Understanding Antibiotics

Supplemental Information for Activities 50-52/ SALI

Prepared by A. L. Grauer, Ph.D.
Department of Anthropology
Loyola University Chicago

The information provided below is intended to supplement the exercises and activities in the textbook. While the book provides information and materials to assist students with the assigned tasks, there are likely to be questions that arise which require a greater understanding of antibiotics. This document is intended to provide instructors with basic information. I have incorporated the words and ideas of many authors here, at times directly using material found on the web. Reference citations for information provided below can be provided upon request.

What is an antibiotic?

Antibiotics are drugs that kill or inhibit infectious organisms. Originally they were organic compounds made from bacteria or molds, though today most are synthetic. Louis Pasteur is credited with discovering the "antibiotic effect" during the 19th century. However, most people associate the beginning of antibiotic therapy with Sir Alexander Fleming, who discovered penicillin in 1928. Difficulties in purification and other technical aspects of making antibiotics caused them to not come into routine usage until the 1950's. The post World War II generations have largely grown up with antibiotics.

Antibiotics work to kill bacteria. Bacteria are single-cell organisms. If bacteria make it past our immune systems and start reproducing inside our bodies, they cause disease. We want to kill the bacteria to eliminate the disease.

Certain bacteria produce chemicals that damage or disable parts of our bodies. In an ear infection, for example, bacteria have gotten into the inner ear. The body is working to fight the bacteria, but the immune system's natural processes produce inflammation. Inflammation in your ear is painful. So you take an antibiotic to kill the bacteria and eliminate the inflammation.

Antibiotics do not work on viruses because viruses are not alive. A bacterium is a living, reproducing lifeform. A virus is just a piece of DNA (or RNA). A virus injects its DNA into a living cell and has that cell reproduce more of the viral DNA. With a virus there is nothing to "kill," so antibiotics don't work on it.

Is penicillin the only antibiotic?

Nope.

Some 150 antibiotics are used in medicine today. However, several hundreds of compounds with antibiotic activity have been isolated from microorganisms over the years, but only a few of them are clinically useful. The reason for this is that only compounds with **selective toxicity** can be used clinically - they must be highly effective against a microorganism but have minimal toxicity to humans. In practice, this is expressed in terms of the **therapeutic** index - the ratio of the toxic dose to the therapeutic dose. The larger the index, the better is its therapeutic value.

Where do antibiotics come from?

There are 3 sources of antibiotics:

- **Natural products.** A number of natural products, penicillin for example, have been discovered that are antibiotics suitable for therapy. They were originally discovered as secretions of fungi or soil bacteria. Soils are complex ecosystems, and it is not surprising that its inhabitants have evolved chemical defenses against each other.
- **Semi-synthetic products.** These are natural products that have been chemically modified in the laboratory (and pharmaceutical facility) to
    - improve the efficacy of the natural product
    - reduce its side effects
    - circumvent developing resistance by the targeted bacteria
    - expand the range of bacteria that can be treated with it
- **Completely synthetic products.** The sulfa drugs are examples

How do antibiotics work?

An antibiotic is a **selective poison**. It has been chosen so that it will kill the desired bacteria, but not the cells in your body. Each different type of antibiotic affects different bacteria in different ways. For example, an antibiotic might inhibit a bacterium's ability to turn glucose into energy, or its ability to construct its cell wall. When this happens, the bacterium dies instead of reproducing. At the same time, the antibiotic acts only on the bacterium's cell-wall-building mechanism, not on a normal cell's.

Antibiotics are compounds that either:

1. kill bacteria directly (**bacteriocidal**)
2. hamper their ability to grow and reproduce (**bacteriostatic**)

When you are fighting off a bacterial infection, your immune system can be overwhelmed by the invading bugs. Antibiotics are thrown into the fray to mount a defense against the invaders until your immune system can recover and finish off the remaining bacteria.

How do antibiotics stave off bacterial growth?

Antibiotics stop or interfere with a number of everyday cellular processes that bacteria rely on for growth and survival, such as:

- crippling production of the bacterial **cell wall** that protects the cell from the external environment
- interfering with **protein synthesis** by binding to the machinery that builds proteins, amino acid by amino acid
- wreaking havoc with metabolic processes, such as the synthesis of **folic acid**, a B vitamin that bacteria need to thrive
- blocking synthesis of **DNA** and **RNA**

Different antibiotics destroy bacteria in different ways. Some short-circuit the processes by which bacteria receive energy. Others disturb the structure of the bacterial cell wall. Still others interfere with the production of essential proteins.

Antibiotic	**Producer organism**	**Activity**	**Site or mode of action**
Penicillin	*Penicillium chrysogenum*	Gram-positive bacteria	Wall synthesis
Cephalosporin	*Cephalosporium acremonium*	Broad spectrum	Wall synthesis
Griseofulvin	*Penicillium griseofulvum*	Dermatophytic fungi	Microtubules
Bacitracin	*Bacillus subtilis*	Gram-positive bacteria	Wall synthesis
Polymyxin B	*Bacillus polymyxa*	Gram-negative bacteria	Cell membrane
Amphotericin B	*Streptomyces nodosus*	Fungi	Cell membrane
Erythromycin	*Streptomyces erythreus*	Gram-positive bacteria	Protein synthesis
Neomycin	*Streptomyces fradiae*	Broa d spectrum	Protein synthesis
Streptomycin	*Streptomyces griseus*	Gram-negative bacteria	Protein synthesis
Tetracycline	*Streptomyces rimosus*	Broad spectrum	Protein synthesis
Vancomycin	*Streptomyces orientalis*	Gram-positive bacteria	Protein synthesis
Rifamycin	*Streptomyces mediterranei*	Tuberculosis	Protein synthesis
Gentamicin	*Micromonospora purpurea*	Broad spectrum	Protein synthesis

Can antibiotics be harmful?

Yup.

Unnecessary antibiotics can be harmful. Antibiotics only fight bacterial infections. They do nothing to help viral illnesses like colds or influenza (flu). If you take an antibiotic when it is not necessary, such as for a cold, you increase the risk of developing an infection caused by antibiotic-resistant bacteria.

The basic problem with antibiotics is summed up in the etymology of the word itself - "antibiotic" means "anti-life." The purpose of antibiotics is to kill bacteria, but as well as destroying the pathogenic bacteria they also kill off the beneficial strains of bacteria within the body. The body has about 400 different types of these beneficial strains, which are found mainly in the digestive tract. These friendly bacteria act as the first line of defense against bacteria, viruses, fungi, and other disease producing microbes. They can synthesize B vitamins and aid in the digestion of insoluble fibre to supply us with extra nutrients. Without these friendly bacteria we find a predominance of unfriendly bacteria in the digestive tract.

With this unnatural imbalance of bacteria, the body can suffer many symptoms. These include fatigue, gastrointestinal upsets, Candida, severe skin rashes, kidney and renal infections, diarrhoea, colitis, hearing loss and many more.

Do antibiotics ALWAYS work?

No. As seen on page C-104 of the SALI textbook, certain antibiotics are effective only on certain bacteria. Also, antibiotics can become ineffective over time because bacteria come up with various ways of countering these actions, such as:

- **Preventing the antibiotic from getting to its target**
  Bacteria do this by changing the **permeability** of their membranes or by reducing the number of channels available for drugs to diffuse through. Another strategy is to create the molecular equivalent of a club bouncer to escort antibiotics out the door if it gets in. Some bacteria use energy from ATP to power **pumps** that shoot antibiotics out of the cell.
- **Changing the target**
  Many antibiotics work by sticking to their target and preventing it from interacting with other molecules inside the cell. Some bacteria respond by changing the structure of the target (or even replacing it within another molecule altogether) so that the antibiotic can no longer recognize it or bind to it.
- **Destroying the antibiotic**
  This tactic takes interfering with the antibiotic to an extreme. Rather than simply pushing the drug aside or setting up molecular blockades, some bacteria survive by neutralizing their enemy directly. For example, some kinds of bacteria produce enzymes called **beta-lactamases** that chew up penicillin.

What is all the hullabaloo about resistance?

And although new antibiotics once seemed to keep a step ahead of resistant bacteria, that's not happening any more -- resistance often occurs faster than new antibiotics can be developed. Today, almost every known disease-causing bacterium is resistant to at least one antibiotic.

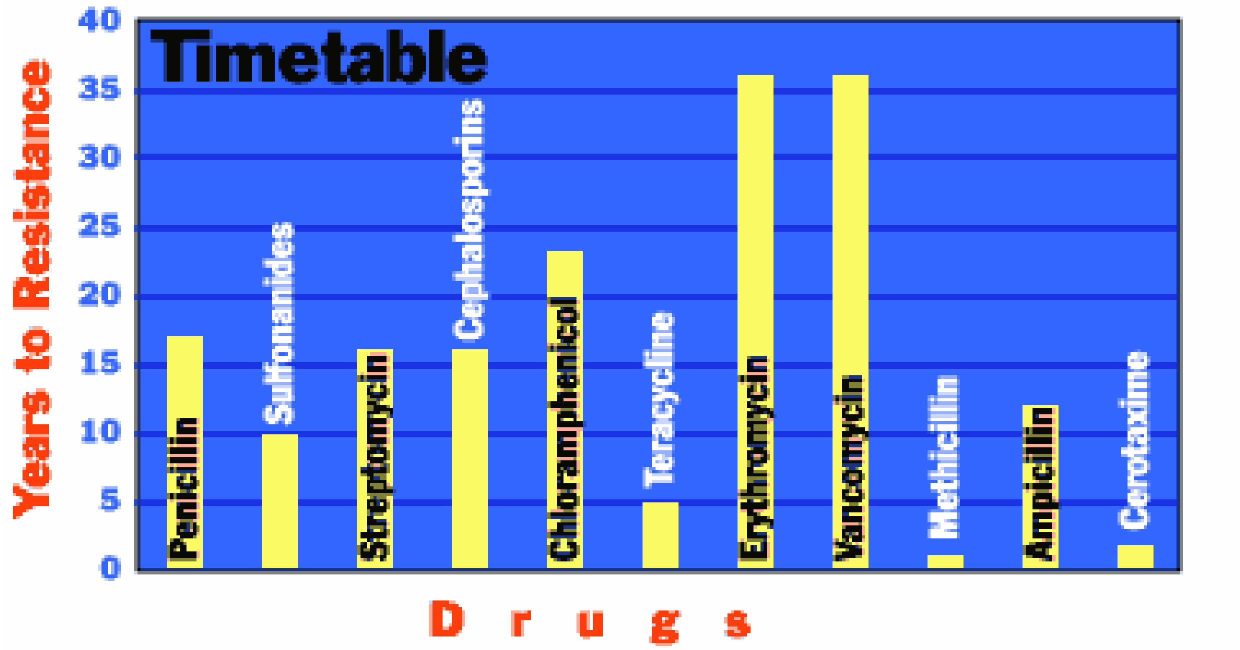
How do bacteria pick up these drug-fighting habits? In some cases, they don't. Some bacteria are simply making use of their own inherent capabilities. Bacteria have two mechanisms for gaining these resistance tricks -- mutation and gene-sharing. A "point mutation" is a change in one base in the DNA molecule. From the bacterium's standpoint, a point mutation is a roll of the dice -- most mutations are harmful; only rarely do these changes give a bug a leg up on the competition.

However, there are many bacteria that didn't start out resistant to a particular antibiotic. Bacteria can **acquire resistance** by getting a copy of a gene encoding an altered protein or an enzyme like beta lactamase from other bacteria, even from those of a different species. There are a number of ways to get a resistance gene:

- During **transformation** - in this process, akin to bacterial sex, microbes can join together and transfer DNA to each other.
- On a small, circular, extrachromosomal piece of DNA, called a **plasmid** - one plasmid can encode resistance to many different antibiotics.
- Through a **transposon** - transposons are "jumping genes," small pieces of DNA that can hop from DNA molecule to DNA molecule. Once in a chromosome or plasmid, they can be integrated stably.
- By scavenging DNA remnants from degraded, dead bacteria.

Unfortunately, if a bacterium gets a resistance gene stuck into its chromosomal DNA or picks one up in a free-floating plasmid, all of its progeny will inherit the gene and the resistance it confers. Why do resistance genes persist and spread throughout bacterial populations? It's basically just Darwin's idea of the **survival of the fittest**, reduced to a microscopic level -- bacteria with these genes survive and outgrow susceptible variants.. The old antibiotic you have may not work at all against the infection you have, so it's best to seek a doctor's advice before trying to treat yourself.

As a result of the overuse of antibiotics resulting in production of these "super germs", over 15,000 people per year die of hospital-caused infections. According to Dr. Robert Mendelsohn in his book, Confessions of a Medical Heretic, your chances of getting an infection while hospitalized are 1 in 20.



http://whyfiles.org/shorties/090antibio_resist/