

# Explore an Issue: Antibiotic-Resistant Bacteria

## Penicillin

The antibiotic penicillin was discovered by Alexander Fleming in 1929. It was once thought of as a “magic bullet,” saving millions of lives. How does it work? Bacteria are constantly rebuilding their cell walls (known as *peptidoglycan synthesis*). An enzyme normally catalyzes the formation of cross-links between the cell wall strands, which is how they protect themselves and maintain their structure. Penicillin works by inhibiting this enzyme, leaving the bacterial cell wall vulnerable and weak, thus killing the bacteria cell.

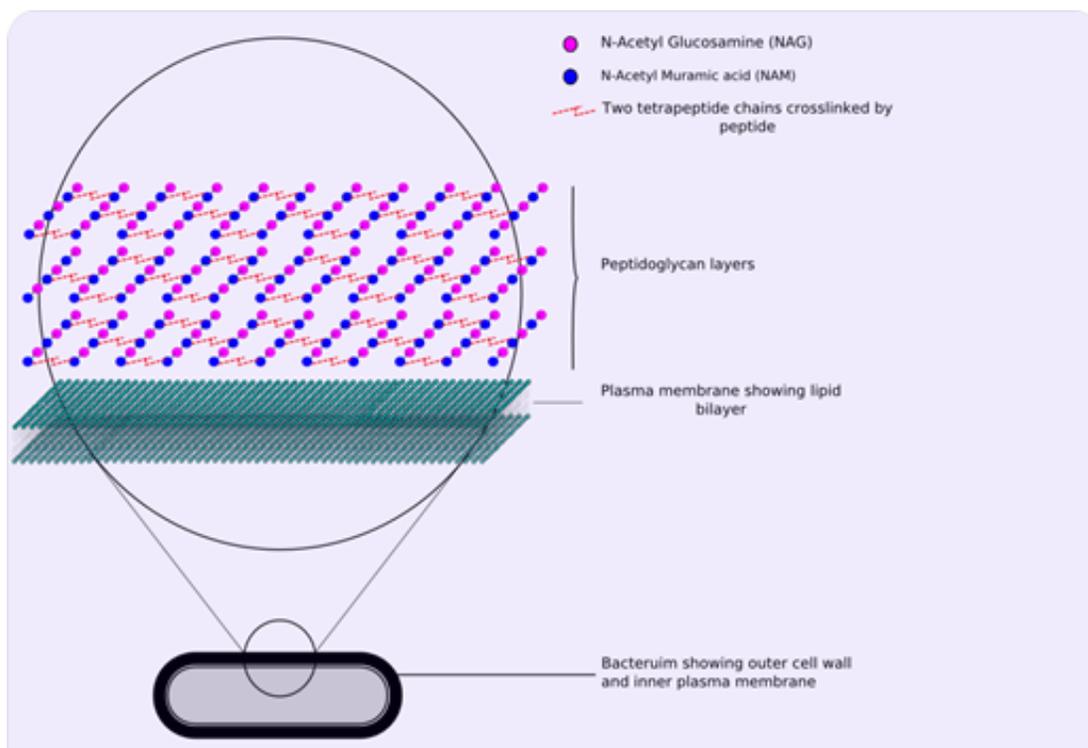
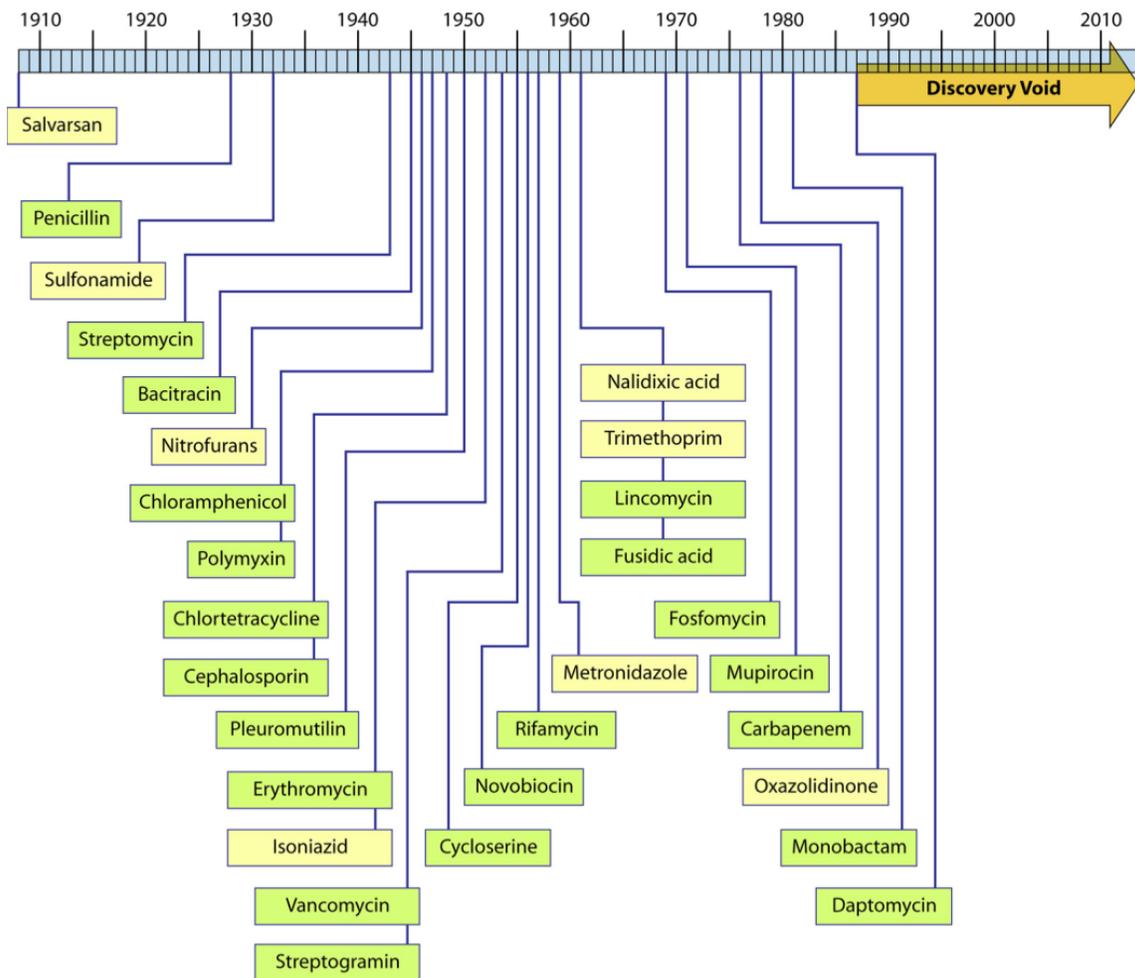


Figure 1 – Simplified schematic of cell wall (showing plasma membrane, teichoic acids not shown)

## Antibiotics

For the past 70 years antibiotics have been successfully used to treat patients with bacterial and infectious diseases. Penicillin directly attacks the bacterial cell wall, while other antibiotics, like erythromycin, block the bacteria's growth or reproduction. While antibiotics have been successful in treating bacterial infections, they are not against viral infections like the flu. Over time, however, we have seen the emergence of many infectious organisms adapting to the drugs designed to kill them, making the products less effective. Unfortunately, after years of success, the pharmaceutical industry is now producing too few antibiotics to replace those that are no longer effective for many types of infection.



## How does Resistance Develop?

Bacteria divide many times a day. Some bacterial cells develop a mutation (change to a gene). While the antibiotics may kill or inhibit the growth of susceptible bacteria, some of these mutations may offer resistance to antibiotics. Bacteria may acquire resistance

from other bacteria by transferring small pieces of DNA called plasmids. Bacteria can resist the effects of antibiotics in several ways. Some bacteria develop the ability to neutralize the antibiotic before it can harm them; others can change the antibiotic attack site so it cannot affect the function of the bacteria; and still others can pump the antibiotic out of the cell or prevent the antibiotic from getting into it.

### Developing Antibiotics Less Susceptible to Antibiotic Resistance

An increasing knowledge of the mechanisms responsible for bacterial resistance to antibiotics is leading research in promising new directions. Several strategies are listed below:



- *Beta-lactamase inhibitors*: Penicillin and similar antibiotics normally act on bacterial enzymes. Beta-lactamase is a bacterial enzyme that breaks down penicillin-type antibiotics and renders them inactive. Therefore, drugs that inhibit this enzyme could help restore antibiotic potency.
- *Anti-infection drugs*: A key to developing antibiotics less susceptible to antibiotic resistance is to understand the survival strategies of bacteria. New technologies can find bacterial genes that switch on at crucial times during infection and ensure the “success” of that infection. For example, scientists have learned that the genes responsible for the virulence of *Staphylococcus aureus* don’t switch on immediately upon infection, when the host’s immune system could eliminate low numbers of bacteria. Instead, the bacteria monitor their own number and density, waiting until they reach a critical mass before switching on their virulence genes. The products (i.e., proteins) of such virulence genes are ideal targets for new anti-infection drugs.
- *Antimicrobial peptides*: Many organisms naturally make and use antimicrobial peptides as part of their normal immune systems. These short proteins can physically damage microbial plasma membranes, much like a needle popping a balloon. Scientists are now working on synthesizing molecules that mimic the activity of the natural peptides.
- *Plasmid expulsion*: Small circular pieces of DNA are called plasmids. Bacteria frequently acquire antibiotic resistance by ingesting plasmids, which contain proteins that prevent antibiotic effectiveness. Researchers are evolving mechanisms to expel the resistance-carrying plasmids from bacteria, thereby re-sensitizing the bacteria to an antibiotic.

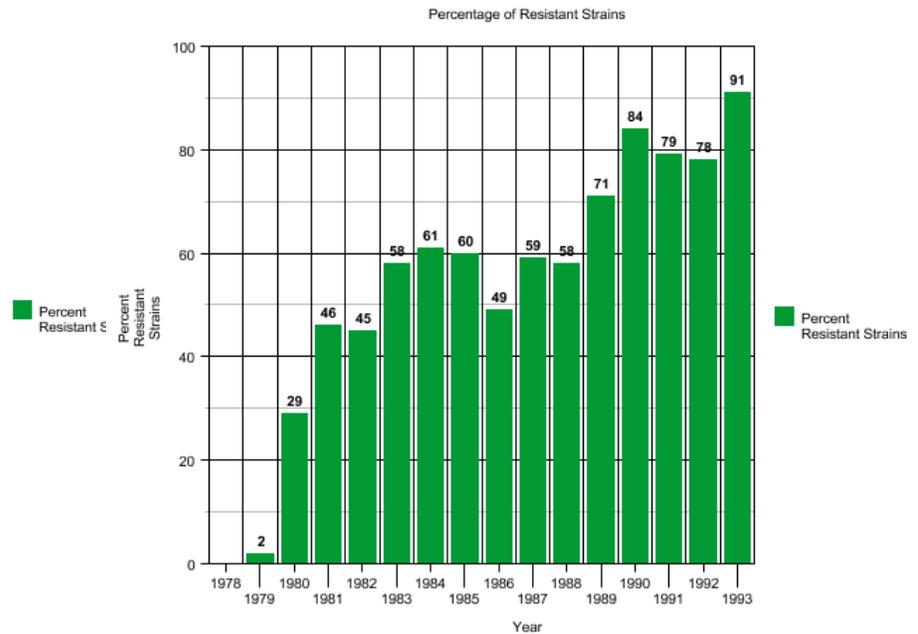
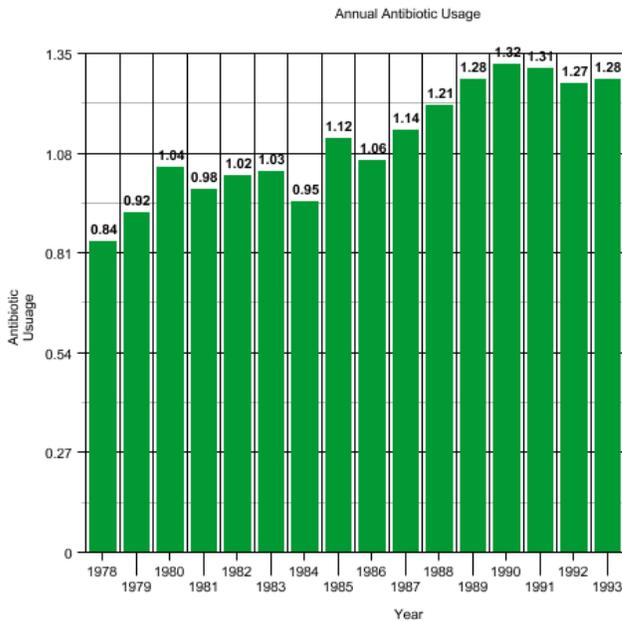
- *Bacterial glycomics*: Nearly all membrane proteins as well as numerous intracellular proteins are modified by the presence of complex saccharides (glycans). Because glycans play such diverse roles in bacterial physiology, the field of bacterial glycomics is indispensable to understanding bacterial pathogenesis, metabolism and cell communities. Advancements in bacterial glycomics have resulted from the improvements in analytical methodologies and the development of new approaches for glycan isolation, characterization and synthesis. Research in bacterial glycomics could lead to the development of innovative drugs.
- *Cell wall teichoic acid*: The peptidoglycan layers of many gram-positive bacteria are tightly packed with glycopolymers called wall teichoic acids (WTAs). These polymers play central roles in cell shape determination, regulation of cell division, and other essential aspects of gram-positive bacterial physiology. Also, WTAs are important in pathogenesis and play key roles in antibiotic resistance. Due to their significance in pathogenesis, WTAs are potential targets for new therapeutics to overcome resistant bacterial infections.

## Questions

1. What is an antibiotic? Define this term and list three examples.
2. How does penicillin work? Is this the only method for eliminating bacteria?
3. The figure on page 2 points to an apparent void in antibiotic development. Why do you think this is?
4. How does antibiotic resistance appear to develop within a bacterial population?
5. Why should I be worried about antibiotic resistance?
6. Use the Internet, your textbook, this article or other sources of information to divide the following list of diseases into two columns under the appropriate headings below: strep throat, common colds, urinary tract infections, chickenpox, anthrax, mumps, tuberculosis, AIDS, syphilis, botulism, whooping cough, measles, foot and mouth disease, influenza.

Effectively treated with antibiotics	Unaffected by antibiotic treatment
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7. Interpreting data: The graphs below show actual data collected from a community in Finland from 1978-1993. Studies were conducted to determine the annual amount of antibiotics used in this community. Bacterial samples of *Moraxella catarrhalis* were also collected from young children with middle ear infections. Bacterial strains were then examined to see if they were susceptible or resistant to these antibiotics. The graphs below show annual antibiotic usage, and the percentage (between 0 - 100%) of bacterial strains that were found to be resistant.



- a. From these graphs, do you think antibiotic usage and the percentage of strains resistant to antibiotics are related?