander Fleming Laboratory Museum, 1999). As a result of their collective work, Chain and Abraham observed that not all bacteria were inhibited by penicillin, as detailed in their 1940 letter to *Nature* (Abraham & Chain, 1988).

In light of this observation, Abraham and Chain conducted additional experimentation that ultimately provided four major pieces of evidence in favor of their contention that antibiotic resistance occurred. These pieces of evidence included the following (Abraham & Chain, 1988):

- An extract made with ***Balantidium coli*** was found to destroy penicillin's growth-inhibiting property.
- The penicillin solution with the enzyme extract lost its growth-inhibiting property.
- The enzyme became denatured in heat and incubation with a pH of 6 and another enzyme.
- The enzyme was present in gram-negative rod bacteria that were insensitive to penicillin.

Based on this evidence, Abraham and Chain concluded that an enzyme, which they termed penicillinase, was the culprit in causing the penicillin-inhibiting properties within some *B. coli* colonies (Abraham & Chain, 1988). In the unit plan (detailed below), students will use these pieces of evidence (shared by means of excerpts from the primary text) to demonstrate that empirical evidence is necessary for scientific knowledge. Analysis of text describing the processes that Abraham and Chain used to gather their evidence will demonstrate that science is a human endeavor and involves creativity and imagination. In the last step, students will relate what they learned in this multiday unit to natural selection.

○ Learning Objectives

This unit plan includes two learning objectives based on the NGSS NOS matrix, as shown in Table 1. It also includes one content learning objective, which is based on the NGSS standard MS-LS4-4: "Construct an explanation based on evidence that describes how genetic variations of traits in a population increase some individuals' probability of surviving and reproducing in a specific environment."

Table 1. NGSS and corresponding learning objectives.

Standard	Learning Objective
Scientific knowledge is based on empirical evidence (NGSS NOS matrix).	Explain how scientific knowledge is based on empirical evidence by writing a paragraph describing how scientists use evidence to support scientific knowledge and by providing at least one example of another area within science where empirical evidence can be used.
Science is a human endeavor (NGSS NOS matrix).	Examine how science is a human endeavor by writing four sentences about how Abraham and Chain used imagination and creativity in discovering the mechanism behind penicillin resistance and by creating a list of four ways that scientists can use imagination and creativity in science.

○ Unit Plan Procedure

The procedure is explained here, and all of the needed materials are given in the Appendix below.

Day 1: Introduction to Historical Narrative

For the Warm-up, students will take the online Pre- and Post-Assessment in a Google Form. The pre-assessment will measure students' understanding of the NOS learning objectives regarding empirical evidence and imagination and creativity in science. Then, students will be introduced to the historical narrative of Abraham and Chain's discovery of antibiotic resistance through an interrupted story, which involves sharing the background of the historical episode while asking questions in between parts. Students will learn about the background of the historical episode, from Alexander Fleming's discovery of penicillin to the work that Abraham and Chain did in the laboratory. However, students will not be given the pieces of evidence that showed Abraham and Chain that antibiotic resistance was happening. The interrupted story was not utilized during the original use of this unit plan in an eighth-grade classroom, because providing students with the historical background information was not considered to be important. However, after utilizing the unit plan in class, the author determined that providing more historical background may have helped students better understand the case study.

Day 2: Case Study Jigsaw & Introduction to Evidence

The Warm-up on the second day of instruction includes asking students to recap the story of penicillin based on the previous day's interrupted story. After reviewing the story, students will complete the Anticipatory Set, a true-false low-stakes self-assessment in Google Forms. The questions asked will seek to determine students' understanding about the functions of antibiotics and enzymes and the terms *antibiotic resistance* and *evidence*.

The teacher will then facilitate a discussion of the self-assessment while viewing the results of the Google Form in real time. The class will come to a consensus on an explanation about the answers for each of the questions after viewing the correct answer.

After the discussion, students will begin the first part of the case study jigsaw in groups. The teacher will introduce the case study jigsaw and provide the students with directions. Students will be divided into "home groups" of four. Each home group will read one of four excerpts from Abraham and Chain's 1940 letter to *Nature,* with three underlined vocabulary terms along with a summary of each excerpt. As students read the excerpts, they will engage in guided close reading strategies.

These strategies include reading the text aloud, reflecting on the text, researching the terms and defining them in their own words, annotating the text, and paraphrasing. Students will also write into their science notebooks answers to research questions provided for their respective excerpts. These research questions provide students the opportunity to explore their excerpts more. Students will also receive homework and closure while they are with their home groups. The homework and closure encourage students to think about and reflect on how Abraham and Chain used evidence to support scientific knowledge. The closure, an activity that closes out the class and provides students with a wrap-up for the day's lesson, will be assessed at the beginning of day 3, as will the homework.

Day 3: Evidence, Imagination & Creativity

The class will begin with a Warm-up asking students to sketch what they read the previous day in their groups and to begin thinking about evidence in those excerpts. A short discussion will follow the sharing of sketches facilitated by the teacher. The closure and homework from day 2 will also be informally assessed at this time through a discussion about them.

After the Warm-up, the case study jigsaw will resume. Students will be placed into "travel groups." The travel groups each contain at least one student expert from each home group, who will share what they learned from their excerpt. Each student will share the evidence that they read in their excerpt and what they felt the evidence suggested. In their travel groups, students will discuss how Abraham and Chain used their individual pieces of evidence to support scientific knowledge, and complete guiding questions.

Next, each travel group will share one piece of the discussion. The teacher will give students the following prompt: "Give one example of how using evidence can be applied in other scientific situations." Students will be given three minutes, on a timer, to write an example in a Google Form. The teacher will then facilitate a whole-class discussion based on students' examples shared in the chat function.

Scaffolding for this question may be necessary to ensure that students can provide examples regarding how using evidence can be applied in other scientific situations. The term *scientific situation* may need to be defined. The teacher can use examples from labs in the course and other well-known examples of scientific situations relevant to the course. Questions that the teacher may use include, What are examples of other scientific situations? What is the outcome of these scientific situations? What is an example of evidence that is used in that scientific situation? Additionally, students may engage in a think-pair-share, where each student discusses a scientific situation with another student and lists examples of evidence that may occur in that scientific situation. Then the students can share their examples in a whole-class discussion.

After the class discussion, the teacher will explicitly explain the NOS concept that scientific knowledge is based on empirical evidence. Students will be asked to define *scientific knowledge* and *empirical evidence* in their own words in their science notebooks. Students will be asked to share their definitions.

Students will revisit their excerpt in each home group. They will begin to think about the process behind their evidence and the use of imagination and creativity by Abraham and Chain to obtain evidence. For the closure, to check for understanding at the end of the class, students will outline at least four parts of Abraham and Chain's process in weighing their evidence. Students will begin their homework, reflecting on specific ways that Abraham and Chain used their imagination and creativity to determine what caused penicillin resistance.

Day 4: Human Endeavors & Construction of Explanation

The fourth day will begin with a Warm-up asking students questions bout how scientists can use creativity. Students will write the answers to these questions in their science notebooks. The teacher will facilitate a class discussion based on the Warm-up questions.

After the Warm-up, the teacher will explicitly explain, in a mini lecture, the NOS concept that science is a human endeavor and that creativity is used by scientists. After the mini lecture, students will explain what the term *human endeavor* means to them. Here it means that people "do" science. These individuals have different backgrounds and experiences that affect how they do science and why they do science.

In their travel groups, students will create a map for a scavenger hunt that will take the audience through the four pieces of evidence that Abraham and Chain used to reach their conclusion. Students will be able to create the map, in Google Slides or on paper, demonstrating how genetic variations in a population increase some individuals' probability of surviving and reproducing in a specific environment (in this case, a laboratory). Students will also explain how Abraham and Chain's discovery demonstrates that "scientific knowledge is based on empirical evidence" and "science is a human endeavor." Students will then complete the closure, demonstrating how natural selection and antibiotic resistance are related, using evidence from the excerpts from Abraham and Chain's paper. Demonstrating the relationship between natural selection and antibiotic resistance is important because this unit can be used as a precursor to a unit on natural selection. Students may take the post-assessment later. However, it can be incorporated into day 4 of the unit plan as a quiz.

○ Appendix

Pre- & Post-Assessment (Google Forms)

Students will be assessed with this rubric-based assessment both before and after they complete the lesson activities:

1. Is empirical evidence necessary for scientific knowledge? Why or why not?
2. Provide one example where empirical evidence can be used in the scientific field. Explain how empirical evidence can be used in the example that you chose.
3. Should imagination and creativity be used in science? Explain the rationale behind your thought process.
4. What does it mean to say that science is a human endeavor? Provide one example.

Pre- & Post-Assessment Rubric

1. Correctly determines that empirical evidence is necessary for scientific knowledge (1 point); explains why (1 point)
2. Provides an example (1 point); explains the example (1 point)
3. Correctly determines that imagination and creativity should be used in science (1 point); explains rationale (1 point)
4. Describes what it means to say that science is a human endeavor (1 point); provides an example (1 point)

Total points: 8 points

Day 2: Introduction to Abraham & Chain & Their Evidence

Anticipatory Set (Google Forms Quiz) Please mark the following statements as true or false, according to the best of your knowledge. We will discuss your choices afterward, and you will ensure you have given the correct answers.

1. Enzymes are proteins that work as catalysts in reactions. **T**/F
2. Enzymes get used up in reactions. T/**F**
3. Antibiotics help bacteria to grow and survive. T/**F**
4. Penicillin is an antibiotic. **T**/F
5. *B. coli* is a type of bacteria. **T**/F
6. Abraham and Chain worked to purify penicillin. **T**/F
7. Evidence is not needed in science. T/**F**

Excerpt Cards (Printed or Google Doc)

Excerpt card 1

An <u>extract</u> of B. coli was made by crushing a <u>suspension</u> of the organisms in the bacterial crushing mill of Booth and Green. This extract was found to contain a substance destroying the growth-inhibiting property of penicillin. The destruction took place on <u>incubating</u> the penicillin preparation with the bacterial extract at 37°, or at room temperature for a longer time.

Excerpt from Abraham, E. P., & Chain, E. (1988). An enzyme from bacteria able to destroy penicillin. *Review of Infectious Diseases, 10*(4), 677. https://www.jstor.org/stable/4454535

Summary of excerpt
A type of bacteria, called *B. coli*, was crushed into an extract. This extract contained a substance that destroyed the ability of penicillin to kill the bacteria.

Excerpt card 2

The <u>growth-inhibiting</u> activity of the solutions was then tested <u>quantitatively</u> on agar plates against Staphylococcus aureus. *The penicillin solution <u>incubated</u> with the enzyme had entirely lost its growth-inhibiting activity, whereas the control solution had retained its full strength.*

Excerpt from Abraham, E. P., & Chain, E. (1988). An enzyme from bacteria able to destroy penicillin. *Review of Infectious Diseases, 10*(4), 677. https://www.jstor.org/stable/4454535

Summary of excerpt
They tested the extract to determine that the enzyme caused the penicillin to not kill the bacteria.

Excerpt card 3

The conclusion that the active substance is an enzyme is drawn from the fact that it is destroyed by heating at 90° for 5 minutes and by <u>incubation</u> with papain activated with potassium cyanide at pH 6, and that it is non-dialysable through "Cellophane" membranes. It can be <u>precipitated</u> by 2 volumes of alcohol, but much of its activity is lost during this operation. The activity of the enzyme, which we term penicillinase, is slight at pH 5, but increases considerably towards the <u>alkaline</u> range of pH. It is very active at pH 8 and 9. Higher pH's could not be tested as penicillin is unstable above pH 9.

Excerpt from Abraham, E. P., & Chain, E. (1988). An enzyme from bacteria able to destroy penicillin. *Review of Infectious Diseases, 10*(4), 677. https://www.jstor.org/stable/4454535

Summary of excerpt
The substance is an enzyme. It was destroyed by heat and by an enzyme that destroys proteins. It did not travel through a thin membrane. It was tested to be active between a pH of 5 and 9.

Excerpt card 4

The enzyme was absent from extracts of the penicillin-sensitive Staphylococcus aureus, *of yeast and of Penicillium notatum.*

It was present in a Gram-negative rod, insensitive to penicillin, found as a contaminant of some Penicillium cultures….

The enzyme was also found in M. lysodeikticus, an organism sensitive to the action of penicillin, though less so than Staphylococcus aureus.

Excerpt from Abraham, E. P., & Chain, E. (1988). An enzyme from bacteria able to destroy penicillin. *Review of Infectious Diseases, 10*(4), 678. https://www.jstor.org/stable/4454535

Summary of excerpt
The enzyme was not in bacteria that is killed by penicillin, in yeast, or in another type of *Penicillium* mold. It was present in bacteria that is not killed by penicillin.

Instructions for Close Reading (Printed or Google Doc)

Please read your excerpt with your group members using the following close reading strategies. Please make any annotations directly on your excerpt card.

1. Read through the text aloud with your group members without writing any annotations. Reflect on how you feel about the passage with your group members. Was it challenging? Easy? Interesting?
2. Research the three underlined terms in the text, and define them in your own words.
3. Read through the text aloud with your partner while writing annotations. Annotations will include (a) one question you are curious about as you read the passage and (b) a numbered list of steps that the researchers took in your passage.
4. Read through the text aloud with your group members for the last time while writing annotations. After that, paraphrase the excerpt in your own words.
5. Congratulations! You are now an expert on your excerpt!

Follow-Up Research Questions (Printed or Google Doc)

Please respond to the following, based on your excerpt:

1. What are three words that you need to define to successfully understand the text? Define these three words in your own words using resources provided.
2. Draw a picture of what happened within the text. Be sure to label each part of the drawing.
3. Describe what happened within the text in your own words in three sentences. You may use what you wrote in your close reading.
4. What did Abraham and Chain find, in the excerpt that you read?
5. What was the evidence found in the text? How do you know?
6. Why is the evidence important? What does the evidence tell us?

Homework & Closure (Printed or Google Form)

Explain in paragraph form (three to four sentences) how the scientists Abraham and Chain used evidence in the excerpt you read to support scientific knowledge. Reflect on your knowledge about science, and determine how evidence can be applied in other scientific situations.

○ Day 3: Evidence, Imagination & Creativity

Warm-up (Printed)

Sketch an image of what you read in your excerpt yesterday. Think about the following questions: What was the evidence that you saw in your excerpt from yesterday? What does this evidence suggest?

Travel Group Discussion: Guiding Questions (Printed or Google Doc)

With your travel group and based on the excerpt you read, please respond to the following:

1. Explain in list form how the scientists Abraham and Chain used evidence to support scientific knowledge.
2. Write down the examples your travel group members selected that show how using evidence can be applied in other scientific situations.
3. How did your specific excerpt display empirical evidence?
4. Give one example of how using evidence can be applied in other scientific situations.

Guided Notes: Scientific Knowledge & Empirical Evidence (Printed or Google Doc)

Scientific ____________________ is based on empirical ____________________.

Define the following terms in your own words.

1. Scientific knowledge:
2. Empirical evidence:

Home Group Discussion (Printed or Google Doc)

1. How did Abraham and Chain use imagination and creativity in their process to determine the empirical evidence?
2. Outline the process in a list of at least four ways that Abraham and Chain determined their evidence.

Homework & Closure (Printed or Google Form)

Reflect on how Abraham and Chain might have used their imagination and creativity in their process to determine what causes penicillin resistance.

1. What are specific ways that Abraham and Chain used imagination and creativity in their process to determine what causes penicillin resistance?
2. Create a list of four ways that you think scientists can use imagination and creativity in science.

○ Day 4: Human Endeavors & Natural Selection

Warm-up (Printed or Google Form)

How can scientists use imagination and creativity in science? What are two examples of ways they can use imagination and creativity in science (besides the ways that Abraham and Chain used them)?

Guided Notes: Science Is a Human Endeavor (Printed or Google Doc)

1. What does it mean that science is a human endeavor?
2. What does the term *human endeavor* mean? Write it in your own words.

○ Closure (Printed or Google Form)

How does antibiotic resistance, such as penicillin resistance, demonstrate natural selection? Please use specific examples and evidence from Abraham and Chain's paper.

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