

Inhalation Aerosols: Physical and Biological Basis for Therapy, 2nd edition. Anthony J Hickey, editor. *Lung Biology in Health and Disease*, volume 221, Claude Lenfant, executive editor. Boca Raton: Informa Healthcare. 2007. Hard cover, illustrated, 472 pages, \$229.95

The field of respiratory drug delivery is important in the treatment of lung diseases. In addition, inhalation aerosols are increasingly viewed as a means of achieving systemic delivery of a wide range of therapeutic agents. Increased interest in aerosols as a route of administration has brought new scientists and clinicians into this field who are interested in learning more about pharmaceutical aerosols. For such newcomers this book does a good job of familiarizing the reader with most of the relevant topics in this field. However, the wide range of topics in the book necessitates that coverage of each topic is brief. Thus, this book is best viewed as a starting point for readers who are new to the field and interested in obtaining a passing knowledge of the relevant material before turning to other sources to learn more about specific subtopics.

The book has 16 chapters in 3 parts: Aerodynamic Behavior (Chapters 1–4), Biological Considerations (Chapters 4–8), and Pharmaceutics and Pharmaceutical Technology (Chapters 9–16). Each chapter is written by a different set of authors and is essentially a review article on a particular topic in the field. As with most review articles, these chapters do not impart a deep level of understanding of the material. Instead, this is a book for those in a hurry to get up to speed as quickly as possible in this field. Of course, speedy learning comes at a price, and the reader should be under no illusion that they have obtained a comprehensive understanding of the material. Indeed, the authors of Chapter 12 nicely sum up the approach throughout the book when they state the material is “discussed without significant attention to the derivation and assumptions required to obtain the result.” Many readers will be happy with such an approach, and for those readers this book does its job.

There is considerable variability in the quality of the chapters; some authors pro-

vided well-balanced, well-written reviews, and others did not. For example, several chapters in Part III are considerably stronger than some of the chapters in Parts I and II. This may in part reflect the fact that 4 chapters in Part III are co-authored by the book’s editor, Hickey, who is one of the most well-respected researchers in this field.

A second disadvantage of the book’s multi-author format is its duplicate coverage of material between chapters. For example, Chapters 1 and 3 have needless overlap on lung deposition models; Chapters 6 and 7 both present material on particle size deposition and lung geometry that is given in Part I; Chapter 7 gives material on devices that is repeated in Part III; Chapter 15 repeats information on drugs and disease states that is given in both Chapters 6 and 8; Chapter 14 repeats information on the physical properties of propellants that is given in Chapter 12, and nebulizer material that is given in Chapter 9. There is even redundancy within some chapters (eg, Chapter 6 presents material on the bioavailability of aerosolized insulin twice). Multiple-author book chapters are difficult to do well, because it is possible that no single author takes on the role of ensuring the quality and avoiding overlap of their chapter material with other chapters. Some of the chapters in this book suffer in this regard. This is unlikely to bother someone who reads only a few chapters, but if reading this book cover-to-cover, such duplication gives it an “absent-minded-professor” flavor, which reduces the otherwise favorable opinion I have of this book.

This is the 2nd edition of this book, so one would expect fewer errors than in the 1st edition. Indeed, the book is relatively free of copy-editing errors; I counted less than 20 such errors; the most glaring was in Chapter 4, where several references to other chapters in the book are made with “dummy” chapter numbers that were not replaced with the actual chapter numbers during copy editing.

Technical errors are also relatively few, and most of them occur in the first half of the book. For example, Chapter 2 overstates the importance of including convective mass transport at the droplet surface in determining the evaporation of liquid droplets. In

fact, such effects are probably important only for high-speed sprays, such as from metered-dose inhalers (MDIs), and can be neglected for typical nebulized droplets. Chapter 7 has several incorrect statements. For instance, it is stated that the MDI canister pressure “will drop during the life of the container,” when in fact this pressure will simply remain constant at the room temperature vapor pressure. It is also stated that “particle velocity in aerosols usually is proportional to droplet or particle size,” which is incorrect, for example, in an accelerating flow. The statement “solution aerosols impact largely in the upper airways” is misleading (eg, consider Qvar). Chapter 8 states that “particles below 0.5 μm are exhaled without deposition in the lungs,” which is incorrect, because it ignores diffusional deposition of particles smaller than a few tenths of a micrometer.

Other errors in the book arise because the authors oversimplify matters without warning the reader of the oversimplification. For example, Chapter 4 reads, “the conducting zone consists of the first 16 generations of airways,” when in fact the number of conducting airways depends on the path taken in the lung. Chapter 4 states that, “as a result of the enormous increase in surface area, bulk flow of air decreases rapidly within the respiratory zone,” when in fact it is the increase in cross-sectional area that causes that decrease.

Comparing this edition to the 1st edition, most of the authors have rewritten their chapters appropriately to include more recent work. However, a few authors chose to update their chapters by tacking on more recent material at the end of the chapter, leaving the early parts largely unchanged. I found this confusing, because these chapters start off with a dated perspective that the reader is likely to assume is the current perspective, and it is only at the end of the chapter that the reader realizes the error in that assumption. There are only a few places where the authors neglected to consider research published since the 1st edition. In Chapter 1 the authors did not include recent advances in mouth and throat deposition prediction, and Chapter 3 focuses on environmental aerosol models rather than recent work on pharmaceutical aerosol models.

Despite the above problems, in general the book will be a useful read for those who want to become familiar with respiratory drug delivery. Many readers of *RESPIRATORY CARE* will focus on the pharmaceutical technology chapters in Part III, and these are in general well written and have good coverage of the relevant material. There is a strong emphasis on MDI formulations; 3 chapters are devoted solely to this topic, compared to one chapter devoted to nebulizers, and one on powder inhalers, plus another chapter that touches on all 3 device types. However, this mix adequately reflects the current prevalence of MDIs in the marketplace. Several chapters in Part III include material on diverse topics that are not well covered elsewhere from an inhalation aerosol perspective (eg, Chapter 10 on alternative aqueous devices, and Chapter 11 on alternative powder processing methods).

In short, this book includes a wealth of information that many readers of *RESPIRATORY CARE* will find useful. Naturally, the book is not without its faults, as mentioned above, so caution needs to be exercised in assimilating some parts the book. However, this book should occupy a well-deserved place on the shelf of anyone starting out in this exciting field.

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Genetics of Asthma and Chronic Obstructive Pulmonary Disease. Dirkje S Postma and Scott T Weiss, editors. *Lung Biology in Health and Disease*, volume 218, Claude Lenfant, executive editor. Boca Raton: Informa Healthcare. 2007. Hard cover, illustrated, 414 pages, \$199.95.

Volume 218 of the *Lung Biology on Health and Disease* series is devoted to the genetics of asthma and chronic obstructive pulmonary disease (COPD). This is a welcome and timely volume in the series. It provides state-of-the-art updates on the genetics of asthma and COPD, which will assist readers in comparing and contrasting these 2 complex conditions, and describes the genetic differences between these 2 common obstructive lung diseases. The editors assembled 41 experts, from the basic animal laboratory to practicing clinicians, who

provided articles that highlight the relevance of the recent advances in the genetics of obstructive lung disease. Understanding the genetics of these 2 conditions is paramount to understanding their pathogenesis, to the development of new therapies, and to determining why some patients respond to some therapies and others do not.

It is hard to do justice to this work in a succinct review, so I have chosen to briefly outline the content and appeal of the various chapters as a guide to the wealth and diversity of knowledge the volume provides, both for the novice and the experienced researcher. All the chapters are well supported with references to pivotal and key publications.

Chapter 1 serves to orient the novice to this field; it provides an excellent introduction to genetics and introduces the terminology and methodology in the rest of the book.

The relevance of genetics to impairment of lung function is outlined in Chapter 2, with some interesting data from studies of twins. Chapters 3 and 4 focus on the gene/environment interaction, the influence of age and gender in asthma, the genetics of the "hygiene hypothesis," and the conundrum of gender differences in COPD and asthma.

Chapters 5 through 7 focus on the latest laboratory molecular techniques and are mostly directed toward basic researchers working with mouse models in the laboratory. These chapters are quite detailed for those unfamiliar with bench research. They are probably most relevant to undergraduates, and they provide a framework of application of basic genetic techniques to the continuum of asthma/COPD laboratory research.

Chapters 8 and 9 address the comparative genomics of asthma and current proteomic techniques. Chapters 10 and 11 provide a detailed schema, from bench to bedside, of the linkage of the complex clinical syndromes of asthma and COPD to genetics research.

Chapters 13 through 18 provide practical information from genetics research for health care workers and clinical researchers in asthma and COPD, and will assist in understanding the recent medical advances. In particular, Chapters 13 and 14 focus on association studies in asthma and COPD and provide a method to understand how targets for new drugs have been identified, and the evolution of potential novel therapies.

These chapters clearly outline the underlying differences in the genetics and pathogenesis of asthma and COPD. This is timely, as presently guidelines and pharmaceutical company research trials seem to be blurring the differences between asthma and COPD. These chapters emphasize the necessity to approach these conditions with different therapies, rather than suggesting almost identical treatment algorithms, particularly the present vogue of early introduction of combination therapy (inhaled corticosteroid and long-acting β_2 agonist in a single inhaler) in both asthma and COPD.

Chapters 15 and 18 are particularly relevant, as they provide background information on the ongoing politically charged debate about potential harmful effects of regular short-acting β agonists, which are the most-used therapy in both acute and chronic asthma. There is extensive individual variability in the response to β agonists, of which genetics is thought to account for as much as 50%. This controversy has recently been extended to cause confusion about the risk/benefit ratio of long-acting β agonists. Both debates focus on β agonists in asthma management but are confounded by factors such as asthma severity, concomitant inhaled corticosteroids use, and (as outlined in this book) genetic and ethnic subgroups.

Both asthma and COPD are common conditions, and their prevalence is increasing substantially. Asthma is rising primarily due to globalization, the gene/environment interaction of groups of patients previously naïve to the western lifestyle moving to western countries or adopting a western lifestyle in their native land. The worldwide COPD rate is also increasing, which is thought to be driven in western countries by our rapidly aging population and an increased smoking rate in women, and in developing countries by industrial pollution and the rising prevalence of smoking.

COPD, which has traditionally been overshadowed by asthma and allergy, is now a major topic of clinical and research interest. We need to better understand genetic susceptibility, gene/environment interactions, and response to therapy in asthma and COPD.

This may be the first time many of us will consider the genetic origin of these 2 contrasting obstructive lung diseases. Many questions remain unanswered. Why do only 18% of smokers develop COPD? Why do asthmatics, and not COPD patients, develop

airway remodeling? With the ongoing advances of genetic research, we are now more capable than ever of discovering the complex answers to these basic questions.

This book provides easy-to-read reviews, with chapters that are relevant to diverse groups, from basic researchers to epidemiologists to clinicians. It introduces what we understand today about the genetics of asthma and COPD. This general appeal may stimulate and foster further collaboration and cross-pollination of ideas between researchers who have focused on asthma or COPD, but not both. Advances in genetics research have substantially advanced our understanding of these conditions and will improve management and prevention.

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Exacerbations of Asthma. Sebastian L Johnston MBBS PhD FRCP, and Paul M O'Byrne MB FRCPI FRCP (C) FRCPE, editors. Boca Raton: Informa Healthcare. 2007. Hard cover, illustrated, 354 pages, \$169.95.

Exacerbations of Asthma is a comprehensive book edited by 2 seasoned writers. With contributions from 38 renowned asthma experts, the editors provide a global view of asthma and its impact on morbidity and mortality. The book has 20 chapters and 6 sections, on epidemiology of asthma exacerbations, pathophysiology, in vitro and in vivo experimentation models of asthma, treatment, prevention, and delivery of care to patients with asthma. Each chapter includes an overview and a concisely written conclusion.

This book is written for a variety of readers. Most chapters are written for health care providers such as asthma educators, respiratory therapists, physicians, and nurses. The information is clearly written and most of the chapters are easily understood, but the chapters on in vivo, in vitro, and murine models for asthma, although well written, require a solid understanding of microbiology, immunology, and biochemistry.

One of this book's strengths is that the chapters are well referenced and have ample discussion of pertinent clinical studies. Most of the studies cited are recent, but a few chapters refer to data from as far back

as the 1960s, which weakens their arguments with outdated statistics.

I had 2 major disappointments about the book. First, the cover art includes a large photograph of a woman using a metered-dose inhaler with the closed-mouth technique and no spacer. Of course, one should never judge a book by its cover, but this photograph illustrates the least effective aerosol delivery method, which would discourage me from purchasing it. I question the editor's intent in using that photograph. My other disappointment is the absence of a chapter on aerosol delivery methods. The pivotal point in asthma management is effective delivery of medications. An evidence-based review of delivery systems and techniques is greatly needed to balance out the topics in this book and provide important information. If I came across this book in a health sciences book store and glanced at the cover and noted the lack of a chapter on aerosol delivery, I would not purchase the book. However, after reading and reviewing it, despite these flaws, I would recommend its purchase.

Chapter 1 clearly defines the nature of asthma exacerbations and their morbidity. Numerous studies are cited on asthma exacerbation frequency, severity, frequency of associated hospital and clinic visits, and financial burden. Unique to this chapter is a discussion on the relationship between thunderstorms and asthma—a concept well supported by studies but not discussed in other books, to my knowledge.

Chapter 1, like several other chapters in the book, contains figures that are confusing and difficult to interpret. For example, Figure 1.1 plots 2 variables at different times of the day: the percent drop in peak expiratory flow, and asthma score. But nowhere does the text or figure legend explain the method for interpreting the 0.0–2.0 range on the Y axis, or define the asthma score. Four graphs plot the effects of 4 different medications on these 2 variables. The legend for the 4 graphs is difficult to discern from the text. The X axis is labeled with a continuum of time, using negative to positive numbers. For example, 15 days prior to the day of asthma exacerbation (which is labeled day 0) is listed as –15 days, and 15 days following the exacerbation is labeled 15. Using a North American orientation for interpreting graphs, this is a nonconventional and difficult approach to present data. Several other chapters also include graphics that are difficult to interpret, lack explanation of

certain variables, symbols, and data points, and are “busy.” These deficits weaken the graphs' and tables' clarity and value. The legend for Table 1.1, which lists data regarding asthma exacerbation rates from 10 studies, does not explain one column of numbers, which rendered the table useless to me.

Chapter 2 differentiates between asthma exacerbation and poorly controlled asthma. This is a clinically important distinction, and this chapter explains the concept well and describes how the pathophysiology of the 2 conditions differ. Tools for diagnosing exacerbations and the use of β agonists and corticosteroids during exacerbations are discussed. This chapter provides an in-depth discussion of the clinical use and limitations of peak flow monitoring. The heart of this chapter is the argument that during an exacerbation the clinician should assess the patient by looking at the differences from the patient's baseline, rather than absolute change, in variables such as peak flow, β agonist use, and symptoms.

Figure 2.10 contains 10 graphs that plot the use of oral corticosteroids, changes in peak flow, symptom score, β agonist use, and inhaled corticosteroid use during exacerbations. As in Chapter 1, the “symptom score” is not defined. The 0–10 scale on the Y axis of the oral steroid graph is not explained. The lack of explanations, along with the graph being printed too small, rendered this figure useless to me.

Chapter 3 addresses the socioeconomic impact of asthma exacerbation. This is discussed in global terms, with emphasis on North America and the European Union. Direct and indirect costs are discussed. This chapter clearly identifies the need for health care providers and decision-makers to identify cost-effective interventions to treat asthma exacerbations.

Chapter 4 discusses the factors that influence the seasonal patterns of asthma exacerbation, such as air pollution, climate, pollen, and viral infections. There is a comprehensive review of studies that have documented global causes of seasonal asthma. The importance of recognizing seasonal asthma risk factors and developing an asthma management plan are highlighted in this well-written chapter. One section on seasonality of respiratory viral infections is discussed with a graph that plots data from 1963–1966. Although this graph illustrates a typical pattern of increased incidence of

viral-induced asthma in September and October, the data are dated.

Chapter 5 provides a good and well-referenced discussion of the differences between childhood and adult asthma exacerbations, the wheezing phenotypes in infants and children, the effects of viral infections on lung development and asthma in children, and the causes of wheezing in older children, such as infection, sinusitis, allergens, and pollution. The emphasis on the uniqueness of the causes and pathophysiology of asthma exacerbation in children makes this a key chapter.

Chapter 6 discusses the etiology of asthma exacerbation in adults and how its causes and pathology differ from that in children. The chapter describes age-specific patterns of exacerbations that require hospital admission. This chapter discusses the trend of increased asthma exacerbation, which began in the 1960s, eventually reached a plateau, and recently began to decline. The causes of this decline are discussed. The role viral infection plays in asthma is discussed at length. The chapter states that some patients with asthma may have an impaired acquired immune response to rhinovirus infections. Every chapter in this book discusses the role of viral infection in asthma, but each chapter has its own focus on that relationship. Other causes of adult asthma, such as pollution, allergens, stress, cigarette smoke, food, aspirin, pregnancy, and gastroesophageal reflux, are discussed.

Chapter 6 also contains several difficult-to-interpret graphs and figures. Figure 6.3 uses 7 shades of gray to illustrate the distribution of viruses and atypical bacteria during single, dual, and triple infections in children. Each shade of gray corresponds to a particular virus, but it is difficult to discern some of the shades in the legend, which makes the graph difficult to interpret. Similar problematic shading compromises some graphs in other chapters.

Chapter 7 discusses the modes of transmission of respiratory viral infections. This chapter cites numerous studies on virus transmission, with emphasis on respiratory syncytial virus, human rhinovirus, and human influenza virus.

Chapter 8 addresses the mechanisms of asthma exacerbation. Detailed discussion covers the normal airway epithelium and the role of mediators and mast cells in inflammation. Discussed at length are how cellular inflammation, airway smooth muscle, pulmonary vasculature, and mucous

cells are altered in asthma. This chapter clearly illustrates the complex pathophysiology of asthma.

Chapter 9 focuses on viral induction of neurogenic inflammation and airway responsiveness. The first section focuses on the receptors and enzymes involved with regulation of the biological response to inflammatory neuropeptides in the respiratory tract, their distribution, function, and biological effects. The second section of this chapter takes the central theme of viral-infection-induced asthma and looks at the effects of viruses on the sensory innervations of the airway. It also discusses the associated pathophysiologic manifestations of these effects on the bronchial wall and pulmonary vasculature during and after an infection. This is one of the more difficult chapters in this book. Topics such as inflammatory neuropeptides and neurogenic airway inflammation are discussed in depth. Also discussed is post-viral inflammation, which is a key concept in adult-onset asthma. The chapter concludes with a comprehensive discussion on therapeutic strategies for treating viral-induced asthma.

Chapter 10 tackles antiviral immunity and protection against asthma exacerbations. Antiviral defenses are discussed, along with explanation of the innate immune response. Although this chapter is well-written and includes 155 references, I found it difficult to understand, due to my limited knowledge of immunology.

Chapter 11 addresses the pathophysiology of bronchiolitis in infants due to respiratory syncytial virus. The causes of wheezing in infants are well-referenced and explained. This chapter discusses the association between bronchiolitis and wheezing in early childhood, with a focus on cause and pathophysiology. The role of active and passive immunization as protection against bronchiolitis is also discussed.

Chapters 12 and 13 focus on *in vitro* models of bronchial epithelial cell infection and macrophage infection. These are the most difficult chapters in the book. To comprehend the information at the depth these topics are presented, the reader should be well-grounded in microbiology, immunology, biology, and biochemistry. The role of rhinoviruses and macrophages in asthma are the foundation of this chapter.

Chapter 14 discusses murine models of allergen exposure and virus infection. Support is provided for the use of murine models to study airway allergen response. The

chapter describes murine models as ideal for determining the role of T cells in allergic response and understanding mediators' roles in asthma exacerbations. In addition the chapter presents murine models to study the association between viral infection and asthma exacerbation. This thorough and in-depth chapter makes the point that murine models offer unique opportunities to identify potential therapeutic approaches, based on cellular and molecular mechanisms.

Chapter 15 explores lessons learned from human experiments with rhinovirus infection in conjunction with exposure to allergens. The chapter expands on the synergy between viral infection and inhaled allergens. It is reported in this chapter that atopic individuals are more susceptible to viral-induced asthma. Emphasis is placed on further exploration of that relationship. This chapter includes several figures that, again, are difficult to interpret. Figure 15.6 contains 6 small graphics with no explanation of the variables on the X axis. The graphs show data from a very limited number of subjects. Even after careful consideration of the data presented, I was unable to see the point of the graphs.

Chapter 16 presents data on leukotriene antagonists in the treatment and prevention of asthma exacerbations. Studies support the use of leukotriene antagonists in asthma. This is a well-referenced chapter on a controversial topic. Though montelukast is experimental in the United States, the chapter discusses several European studies that found intravenous montelukast effective for asthma exacerbation. The chapter concludes that adding leukotriene antagonists may benefit patients who do not respond to other asthma exacerbation therapies.

Chapter 17 addresses the key issue of the role of corticosteroids in preventing asthma exacerbations. This chapter supports the use of high-dose inhaled corticosteroids with the onset of an upper-airway infection. The use of low-dose inhaled corticosteroids in children with airway infection is also discussed. The authors make a good argument for low-dose corticosteroids for preventing asthma exacerbations. This chapter is well-written and thorough.

Chapter 18 looks at the combination of inhaled corticosteroids and long-acting β_2 agonists. This chapter is written by one of the book's editors (O'Byrne, who is well known for his expertise in asthma), who expands on the importance of adding a long-

acting β agonist to inhaled corticosteroids. This chapter is well-written and concise.

Chapter 19 explores the importance of self-management in minimizing asthma exacerbations and the use of asthma action plans. The pros and cons of having the patient self-adjust therapy are presented. I think this chapter will be extremely valuable to asthma educators. This chapter contains several figures that, despite my grounding in statistics, I could not interpret. In particular, Figures 19.3 and 19.4 are comparison graphs for which no explanation is provided in the text or legend. I presented Figures 19.5 and 19.6 to our campus statistician, and she also had difficulty interpreting their intent.

The book concludes with a chapter on psychosocial issues associated with asthma, which is a topic not well-documented in the literature. This chapter does a good job identifying the psychological issues experienced by patients with chronic asthma. Most clinicians who treat patients with asthma tend not to recognize how these factors affect patients. This chapter emphasizes the need to evaluate the psychological, social, and behavioral problems associated with chronic asthma. I think this is a pivotal chapter for understanding how psychosocial issues influence the management of patients with asthma.

In summary, I found **Exacerbations of Asthma** to be a well-referenced book that

deals with a broad list of asthma topics. Overall the writing is clear, thorough, and well-organized. The content is timely and accurate. The weaknesses discussed above should be addressed in a subsequent edition.

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