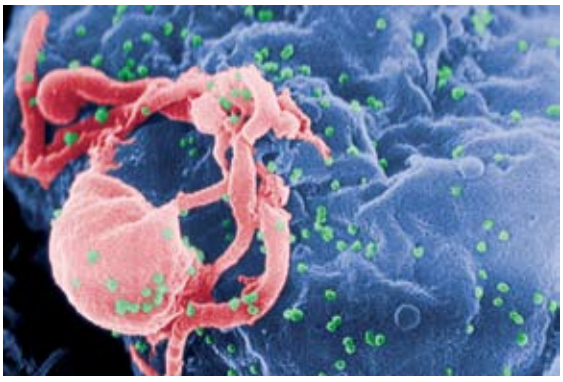
When the drugs don't work

Helen Fry

There are millions of bacteria everywhere – on your skin, in your guts, on your lunch. Bacteria have been troubling us for as long as we've been around, so we have put a lot of effort into finding ways to fight back at them.

We have developed thousands of different antibiotics since their discovery in 1928, to treat everything from boils to leprosy. However, bacteria are not the most abundant nor the most troublesome of microbes – this dubious title belongs to the virus. Viruses cause colds, flu, cold sores, AIDS, chicken pox, measles and a host of other common or serious diseases.

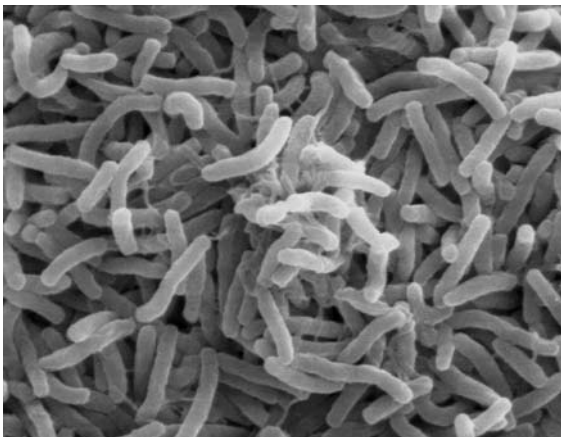
With the swine flu pandemic well under way, it has become even more obvious how defenceless we are against viral adversaries. To put this in context, if you have a bacterial chest infection there are over 100 antibiotics available to treat this. If you get influenza, there are only two. Of the hundreds of viruses that cause disease in humans, there are effective drugs against just six of them.



A human cell infected with HIV (shown in green) which causes AIDS.

Developing antivirals

So why are there so few decent drugs, when viruses are clearly such a pest? Firstly, in order to make a drug against a particular virus, it needs to be well understood, so that a specific part of its lifecycle can be targeted. However, researching viruses is difficult, as they will not simply grow in a dish like most bacteria, they have to be grown inside living cells, and they cannot be seen with a normal microscope.

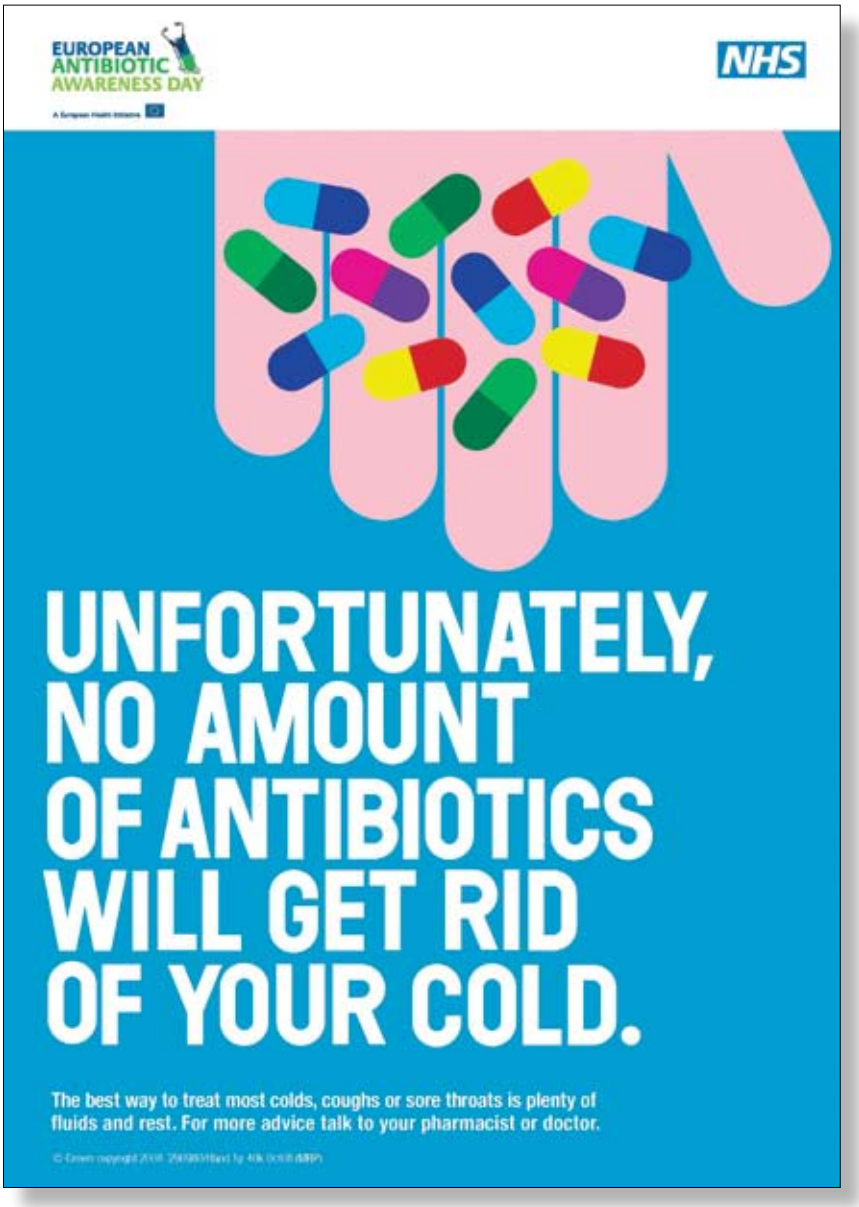


Cholera bacteria, seen using a scanning electron microscope.

They do not produce any toxins or compounds of their own which could be detected, so they are very hard to study well. On the other hand, they have very small genomes, which can be easily sequenced, so some information can be gained this way. The difficulty of studying viruses means that not a lot is known about them, making it hard to find ways of killing them.

Even when a virus is well studied, it is still difficult to make good antivirals. This is because viruses live and multiply inside host cells, so for a drug to be

Key words
bacteria
viruses
antibiotics
antivirals



This poster attempts to persuade patients that there is no point in asking for antibiotics to cure a viral infection.

effective it needs to enter the host cell to find the virus. However, if a drug enters a cell it is likely to harm it, so a drug has to target cells infected with virus. This is difficult to do, so antivirals are often quite toxic, generally killing off cells that are dividing rapidly, such as bone marrow and hair follicles. In fact, the side effects of some drugs can be worse than the disease itself.

There is also, of course, the issue of money. It takes millions of pounds and close to 15 years to make a drug and bring it to market, partly due to strict safety tests. Drugs are developed by companies, so have to be profitable. Most profit comes from drugs that have to be taken for a long time, so drugs for all kinds of infectious diseases are under-researched as they generally require a short course. The exception to this is HIV, which requires life-long drug therapy and is therefore more profitable and better researched. There are more agents to treat HIV than any other virus.

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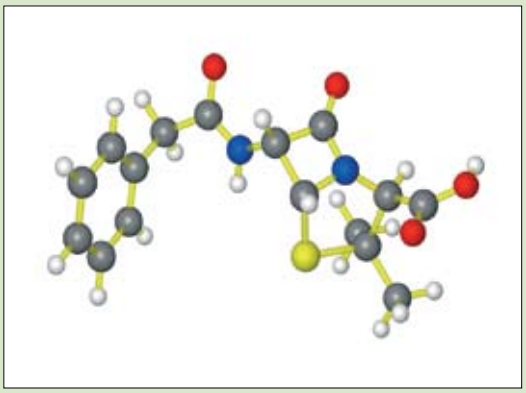
Antiretrovirals are drugs developed to fight retroviruses such as HIV, which causes AIDS.

Antibiotics

- The first antibiotic to be discovered was penicillin, by Alexander Fleming in 1928.
- Penicillin was first purified during the Second World War and made available for general use.
- Penicillin is a natural substance; most modern antibiotics are chemically-modified versions of natural substances.
- Antibiotics work either by killing bacterial cells (bactericides) or by preventing their growth (bacteriostatics).
- Bacterial cells are rather different from mammalian cells so antibiotics can attack bacteria without affecting the host mammal (such as a human).



The chemical structure of a penicillin molecule.
Key: grey = carbon; white = hydrogen; red = oxygen; blue = nitrogen; yellow = sulphur.