# Preface

One of the greatest medical achievements of the 20th century undoubtedly was the rapid and effective introduction of antiinfective chemotherapy subsequent to Fleming's discovery of penicillin. Clearly untold numbers of lives have been saved by the application of natural product, semisynthetic, and synthetic antimicrobial compounds to the treatment of infectious disease. Academic, industrial, and government scientists, physicians and associated healthcare workers, and administrators all contributed to these efforts that have served humankind so well.

This success in some way belies the effectiveness of the agents that were discovered and developed into powerful therapies because we have often overlooked the complexity of the pathogenic microorganisms and their interactions with human and animal hosts. The clearest example of this was our very slow grasp of the significance of microbial biofilms. Von Leeuwenhoek alluded to biofilms in his writings (circa 1650), and later reports by Zobell (1942) and others clearly described multicellular prokaryotic communities from natural environments. Another 30 years passed before Costerton and colleagues began to emphasize the very significant role of adherent microbial communities in human infectious disease. In the 20 years subsequent to that declaration, many advances have been made, and yet much of the antimicrobial research continues to focus on methods utilizing planktonic bacteria. This phenomenon is due in part to the often good correlations of minimal inhibitory concentration (MIC) breakpoints for antibiotics with clinical outcomes, and takes into account exposure at the site of infection as well as activity against the target. However, the successful use of the MIC value may also have been due to the nature of infections and patient's status. As the infectious disease landscape continues to evolve such that biofilm-related infections become more predominant, the correlation between *in vitro* susceptibility results and clinical outcomes may likely decline. The erosion of the basis for effective antimicrobial therapy has arisen from the nature of the patient population due to underlying debilitation and impaired immune status, but also from the increasing emphasis on the use of indwelling medical devices (IMD). This trend at least is well known and has been recognized by governmental agencies including the Food and Drug Administration and the Centers for Disease Control and Prevention, and behooves the scientific and medical community to reflect on future approaches to addressing this problem.

In this book we have attempted to develop a general understanding of the problems for a broad audience. Thomas and colleagues have contributed an excellent overview of economic burden associated with treating biofilm-related infections. Schinabeck and Ghannoum have described the central role of IMD in the infections, and Gorman and Jones have provided us with detailed descriptions of how implant surface characteristics contribute to the adherence of pathogens and initiation of infections. In addition to the major principles, discussion of cutting edge aspects have been provided by Lewis and colleagues in the area of antibacterial tolerance and persisters,

which is central to the problem of treating biofilm-related infections. Animal models have been described by Handke and Rupp essential for identification of new effective therapeutic regimens. Discussion of the effectiveness of various antimicrobial agents for therapy of associated infections and extensive clinical protocols have been included as well. Finch and Gander have described how an understanding of antimicrobial pharmacodynamics can lead to improved efficacy, and the chapter by Dodge et al. on beta-lactam therapy is insightful. The detailed protocols provided by Lewis and Raad, Stryjewski and Corey, and Antonios et al. should aid physicians in the treatment of these refractory and often difficult-to-treat infections. It is our hope that this book will provoke thought and lead to more research resulting in improved therapies for infections where biofilms play a substantial role.