

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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#### REFERENCES

1. Ryan F. Tuberculosis: the greatest story never told. Worcestershire, England: Swift; 1992.
2. Ryan F. The forgotten plague: how the battle against tuberculosis was won and lost. Boston: Little Brown & Company; 1993.
3. Geiter L (ed). Ending neglect: the elimination of tuberculosis in the United States. Washington DC: National Academy Press; 2000.
4. Reichman L, Tanne J. Timebomb: the global epidemic of multi-drug resistant tuberculosis. New York: McGraw-Hill; 2002.
5. Dubos J, Dubos R. The white plague: tuberculosis, man, and society. Boston: Little, Brown and Company; 1953.
6. Dormandy T. The white death. New York: New York University Press; 2000.
7. Roberts CA, Buikstra JE. Bioarchaeology of tuberculosis: a global view on a re-emerging disease. Gainesville, Florida: University Press of Florida; 2003.
8. Centers for Disease Control and Prevention (CDC); American Thoracic Society. Update: adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States, 2003. *MMWR Morb Mortal Wkly Rep* 2003; 52(31):735–739.

**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*