

Antibiotics and Antimicrobial Resistance

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Annotation. Antimicrobials, such as antibiotics, are substances used to kill microorganisms or to stop them from growing and multiplying. They are commonly used in human and veterinary medicine to treat a wide variety of infectious diseases. Antimicrobial resistance (AMR) refers to the ability of microorganisms to withstand antimicrobial treatments. The overuse or misuse of antibiotics has been linked to the emergence and spread of microorganisms which are resistant to them, rendering treatment ineffective and posing a serious risk to public health. A well known example of a bacterium that has acquired resistance to multiple antibiotics is *Meticillin-resistant Staphylococcus aureus (MRSA)*.

Keywords. antibiotic, microorganisms, protein synthesis, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Salmonella typhi*, *Shigella*

Since the initiation of widespread use of penicillin during World War II, antibiotics have significantly prevented the spread of infections. Antibiotics are natural products of fungi, bacteria, and related microorganisms that affect the growth of other microorganisms. Some antibacterial antibiotics are bactericidal (kill the microorganism), whereas others are bacteriostatic (inhibit growth until the microorganism is destroyed by the individual's own protective mechanisms). The mechanisms of action of most antibiotics are inhibition of the function or production of the cell wall/membrane, prevention of protein synthesis, blockage of DNA replication or interference with folic acid metabolism. Because viruses use the enzymes of the host's cells, there has been far less success in developing antiviral antibiotics.

Many other infections considered routine and easily treatable with penicillin are now resistant to almost all currently available antibiotics, including methicillin-resistant *Staphylococcus aureus* and *Streptococcus pneumoniae*, which causes pneumonia, meningitis, and acute otitis media (middle ear infection). Additionally, there are major increases in resistant *Salmonella typhi* (typhoid fever), *Shigella* (bloody diarrhea), *Acinetobacter* (pneumonia), *Campylobacter* (bloody diarrhea), *Enterococcus* (sepsis, wound infection, urinary tract infection), *Pseudomonas aeruginosa* (burn infection, sepsis), and *M. tuberculosis* (tuberculosis). Antibiotic-resistant fungi (e.g., fluconazole-resistant *C. albicans*) have evolved and malarial parasites have recently developed broad drug resistance, including to chloroquine—the previous mainstay of the preventive and therapeutic arsenal of antimalarial drugs.

Microbes can use various mechanisms to resist or inactivate antibiotics. The type of antibiotic affected by these resistance mechanisms is primarily determined by how the drug enters the microorganism or its mechanisms of action. For example, an enzyme called beta-lactamase, which is produced by most *S. aureus* species, prevents the action of penicillin on the microorganismal cell wall.



Other antibiotics, such as fluoroquinolones and macrolides, are rendered ineffective by multiple resistance mechanisms.

Why have multiple antibiotic-resistant microorganisms emerged? Lack of compliance in completing the therapeutic regimen with antibiotics allows the selective resurgence of microorganisms that are more relatively resistant to the antibiotic. Overuse of antibiotics can lead to the destruction of the normal microbiome, allowing the selective overgrowth of antibiotic-resistant strains or pathogens that had previously been controlled. There also is concern that overuse of antibiotics to promote growth in animals used for food may result in ingestion of antibiotic-containing meat.

Vaccines and Protection Against Infection.

Active Immunization Recovery from an infection generally results in the strongest resistance to a future infection with the same microbe. Vaccines are biologic preparations of antigens that, when administered, stimulate production of protective antibodies or cellular immunity against a specific pathogen without causing potentially life-threatening disease. The purpose of vaccination is to induce long-lasting protective immune responses under safe conditions. The primary immune response from vaccination is generally short lived; therefore booster injections are used to push the immune response through multiple secondary responses that result in large numbers of memory cells and sustained protective levels of antibody or T cells, or both.

Passive Immunotherapy

Passive immunotherapy is a form of countermeasure against pathogens in which preformed antibodies are given to the individual. Passive immunotherapy with human immunoglobulin has been approved for several infections, including hepatitis A and hepatitis B. Treatment of potential rabies infection after a bite combines passive and active immunization. Individuals who have been bitten receive a one-time injection with human rabies immunoglobulin, or, more recently, with monoclonal antibody to slow further viral proliferation, followed by multiple injections with a killed viral vaccine to induce greater protective immunity. More specific therapy with monoclonal antibodies is being evaluated for other infectious diseases. A monoclonal antibody against RSV has been approved for therapy, and recently an experimental monoclonal antibody preparation is available for the treatment of Ebola virus infection. A vaccine also is available to control outbreaks of Ebola virus infections. In the past, vaccines and therapeutic antibodies were developed only for the most deadly pathogens. With the increase in antibiotic-resistant microorganisms, the development and widespread use of new vaccines and antibodies against these microorganisms must be considered.

In conclusion, antimicrobial resistance (AMR) - the ability of microbes to resist antimicrobials – remains a key threat to population health and economies globally. AMR strains health systems, overburdens healthcare resources and inflates health expenditure while exerting tremendous pressure on the economy.

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