Front cover figure: Adhesion of bacteria to substrata is a remarkably specific phenomenon. The scanning electron micrograph on the cover illustrates type 1 fimbria-mediated adhesion of uropathogenic *Escherichia coli* to murine bladder epithelial cells. An epithelial cell near the center of the field is covered by hundreds of *E. coli* cells, while the five surrounding cells are virtually devoid of adherent bacteria. To date, there is no molecular explanation for this mosaic pattern of *E. coli* adhesion. Both commensal and pathoadaptive alleles of the adhesin subunit of type 1 fimbriae, FimH, can be found within the overall *E. coli* population. The strain illustrated in this micrograph expresses a pathoadaptive allele of FimH that is typical of uropathogenic *E. coli*. Strains expressing commensal alleles of FimH adhere in extremely small numbers to uroepithelial cells. See chapters 4 and 6 for more information. Micrograph courtesy of D. L. Hasty (University of Tennessee and Veterans Administration Medical Center, Memphis, Tenn.), E. V. Sokurenko (University of Washington, Seattle, Wash.), and Lou Boykins (University of Memphis Integrated Microscopy Center, Memphis, Tenn.). Tim Higgins (Illustrator, University of Tennessee Health Science Center, Memphis) contributed to the cover design.

Back cover figure: Surface view of the FimH molecule (purple), crystallized in the presence of the FimC chaperone (yellow) and a molecule of C-HEGA (green) occupying the mannose-binding site of the lectin. The figure was created with the PyMOL molecular graphics system program of W. L. Delano (http://www.pymol.org) and is provided courtesy of Stefan Knight, Department of Molecular Biology, Swedish University of Agricultural Sciences, Uppsala Biomedical Centre, Uppsala, Sweden.

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We dedicate this volume to our coauthor and great friend, Ron Doyle. We first became aware that Ron was suffering from amyotrophic lateral sclerosis (Lou Gehrig’s disease) in the fall of 2000, when he told us of some weakness in his right arm. The rapidity with which he succumbed to this terrible disease makes us wish we could change our field of research to search for a treatment or cure. The grace with which he accepted his fate makes us wish to have a fraction of his strength of character. With the untimely death of Ron Doyle on 18 January 2002, microbiology lost one of its leaders and we, and many, many others, lost a valued friend and colleague. We miss him tremendously.

Ron was born in Calvert City, Ky., and attended Northeast Louisiana University, Monroe, La., where he studied chemistry and played basketball. He obtained his Ph.D. in microbiology at the University of Louisville Medical School in 1967. He then moved to Roswell Park Institute in Buffalo, N.Y., for postdoctoral studies in protein chemistry. In 1969 he moved back to Kentucky and started his 33-year career in the Department of Microbiology at the University of Louisville, where he became full professor in 1979. During Ron’s career in Louisville, he was heavily involved in teaching assignments and directed a very active research laboratory. Ron also served in a variety of administrative posts, including associate dean for research in the University of Louisville School of Dentistry, a Sigma Xi National Lecturer, an American Society for Microbiology division chair, and a Canadian Society of Microbiology section chair. He was also elected to membership in ASM’s prestigious American Academy of Microbiology. To say that Ron liked to travel is a major understatement. He traveled all over the world, becoming involved in international research and teaching projects. He lectured widely throughout the world and participated in joint research projects with scientists in various countries. He was an honorary member of the Israeli Society of Microbiology and the Romanian Academy of Medicine.

Although Ron traveled to many different countries around the world, everyone who knew him could attest to the fact that Israel was his favorite. In
DEDICATION

fact, his determination to write this book on bacterial adhesion, and the 1994 Ofek–Doyle book, was very possibly because it gave him a good excuse to return to Israel year after year. His first contact with Israel was during a 1984 sabbatical at the Weizmann Institute of Science. This initial visit led to continuing collaborations with scientists at the Weizmann Institute, Tel Aviv University, the University of Jerusalem, and Bar-Ilan University. Several of the collaborative projects were supported by joint U.S.-Israel grants. Ron also initiated research projects with scientists from the Arab community of Israel, focusing on rapid diagnosis of mycobacteria, funded by a grant from the Israeli Ministry of Health. Ron went to Israel to write and work and experience its cultures and its history even during times when almost no one else would come.

Ron’s early studies focused on cell wall constituents, particularly those of gram-positive bacteria, such as peptidoglycan, teichoic acid, and teichuronic acid. His work greatly advanced our knowledge about the function of these constituents in cell growth and division. His interest in bacterial adhesion originated in the late 1960s, when it became clear that bacterial lectins were involved in the mechanisms used by oral bacteria to cause disease. His interest in this subject was undoubtedly influenced by his earlier studies of lectin-sugar interactions. Ron was an early proponent of using mathematical approaches developed for ligand-receptor interactions for studying bacterial attachment to substrata. Thanks to his contributions, adhesion data can now be analyzed using Scatchard, Hill, and related plots to estimate the affinity, cooperativity, and other parameters of the adhesion. Ron was also one of the first to point out the importance of hydrophobicity in the adhesion process. This was a concept initially dismissed as irrelevant by many researchers in the field, but Ron stood his ground and has long since been vindicated, as the importance of the hydrophobic effect became widely accepted. In more recent years, Ron collaborated with scientists in Mexico, Israel, Romania, and Bulgaria to develop rapid diagnostic tools involving lectin recognition of microbial surfaces. Ron also worked on antiadhesion therapies for bacterial infections. As a variation on this theme, he found that fluoride, at concentrations present in fluoridated tap water, suppresses the ability of streptococci to express adhesins and other virulence factors.

These are a few examples of Ron’s contributions to the field of microbiology, many of which have had a marked impact on the field. Ron’s legacy includes some 200 primary publications and many reviews and books. His books dealt with a great diversity of subjects, including a number of different areas of current microbiological research and also with the far-reaching consequences of microbiology on culture and history. Family, friends, and colleagues all miss Ron, as do the many dozens of scientists and students from around the world who were the beneficiaries of his generosity. Microbiology has lost a pioneering spirit, and we have lost a very dear friend.

ITZHAK OFEK AND DAVID HASTY
September 2002
It will be clear from our Dedication that the preface to this book is being written one year after the death of Ron Doyle. Ron played an instrumental role in much of the writing of the text. Even throughout 2001, the year in which he was most afflicted by the debilitating effects of amyotrophic lateral sclerosis, he worked with us on various sections of this book. On several occasions, we visited Ron in Louisville or he visited us during Ofek’s sabbatical in Memphis. He had even planned one final trip to Israel for the fall of 2001 to continue working on the book, as well as to visit the country he loved. He continued to play a very important role in writing this book and remained much more active than we had any right to expect, almost until the end of his life.

This text represents an effort to update a 1994 text, *Bacterial Adhesion to Cells and Tissues*, by Ofek and Doyle. The literature surveyed for the previous publication ended on 1 January 1992. The literature surveyed in this volume ended, with some exceptions, on 1 January 2002. Thus, the period covered was a full decade of very active investigation in the field of bacterial adhesion. Many achievements were made over this 10-year period, as evidenced from the many publications cited. We have endeavored to cover as many important issues as possible, but a complete overview of the field became impossible. Although a wholehearted effort was made to review all of the pertinent publications, undoubtedly there were some that escaped our attention, and we apologize in advance to the investigators whose work we did not include. The chapters cover general principles, methodology, characteristics of target cells and tissues, characteristics of bacterial surfaces and the regulation of surface protein expression and biogenesis, and several common themes that emerged during the last decade or two and are under very active investigation. The final chapter compiles, primarily in table form, a list all of the pathogenic bacterial species that were tested for their ability to adhere, the test substrata used, and the adhesins involved in the cases where they were known. It will only take a cursory glance to see which species have received the most attention.
and to indicate, perhaps, which species offer an opportunity for more active investigation.

We express our gratitude to a number of people who have contributed to our project in various ways. Large parts of this book were written in countries other than the United States and Israel due to the hospitality and inspiration of many of our international colleagues, and our very special thanks go to them: Giuseppi Teti and colleagues at the University of Messina, Messina, Italy; Karen Krogfelt at the Statens Serum Institut, Copenhagen, Denmark; Hany Sahly at the University of Kiel, Kiel, Germany; and Thomas Hartung at the University of Konstanz, Konstanz, Germany. The hospitality of Erika Crouch, Washington University Medical School, St. Louis, Mo., is also gratefully acknowledged. We are grateful to Kelly Cowan (Department of Microbiology, Miami University, Oxford, Ohio) for writing the Mathematical Analyses section of chapter 2. Naomi Balaban (Department of Human Microbiology, Tel Aviv University, Tel Aviv, Israel), Kevin McIver (Department of Microbiology and Immunology, University of Texas, Southwestern, Dallas, Tex.), and Mark Schembri (Department of Microbiology, Technical University of Denmark, Lyngby, Denmark) were kind enough to read and offer advice on various sections of chapter 4. Evgeni V. Sokurenko provided help with the discussion of probiotics as antiadhesion therapeutic agents in chapter 11. A special debt of gratitude goes to Memphis coworkers, especially Loretta Hatmaker, Tim Higgins, Susan Price, and Linda Snyder, for the variety of important ways in which they helped.

Finally, we acknowledge granting agencies (NIH, Department of Veterans Affairs, U.S.-Israel Bi-National Science Foundation, Ocean Spray Cranberry Co.) for funding work on mechanisms of bacterial adhesion and antiadhesion-based therapy in our laboratories.

ITZHAK OFEK AND DAVID HASTY

January 2003
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