Pharmacotherapy of Asthma. James T Li, editor. *Lung Biology in Health and Disease* series, volume 212. Claude Lenfant, series editor. New York: Taylor & Francis. 2006. Hard cover, illustrated, 400 pages, $179.95.

This book describes the pharmacotherapy of asthma. The introductory chapter provides the reader with the perspective of the national and international asthma management guidelines, then the following 10 chapters cover specific drug classes and their basic mechanisms of action and efficacy in asthma. Then 2 chapters outline out-patient and in-patient asthma therapy and provide the appropriate perspective on the relative efficacy of the various pharmacologic classes and which agents are first-line and second-line choices. This objective perspective is missing in some of the chapters on specific agents. Thus, I would recommend that any reader relatively new to the topic read the first and last 2 chapters prior to immersing themselves in the drug-specific chapters.

Pharmacotherapy of Asthma is the 212th volume in this established series on lung diseases. It has been 20 years since the publication of *Drug Therapy for Asthma*, the 31st volume in this series, which explored asthma therapy in a similar though much larger text (800 pages). Since that time most volumes in this series that have discussed asthma pharmacotherapy did so as treatises on specific aspects, such as exercise-induced asthma or a specific class of drugs, such as inhaled corticosteroids, β_2 agonists, or the leukotriene receptor antagonists. It therefore must have been a daunting task to cover such a large topic in such a limited space, and in this book, coverage of certain aspects of pharmacotherapy are sacrificed in favor of others. Practical aspects of drug administration, such as drug delivery techniques, which agent to use in specific patient situations (with the exception of the chapter on management of acute severe asthma), and patient education are sacrificed for coverage of the mechanisms of action (both proven and theoretical), and general efficacy and approach to therapy with the agents is emphasized. This book is targeted at clinicians who care for patients with asthma. The editor included nurses, asthma educators, and respiratory therapists in the list of persons who would find the recommendations helpful. Pharmacists were notably left off the list. Because the most useful aspects of the drug-specific chapters were the discussions of basic mechanisms of action, pharmacists would be a good target audience.

One weakness of the book is that many of the authors wrote in advocacy for specific drug classes, as opposed to a more balanced approach of describing the proven relative efficacies of the various agents. However, the reader can go to the more recent guidelines to obtain more evidence-based, balanced recommendations. Notable exceptions to the advocacy found in many chapters include the chapters on inhaled and systemic corticosteroids, and on immunosuppressive and alternative treatments.

The first chapter reviews the national (National Asthma Education and Prevention Program) and international (primarily the Global Initiative for Asthma) guidelines. The most interesting aspect of this chapter is that the last few sections on the guidelines have influenced physician prescribing and patient outcomes on a global scale. Author Bernstein notes that we have seen improvement but that we still have a long way to go to improve asthma outcomes.

The chapter on β_2 agonists discusses the newer dynamic model of the mechanism of action, as opposed to the older "lock and key" model of agonists, antagonists, and receptors. However, the chapter authors could only theorize about how full agonists and partial agonists differ in this model, so it is not clear how to explain all clinical aspects by the newer model. They provide excellent discussions of the mechanisms of and differences between inhaled long-acting β_2 agonists, formoterol and salmeterol, and the relative clinical importance of tolerance (minimal) to their overall efficacy. They cover long-acting β_2 agonist use as an adjunctive therapy with inhaled corticosteroids and the issue of potential masking of inflammation, because they treat only bronchoconstriction. There is no discussion of the new "black box" warning on the package inserts for long-acting β_2 agonists that was recently mandated by the Food and Drug Administration (FDA), based on the results of the Salmeterol Multi-center Asthma Research Trial (SMART) and an FDA advisory panel meeting,[1–3] which came out after this book went to press; this demonstrates the difficulty of keeping a textbook current. The discussion on the newest issue concerning the pharmacogenetics of β_2 agonist response is similarly limited, in that it does not include the recent studies by the National Heart, Lung, and Blood Institute's Asthma Clinical Research Network.

The chapter on anticholinergics could have been easily eliminated, as none of the current anticholinergics has an FDA approved indication for chronic asthma, nor is there adequate data on their use in asthma, as the text makes clear. The various guidelines recommend ipratropium bromide as adjunctive therapy in moderate-to-severe asthma exacerbations in the emergency department, and that could have been adequately dealt with in the chapter on emergency-department treatment. An entire chapter on a drug that is primarily for chronic obstructive pulmonary disease (COPD) was unwarranted, in my opinion, and added little.

Both chapters on corticosteroids (inhaled and systemic) are very good and fairly balanced in their discussion of relative efficacy and safety. Unfortunately, there is no discussion of the use of inhaled corticosteroids in children. The editors may have thought that subject was adequately covered in volume 209 of this series, *Childhood Asthma.* However, some of the other chapters discuss asthma drugs in children.

Unfortunately, in the chapter on systemic corticosteroids, starting on page 245, the references starting at 82 are off by one through the rest of the text (reference 82 should be 81, and so on).

The chapter on leukotriene modifiers was particularly one-sided. The section on their history and basic mechanisms is excellent, but, starting in section 5-III, on leukotriene modifier effects in various types of asthma, the advocacy for these agents is particularly egregious. The author states (page 22) that "the bronchoprotective effect of β_2 agonists in exercise-induced asthma is lost with recurrent use." However, the cited reference clearly shows that pretreatment with albuterol results in a 1.1% drop in forced expiratory volume in the first second (FEV_1) after long-term placebo treatment and a 5.5% drop in FEV_1 after long-term albuterol treatment. A drop of $\geq$ 15% is considered exercise-induced bronchospasm, so both a 1% and a 5% drop would be considered complete blocking. It is then stated that zileuton completely blocks the physiologic consequence of aspirin challenge in aspirin-sensitive individuals, but the author fails to point out that the study was done by titrating to the dose of aspirin-caused adverse effects, then that dose was used in the subsequent challenge, and completely ignores other studies that clearly showed that these agents

do not protect against aspirin challenge if one titrates the aspirin dose upward.[4–6] These studies showed that just the threshold dose of aspirin is altered, and it is still considerably below the standard dose of 325 mg in adults. Further, in the discussion of its use as adjunctive therapy with inhaled corticosteroids, the studies that have demonstrated greater efficacy of the long-acting β_2 agonists as adjunctive therapy were left out of the references.

The chapter on theophylline and phosphodiesterase inhibitors covers much of the same territory covered in previous reviews by the same author. The discussions of the airway anti-inflammatory effects of theophylline are interesting, yet the clinical importance is still unknown, particularly when the selective phosphodiesterase 4 inhibitors (given short shrift at the end of the chapter), which are relatively selective for the anti-inflammatory activity, have shown little to no clinically important activity in asthma. On page 156 the author equates the addition of theophylline to inhaled corticosteroids similar to that of long-acting β_2 agonists, yet studies show that it is no more effective than doubling the dose of inhaled corticosteroids, whereas the addition of long-acting β_2 agonist generally provides better efficacy than doubling the inhaled corticosteroid dose. The statement on page 152 that theophylline can completely block exercise-induced bronchospasm is not supported by the referenced study, which shows that some patients with that level have no blocking effect. Other statements about theophylline attenuating exercise-induced bronchospasm are more accurate.

The sections on toxicity and pharmacokinetics are well written concise reviews of these topics. However, the author downplays the potential adverse effects and toxicities—a view not necessarily shared by others; the potential for serious toxicity is the main reason theophylline is seldom used anymore.

The chapter on the chromones, cromolyn and nedocromil, extensively reviews the basic mechanisms and the various in vitro and in vivo findings on inflammatory cells and mediators, and the chapter puts these findings in proper perspective by pointing out the limited efficacy in clinical asthma, compared to the inhaled corticosteroids. In section 7-VIII, "Allergen Challenge Clinical Trials," the authors discuss effects on other challenges, such as exercise and sulfur dioxide. On page 210 the authors reverse references 98 and 99. On page 215 the authors state there has been only one study that compared nedocromil to inhaled corticosteroids, but then they discuss the Childhood Asthma Management Program (CAMP) trial,[7] which, although not designed as a double-dummy study, was a parallel trial that compared nedocromil and budesonide to their respective placebos, and so provided the best available perspective on how each compared to placebo over an extended period.

The chapter on omalizumab, which is the newest therapy for asthma, is very good. However, all of their selected figures reference the paper by Milgrom et al[8] that suggested that omalizumab is as effective in children as in adults, although the FDA thought the data insufficient to warrant an indication in children. Dykewicz wrote an excellent chapter on the broad category of alternative treatments. The balance between mechanisms and actual clinical efficacy is very valuable.

The final 2 chapters, on out-patient and in-patient asthma management, could also be called beyond the guidelines, as they address data more recent than the publication of the guidelines. They both provide balanced perspective on the potential therapies, and the chapter on in-patients provides some excellent information on asthma treatment in the intensive care unit that is missing from the guidelines.

In conclusion, the strength of this text is its discussion of the basic pharmacology mechanisms of asthma drugs. All of the authors wrote concise, easy-to-understand sections on complicated information. However, in a number of chapters the authors' zeal for certain therapies prevented a balanced discussion on how the basic mechanisms translate into relative efficacy. Thus, my recommendation about this book is limited to those interested in knowing the basic pharmacology for the specific chapters and reading the first and last 2 chapters for perspective on each of the agents for the general treatment of asthma.

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REFERENCES

1. Murphy S, Roberts R. "Black box" 101: how the Food and Drug Administration evaluates, communicates, and manages drug benefit/risk. J Allergy Clin Immunol 2006;117(1):34–39.
2. Nelson HS, Weiss ST, Bleecker ER, Yancey SW, Dorinsky PM; SMART Study Group. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest 2006; 129(1):15–26. *Erratum in Chest 2006; 129(5):1393*.
3. US Food and Drug Administration. Medical officer review. Provided for meeting of Pulmonary-Allergy Drugs Advisory Committee, July 13, 2005. http://www.fda.gov/ohrms/dockets/ac/05/briefing/. *Accessed March 11, 2006*.
4. Pauls JD, Simon RA, Daffern PJ, Stevenson DD. Lack of effect of the 5-lipoxygenase inhibitor zileuton in blocking oral aspirin challenges in aspirin-sensitive asthmatics. Ann Allergy Asthma Immunol 2000;85(1):40–45.
5. Stevenson DD, Simon RA, Mathison DA, Christiansen SC. Montelukast is only partially effective in inhibiting aspirin response in aspirin-sensitive asthmatics. Ann Allergy Asthma Immunol 2000;85(6 Pt 1):477–482.
6. Berges-Gimeno MP, Simon RA, Stevenson DD. The effect of leukotriene-modifier drugs on aspirin-induced asthma and rhinitis reactions. Clin Exp Allergy 2002;32(10): 1491–1496.
7. The Childhood Asthma Management Program (CAMP): design, rationale, and methods. Childhood Asthma Management Program Research Group. Control Clin Trials 1999;20(1):91–120.
8. Milgrom H, Berger W, Nayak A, Gupta N, Pollard S, McAlary M, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody (omalizumab). Pediatrics 2001;108(2):E36.

Allergy and Asthma in Modern Society: A Scientific Approach. Reto Crameri, editor. *Clinical Immunology and Allergy* series, volume 91. Basel: Karger. 2006. Hard cover, illustrated, 224 pages, $167.25.

Allergy and Asthma in Modern Society: A Scientific Approach is volume 91 in this series. The editor selected some of the best in their field to write the book's 18 chapters, which include such timely topics as environmental factors that influence allergy and asthma (Platts-Mills, Erwin, Woodfolk, and Heymann), the immunologic basis of the hygiene hypothesis (Renz, Blümer, Virna, Sel, and Garn), the role of T lymphocytes in asthma (Kay), allergic manifestations of skin diseases (Breuer, Werfel, and Kapp), allergic conjunctivitis (Bonini), and fungal allergies (Crameri,