I BET YOU DIDN'T KNOW...

Bacteria get viral infections as well

Paul Tyler, PSTT College Fellow, links **cutting-edge research** with the **principles of primary science**

paul.tyler@pstt.org.uk

In 2016, a group of scientific experts from different fields came together to explore the most likely replacements for antibiotics. They put together a list of 19 possible alternatives and narrowed it down to 10 that they felt were worth pursuing, and therefore funding.

One of the possible alternatives considered is to use *bacteriophages*; viruses that attack and kill bacteria. This has been a common medical practice in some Eastern European countries for nearly 100 years but research into bacteriophages in Western countries stopped when antibiotics were discovered.

One of the world's leading experts on bacteriophages is Professor Martha Clokie, a *microbiologist* at the University of Leicester. Her research team are working to understand the complex interactions between bacteria and bacteriophages in different environments. There is increasing evidence that viruses can control their bacterial hosts in a variety of ways, even in the human body.

We all know that humans are infected by viruses but it's not just us that battle against constant strains of viruses making us ill. Every living thing on planet Earth has viruses that attack it. Some viruses are very specific to a single species, others can attack a broader range of species and sometimes viruses can even jump from one species to another.

Bacteria don't escape either; every species of bacteria has its own set of viruses, bacteriophages, that infect it and scientists are working to understand more about the complex battle that goes on between bacterial species and their viruses.

Humans have a complex immune system that can help us fight viral infections when they happen. We are just beginning to understand the defence systems that bacteria also possess to defend themselves from viral attack.

Questions to ask children.

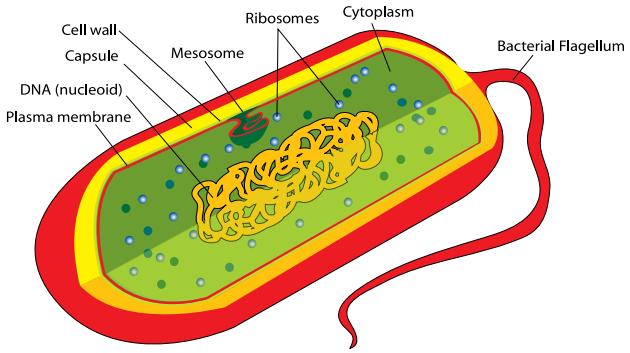
What bacteria and viruses do you know?

What do bacteria and viruses do?

What is the difference between bacteria and virus?

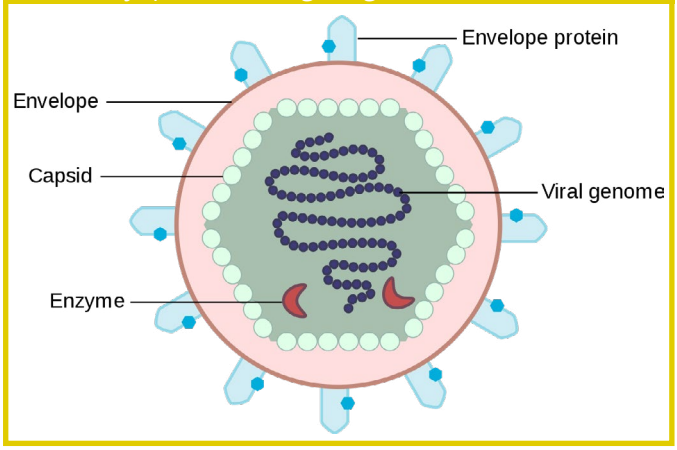
There are more than 30,000 species of bacteria defined on Earth and they are found just about everywhere from the freezing Antarctic to the hottest volcanic environments. They are simple single celled organisms that reproduce by copying their *DNA* and then splitting into two identical offspring cells (Figure 1).

Figure 1. Bacteria are types of single-celled organism.



Viruses are tiny infectious agents, about 100 times smaller than bacteria (Figure 2). They are made up of genetic material, often DNA, inside a protein capsule. They are not able to reproduce themselves and have to infect another organism's cells in order to make more viral particles.

Figure 2. Viruses are tiny infectious agents that interact with every species of living thing.



Every living organism on Earth has viruses that infect it, from humans to trees, whales to bacteria – 1 millilitre of sea water contains several million virus particles and if all the viral particles on Earth were lined up, they would extend over 100 light years (the distance that light travels in 1 year - 9.46 trillion kilometres).

The bacteria vs virus battle

For a bacteriophage to succeed it needs a host cell that it can infect and take over to produce more viral particles.

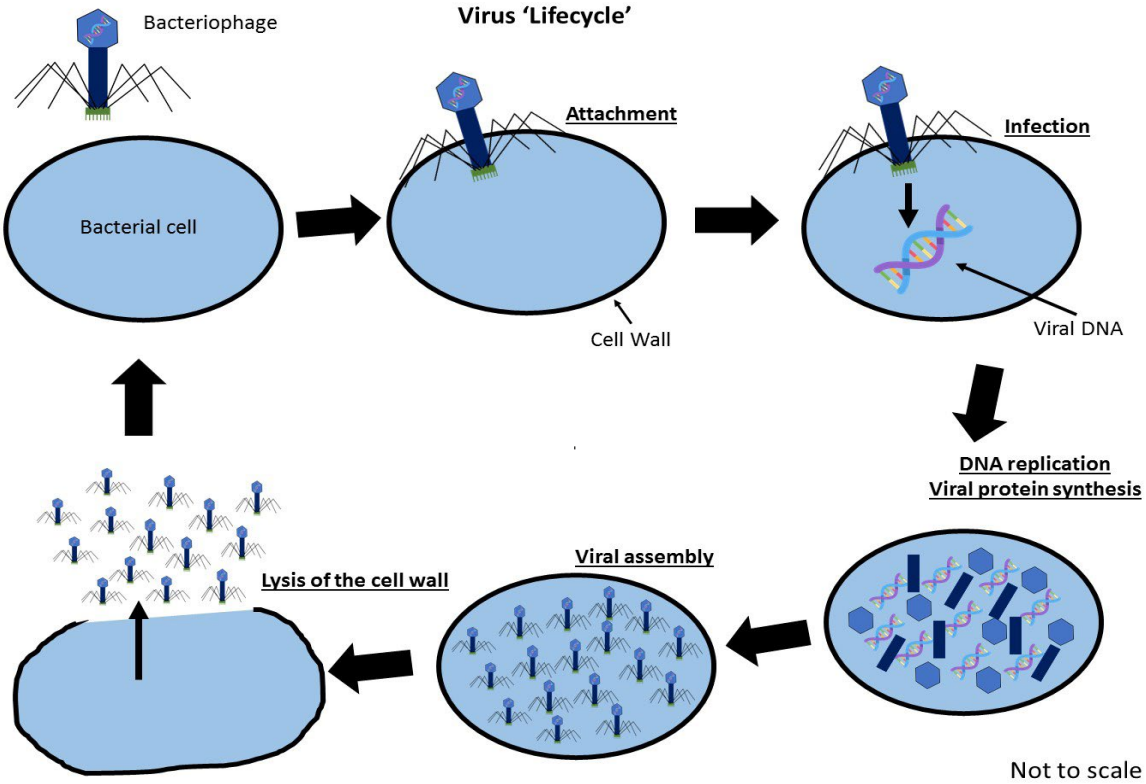
The 'lifecycle' of a bacteriophage starts with attachment to the cell wall of the bacterial cell. It then injects its DNA into the cell (Figure 3). The bacteria start to copy the viral DNA and then read the DNA to produce the protein structures that make up a new viral particle. Finally, the bacterial cell constructs new viral particles before it breaks open (a process called lysis) and releases the virus to infect other cells. Hundreds of new viral particles can be made and released in a matter of hours, allowing the infection to spread very quickly.

Bacteria and viruses have coexisted and coevolved for approximately 3.9 billion years and over that time there has been a constant evolutionary battle between the two. Bacteria have *evolved* defences that stop viruses attaching to the cell surface and infecting them, viruses have evolved to overcome these defences. Bacteria have evolved defensive systems that recognised viral *genetic material* after it had been injected and destroyed it, viruses have evolved to overcome these defences.

Most of the bacterial defence systems that have been discovered protect a single bacterial cell against attack, but there some documented examples that act in a broader way. In one of these, bacteria within an environment can release chemicals that can enter neighbouring bacterial cells and stop infection. Researchers are particularly interested in the mechanism of this process and why is occurs. They are asking the question, does it happen all the time, or only in response to a phage infection?

Understanding this process in *Streptomyces* bacteria, a group of bacteria that are mostly found in soil and decaying vegetation, has helped scientists uncover more about the complex relationship between bacteria and the phages that infect them.

Figure 3. Diagram showing how bacteriophages multiply inside a bacterial cell.



The antibiotic issue

There are a wide range of bacterial pathogens that infect humans and make them ill. From food poisoning caused by *Escherichia coli* or *Salmonella*, to tuberculosis caused by *Mycobacterium* tuberculosis, and cholera, caused by *Vibrio cholerae*, bacterial infections have been fatal for humans for thousands of years.

All that changed with the discovery of penicillin in 1928 and since then, billions of human lives have been saved by antibiotics. However, antibiotics are rapidly becoming less effective for treating infections for two main reasons:

1. Bacteria reproduce very quickly, a new generation every 24 hours or less, and so they can *mutate* very quickly and become resistant to the antibiotics being used.
2. The increased use of antibiotics in farming and over prescription by doctors increases the mutation rate significantly.

Bacteria that are resistant to antibiotics are called *superbugs* and, according to the World Health Organisation, they are responsible for over 700,000 deaths worldwide every year. If left unchecked, it is estimated that superbugs could be responsible for 10 million deaths a year globally by 2050.

Finding alternative treatments for bacterial infections has become a major priority for scientists across the world.

Questions to discuss with children.

Have you ever taken antibiotics?

What can you find out about different ways in which antibiotics are used?

A bacteriophage solution

Bacteriophages are efficient bacteria killers but they can also change the outside of bacteria so the human immune system cannot recognise them. For example, they can make their bacterial host produce toxic chemicals and in cystic fibrosis, a disorder with issues including difficulty breathing due to mucus in the lungs and frequent lung infections; a bacteriophage lets the bacterial host survive in the *anaerobic* conditions found in mucus filled lungs.

Despite the obvious harm that viruses can do to humans, their ability to selectively kill bacteria means they could have a critical role in solving the current antibiotic crisis.

GLOSSARY

Anaerobic
without oxygen

Antibiotic
a type of medicine used to treat bacterial infections

Bacteria
a type of simple single-celled organism

Bacteriophage
a virus that infects bacteria (usually just called phages)

DNA
deoxyribose nucleic acid, material that carries the instructions for every living thing

Evolved
something has changed slowly over time, often in response to a threat

Genetic material
material found in every living cell that carries the instructions to make more of that living thing

Microbiologist
a scientist who studies microorganisms such as bacteria, viruses, algae, fungi and some types of parasites

Mutate
small but permanent changes to the genetic material of an organism that change the organism's characteristics or behaviour

Pathogen
a microorganism that causes disease

Virus
a tiny infectious particle made up of genetic material in a protein capsule

The research paper that inspired this work was:

Bacterial defence molecules target viral DNA.

By Clokie, Martha R.J.

Nature, 564, 199 – 200 (2018) https://doi.org/10.1038/d41586-018-07576-7 Accessed October 2020

Martha R. J. Clokie works in the Department of Genetics and Genome Biology, University of Leicester, Leicester, UK

Further information in this work came from the following papers:

1. Alternatives to antibiotics—a pipeline portfolio review.

By Lloyd Czaplewski[1,2,3], Richard Bax[4], Martha Clokie[5], Mike Dawson[6], Heather Fairhead[7], Vincent A Fischetti[9], Simon Foster[10,11], Brendan F Gilmore[12], Robert E W Hancock[13], David Harper[14], Ian R Henderson[15], Kai Hilpert[16,17], Brian V Jones[18,19], Aras Kadioglu[20], David Knowles[11,21], Sigríður Ólafsdóttir[22], David Payne[23], Steve Projan[24], Sunil Shaunak[25], Jared Silverman[26], Christopher M Thomas[15,27], Trevor J Trust[28], Peter Warn[29], John H Rex[30,31].

Lancet Infectious Diseases 16: 239–51 (2016) https://doi.org/10.1016/S1473-3099(15)00466-1 Accessed October 2020

1. *Chemical Biology Ventures, Abingdon, Oxfordshire, UK*
2. *Abgentis, Edgbaston, Birmingham, UK*
3. *Persica Pharmaceuticals, Canterbury, Kent, UK*
4. *Transcrip Partners Reading, Berkshire, UK*
5. *Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, UK*
6. *Novacta Biosystems, Welwyn Garden City, Hertfordshire, UK*
7. *Cantab Anti-infectives, Welwyn Garden City, Hertfordshire, UK*
8. *Phico Therapeutics, Babraham, Cambridge, UK*
9. *Laboratory of Bacterial Pathogenesis and Immunology, The Rockefeller University, New York, NY, USA*
10. *Department of Molecular Biology and Biotechnology, University of Sheffield, Sheffield, UK*
11. *Absynth Biologics, Liverpool, UK*
12. *School of Pharmacy, Queen's University, Belfast, UK*
13. *Department of Microbiology and Immunology, University of British Columbia, Vancouver, BC, Canada*
14. *Evolution Biotechnologies, Ampthill, Bedfordshire, UK*
15. *Institute of Microbiology and Infection, University of Birmingham, Edgbaston, Birmingham, UK*
16. *Institute of Infection and Immunity, St George's, University of London, London, UK*
17. *TiKa Diagnostics, London, UK*
18. *School of Pharmacy and Biomolecular Sciences, University of Brighton, Brighton, UK*
19. *Queen Victoria Hospital NHS Foundation Trust, East Grinstead, West Sussex, UK*
20. *Institute of Infection and Global Health, University of Liverpool, Liverpool, UK*
21. *Procarta Biosystems, Norwich, UK*
22. *Icelandic Medicines Agency, Reykjavik, Iceland*
23. *GlaxoSmithKline, Collegeville, Pennsylvania, PA, USA*
24. *MedImmune, Gaithersburg, MD, USA*
25. *Department of Medicine, Imperial College London, London, UK*
26. *Kaleido Biosciences, Cambridge, MA, USA*
27. *Plasgene, Edgbaston, Birmingham, UK*
28. *Pan-Provincial Vaccine Enterprise, Saskatoon, SK, Canada*
29. *Evotec, Manchester, UK*
30. *AstraZeneca, Boston, MA, USA*
31. *F2G, Manchester, UK*

2. The Third Annual Meeting of the European Virus Bioinformatics Center.

By Franziska Hufsky[1,2], Bashar Ibrahim[1,3], Sejal Modha[4], Martha R. J. Clokie[5], Stefanie Deinhardt-Emmer[1,6,7,8], Bas E. Dutilh[1,9,10], Samantha Lycett[11], Peter Simmonds[12], Volker Thiel[13,14], Aare Abroi[15], Evelien M. Adriaenssens[1,16], Marina Escalera-Zamudio[17], Jenna Nicole Kelly[13,14], Kevin Lamkiewicz [1,2], Lu Lu[18], Julian Susat[19], Thomas Sicheritz[20], David L. Robertson[1,4], and Manja Marz[1,2].

Viruses 11, 420 (2019) https://doi.org/10.3390/v11050420 Accessed October 2020

1. *European Virus Bioinformatics Center, 07743 Jena, Germany*
2. *RNA Bioinformatics and High-Throughput Analysis, Friedrich Schiller University Jena, 07743 Jena, Germany*
3. *Chair of Bioinformatics, Matthias-Schleiden-Institute, Friedrich Schiller University Jena, 07743 Jena, Germany*
4. *MRC-University of Glasgow Centre for Virus Research, Glasgow G61 1QH, UK*
5. *Department of Genetics and Genome Biology, University of Leicester, Leicester LE1 7RH, UK*
6. *Institute of Medical Microbiology, Jena University Hospital, Am Klinikum 1, D-07747 Jena, Germany*
7. *Section for Experimental Virology, Jena University Hospital, Hans-Knöll-Straße 2, D-07745 Jena, Germany*
8. *Center for Sepsis Control and Care, Jena University Hospital, D-07747 Jena, Germany*
9. *Theoretical Biology and Bioinformatics, Science4Life, Utrecht University, Padualaan 8, Utrecht 3584 CH, The Netherlands*
10. *Centre for Molecular and Biomolecular Informatics, Radboud Institute for Molecular Life Sciences, Radboud University Medical Centre, Geert Grooteplein 26, Nijmegen 6525 GA, The Netherlands*
11. *Infection & Immunity Division, Roslin Institute, University of Edinburgh, Midlothian EH25 9RG, UK*
12. *Nuffield Department of Medicine, University of Oxford, Peter Medawar Building, South Parks Road, Oxford OX1 3SY, UK*
13. *Institute of Virology and Immunology, 3012 Bern, Switzerland*
14. *Department of Infectious Diseases and Pathobiology, Vetsuisse Facility, University of Bern, 3012 Bern, Switzerland*

15. *University of Tartu, Institute of Technology, 50411 Tartu, Estonia*
16. *Quadram Institute Bioscience, Norwich Research Park, Norwich NR4 7UQ, UK*
17. *Department of Zoology, University of Oxford, Parks Rd, Oxford OX1 3PS, UK*
18. *Usher Institute of Population Health Sciences & Informatics, Ashworth Laboratories, Kings Buildings, University of Edinburgh, Charlotte Auerbach Road, Edinburgh EH9 3FL, UK*
19. *Institute of Clinical Molecular Biology, Kiel University, 24118 Kiel, Germany*
20. *Natural History Museum of Denmark, University of Copenhagen, DK-1123 Copenhagen, Denmark*