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Antibiotics

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I. INTRODUCTION

Antibiotics are chemical substances produced by living organisms (generally microorganisms) or derivatives of these substances that suppress the growth of or kill other microorganisms in low concentrations. Nowadays the term antibiotics is extended to synthetic antibacterial agents such as the sulfonamides or quinolones.

Antibiotics are very common substances in the microbial world, but it was not until the 1940s that their true potential was acknowledged and large-scale production was developed. Penicillin was the first antibiotic, discovered by Alexander Fleming in 1928. The first sulfonamide drug, tested in 1932 by Gerhard Domagk and patented in 1935 by Bayer (Germany), was a red azo dye called prontosil. In 1939 René Dubos obtained tyrothricin, a mixture of two peptide antibiotics, gramicidin and tyrocidine. That same year penicillin was isolated by Ernst Chain, Howard Florey, and others. In 1944 Selman Waksman and Albert Schatz isolated streptomycin from *Streptomyces griseus*. The Nobel prizes for medicine were awarded to Domagk (1939); Fleming, Chain, and Florey (1945); and Waksman (1952). Most classes of antibiotics were discovered in the 1940s, 1950s, and 1960s.

The large number of antibiotics currently available can be classified in a variety of ways, e.g., by their chemical structure, their microbial origin, or their mode of action. They are also designated by their effective range: broad-spectrum antibiotics such as tetracyclines, medium-spectrum such as penicillins, and narrow-spectrum such as polymyxins. The most common classification is based on chemical structure and mechanism of action, as follows (1):

1. *Bactericidal cell wall agents* inhibit synthesis of bacterial cell walls (penicillin, cephalosporins, cycloserine, vancomycin, bacitracin, and the imidazole antifungal agents miconazole, ketoconazole, and clotrimazole).
2. *Bactericidal cell membrane agents* act directly on the cell membrane of microorganisms, affecting membrane permeability and leading to leakage of intracellular compounds (polymyxin, colistimethate, and the polyene antifungal agents nystatin and amphotericin B).
3. *Bacterial protein synthesis inhibitors* include
   a. Bactericidal agents that alter protein synthesis, leading to cell death (the aminoglycosides streptomycin, neomycin, kanamycin, gentamicin, tobramycin, amikacin, and kasugamycin).
   b. Bacteriostatic agents that inhibit protein synthesis (chloamphenicol, the tetracyclines, and the macrolides).
4. Bactericidal agents that affect nucleic acid metabolism (rifamycins and quinolones).
5. Bacteriostatic antimetabolites, which block metabolic steps essential to microorganisms (trimetoprim and the sulfonamides).