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# K-12 Partnership Lesson Plan

# Heather Kittredge

# *Microbial Connections*

# *The Evolution of Antibiotic Resistance*

## Overview

Antibiotic resistance is becoming known as a worldwide threat to public health. Humans rely on antibiotics for many medical procedures, including knee and hip replacements, cancer and other sicknesses that suppress the immune system, all the way down to simple bacterial infections. Bacteria quickly regenerate though, which allows mutations to quickly arise in a population. When one bacteria accumulates a mutation that allows it to be resistant to antibiotics, it will not be killed when all of the other members of the population are killed by the antibiotic. This creates an environment for resistant bacteria to successfully multiple and contribute to the problem of antibiotic resistance.

In this lesson, we discuss different types of antibiotics and their cellular targets, followed by an overview of how bacterial evolution leads to antibiotic resistance and finally what the future holds for combating antibiotic resistance around the world. After this material is covered the lesson plan moves on to an activity using marshmallows and M&Ms to model the evolution of antibiotic resistance. In the model, M&Ms have a mutation that prevents antibiotics from entering their cell walls, making them resistant to antibiotics.

**Objectives**

At the conclusion of the lesson, students will be able to:

* Understand that antibiotic resistance is a product of evolution (natural selection)
* Discuss the different types of antibiotics and their cellular targets
* Discuss the role humans play in the rise of antibiotic resistance
* Comprehend the next steps in dealing with antibiotic resistance as a public health concern
* Generate a hypothesis and prediction for how antibiotic resistance will change bacterial survival and population dynamics
* Collect data from an experiment and put into a table
* Convert a data table into a figure and draw conclusions about the severity of antibiotic resistance

**Length of Lesson**

This lesson will require one hour long class period. The first half hour will include an overview of antibiotic resistance including a PowerPoint. The second half hour will be for the marshmallow and M&M activity. The lesson plan provided here simply models the change in the ratio of marshmallows to M&Ms in a population over time, but this model could easily be modified for higher lever learning. For example, by including a variety of antibiotics represented by tools other than a toothpick, different types of cells using different colored marshmallows or catered to building a model for natural selection from the supplies, but with minimal instruction.

**Grade Levels**

This lesson is designed for high school students based on the language in the PowerPoint, but can easily be modified for middle schoolers without much change to the activity.

**Standards covered (NGSS)**

Disciplinary Core Ideas:

**MS-LS4-5**

Gather and synthesize information about the technologies that have changed the way humans influence the inheritance of desired traits in organisms.

**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.

**HS-LS4-1**

Communicate scientific information that common ancestry and biological evolution are supported by multiple lines of empirical evidence.

**HS-LS4-2**

Construct an explanation based on evidence that the process of evolution primarily results from four factors: (1) the potential for a species to increase in number, (2) the heritable genetic variation of individuals in a species due to mutation and sexual reproduction, (3) competition for limited resources, and (4) the proliferation of those organisms that are better able to survive and reproduce in the environment.

**HS-LS4-3**

Apply concepts of statistics and probability to support explanations that organisms with an advantageous heritable trait tend to increase in proportion to organisms lacking this trait.

**HS-LS4-4**

Construct an explanation based on evidence for how natural selection leads to adaptation of populations.

**HS-LS4-5** Evaluate the evidence supporting claims that changes in environmental conditions may result in: (1) increases in the number of individuals of some species, (2) the emergence of new species over time, and (3) the extinction of other species.

Cross Cutting Concepts:

* Cause and effect
* Systems and System Models
* Stability and Change of Systems

Science and Engineering Practices

* Asking questions and defining problems
* Planning and carrying out investigations
* Analyzing and interpreting data
* Engaging in argument from evidence

**PowerPoint Notes (by slide)**

1. Title Slide: the background is a blood agar plate. The yellowish parts of the plate indicate the bacteria are capable of lysing blood cells.
2. The presentation has three main parts. First, we will go over a brief introduction to what an antibiotic is and what it means to be resistant to antibiotics. Second, we cover why antibiotic resistance is such a large health concern and how a world with no functional antibiotics would be a very unpleasant place to live. Third, we cover what is currently being done to combat the antibiotic resistant crisis. Lastly, the pictures of the M&Ms and marshmallows introduce the game that the students will get to play after the lecture is finished.
3. Introduce the idea that bacteria live in very harsh environments that are often nutrient poor and bacteria must compete with each other for these limited nutrients. Over the years, bacteria have evolved the ability to harm other bacteria in order to increase their odds of surviving. Secreting chemical toxins is one way that bacteria can protect themselves. The introduction of antibiotics was catalyzed by the idea that humans could capture these chemical toxins and use them to kill harmful bacteria found in mammals. The scientists that worked on the first antibiotic are often quoted as predicting that harmful bacteria would quickly evolve to combat any antibiotic humans began using in large quantities.
4. Penicillin was the first antibiotic discovered and it was completely unintentional. Fleming realized the potential for penicillin after he witnessed the fungus kill pathogenic bacteria on an agar plate.
5. This agar plate demonstrates the power of antibiotics as you can see the circular disks that are soaked in antibiotics are able to kill all the bacteria around the disk. This is similar to the phenomenon Fleming observed with penicillium on a lawn of pathogenic bacteria.
6. This is a very important slide. In order, for students to understand that antibiotic ressitance is an evolutionary process they have to understand that humans are incapable of becoming resistant to antibiotics, only bacteria living in your body can become resistant to antibiotics. These bacteria can stick around in your body until the next round of antibiotics, rendering the antibiotics virtually useless.
7. This figure demonstrates how quickly resistance strains of pathogenic bacteria can arise in the human population. Note to students how many antibiotics have been created over the years and that no new antibiotics have come to market since 2005.
8. This slide helps to explain why we can keep producing antibiotics. Different classes of antibiotics have different cellular targets, so even when a mutation evolves that inhibits folate synthesis, there is still the potential to use an antibiotic that targets another cellular component like protein synthesis. A world without antibiotics means that many pathogenic bacteria had evolved to be resistant to a variety of cellular targets.
9. Without antibiotics many now simple medical procedures would be considered life threatening. This includes transplants, dialysis, any immune suppressing sicknesses including cancer as well as hip and knee replacements.
10. Antibiotic overuse is a major factor contributing to antibiotic resistance. While humans can be overprescribed antibiotics (when they do not have an illness caused by a bacterial infection), the majority of antibiotics (70%) are fed to animals in their feed. Antibiotics were created to fit like a key, destroying only certain pathogens. Using antibiotics as a means of preventing disease is not how they were intended to be used and is a major problem contributing to ressitance.
11. Animation shows how two bacterial cells survive a first round of antibiotics, one of them survives because of a mutation (this cell turns green) and then can survive the second round of antibiotics to continue to replicate. Note how the population turns from all susceptible cells (orange) to resistant cells (green).
12. This is a really cool video that demonstrates how quickly antibiotic resistance can spread. Might want a different video for the middle school audience.
13. Finally, tie together the second part of the lecture by explicitly pointing out that both mutations and natural selection (both evolutionary mechanisms) are responsible for antibiotic resistance. This is really just a classic case of survival of the fittest. You can also point out that the antibiotic rifampicin (pictured), which we common work with in the lab only requires one base pair to mutate in order to confer resistance.
14. Introduce the third part – there is some hope!
15. The combination of resistance and lack of new antibiotics is drawing the world’s attention towards dealing with antibiotic resistance. One big reason that no new antibiotics have come out in the last few years is that pharmaceutical companies can make more profit off of old antibiotics that are less effective – meaning people will buy more. In addition, it is very difficult to find new antibiotics and often is an endeavoring in losing money.
16. Examples of what could happen in a post antibiotic era (could probably move this slide if you wanted).
17. Corporation are not all bad, really they are just doing their job by trying to maximize their profits, but recently large pharmaceutical companies have come to agree that something needs to be done to combat antibiotic resistance and hence The Davos Declaration came about.
18. This last slide introduces the most important glimmer of hope! That a new antibiotic class has been discovered within the last year and in preliminary studies it did not show any signs of resistance. This indicates that it might take longer than usual for resistance to evolve in response to Teixobactin. What is even cooler though, is the way that teixobactin was discovered – using the iChip. It is like 1000s of small petri dishes and it increases the number of bacteria we can isolate from the environment because the environment supplies the nutrients for specialist bacteria to grow. On agar plates, it is estimated that 1% of bacteria can grow, but with the iChip it is estimated that around 50% of the world’s bacteria will grow.
19. Moving onto the game!

**Materials**

* One large bag of small marshmallows
* One bag of M&Ms (need less than marshmallows)
* Toothpicks
* Powerpoint introduction
* Student handout
* Scientific literature to assign before class

**Worksheet Notes**

1. Hand out the worksheet and let them begin reading before you hand out the materials.
2. Give each pair around 20 M&Ms and 40 marshmallows. It’s ideal if you have out two different colored paper plates, one plate is for the extra’s and the other is for the actual population (might be best to have them draw a human on this plate).
3. \*Before they begin, you will probably want to explain that you can only kill bacteria by stabbing it with the toothpick you cannot just pick it up with the extra marshmallow (very sticky) attached to the end of the toothpick.
4. Once they have finished the worksheet, ask different groups how many susceptible bacteria were alive at the end. This should be highly variable based on how quickly they were able to stab, this process can be compared to the strength of different antibiotics or even a quick lesson in the stochastic nature of population dynamics (bring up genetic drift as another evolutionary mechanism).

**Resources (email** **kittred8@msu.edu** **for PDFs)**

* A new antibiotic kills pathogens without detectable resistance. Nature 2015.
	+ Nature paper for Teixobactin results
* Molecular Mechanisms of Antibiotic Resistance. Nature Reviews 2015.
	+ Good overview of cellular targets of antibiotic resistance
* Entering a Post-Antibiotic Era? Nature Reviews Microbiology 2013.
* Resistance to Antibiotics: Are we in a Post-Antibiotic Era? Archives of Medical Research 2005.
* Update on the current antibiotic crisis? Current Opinion in Pharmacology 2014.
* The True Cost of Antimicrobial Resistance. Biomedical Journal 2015.

**Assessment**

* Can students describe the evolutionary mechanisms that lead to antibiotic resistance?
	+ Mutation and genetic drift
* Can students project the trend of a population of susceptible pathogens after a dose of antibiotics?
	+ Decrease
* Can students project the trend of a population of resistant pathogens after a dose of antibiotics?
	+ Increase
* Does a student understand why you can’t take antibiotics when you are not sick?
	+ Decreases competition with susceptible pathogens (there is often a tradeoff – it is costly to be resistant so you might be worse under normal conditions).