Clinical Approach to Infection in the Compromised Host

Third Edition

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Foreword to the Third Edition

Not long ago it was a common opinion that the subject of controlling infections in the "compromised host" was a rather obscure corner of medicine occupied only with bizarre examples of rarities that the ordinary clinician could probably ignore without much damage to his working knowledge or to the safety of his patients. Recent experience has piled up in an overwhelming way on the other side of this question. It is now, of course, abundantly clear that such patients, far from being scarce, are likely to become increasingly central to the responsibility of medicine as a whole. Patients in this class offer the utmost challenge to those responsible for their care and are fascinating subjects of study and strong goads toward further learning. The compromised host lies open, as a form of exposed, all-purpose culture plate. Not only do such patients admit many kinds of ambient organisms with startling ease, but they usually do so in relative silence. Thus, in their early stages, only muted signals of trouble may be detectable by even the most observant physician. If these weren't enough, the picture is further confounded by the fact that the ability of such patients to throw off extraneous pathogens is, by definition, compromised. The nature of the compromise enlists still more variables and complexities, making the analysis of the circumstances presented by an individual patient all the more demanding. What is demanded most is an expert in situations like this, and the collection of expert views in this volume is the kind of help that the nonexpert sorely needs. What the generalist soon finds in working with an expert in this field is that the special strength of his opinion can be carried over to the management of ordinary patients with common infections. The presence of such an expert gives one a comfortable feeling that is probably akin to what a coach might feel if he could summon a pinch hitter to the plate who can hit home runs with two bats in his hands instead of one.

This third edition of Rubin and Young's widely read volume fully reflects the broad range of the subject at hand, giving special, and entirely justified, emphasis to the most prevalent immunocompromising situation of all, the individual infected with the human immunodeficiency virus. On reflection, this class of infections offers a particular curiosity because it is the primary infection itself that brings on immunological compromise, thereby generating a kind of "open season" for further invasion by still other organisms, and a dazzling array of organisms has to be considered. Intentionally immunosuppressed patients offer another class in which infections represent a secondary result from a primary, well-defined factor that is especially frustrating since it is usually quite resistant to change. Thus, the AIDS patient and the heart transplant recipient have several features in common, including a significant, and still incompletely explained, risk of developing malignant neoplasms.

In the early days of transplantation the doses of immunosuppressive agents that would be required for optimal control of rejection reactions were unknown. Not surprisingly, we were quite ill prepared to deal with the infectious complications of their use. As the doses of these agents tended to be larger than they are now, devastating infections were all too common. In retrospect, this situation proved to offer remarkable opportunities for the pioneering infectious disease specialists who entered the field at that time. The transplant recipient usually begins his period of immunocompromise at a time that can be anticipated in advance. This gives the expert in immunosuppression for transplantation valuable insights in handling patients already suffering from advanced immunocompromise from other causes. Thus, handling the problems presented by patients who have suffered immunocompromise, either in the course of their underlying illnesses or because of intentional immunosuppression, falls naturally into the same book and into the same growing medical specialty.

Current approaches to the evaluation of infections in compromised hosts and the substantial advances in their treatment are impressive. They are much superior to the best available only a few years ago. Nevertheless, one has the feeling that our present circumstances must represent a fairly early stage along the visible road to further improvements. The limited place now occupied by isolation techniques and the use of chronic antibiotic treatment to suppress, but not eliminate, certain types of infections will be interesting to watch in the future. These modalities may be used even less than they are today. Perhaps the biggest question for the future, how-

ever, will be the place of new approaches to heightening or restoring the intrinsic defenses of the host. With the identification and production of a growing number of cytokines, and greatly expanded information about the complex world of intercellular signaling, many new opportunities are unfolding. One already sees the value of this knowledge in situations where leukopenias are rapidly reversed by treatments with granulocyte-stimulating factors. Accordingly, it now seems likely that a valuable part of the management of compromised patients will soon include the individualized restoration of immune competence in addition to direct assaults on the offending organisms from without.

I look for this authoritative and up-to-date account of the management of infections in compromised hosts to be as thoroughly useful as were its predecessors. I must express the hope, however, that the subject will continue to advance in such a way that yet another volume will be called for by acclamation.

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Preface

In the spring of 1977, at the annual Epidemic Intelligence Service Conference of the Centers for Disease Control, two friends from medical school days, one now in California and one still in Boston, met and began to discuss their current clinical and research interests. By happy coincidence, we had both become immersed in what was then deemed a highly esoteric, ivory tower series of problems—those of the immunocompromised host. We belonged to a small community of clinical investigators who were part infectious disease clinicians, part microbiologists, part clinical immunologists, and part white cell biologists. We regarded the infections that were being seen in the transplant patient, the cancer patient, and the child with a congenital immunodeficiency disorder as both important clinical problems and as an opportunity for studying host–pathogen interactions.

Already there was a burgeoning literature from this small community of scholars, and there were beginning hints that because of strides being made in transplantation, cancer chemotherapy, and the use of immunosuppressive drugs for the treatment of autoimmune disease, the infectious disease problems of these patients would be of increasing interest and importance to the general medical community. We felt that a critical review of these subjects, the combination of a practical management strategy with the most up-to-date scientific information, and a delineation of the areas most needing further study, would help in advancing this area of clinical medicine. Thus, the first edition of this book was born.

In the nearly two decades that have elapsed since our first conversation and this, the third edition of *Clinical Approach to Infection in the Compromised Host,* this field has burgeoned in remarkable fashion. The infectious disease problems of the immunocompromised host have indeed become the concern of all practitioners of medicine, of as much concern to the primary care physician as the tertiary care specialist. The population of patients at risk has grown logarithmically because of the tragedy of AIDS and the remarkable success being achieved with modern immunosuppressive therapy in so many areas of medicine. Gratifyingly, there has been an accompanying explosion of information on the science and practice of caring for the infectious disease problems of these patients. Despite the medical conferences, new journals, newsletters, cassettes, videotapes, and other multimedia attempts to convey the necessary information to the expanding group of physicians who need such knowledge, we continue to believe that there is a compelling need for the clinician to have access in the dead of night or the heat of day to well-written, sage advice from veterans of battles similar to those they are now undertaking. This book continues to attempt to fulfill these needs. We have previously stated that the best way to learn is to sit at the feet of a master for several years—like Mark Hopkins and the Log. It is our hope that we have been able to bring together a group of Mark Hopkinses, all veterans of these battles and distinguished contributors to the field, with this book serving as a Log for all those with a need to know. All credit for achieving these objectives is owed to our contributors. We accept responsibility for any inadequacies.

As we have been privileged to contribute and to edit all three editions of this book, it is of interest to chronicle the changes that have occurred. At the time the first edition went to press, we had never heard of AIDS; in the current edition there are five separate chapters dealing with this subject, and issues related to HIV infection and AIDS can be found in virtually every other chapter as well. In the first edition, the only organ being transplanted was the kidney; now we discuss the liver, the heart, and the lungs as well, and begin to touch on the pancreas and the small bowel. Our understanding of host–parasite interactions and principles of patient management has likewise grown extensively. It is little wonder that this edition is at least 75% larger than the original volume, despite intensive efforts at editing. We are excited that the expansion in this field has necessitated and justified such an increase in material.

As we peruse this edition, we are also reminded that as in any dynamic field of medicine and science we stand on the shoulders of those who have gone before. These include our teachers, our patients, and our colleagues. Unfortunately, much of what we have learned has come from the study of patients who, despite the best efforts that could be made, have succumbed to their infections. Memories of them and their courage in the face of ex-

treme adversity continue to inspire us, and this book is in part dedicated to them. It is also dedicated to two friends and colleagues, whose contributions to this book, to medicine, and to our community continue, but who have been taken from us prematurely at the peaks of their careers. This book honors the memories of Dr. Joel Meyers and Dr. John Wolfson—gentlemen, scholars, and compassionate physicians; we are all poorer for their absence, and are grateful for the time we had with them.

Robert H. Rubin
Lowell S. Young

Boston and San Francisco

Preface to the First Edition

The science and practice of infectious disease cut across all medical disciplines, from medicine to surgery, and from cardiology to neurology. Because of the diverse nature of infection and the clinical settings in which it occurs, the acquisition of the skills needed to become expert in clinical infectious diseases has usually required a lengthy apprenticeship. As one of us has noted, "The practice of infectious disease is akin to many primitive arts, being handed down by oral traditions from generation to generation. The best way to learn is to sit at the feet of a master for several years, asking, observing, and studying—the medical equivalent of Mark Hopkins and the Log."

However, increasingly it has become apparent that a more efficient means of communicating the art and science of clinical infectious disease to the general medical community is necessary. The infections themselves, the potential therapeutic modalities, the clinical settings in which they occur, and the occurrence of such infections far away from the academic medical center—all these have put a new emphasis on disseminating the most up-to-date information available to diagnose and treat clinical infection. This is particularly true when one considers the gamut of infections that afflict the patient with a defect in host defense. Those of us with a particular interest in this area of medicine and infectious diseases are painfully aware of the special nature of these patients and their problems and the rather extended apprenticeship we have served in learning to deal with these problems. We have been impressed that although great strides had been taken in general infectious disease in moving beyond the Log and the oral tradition, in this area of infectious disease such efforts are just beginning. Thus, the idea for this book was conceived to attempt to meld the scientific advances in this area with the experience that we had had in dealing with such patients to construct a useful, practical guide to the problem of infection in the compromised host. We wanted to share the fruits of our apprenticeship with the rest of the medical community who increasingly are being called upon to deal with these clinical problems.

The next step was to find out whether a publisher would be interested. Ms. Hilary Evans of Plenum was quickly recruited to the effort. She has been a bulwark of strength and encouragement during the lengthy gestation period. Finally, there comes the recruitment of the other contributors. Perhaps the most pleasant surprise in this whole experience was the enthusiasm with which our contributors brought their expertise to the endeavor—all of us agreeing that a need existed for a practical guide to patient management in the immunosuppressed host that was based upon firm scientific data whenever this was available and on the art and judgment of medicine when such data was unavailable. With admiration and gratitude we thank our contributors, who have taught us so much in the preparation of this book.

Finally, it is fitting that we express our gratitude to three different groups of individuals who have made this book possible—our teachers, Mort Swartz, Louis Weinstein, Alex Langmuir, Don Armstrong, and Don Louria, who have served as our models in their ability to blend the sciences of microbiology, immunology, and epidemiology with the art of clinical medicine; our families, who have supported us in this effort and whose time has been stolen to prepare this work; and, perhaps most of all, our patients, the immunocompromised patients with life-threatening infections who continue to teach us and inspire us with their courage and faith as we painfully learn how best to deal with infection in the compromised host.

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