

ANTI-INFECTIVE THERAPY

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PREFACE

This book fills an urgent need for a comprehensive, well-referenced, up-to-date book on antibacterial agents, antivirals, and antifungal agents. Although a number of sources for such drugs are available ranging from tabular summaries of information to detailed treatises of basic pharmacology, a book by infectious disease physicians emphasizing thorough discussion of the commonly and not so commonly used drugs is lacking.

Anti-infective Therapy is organized by drugs or groups of drugs. There is complete coverage of currently licensed (U.S.), soon to be licensed, and promising anti-infective agents written from the point of view of the practicing infectious diseases consultant. Experts in their fields will find the information contained here essential to their practice. The treatment of each agent is up-to-date, comprehensive, and extensively referenced. In addition, chapters are devoted to such topics as principles of anti-infective therapy, pharmacokinetics, the use and abuse of antibiotics, and cost issues related to antibiotic therapy. It is not a "cookbook" manual. The book is scholarly yet highly practical because of the physician authorship and the liberal use of tables and charts to help the reader find key or often used information concerning each of the major drugs. Specific tables on the pharmacology of anti-infective agents should prove especially useful. A complete list of tables and their location is included in the front matter, and a special index has been prepared for easy access to information on specific clinical problems. This work, a reproduction of the section on anti-infective therapy from the complete infectious disease textbook *Principles and Practices of Infectious Diseases*, will be helpful to internists, family practitioners, pediatricians, surgeons, obstetrician-gynecologists, and pharmacists.

We are grateful to our contributors for their skillful handling of the material, to our secretaries for their careful work, to our wives and children for their continued support, and to Andrew Ford and others at John Wiley & Sons for their support and encouragement in this project.

Gerald L. Mandell
R. Gordon Douglas, Jr.
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PRINCIPLES OF ANTI-INFECTIVE THERAPY

ROBERT C. MOELLERING, JR.

Although the discovery of effective agents to prevent and treat infection caused by bacteria and other pathogenic microorganisms is one of the most important developments of modern medicine, the use of such agents has not been limited to the present era. Substances with anti-infective potential have been applied medically for thousands of years. Indeed, more than 2500 years ago the Chinese were aware of the therapeutic properties of moldy soybean curd applied to carbuncles, boils, and other infections (1), and the ancient Greek physicians, including Hypocrates, routinely used substances with antimicrobial activity including wine, myrrh, and inorganic salts in their treatment of wounds (2). Until the discovery of the microbiologic basis of infections in the nineteenth century, however, the therapy for infections remained strictly empiric. Heavy metals such as arsenic and bismuth were found to be useful against a number of infections, including syphilis, in the early 1900s; but the modern era of chemotherapy did not really begin until the discovery and initial clinical use of the sulfonamides in 1936 (1). This was followed in the 1940s by the discovery of the therapeutic value of penicillin and streptomycin, and by 1950 the "golden age" of antimicrobial chemotherapy was well underway.

It is the result of the relatively recent work in this area since 1936 that forms the basis for this and each of the succeeding chapters on anti-infective therapy. The major emphasis in this chapter is on antibacterial agents because there are more data available on these drugs. However, many of the principles to be discussed can also be applied to the use of antifungal, antiviral, and, to some extent, antiparasitic drugs.

CHOICE OF THE PROPER ANTIMICROBIAL AGENT

In choosing the appropriate antimicrobial agent for the therapy of a given infection, a number of important factors must be considered. First, the identity of the infecting organism must be known or, at the very least, it must be possible to arrive at a reasonable statistical guess as to its identity, based on clinical information. Second, we must have as accurate information as possible about the antimicrobial susceptibility (or potential susceptibility) of the infecting organism. Finally, a series of so-called host factors must be taken into consideration to arrive at the optimal choice of antimicrobial agent. Each of these items will be considered in this book.

Identification of the Infecting Organism

Several methods for the rapid identification of pathogenic bacteria in clinical specimens are available. A Gram's stain preparation is perhaps the simplest, least expensive, and most useful of all the "rapid methods" of identification of bacterial (and some fungal) pathogens. This technique can be used to identify the presence and morphologic features of microorganisms in body fluids that are normally sterile (cerebrospinal fluid, pleural fluid, synovial fluid, peritoneal fluid, urine). On occasion, Gram's stain of a buffy-coat preparation of blood will reveal phagocytosed organisms in the polymorphonuclear leukocytes of patients with bacteremia or fungemia. Similar preparations of sputum will also be helpful in revealing the nature of the infecting organism in patients with bacterial bronchitis or pneumonia. Gram's stain of a stool specimen may also produce useful information. In patients with staphylococcal enterocolitis, the Gram's stain reveals sheets of gram-positive cocci replacing the normal stool flora. The presence of polymorphonuclear leukocytes in the stool also provides a helpful clue to the cause of certain cases of diarrhea. Polymorphonuclear leukocytes are not found in normal stools. When present, they suggest the possibility of a bacterial gastroenteritis such as shigellosis, salmonellosis, or *Campylobacter*, or invasive *Escherichia coli* gastroenteritis. Polymorphonuclear leukocytes are not found in the stools of patients with viral gastroenteritis, food poisoning, cholera, and diarrhea due to noninvasive toxigenic *E. coli* (3). *Campylobacter* may be identified in the stools of patients by its characteristic gull-wing appearance on smears of stool (4).

Immunologic methods for antigen detection [such as enzyme-linked immunosorbent assay (ELISA) or latex agglutination] may also provide clues for the rapid identification of the infecting pathogens. Final and definitive identification of pathogenic organisms usually requires cultural techniques. It is thus imperative that appropriate specimens be obtained for culture before beginning antimicrobial therapy. Once anti-infective agents have been started, cultures often are rendered sterile, even though viable organisms remain in the host.

In most cases, it may be impossible to determine the exact nature of the infecting organisms before the institution of antimicrobial therapy. In these