NHS
National Institute for
Health Research

Health Protection Research Unit in Healthcare Associated Infections & Antimicrobial Resistance

Public Health England
wellcome trust sanger institute
IMPERIAL COLLEGE HEALTH PARTNERS
UNIVERSITY OF CAMBRIDGE
Imperial College London

Lesson plans and learning resources
Micro-organisms, evolution and antibiotic resistance

KS2

Time needed: 1 x 60 minutes

Micro-organisms, evolution and antibiotic resistance

This lesson aims to help pupils understand how animals evolve and specifically how antibiotic resistance among micro-organisms occurs. Pupils 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.

Members of the Imperial College Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance can help deliver these lessons at West London locations as part of our Patient and Public Engagement Activities. To request our involvement please contact head.ops@imperial.ac.uk

National Curriculum Links- KS2

Cells and Organisation

- the structural adaptations of some unicellular organisms

Living things and their habitats

- Pupils should be taught to describe how living things are classified into broad groups according to common observable characteristics and based on similarities and differences, including micro-organisms, plants and animals

Evolution and inheritance

- Pupils should be taught to recognise that living things have changed over time and that living things produce offspring of the same kind, but normally offspring vary and are not identical to their parents. They should identify how animals and plants are adapted to suit their environment in different ways and that adaptation may lead to evolution

Lesson 1 Objectives

The objective of the lesson is to teach students a bit about microbes and how they can evolve to become drug resistant.

We aim to educate that antibiotic use drives drug resistance.

By the end of the lesson:

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

Lesson variations

This lesson can be delivered as a simple interactive demonstration of evolution using pom-poms and pipe cleaners. Printable resources are also appended at the end of this document for an extension activity allowing pupils to design their own super-bug with super powers.

Alternatively the lesson can be supported by the Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance. Representatives from the unit can bring pom-poms, pipe-cleaners and printed resources. Contact head.ops@imperial.ac.uk

Background teacher Information

Microbes are tiny organisms; too tiny 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 microbe; bacteria, viruses, fungi and protozoa. Some microbes are harmful to health. A common names for these harmful microbes that the children are likely to have heard of 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 duplicate themselves in as little as 20 minutes. The speed of reproduction means that bacteria which cause illnesses can spread rapidly. It also means that bacteria can respond to changes in their environment by also changing rapidly.

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 the penicillins) 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 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

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 penicillin's.

When a bacterium is no long 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 the children may have heard of these bacteria referred to as "superbugs".

Antimicrobial resistance it poses a catastrophic threat, which if it isn't addressed, could lead to a scenario where any one of us could go into hospital in 20 years for minor surgery and die because of an ordinary infection that can't be treated by antibiotics. Routine operations like hip replacements, organ transplants or caesarean section could be deadly because of the risk of infection.

Bacteria are able to share the DNA which makes them resistant with other bacteria, even bacteria of another species. This and the speed with which bacteria are able to evolve, means both that resistance can quickly spread. Antibiotic resistant bacteria currently kill around 700,000 people every year and this figure is predicted to rise to 10 million by 2050. Bacteria can also become resistant to more than one kind of antibiotic. This is called a multidrug resistant organism. There are a number of disease causing bacteria, which were previously treatable, but are now multidrug resistant. For example, multi-drug resistant tuberculosis (TB) is resistant to two of the main antibiotics, soniazid (INH) and rifampin (RIF), commonly used to treat TB. Increasingly, hospitals are encountering patients with bacteria which are resistant to a number of antibiotics including the antibiotics of last resort.

Lesson 1 Plan

<table>
<tr><th>Timing</th><th>Activity</th><th>Resources</th></tr>
<tr><td>Introduction</td><td></td><td></td></tr>
<tr><td></td><td>Lesson aims and objectives to be clearly explained to children and displayed</td><td>Sides provided</td></tr>
<tr><td>5 minutes</td><td>Using the slides provided and the introductory video explain what microbes are. They are sometimes called germs or bugs. There are 4 main classes of microbes, bacteria, viruses, protozoa and fungi. The first two are so tiny that they can only be seen under a microscope.</td><td>Video/Slides provided</td></tr>
<tr><td>10 minutes</td><td>You might then initiate a discussion around how microbes can be helpful or unhelpful

The children will have experienced both kinds –
Helpful microbes are used to make bread (yeast), and yogurt (live yogurt cultures) as per the video and also beer and wine.
Microbes can be made into medicine (e.g. the antibiotic penicillin).
Microbes are an essential part of the immune system, mentioned in the video- our body is full of friendly bacteria which keep your tummy well (this is what probiotics drinks are supposed to “top up”) and friendly bacteria on your skin which help keep out unhelpful bacteria.
Unhelpful microbes can make you ill if they get inside your body. Examples include the food poisoning mentioned in the video (often E.Coli or salmonella bacteria). Viruses are nearly all unhelpful and the children will have experienced some of them- influenza which cause ‘flu and rhinoviruses which can cause the common cold and pneumonia and bronchitis (although the latter can also be caused by bacteria!)</td><td>Slides provided</td></tr>
<tr><td>20 minutes</td><td>Using the slides provided and your pre-prepared resources of pom-poms and pipe-cleaners, move on to build your bug.

Ask all the pupils in the class to take 2 pom-poms and a pipe cleaner and make a bacterium in the way described on the slide.</td><td></td></tr>
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	Ask the children to each hold up their bacteria so that the group can see what has been produced, noting the **natural variation** between the bacteria (slides 7 and 8). Explain **naturally occurring resistant** (slide 9) before demonstrating by introducing "wonderdrug no 1" into the environment (slide 10) **As the demonstrator YOU choose which colour pom-pom denotes natural resistance. It is suggested you choose a colour which is "rare" to force the majority of children to re-make the bacteria.** Continue through the slides, highlighting that those bacteria which survived had **naturally occurring resistance** (i.e. something about that bacterium enabled it to survive a dose of antibiotics). Ask pupils 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. High-light 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** (slide 12) Some pupils 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) and give them a pom-pom of the "right" colour to denote resistance. Now introduce "wonderdrug no 2" into the environment (slide 15) in the same way, this time choosing a pipe-cleaner (cell wall colour) to denote resistance. Once most of the bacteria are killed, highlight 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. Ask pupils whose bacteria have been destroyed by "wonderdrug no. 2" to make a new bacteria (slide 17) 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.	

	Explain that you have now, as a class, 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. 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. Use the video to show the pupils bacterial evolution in process.	
10 minutes	Optional- use the extension material to ask pupils in groups or as individuals to design their own superbug.	
15 minutes	Discussion- the super-powers which each group or pupil has come up with should be fed back and discussed by the whole class. Using the "mechanisms of action of antibiotics and the mechanisms of resistance" information, discuss how many of the super-powers the students have come up with, actually exist for real, among resistant bacteria.	

Preparing for the lesson: Materials and Instructions

At least a week in advance

- Contact head.ops@imperial.ac.uk. If you would like Imperial College to support the lesson.

On the day of lesson delivery you will need:

- Pipe cleaners (assorted colours)
- Pom-poms (assorted colours and sizes)
- Optional- Physical "wonderdrug no 1" and "wonderdrug no 2" labels provided for you to print out
- Optional – printed extension material to design a superbug

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 LESSON

- 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 lesson
- 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 the classroom
- Check slides are working and videos
- Print extension material if you are using it

WONDER-DRUG LABLES

These can be printed and stuck to bottles of your choice to give the demonstrator a physical antibiotic to present to the class

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 Β-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

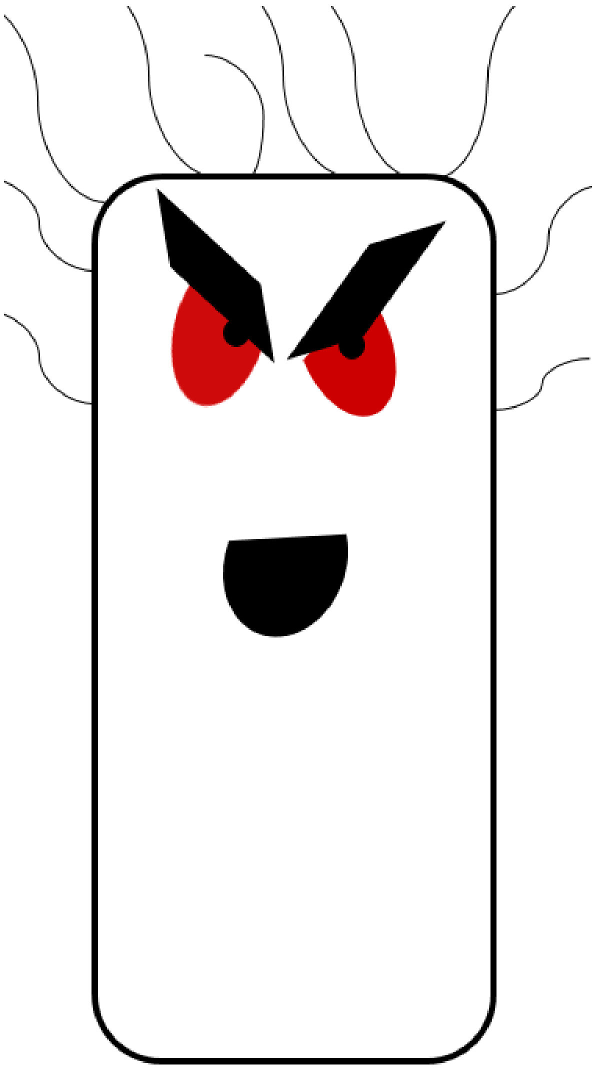
HOW IT WORKS- this group of antibiotics affect ribosomes, the cell's protein-building machines. Ribosomes build proteins in both bacteria and human cells, but there are differences between bacterial and human ribosomes. Macrolides block only bacterial ribosomes and prevent them from building proteins. 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.

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 super-heroes or super-villains you know about then draw, or write down, some super-powers 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?

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?

Does your superbug have some sort of super-weapon ?

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 penicillins. These enzymes can degrade a wide spectrum of β-lactam antibiotics, sometimes including the last resort drugs available for infections with these bacteria.