NIHR | National Institute for Health Research

Health Protection Research Unit in Healthcare Associated Infections & Antimicrobial Resistance

Imperial College London

Patient and Public Engagement Activity Pack

Microorganisms, evolution and antibiotic resistance: Build a Bug

Microorganisms, evolution and antibiotic resistance: Build a bug

This pack is designed as a free guide, with printable resources, to allow you to run your own engagement activity about antimicrobial resistance.

The activity aims to educate participants and help them to understand how bacteria evolve and specifically how antibiotic resistance among microorganisms occurs. Participants will carry out a simple activity using pom-poms and pipe cleaners, which will explain evolution and selection pressure and the difference between naturally occurring resistance and acquired resistance.

Antibiotic resistance has serious implications at individual as well as global levels that the participants might not be aware of. This activity will highlight these.

This activity is also available in a lesson plan format for schools. Please check our website.

Crediting the HPRU in HCAI and AMR at Imperial College.

We would be delighted to hear from you if you choose to use our resources. Please do contact us at head.ops@imperial.ac.uk and tweet pictures of the activity and tag us: @HPRUamr

Activity Objectives

This activity aims to help participants understand how bacteria evolve and specifically how antibiotic resistance among micro-organisms occurs. Participants will carry out a simple activity using pom-poms and pipe cleaners, which will explain evolution and selection pressure and the difference between naturally occurring resistance and acquired resistance.

By the end of the activity:

- All participants should understand how environmental conditions can drive adaption and evolution.
- All participants should understand that antibiotic use drives antibiotic resistance and should **only** be used when really needed.
- Most participants should be able to describe the difference between naturally occurring and acquired resistance.

Background Information

Antibiotics are used to treat infections caused by bacteria. They also underpin much of modern medicine from routine surgery to cancer treatment.

If used too often or incorrectly then bacteria can develop (evolve) ways to avoid being killed by antibiotics. This is called resistance. Drug resistant bacteria are harder to kill than non-resistant bacteria. If bacteria become resistant to several different types of antibiotics, this is called multi-drug resistance and can eventually become impossible to treat.

This activity demonstrates how microbes adapt and how their environment drives them to become drug resistant.

Microbes are tiny organisms; too small to see without a microscope. They live everywhere, in air, soil, rock and water, on plants and animals, even on our skin. Microbes are essential for healthy life, we could not exist without them. There are four main types of microbes: bacteria, viruses, fungi and protozoa. Some microbes are harmful to health. Common names for these harmful microbes that the children are likely to have heard are ‘germs’ or ‘bugs’.

Bacteria are tiny and it is estimated that the total number of bacteria on the average human at any one time is around 1 trillion! Bacteria can reproduce rapidly—some species can replicate themselves in as little as 20 minutes. The speed of reproduction means that bacteria that cause illness can spread rapidly. It also means that bacteria can respond to changes in their environment by also changing rapidly. This is called **natural variation**. This natural variation can be seen in all groups of living things which are the same species. Sometimes, these small variations, can lead to one bacteria having some sort of advantage over another when it comes to survival. These “mutants” may replicate faster than the others, or be better at fighting off other bacteria, or better at surviving in a tough environment.

Antibiotics are a family of drugs which work against bacteria. They have been the cornerstone of much of modern medicine, allowing routine surgery to be conducted without the risk of infection and the development of new treatments such as chemotherapy and transplantation which in weakening the immune system rely on antibiotics to stop the patients succumbing to illness. Along with better diets and sanitation, antibiotics are one of the key reasons for the dramatic increase in life-expectancy over the past century.

Different types of antibiotics work in different ways. For example Beta-lactam antibiotics (this group includes penicillin) kill bacteria by destroying their cell wall. Bacteria build cell walls by linking molecules together—beta-lactams block this process. Without support from a cell wall, pressure inside the cell becomes too much and the membrane bursts. Antibiotics in the macrolide group (this group includes erythromycin) stop the bacteria from building proteins. Since proteins do all the cell's work, a bacterium that cannot build proteins cannot survive. Quinolones (antibiotics like ciprofloxacin) stop break the DNA of bacteria when they start copying their DNA which they need to do to reproduce. Quinolones cause the strands to break and then prevent the breaks from being repaired. Without intact DNA, bacteria cannot live or reproduce.

Every time bacteria are exposed to non-lethal doses of antibiotics they have an opportunity to adapt (evolve) so that they are not affected by the drug. They may do this in a number of ways; some bacteria can produce enzymes that are capable of adding different chemical groups to antibiotics. This stops the antibiotic binding to its "target" in the bacterial cell. Other bacteria can change the composition or structure of the target the antibiotic is looking for, shielding it from the antibiotic. Some bacteria are able to produce alternative proteins that can be used instead of the ones that are targeted by the antibiotic. This type of resistance is the basis in MRSA (methicillin-resistant *Staphylococcus aureus*). Other bacteria produce pumps that sit in their membrane or cell wall transporting antibiotics out from the bacterium, in this way lowering the antibiotic concentration inside the bacterial cell and others produce enzymes that destroys the active component of antibiotics (like for penicillin).

When a bacterium is no longer susceptible to treatment by an antibiotic this is called **antibiotic resistance**, it is the bacteria NOT the person who has become resistant to the antibiotics, you and may have heard of these bacteria referred to as "superbugs".

Activity Preparation

You will need:

- Pipe cleaners (assorted colours)
- Pom-poms (assorted colours and sizes)
- Physical "wonderdrug no 1" and "wonderdrug no 2" labels provided for you to print out
- Table to display and carry out activity

Optional

- Accessories such as stick on eyes to personalise the bugs

A wide range of suppliers of pom-poms and pipe cleaners for craft can be found on www.amazon.com. High street retailers include Tiger stores, WHSmith and arts and crafts shops.

ON THE DAY OF THE ACTIVITY

- Cut one each of the different coloured pipe-cleaners into smaller pieces to represent the plasmid DNA and keep them separately – or alternatively keep a pair of scissors handy to snip bits off during the demonstration.
- Sort a few of the smallest pom-poms of each colour and keep them separately to represent the plasmid DNA.
- Have your physical "wonderdrugs" ready if you are using them.
- We also suggest you have containers or bowls for the pipe cleaners and pom-poms to make them easier to hand around to participants.

Activity in action:

1. Ask all the participants to take 2 pom-poms and a pipe cleaner and make a bacterium following these steps:

- Use a pipe-cleaner to represent the cell wall.
- Use any two pom-poms to represent your bacterial plasmid and chromosomal DNA.
- Squash the pom-poms together and wrap the pipe-cleaner around the outside to hold them together.

2. Next, ask the participants to each hold up their bacteria so that the group can see what has been produced, noting the **natural variation** between the bacteria:

- The DNA (pom-pom) colours chosen may differ from one to another.
- The colour of the cell wall (pipe cleaner) may be different.
- Some cell walls may be wrapped tighter than others.

3. Explain **naturally occurring resistance** by introducing "wonderdrug no 1" into the environment:

- Wonderdrug no 1, is an antibiotic. Antibiotics are compounds which kill bacteria. They are developed into medicines to kill disease-causing bacteria.
- Antibiotics have allowed us to effectively treat disease since their discovery in the 1920s.
- They have prevented us from dying from minor infections and allowed us to develop modern medical procedures including all kinds of surgery and cancer medicine.
- Some naturally occurring variations, as noted in step 2, allow some bacteria to naturally survive the presence of some **ANTIBIOTICS.**

4. **As the demonstrator YOU now choose any colour pom-pom on display, to denote natural resistance. It is suggested you choose a colour which is "rare" to force the majority of participants to re-make the bacteria.**

- Ask all participants whose bugs do not contain the chosen colour to take them apart.
- Highlight to your participants that those bacteria which survived had **naturally occurring resistance** (i.e. something about that bacterium enabled it to survive a dose of antibiotics).
- Ask participants whose bacteria have been destroyed by "wonderdrug no 1" to make another in the same way, **bearing in mind that "wonderdrug no 1**" is still in the environment.

5. As participants build a new bug, highlight that those who have chosen the "correct" colour pom-pom in order to survive, have responded to **selection pressure** and that this is called **acquired resistance.**

6. Some participants will not chose the "correct" colour pom-pom which denotes resistance. This is fine. Use this as an opportunity to explain how bacteria can **transfer resistance** DNA (plasmid transfer) to each other and to bacteria of other species. To denote this, give them a pom-pom of the "right" colour to denote resistance which you set aside at the beginning of the activity.

7. Now introduce “wonderdrug no 2” into the environment in the same way, this time choosing a pipe-cleaner (cell wall colour) to denote resistance to this new antibiotic. Again try to choose a rare colour to force the majority of the participants to remake their bug.

- As before ask all participants whose bugs do not contain the chosen colour cell well to take them apart.
- Highlight to your participants that those bacteria which survived had **naturally occurring resistance** as before (i.e. something about that bacterium enabled it to survive a dose of antibiotics) and that those remaining bacteria are now **multi-drug resistant –** as they acquired resistance to the first drug and have natural resistance to the second drug.

8. Ask participants whose bacteria have been destroyed by “wonderdrug no. 2” to make a new bacteria either by responding to selection pressure, i.e. making it again from scratch, or by acquiring the necessary resistance by DNA transfer, i.e. by incorporating a little section of the “correct” coloured pipe-cleaner.

9. Explain that you have now, as a group, made a group of multi-drug resistant bacteria. These are pretty scary and if you went to hospital with an illness caused by these, the hospital might not be able to treat you.

10. Highlight that if we introduced a “wonderdrug no.3” the pattern would be the same: **antibiotic use drives antibiotic resistance** and therefore we should only use antibiotics when they are really needed and should ALWAYS ensure we use them properly.

WONDER-DRUG LABLES

These can be printed and stuck to bottles of your choice to give the demonstrator a physical antibiotic to use during the activity.

WONDER DRUG NUMBER 1

Kills bacteria! This medical marvel saved millions of lives during the Second World War when it went into mass production. It is the corner stone of modern medicine

HOW IT WORKS: Bacteria constantly remodel their peptidoglycan cell walls, simultaneously building and breaking down portions of the cell wall as they grow and divide. Penicillin and other B-lactam antibiotics inhibit the formation of peptidoglycan cross-links in the bacterial cell wall

WONDER DRUG NUMBER 2

Useful in treating respiratory, skin, soft tissue and other diseases. Can be used as a substitute for patients with a penicillin allergy. Unlike Penicillin is effective against Legionelle pneumophila, mycoplasma, mycobacteria some riskettsia and chlamydia

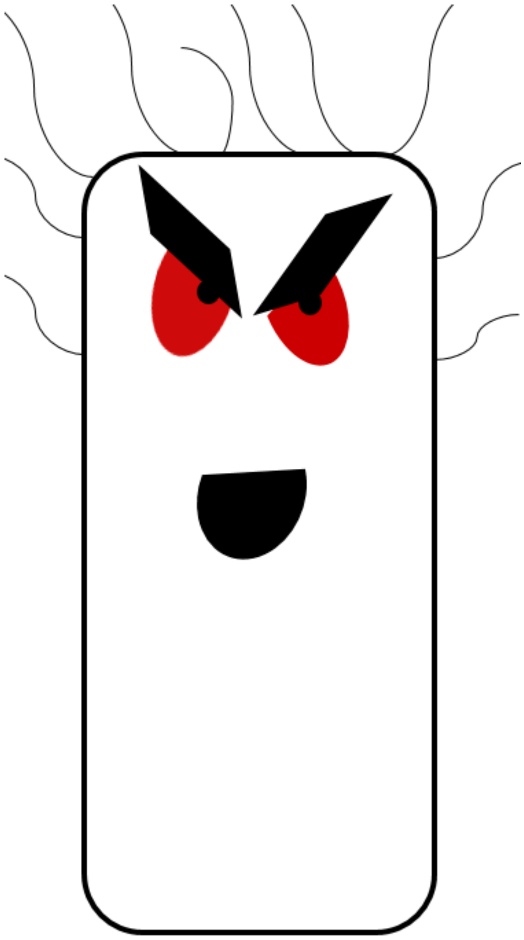
HOW IT WORKS: This group of antibiotics affect ribosomes, the cell's protein-building machines. Ribosomes build proteins in both bacteria and human cells, but there are differences between bacterial and human ribosomes. Macrolides block only bacterial ribosomes and prevent them from building proteins. Since proteins do all the cell's work, a bacterium that cannot build proteins cannot survive. Erythromycin, which is commonly used to treat respiratory tract and skins infections is a macrolide.

FOLLOW ON ACTIVITY—DESIGN YOUR SUPERBUG.

Like superheroes, superbugs have special powers. These powers mean that they cannot be harmed by drugs called antibiotics which have been designed to kill them.

Like the superheroes, the X-men, these special powers are the result of genetic mutations which happen naturally or in response to the environment.

Think about the superheroes or supervillains you know about then draw, or write down, some superpowers you want to give your superbug to make it resistant to antibiotics.



Some ideas and inspiration

Can your superbug change its shape like Elastigirl of the Incredibles?

Can your superbug disguise itself like Mystic from the X-men, or have a camouflage or cloaking device like Batman's suit?

Does your superbug have a protective shield like Captain America or some sort of superweapon?

Can your superbug heal itself, or regenerate like Wolverine?

Can your superbug absorb powers without getting hurt like Jean Grey from the X-men?

Can your superbug use mind-control to fool the antibiotic, like Professor Xavier?

The mechanisms of action of antibiotics and the mechanisms of resistance.

HOW DIFFERENT CLASSES OF ANTIBIOTIC WORK

Beta-lactam antibiotics (this group includes the penicillins) kill bacteria that are surrounded by a cell wall.

Bacteria build cell walls by linking molecules together—beta-lactams block this process. Without support from a cell wall, pressure inside the cell becomes too much and the membrane bursts.

Antibiotics in the macrolide group (this groups includes erythromycin) stop the bacteria from building proteins.

Since proteins do all the cell's work, a bacterium that cannot build proteins cannot survive.

Quinolones (antibiotics like ciprofloxacin) stop break the DNA of bacteria when they start copying their DNA which they need to do to reproduce. Quinolones cause the strands to break and then prevent the breaks from being repaired. Without intact DNA, bacteria cannot live or reproduce

THE "SUPER-POWERS" OF BACTERIA WHICH ENABLE THEM TO BECOME DRUG-RESISTANT

Modify the antibiotic. Bacteria can sometimes produce enzymes that are capable of adding different chemical groups to antibiotics. This in turn stop the antibiotic binding to its "target" in the bacterial cell.

Camouflage the target. Bacteria can change the composition or structure of the target the antibiotic is looking for. This results from mutations in the bacterial DNA and can stop the antibiotic from interacting with the target, or sometimes bacteria can add different chemical groups to the target structure, shielding it from the antibiotic.

Express alternative proteins. Some bacteria are able to produce alternative proteins that can be used instead of the ones that are targeted by the antibiotic. This type of resistance is the basis in MRSA (methicillin-resistant *Staphylococcus aureus*).

Reprogram target. Sometimes bacteria can produce a different variant of a structure it needs. For example, Vancomycin-resistant bacteria make a different cell wall compared to susceptible bacteria. The antibiotic is not able to interact as well with this type of cell wall.

Pump the antibiotic out from the bacterial cell. Bacteria can produce pumps that sit in their membrane or cell wall. They are used to transport signals and nutrients but can also sometimes be used to transport antibiotics out from the bacterium, in this way lowering the antibiotic concentration inside the bacterial cell.

Decrease permeability of the cell wall. Bacterial can develop their external membrane making it more difficult for the antibiotic to get into the bacteria.

Destroy the antibiotic. There are enzymes that bacteria can produce which stop antibiotics working. One example is β-lactamase that destroys the active component of penicillin. These enzymes can degrade a wide spectrum of β-lactam antibiotics, sometimes including the last resort drugs available for infections with these bacteria.