

Antibiotics Attack



What are antibiotics?

Antibiotics are any natural substances secreted by one microorganism to ward off other microorganisms. Bacteria or molds might secrete chemicals that interfere with attacking microorganism to harm, kill, or slow them down. In the micro world, antibiotics are ammunition.

Antibiotic is a substance or compound that kills bacteria or inhibits their growth. Antibiotics belong to the broader group of antimicrobial compounds, used to treat infections caused by microorganisms, including fungi and protozoa.

Antibiotic age began in the late 1920s when Alexander Fleming saw that the mold, *Penicillium*, was inhibiting bacterial growth and when René Dubos purified gramicidin as an antibiotic.

Source of Antibiotics:

The antibiotics we take are primarily produced by bacterial microorganisms.

With advances in medicinal chemistry, most antibiotics are now semisynthetic. Some antibiotics are still produced and isolated from living organisms, such as the aminoglycosides, and others have been created through purely synthetic means: the sulfonamides, the quinolones, and the oxazolidinones.

In addition to this origin-based classification into natural, semisynthetic, and synthetic, antibiotics may be divided into two broad groups according to their effect on microorganisms:

- ▶ Those that kill bacteria are bactericidal agents
- ▶ Those that only impair bacterial growth are known as bacteriostatic agents.

Molds such as *Penicillium Chrysogenum* and soil organisms such as *Bacillus brevis* were grown to collect the first crude samples of antibiotics and are still grown by commercial companies to produce antibiotics.

The challenge that early researchers faced in antibiotic production was purification from other supernatant proteins. As cells release antibiotics, they undergo other cellular functions, expelling wastes, taking in nutrients, and undergoing cell death, all of which leave debris and result in impure samples of antibiotics. René Dubos was victorious in isolating gramicidin, although the process was complex.

Significance

Antibiotics have acted as miracle drugs, from first curing wounded soldiers suffering from infectious disease in World War II to helping people in Singapore with typhus fever.

The significance of antibiotics is immeasurable considering their effectiveness against harmful gram-positive and gram-negative bacteria. Penicillin and gramicillin neither had been discovered nor isolated before World War II, at least 300,000 more people would have died. If we didn't have antibiotics today, many more men, women, and children would be very sick from bacterial infections.



Specificity

Antibiotics, such as penicillin, streptomycin, and ampicillin, attack bacterial processes of growth and reproduction such as DNA replication, DNA transcription, RNA translation, ribosomal protein synthesis, and peptidoglycan cross-linking.

The reason that antibiotics are not effective against viruses is that viruses are not living; viruses can reproduce only when they are inside other living cells. Antibiotics aim to interfere with cellular functions, which viruses lack. Another aspect of antibiotic specificity has to do with the fact that some bacterial infections can be only treated by certain antibiotics.

Pathways of Attack

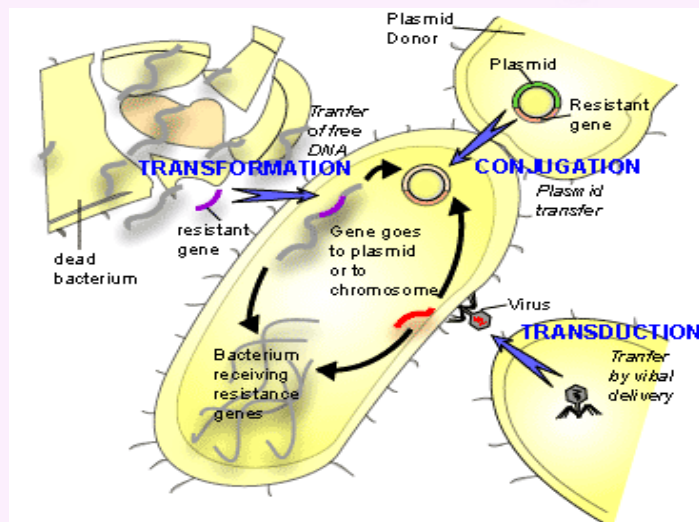
The basic theory of antibiotic attack is to target microbial functions and structures that are different from the host.

Antibiotics aim to interfere with the normal cellular functions of bacteria and fungi so as to prevent further infection of the host.

Those regular functions include cell wall biosynthesis, membrane function, DNA replication, DNA transcription, and RNA translation or protein synthesis.

Simply, antimicrobial treatments look to stop infectious agents by throwing sticks in the spokes of their cellular wheels.

In the following few frames, you will see the mechanisms of attack of some common antibiotics.



Antibiotics Resistance:

As we use antibiotics and other antibacterial agents such as antibacterial lotions, soaps, and sprays to kill bacteria, we are pruning the species pool for the stronger bacteria. Since antibacterial agents do not kill 100% of bacteria, they leave a few of the bacteria that are resistant. These bacteria continue to grow, and in fact, they flourish due to an increase in nutrients that their weaker counterparts would have competed for.

The primary cause of antibiotic resistance is antibiotic use both within medicine and veterinary medicine.

The greater the duration of exposure the greater the risk of the development of resistance irrespective of the severity of the need for antibiotics.

Besides antibacterial agent use, over-prescription of antibiotics weeds out weak bacteria and leaves resistant strains. However, more commonly, bacteria that are targeted by antibiotics develop mechanisms to fight back against antibiotics. Bacteria become antibiotic-resistant by mutating existing genes or acquiring new ones that can encode for efflux pumps or deactivating enzymes, for example.

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Bacteria fight back

Once antibiotics are administered, bacteria do not just accept the drugs and die. Many bacteria actively resist antibiotics by producing enzymes that bind to antibiotics, expel antibiotics, or even change target sites. These activities are coded for by resistance genes (R genes) located on transferable transposons (bits of DNA that can jump) or plasmids.

Target site alteration:

While R genes code for new proteins to fight antibiotics, they can also code for the alteration or mutation of existing target sites. In order for an antibiotic to effectively inhibit a cellular mechanism, the mechanism must be identifiable.

An interesting example is the group of macrolide antibiotics, including erythromycin, lincomycin, and clindamycin. Bacteria resistant to these macrolides produce methylase, which causes the methylation of the 23S ribosomal RNA in gram-positive bacteria. By methylating the ribosomal RNA, the bacteria make the 50S ribosomal subunit resistant to binding by the macrolide antibiotics. The drugs are no longer able to interfere with ribosomal RNA processes.



Magna-Biotic (Clavulanic acid + Amoxicillin)

Magna-Biotic is an antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the (beta)-lactamase inhibitor, clavulanate potassium (the potassium salt of clavulanic acid). Amoxicillin is an analog of ampicillin, derived from the basic penicillin nucleus, 6-aminopenicillanic acid.

Clavulanic acid is produced by the fermentation of *Streptomyces clavuligerus*. It is a β -lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of β -lactamases by blocking the active sites of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-mediated β -lactamases frequently responsible for transferred drug resistance to penicillins and cephalosporins.

Clinical Pharmacology

Amoxicillin and clavulanate potassium are well absorbed from the gastrointestinal tract after oral administration of Magna-Biotic. Dosing in the fasted or fed state has minimal effect on the pharmacokinetics of amoxicillin.

While Magna-Biotic can be given without regard to meals, absorption of clavulanate potassium when taken with food is greater relative to the fasted state. In 1 study, the relative bioavailability of clavulanate was reduced when Magna-Biotic was dosed at 30 and 150 minutes after the start of a high-fat breakfast. The safety and efficacy of Magna-Biotic have been established in clinical trials where Magna-Biotic was taken without regard to meals.