

**Pharmacology and Therapeutics of Asthma and COPD.** Clive P Page and Peter J Barnes, editors. (Handbook of Experimental Pharmacology series, volume 161. K Starke, series editor) Berlin: Springer-Verlag. 2004. Hard cover, illustrated, 376 pages, \$349.

There are many books, review articles, Internet sites, and traveling lecturers offering information on every practical aspect of therapy for asthma and chronic obstructive pulmonary disease (COPD), so why is there a need for another 376-page book on the topic? A second question is, who will benefit by referring to this book? And a third question is, does it offer any important new insights into the practical treatment of these common bronchospastic diseases?

The first question is partly answered in the preface, which points out that the editors previously published a book on the pharmacology of asthma, in 1991, and that the subsequent decade had been one in which an enormous mountain of new information had been generated. It would have been of interest if the authors had written a summary chapter detailing pharmacologic advances over the decade and explaining the relatively scant progress in drugs for asthma and COPD with the deluge of advances in other major therapeutic battlefields such as heart failure and peptic ulcer. It is notable that this new book can list only the leukotriene drugs as an important new class of traditional therapeutic molecular agent, whereas most of the other marketed agents of the 1990s and early 21st century are drugs similar to the old ones and simply offer the one major advantage of greater persistence of effect.

So why is there a need for a new book? The main justification is that the 2 editors are the foremost investigators of respiratory pharmacology in the world, and they wrote or contributed to half of the chapters. The remaining 7 chapters were written or contributed to in similar style by a total of 17 other authors, all of whom were selected for their depth of knowledge of the literature in their topics. The book is relatively unique in providing a critical discussion of a huge number of published articles, with the reference list for each chapter being similar in length to the text. What is extraordinary is

that in each chapter this enormous literature has been evaluated and then woven into a logical text that places the huge body of work into a meaningful context that very few individual readers could have generated on their own by delving into the wide range of journals that the authors have scoured, devoured, and absorbed. This is a scholarly tome that compresses a mass of disorderly facts into a cogent narrative history, which, not unexpectedly, does not always make for easy reading.

Who will gain by looking into this book? The editors suggest that it will be of value to research scientists and research clinicians, and those involved in the development of new drugs. Undoubtedly this is correct. They also express the hope that it will be invaluable for clinicians and respiratory physicians who treat asthma and COPD, but undoubtedly this is doubtful. Through their analysis of the exhaustive burden of increasing information on drug mechanisms, and the reported properties of individual agents that have been subjected to research studies, the authors have provided investigators with extremely valuable reviews. One is awed by the insights provided in this book's analysis of the ever-burgeoning information on pharmacology and molecular biology, and the innovations that have emerged from university and industrial research laboratories. Clinician readers will find much of this information to be impressive, but they are likely to be overwhelmed by the detail. Moreover, it is disappointing to find that very little of the current understanding of bronchospasm and inflammation is being translated into dramatically innovative therapy in the clinic or in the intensive care unit. However, it can be envisaged that a keen fellow in training would be happy to read and retain some of this emerging knowledge so as to regurgitate it to impress juniors and to confuse seniors, although such erudition will not influence patient care.

This leads to the third question regarding new insights into treatment. The information is at best encouraging, but very little in the way of practical information can be extracted that will influence the experienced practitioner. Clinicians who treat patients will perhaps read the first half of this book on the current drugs and therapies of asthma

and COPD to gain a thoughtful view of standard drugs. They will be particularly impressed with the chapter on corticosteroids, which makes the complex actions of these agents surprisingly understandable. The 5 figures provided by Barnes will be borrowed by lecturers who will like the clarity of his drawings. In contrast, the chapter on  $\beta$ -adrenoceptor agonists has only one good figure, explaining the molecular pathways, while the chapters on anticholinergics and theophylline are not illustrated. The chapter on mediator antagonists and anti-allergy drugs lacks illustrations and only offers relatively brief attention to the antihistamines, leukotriene receptor antagonists, and chromones. Furthermore, this chapter leaves the impression that these "advances" are doomed to be therapeutically disappointing.

The second half of the book is totally different. Eight chapters discuss the wealth of research information on new drugs, most of which, however, are never going to be used in the clinical setting. These include the familiar classes such as bronchodilators, phosphodiesterase inhibitors, anti-allergic drugs, and novel anti-inflammatory agents. The new bronchodilators encompass the fashionable nitric oxide and less impressive agents such as vasoactive intestinal peptide, atrial natriuretic peptide, and potassium channel openers. This is certainly grist for the researcher, with discussion on agents such as Ro25-1553 (Ac-Glu, Lys, Nle, Ala, Asp, Leu, Lys, Gly, Thr-vasoactive intestinal peptide (cyclo 21-25)). (Note: Some reference numbers are included inappropriately, and the final bracket is missing in the text on page 157). This complex chapter is dignified with one figure, which is partly colored green to make it more palatable, but it is still a digestive challenge. The chapter on new phosphodiesterase inhibitors (which are also covered to some degree in the preceding chapter) is certainly for the intrepid. If you can cope with single sentences that include information on AH-2132 (benzafentrine), ibudilast, and MKS492, or sentences that discuss PDE4 (phosphodiesterase) or IL-2mRNA (interleukin-2 messenger ribonucleic acid), this is the chapter for you.

The chapter by Barnes on cytokine inhibitors dilutes the intellectual assault with 12 of his characteristic "Barnesograms,"

which illustrate the bewildering complexity of the inflammatory reaction. However, the findings are not very encouraging, since novel drugs that inhibit single cytokines seem to have little therapeutic promise, although emerging research drugs that inhibit multiple cytokines may be more successful.

A novel aspect of the airway inflammatory response is discussed in the chapter on inhibitors of leukocyte endothelial adhesion. Such drugs could inhibit the migration of white cells into pulmonary tissue and thereby abort the bronchospastic response. This avant-garde approach to asthma introduces us to the various adhesion molecules, such as selectins and glycoprotein ligands, and to integrins, while epidermal growth factor and novel statins make cameo appearances. At this point the reader is sufficiently impressed with the ranks of dangerous cell invaders that it becomes disappointingly easy to envisage new drugs serving as hopelessly outnumbered border police that are designed to inhibit this dangerous trafficking across cell membranes.

The chapter on new anti-allergic drugs is slightly out of date, since the only truly interesting and innovative agent to emerge from research is the recently released rhuMab-E25, which we know as omalizumab. This should have been greeted with a greater fanfare, since it is the sole truly original asthma drug to be marketed, and it would have been useful if this chapter included more suggestions on how to position this agent in clinical therapy. The authors go on to provide an interesting discussion on deoxyribonucleic (DNA) acid vaccination, plasmid vaccination, and immunostimulatory DNA sequences combined with allergenic protein. However, much more clinical research will be needed before such agents enter into the daily practice of the allergist or pulmonologist. Similarly, as the following chapter on gene therapy points out, such cutting-edge research may have a relatively limited value in therapeutics, since the derived treatments would be cost-effective in only a small proportion of patients.

Clinical researchers will find the chapter on new drug evaluation to be very valuable, and this chapter is likely to be the one that is most appreciated by those who refer to this book selectively. It provides a general review of all the current tests and clarifies what end points should be sought. Although details are generally skimpy, the well-selected reference list will direct readers to relevant airway function tests, exercise eval-

uations, blood analyses, and even sputum analysis reports. Allergen challenge tests and herbal medicine challenge tests are also alluded to in this comprehensive review.

The final chapter by the 2 editors refers to about 100 references on novel anti-inflammatory therapies. The agents considered are a bewildering array of mediator antagonists, protease inhibitors, transcription factor inhibitors, signal transduction inhibitors, immunomodulators, vaccines, and remodeling agents. This skillfully organized account includes a variety of newly emerging terms that might be destined to become more commonplace, such as metalloproteinases, mitogen-activated protein kinase, GATA-3 (DNA sequence), calcineurin, nuclear factor (NF)-kappa  $\beta$ , c-Jun N-terminal kinase (JNK), and chaperonins. Unfortunately, an enormous number of drugs that have been designed to work on molecular pathways involving these agents have been shown to be unsuitable for clinical use. This information, however, could help the public understand how much effort with so many frustrating journeys into pharmacologic cul-de-sacs goes into bringing a suitable medication into the advertising pages of medical journals.

Overall, one must question the role of a book that evaluates such a wealth of material. Much of the research information is available in reviews or state-of-the-art articles in scientific or clinical journals, and the therapeutic uses of available drugs is presented in more practical format in numerous books and other published articles. Such a book can never be up to date, although a few of its listed references are as recent as 2002. Clinicians and investigators will be able to find most of the information on the Internet or in the abstracts of presentations at national meetings. This book could have made it easier to access its complex information by presenting more summaries in detailed tables or with more explanatory diagrams or cartoons. It is regrettable that the index in this book is a disaster, and it raises the question of whether an index is necessary, since each chapter provides a detailed tabulation of the chapter contents and a concise abstract that reviews the information.

Although I was pleased to have had the opportunity to review this book, it is evident that its main market will be research libraries rather than individuals or hospital libraries. More important, it makes one wonder if books such as this will be published in the future, since information retrieval is

becoming far less dependent on volumes that are filled with a mixture of chapters, each of which is likely to appeal only to a very selective audience, with most readers having little interest in the rest of the book. The volume is listed as number 161 in the series *Handbook of Experimental Pharmacology*, but it is now time to reclassify the series as "Shelfbook," since the truly useful books are metamorphosing into handheld personal libraries. For those who enjoy books for their evocative decorative appearance, this book may provide a welcome addition to this erudite series.

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**ACSM's Exercise Management for Persons with Chronic Diseases and Disabilities**, 2nd edition. J Larry Durstine PhD and Geoffrey E Moore MD. Champaign, Illinois: Human Kinetics. 2003. Hard cover, illustrated, 374 pages, \$49.

This is the second edition of this title, which surveys a broad range of chronic diseases and disabilities that may be represented among the expanding spectrum of persons referred for exercise testing or exercise prescription. The conditions covered range from cardiovascular diseases to orthopedic conditions to mental illness. The number of chapters has increased from 42 in the first edition to 49 in this edition, due to splitting some of the earlier edition topics into subsets and adding a few additional conditions.

The book is intended for exercise specialists, which would include respiratory therapists involved in an exercise testing laboratory or a rehabilitation service, as well as individuals with primary training in exercise science. It is written at a level that requires some familiarity with medical terminology but not extensive medical expertise. It does assume that the reader is familiar with exercise physiology and has the technical knowledge and proficiency for performing exercise testing and/or training.

The content is organized into 8 sections. The first section is mainly introductory, with considerable space given to explaining the editors' intent, the terminology used in the text, and the structuring of the individual chapters. A chapter on testing children is included here, apparently because it didn't fit neatly anywhere else. Subsequent sections include cardiovascular diseases, pul-

monary diseases, metabolic diseases, immunologic and hematologic disorders, orthopedic conditions, neuromuscular disorders, and cognitive, psychological, and sensory disorders. The large number of conditions included in the book dictates that no condition is discussed in detail, so this is not an in-depth reference on any one of the particular patient ("client" is the term used exclusively throughout this volume) populations.

To cover this broad range of topics there are approximately 60 contributors. A common problem of multi-authored texts is lack of uniformity in quality and style, and overlap in content from one chapter to another. The editors have made an explicit attempt to address this problem in their structuring of the book. Each individual chapter is organized in a highly standardized manner, using the following headings:

- Overview of the Pathophysiology
- Effects on the Exercise Response
- Effects of Exercise Training
- Management and Medications
- Recommendations for Exercise Testing
- Recommendations for Exercise Programming
- Special Considerations

Standardized tables of testing protocols and programming (training) goals are also included in most chapters, as is an example case study of an individual with the condition of interest. At the end of each chapter is a short list of references.

This standardized approach results in a uniform format and appearance in each chapter. The trade-off, of course, is that the standard outline isn't uniformly appropriate for each of the conditions addressed, and it results in some chapters having an awkward and artificial flow. For example, cancer and its treatments represent a heterogeneous set of conditions that may have diverse effects on exercise function, whereas bleeding disorders would not be expected to affect exercise function in any specific manner, and exercise in subjects with visual impairment represents a far more narrowly focused set of issues than the standard format was designed to address. The standardized format also results in chapters having roughly uniform length, even though some conditions, such as diabetes or obesity, could reason-

ably warrant a more extensive discussion because they are more common and/or more complex than others.

By far the most useful aspect of most chapters is the background information provided in the first half of each chapter. While this information will certainly be too limited to be a sufficient knowledge base for someone whose day-to-day work focuses on patients with a particular condition (eg, someone working in a pulmonary rehabilitation facility would want a more extensive understanding of chronic obstructive pulmonary disease than presented in this book chapter), it is a good starting point for someone who encounters individuals with a wide variety of medical histories and needs a resource for a quick introduction to different conditions. For example, reading the 3 pages of text in the chapter on cardiac transplant could quickly give an exercise professional unfamiliar with this population important information about what to expect during an exercise test on a transplant recipient. There are also chapters that are useful because they apply to a broad range of individuals, such as the excellent chapter on diabetes. Only a limited number of references are provided at the end of each chapter. The advantage of this is that they tend to be carefully selected reviews that provide the reader with a reasonable next step for finding more in-depth information. No references are cited in the body of the chapter, however, and the various authors do not always identify for the reader which statements are opinions and which carry the weight of scientific evidence.

In contrast to the narrative portions of each chapter, the standardized tables related to testing protocols and training programs are less useful. They take up considerable space in each chapter and in many cases contain redundant or unnecessary information. For example, almost every chapter's table on exercise programming contains a nearly identical row describing aerobic exercise as exercise involving large muscle mass for the purpose of increasing exercise tolerance. In addition, information within the tables, such as the recommended test protocol for determining peak oxygen uptake, is inconsistent from chapter to chapter. While in some cases this variability reflects important functional differences between different populations, it sometimes simply reflects idiosyncratic differences in the way individual chapter authors chose to fill in the table, and it is not always clear to

the reader which of these is the case. Using this reference as a guide to conducting tests in individual subjects could be confusing, therefore, and would result in systematic differences in testing protocols applied to persons having different diagnoses, even if their functional capacity and exercise needs were actually similar. The tabular presentations would certainly be more useful if related conditions were consolidated into summary tables that highlighted important differences between populations. The task of producing such a consistent set of guidelines relevant to a varied clientele is challenging indeed, and unfortunately is not accomplished in this volume.

The case studies at the end of each chapter were included specifically to highlight the editors' recommended approach to management of exercise problems using the S (subjective) O (objective) A (assessment) and P (plan) format, and are presented accordingly. The importance of this goal is a matter of opinion, but the cases seem to me of limited utility for illustrating either the diseases themselves or the exercise professional's assessment process. In some chapters the cases are presented as they might be written by the exercise specialist, while others contain elements such as plans for prescription of new drug therapies or medical interventions that imply the assessment of the treating physician. Some of the cases are simply not well integrated with the chapter information. For example, the chapter on vascular aneurysms indicates that maximum testing should not be performed in the presence of this condition, but results of maximum testing appear in the case study nonetheless. Overall I wish the space devoted to the cases had instead been offered to the chapter authors for discretionary use. Perhaps then some omissions that are probably due to space constraints could be remedied. For example, the chapter on cardiac pacemakers could benefit from illustrations of the appearance of pacemaker activity on the electrocardiogram tracing.

At the end of the book is a series of appendixes with supplementary information. The first is a compendium of drugs; these are organized by class, which makes it difficult to locate a particular drug by its name. It is followed by a more useful set of tables showing expected effects of cardiovascular drugs on selected cardiovascular responses to exercise. The third appendix is an ambitious but failed attempt to identify the effects of a wide range of medications

on exercise function. No distinction is made between statements extrapolated from isolated experimental conditions and information relevant to the clinical use of the drugs, nor is there any distinction made between Food and Drug Administration-approved uses and nonapproved uses for specific drugs. As a result, much information in this section is alarmingly misleading. The reader would be better served by having a *Physicians' Desk Reference* or similar drug guide at hand. The final appendix contains Web sites of major organizations relevant to the conditions covered in the book.

All in all, this would be a useful book to have on the shelf of the multi-function exercise laboratory. I would consider it a second-tier reference, after the more fundamental needs for technical and physiologic references are covered, and not a definitive reference for any of the conditions it reviews. The wide range of the subject matter makes it a unique resource, however, and its accessibility would be difficult to duplicate from any other source. Its most likely role will be as a quick guide to turn to when laboratory personnel find themselves faced with an individual with an unfamiliar diagnosis referred for evaluation or rehabilitation.

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**Clinical Tuberculosis**, 3rd edition. Peter DO Davies, editor. London: Hodder/Arnold/Oxford University Press. 2003. Hard cover, illustrated, 476 pages, \$149.50.

How often does a book not only inform and teach but also recruit new characters into the evolving story of an old disease? Peter Davies has brought together a selection of international leaders in tuberculosis (TB) research and control to contribute to the 3rd edition of a major international textbook. It is an excellent work, addressing the major issues with authority and diversity. It especially addresses the problems of TB outside of the most wealthy countries. Some readers may find that selected issues, including contact investigations and preventing transmission in institutions, require more thorough treatment than it provides. The tone and content of the text, however, more than make up for relatively minor limitations, in

showing how and why this global plight needs more attention from those with resources.

More explicitly than most textbooks, **Clinical Tuberculosis** targets a broader audience than its title implies, from its dedications and preface, through its content and conclusions. The clinicians and other practitioners who diagnose and treat TB and who implement the public health practices of TB control may compose the largest audience, but its most important target audience is more likely the policy makers who enable or restrain those efforts. Davies dedicates his 3rd edition of **Clinical Tuberculosis** to "the people of the United States of America in the hope that they will lead the world into greater equality of health and resources." Many authors have pointed out that TB control is a measure of resources and political will, since this disease, which has been preventable and curable for half a century, infects one third of the world's population and *continues to kill 2 million people every year*.

When the 1st edition was published in 1994, the industrialized world was just recovering from a historic resurgence of TB that has been attributed to several converging factors: the breakdown of public health infrastructure during the previous 2 decades; the emergence of a new virus, human immunodeficiency virus (HIV), which makes humans much more vulnerable than normal to TB infection and disease; the persistence of TB in most of the world, where the public in resource-rich countries paid it little attention; and migration of infected people to these resource-rich countries. Demonstrating one measure of this lack of attention, **Clinical Tuberculosis** was the first standard textbook on TB to be published in the United Kingdom since 1953.

Just 2 years earlier, another book came out in the United Kingdom, *Tuberculosis: The Greatest Story Never Told*, by Frank Ryan.<sup>1</sup> Dr Ryan recognized the historical importance of the resurgence and took the opportunity to engage the public by changing the title for the American edition to *The Forgotten Plague: How the Battle Against Tuberculosis Was Won and Lost*.<sup>2</sup> This popular book is a biographical and historical description of the discovery of modern diagnostics and treatments of TB. The attempt to influence readers through the persuasive power of a title subsequently was made by the Institute of Medicine in its authoritative assessment of TB control efforts, *Ending*

*Neglect: The Elimination of Tuberculosis in the United States*,<sup>3</sup> and by Lee Reichman and Janice Tanne in *Timebomb: The Global Epidemic of Multi-Drug Resistant Tuberculosis*.<sup>4</sup> In 3 editions of **Clinical Tuberculosis**, the title has been generic, but Davies has started to communicate his message just inside the front cover, with his dedications.

The 2nd edition of **Clinical Tuberculosis** was much longer than the first, with 11 chapters devoted to specific countries and regions of the developing world where TB is especially prevalent. These chapters were written mostly by specialists from those countries and regions, as part of an effort to maximize usefulness to TB control where it is most needed. That edition was dedicated to "Gordon Leitch [a contributor to the first edition], who died while helping to rescue friends in a swimming accident, Cyprus, July, 1996." This dedication invokes humanity's altruistic instinct and recalls another TB-related death from drowning in the Mediterranean 174 years earlier—that of the poet Shelley, who was seeking the prescribed cure for TB in the warm climate along the coast of Italy. His body was found with a book in his pocket by Keats, perhaps the most famous of the 19th century Romantic consumptives who died young, as described beautifully by Renee and Jean Dubos in *The White Plague: Tuberculosis, Man, and Society*.<sup>5</sup>

The publication of a 3rd edition of **Clinical Tuberculosis** attests to the success of the second. In his preface to this edition, Davies expresses the intention to provide "the essential information for the clinician managing tuberculosis wherever he or she may be working. The most important reason for the smaller size is to make it affordable to those working in poorly resourced countries, where tuberculosis is likely to be most prevalent." This edition is smaller than the second edition, largely from omission of most of the country- and region-specific chapters. However, it remains a substantial volume and is unfortunately more expensive, perhaps owing to rising publishing costs, than the 2nd edition, which is still available in the United States (at the time of this writing) for \$125.

The 3rd edition starts with a novel approach to understanding the history of TB, by Charlotte Roberts, reader in archaeology in Durham, United Kingdom, and Jane Buikstra, professor of anthropology in Albuquerque, New Mexico. Most histories of the disease in TB textbooks chronicle the social

and cultural history of the disease in Western civilization, as Dubos and Dubos do in *The White Plague*, or the history of medical advances against the disease, as Ryan does in *The Forgotten Plague*. A good recent combination of these approaches is Thomas Dormandy's *The White Death*.<sup>6</sup> What these approaches miss, however, is a full picture of the breadth and depth of human suffering from this disease across the world.

Roberts and Buikstra cite the growing accumulation of evidence of TB in skeletal remains around the world, taking advantage of the typical findings of TB of bones and joints, in the context of known frequencies and specificities of those findings. In fact, part of their chapter reads like an introduction to extrapulmonary TB of bones and joints. They list the limitations of this approach very carefully, but at the same time show that the study of ancient human remains from sites around the world is revealing the disease to be more ancient and more widespread than previously thought, probably predating the domestication of cattle, which has been hypothesized elsewhere to be the source of TB in humans. Advances in molecular biology are permitting analysis of ancient DNA, to confirm the tuberculous origin of gross pathology findings such as in skeletal deformities and abnormal lymph nodes. The authors expect current work will soon be able to distinguish between *Mycobacterium tuberculosis* and *M. bovis* and to be able to compare current strain types with ancient strain types, to show more clearly the trajectory of this plague.

While this chapter focuses mostly on the physical evidence of human remains, it refers to history, art, and literature, exploring, for example, the connection between urbanization, poverty, and the incidence of TB. This newly developing approach to the history of TB, and its dissemination, may help to achieve the editor's goal of helping the public in countries with resources to understand the global impact of the disease and the need for a global approach to its control. (The material in this chapter is also in book form by the same authors in *Bioarchaeology of Tuberculosis: a Global View on a Re-emerging Disease*.<sup>7</sup>)

The second chapter of the book is entitled "Epidemiology," by Christopher Dye of the World Health Organization. He follows a useful format of trying to answer "10 leading questions about TB epidemiology," and provides useful tools for further epidemiological work. One of these is his graph-

ical depiction of the theoretical impact of different interventions against TB, in the presence of varying rates of HIV infection in a high-incidence country. This chart shows the preeminent importance of TB detection and TB cure, an old message but one that bears periodic reexamination and broader dissemination. This message is of course one of the main messages of the book: expand the use of well-known methods of TB detection and cure, even while research continues to look for new ones. Dye also calls for increased use of cross-disciplinary analytical models, including economic and social factors, in order to "find new areas of vulnerability that can be exploited for better TB control."

After Dye has shown that the impact of TB detection may be even greater than the impact of TB cure, the reader may expect to find a substantial emphasis on detection in subsequent chapters, especially in Chapter 3, on laboratory diagnosis. The 18 color plates show very clearly some of the standard laboratory and clinical images of TB, from typical acid-fast stains under sputum microscopy and histopathology to the haunting cachexia of consumption, the angular spinal distortion of Pott's disease, and several examples of cervical lymphatic disease (scrofula). The laboratory diagnosis chapter describes traditional methods of microscopy, culture, and specimen issues, along with newer liquid broth systems and drug susceptibility testing. It also addresses nucleic acid amplification techniques for rapid diagnosis, research on serodiagnosis, and developments in laboratory detection of latent TB infection, along with other new molecular and phage-based techniques.

As a tool for clinicians in resource-poor areas, the book's abbreviation of advanced methodologies is appropriate, but it would be more useful if the basic techniques were expanded upon a little more, explaining why, for example, and in what circumstances, "3 consecutive sputa are still required for the diagnosis of TB." A few graphic illustrations would be helpful. Clinicians in most of the world, where the acid-fast smear is the only laboratory technique available for TB diagnosis, may require a more complete discussion of its use. Clinicians in the developed world have such a variable range of laboratory services that they would benefit from a more flexible algorithm of laboratory diagnosis than is presented in this chapter. As traditional and more expensive techniques continue to be evaluated for their

appropriate place in national and international guidelines for TB control, one has the expectation that the laboratory diagnosis chapter in the next edition of **Clinical Tuberculosis** may be more robust.

The chapter on deoxyribonucleic acid (DNA) fingerprinting serves this new epidemiological tool well. Chapters on respiratory TB, extrapulmonary TB, and childhood TB are thorough, with useful illustrations, case histories, and references. The chapter on pediatric TB presents a perspective from South Africa by H Simon Schaaf, Robert Gie, and Nulda Beyers, from the University of Stellenbosch, where unfortunately the experience with pediatric TB is vast. It includes excellent material on epidemiology and mortality, in addition to practical approaches to diagnosis and treatment, including drug-resistant TB. Here or in the pharmacology chapter, however, it would be useful to add comments and references on the safety of quinolones, an important class of second-line drugs for TB, for prolonged use in children, perhaps citing, for example, their use for chronic infections in children with cystic fibrosis.

The clinical pharmacology chapter is brief, well referenced, and to the point. It starts with an introduction of principles and issues, outlining the differences between the development of TB treatment and of treatment for other bacterial infections, which has often been based on better understanding of pharmacodynamics, the study of relationships between drug concentrations and drug effects. The author, Charles Peloquin, from Denver, Colorado, makes the point that TB regimens were developed by incremental improvement through clinical trials before mechanisms of action and pharmacodynamic relationships were discovered. This approach has left room for improvement in designing treatment regimens, even with the drugs available today. Most of the chapter presents the basic and applied pharmacology of the standard first- and second-line TB drugs, with an instructive case history showing a practical approach to common issues of treating TB in an HIV-infected person, and tables outlining drug interactions, especially those between rifamycins and antiretroviral drugs.

Two figures at the beginning of the chapter on TB chemotherapy, by Wing Wai Yew, chief of the Tuberculosis and Chest Unit at Grantham Hospital in Hong Kong, China, put patients with TB in the contexts of the community and of the economy. The first

shows a structure of community support providing incentives at the top and government commitment providing funding and training through the National Tuberculosis Programme at the foundation. The other elements of treatment fill out this framework in order to reach the patient, at the center, with complete treatment. The second figure, the vicious circle of poverty and TB, shows the consequences of failure. Although this chapter and the following chapters on important aspects of treatment and management bring current and fresh perspectives and information to clinicians treating TB, these figures at the heart of a current major international textbook on TB may inspire individuals in positions of influence to recognize that the most important elements of TB treatment are public support and government commitment. Yew credits new public-private partnerships such as the Global Alliance for Tuberculosis Drug Development with developing effective infrastructures for supporting research and development of new TB drugs.

The chapters on Bacille Calmette-Guérin (BCG) and treatment of latent TB infection are very important and useful, since a long but unpredictable period of latency is one of the hallmarks of TB, and since these 2 interventions have been shown to have a protective effect. BCG vaccination for TB is currently administered to 100 million children worldwide. The author of this chapter, Hans Rieder, of the International Union Against TB and Lung Disease, presents the history and evidence supporting this intervention and the reasons for continuing it, in spite of its limitations, in resource-poor settings. BCG has been proven to help protect infants and small children from the most severe forms of TB. Clinicians in settings where BCG is not routinely used will find this chapter very useful in helping them work with patients who come with histories of BCG vaccination.

Chapter 18 is by the same author of the corresponding chapter in the previous editions, Richard O'Brien, recently of the United States Centers for Disease Control and Prevention (CDC) and now with the Foundation for Innovative New Diagnostics, in Switzerland. This chapter shows a point in the evolution of TB control in its title, "Treatment of Latent Tuberculosis Infections," acknowledging the principle that presentation may change practice more effectively than data. O'Brien's chapter in the 1994 and 1998 editions was entitled "Pre-

ventive Therapy." This change in terminology was adopted in 2000 in the United States in order to emphasize that latent TB infection (LTBI) is a condition that should be actively diagnosed and treated. Although treatment of LTBI has been shown to reduce the development of active disease by as much as 90% in large multinational studies since the 1960s, and widespread implementation is known to be necessary to achieve eradication of TB, acceptance of this intervention has been mixed. The most highly recommended regimens, a year after publication of the book, remain the same as those described in this chapter: 9 months of isoniazid in the United States and Canada, and 3 months of rifampin and isoniazid in the United Kingdom. However, the real and the perceived challenges of toxicity, adherence, and drug resistance have led to the development of shorter regimens. One of these showed tremendous promise in studies of HIV-infected individuals (2 months of rifampin and pyrazinamide), and it was still included among currently recommended regimens in the United States at the time of publication, though with strong caveats. Early cases of severe and fatal hepatotoxicity with this regimen are well-described and documented in this chapter, along with recommended precautions, showing the accumulation of evidence during an episode of transition in TB control. Updates to the 2000 statement on targeted testing and treatment of LTBI subsequently have been published and widely disseminated by CDC, advising, based on demonstrations that it is associated with unacceptably high rates of hepatotoxicity, that, "... this regimen should generally not be offered to persons with LTBI for either HIV-negative or HIV-infected persons."<sup>8</sup>

**Clinical Tuberculosis** presents the current state of the art in international TB control from the perspectives of well-recognized experts in the field. It reaches out to a wide range of audiences: to subspecialty physicians receiving referrals for diagnosis and treatment of TB as well as to interested non-specialists who might or might not see an occasional case, both in wealthy low-incidence countries and to the far more numerous community practitioners in high-incidence areas with minimal resources, who diagnose and treat new cases of TB every day. However, it has the potential to be most useful in the hands of members of the public who may not understand much of the technical detail but who have the capacity

to recognize the tragedy of the global TB epidemic. They will find this book to be an excellent current compendium of tools for fighting that tragedy and may find the inspiration and summon the energy and creativity to participate in the continuing story.

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**The Mold Survival Guide for Your Home and for Your Health.** Jeffrey C May and Connie L May. With a contribution by John J Ouellette MD and Charles E Reed MD. Baltimore, Maryland: The Johns Hopkins University Press. 2004. Soft cover, illustrated, 215 pages, \$18.95.

This is the second book from Jeffery May on indoor environmental hazards, following *My House is Killing Me! The Home Guide*

for *Families with Allergies and Asthma*,<sup>1</sup> a guide for the prospective homebuyer or homeowner with indoor air problems. That volume was a readable survey of home indoor issues that join the burgeoning literature on indoor air problems. This new volume focuses on one of the most controversial and litigated aspects of indoor air health complaints: mold. The book's publication is particularly timely, with the recent publication of the Institute of Medicine's report, *Damp Indoor Spaces and Health*,<sup>2</sup> which nicely summarizes the evidence that moisture and mold are associated with upper-airway complaints and asthma exacerbation.

The Mays have peppered **The Mold Survival Guide** with fascinating personal anecdotes from their experience as home inspectors. The book brings a complex and fascinating science alive and is accessible to most readers. As in the previous volume, this one is directed toward home or condominium owners facing mold and moisture problems. The book may also be helpful to alert practitioners who must address this increasingly common complaint in their practice and the building contractors who are considering adding mold remediation to their repertoire. The book does provide some helpful references, from both the lay and scientific literature, but it is not meant as a reference guide to mold biology, exposure assessment, or health effects. As the authors note, it will help one stay "abreast of the news in medicine, legislation, and the insurance industry," and "will help you defend your physical and economic health against mold."

The book is organized into 3 parts. Part I, "The World of Mold," provides a survey of mold biology and health effects. The authors' vast field experience inspecting and documenting mold contamination is exhibited in Part II, "The Search for Mold," and they appropriately finish with "The Cleanup," describing what options one has for safely addressing the problems identified in Part II.

Part I is a succinct introduction to the problem and review of mold biology and health effects. The health effects chapter is a brief, reasonably balanced summary of immune response, focusing on respiratory effects. It is consistent with the aforementioned Institute of Medicine report, and would benefit from references (there are

none). It leaves the raging controversy over nonrespiratory complaints (often neurological) to one sentence, noting that such effects "are still being debated." The Institute of Medicine found insufficient evidence for such effects. The final chapter of this section nicely outlines why "the mold landscape is in chaos," with legal and scientific wrangling and the emergence of congressional action demanding research and guidelines to help the public navigate this landscape. It points out the evolution of concern at the National Institute for Occupational Safety and Health, which has increased its percentage of "sick building syndrome" cases caused by microbiological exposure from 5% to 35–50% in recent years.

Part II entitled, "The Search for Mold," demonstrated the authors' enthusiasm for the detective work required for moisture and mold remediation in homes. Their descriptions of what to look for and where are easy to follow. There are many stunning color photographs and horror stories involving water intrusion and subsequent structural damage. In addition to description of hazards in living spaces, the authors spend even more time focusing on those out-of-sight-out-of-mind areas of housing where mold problems can be missed by incompetent inspectors and fester for years before being noticed. The chapters include "What Lurks Below," "Mold in the Mechanicals," and "The Spaces We Don't Live In." As visible damage is often the tip of the iceberg of mold problems, this emphasis is well-founded. There are good discussions on crawl spaces, along with ventilation, heating, and air-conditioning-system pitfalls. The final chapter of the section wades into the controversy over mold measurement. The authors do recognize the uncertainty in this matter and note when referring to the lack of importance of mold speciation, "and here mycologist and indoor air quality professionals will probably disagree with me." In clinical practice, despite the absence of accepted safe or dangerous levels, mold measurements will be taken, and the chapter does aid in interpretation. Another recent source for clinicians is, *Guidance for Clinicians on the Recognition and Management of Health Effects Related to Mold Exposure and Moisture Indoors*,<sup>3</sup> which was published after **The Mold Survival Guide for Your Home and for Your Health** went to press. Each chapter in this part ends with

a helpful question-and-answer section to help one address common problems and recognize and avoid shoddy contracting. The question-and-answer format gives a "real-world" character to the more didactic text. Much of the content here is drawn from Jeffrey May's first book and amply informs this subject matter as well.

The final section is aptly named "The Cleanup." These chapters briefly address frequent concerns about the health (and economic) impacts of cleaning up after mold and water damage. It provides the homeowner with a rough guide of when to call for professional help when dealing with your own personal flood or "black mold" intrusion. The section is organized by cleanup task (eg, furniture, carpet, stored goods) and also includes advice on talking to your insurance company. A question-and-answer section for this part of the book would be very helpful.

**The Mold Survival Guide for Your Home and for Your Health** is an excellent effort and puts into perspective the public's fears and uncertainties about mold. It is readable, not sensationalized, and reasonably well referenced, with a useful index. The volume is most timely, as health professionals are beginning to get mainstream guidance on what should be done with their patients who are concerned and sometimes made ill by the mold that "lurks within."

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