

Practical Handbook of Nebulizer Therapy. Jacob Boe, B Ronan O'Driscoll, John H Dennis. New York: Martin Dunitz/Taylor & Francis. 2004. Hard cover, illustrated, 323 pages, \$63.95.

Nebulizers are the "Rodney Dangerfield" of aerosol delivery devices: they *get no respect!* The introductory paragraph of almost every recently published paper on new aerosol delivery devices seems to include an obligatory derogatory remark about the inefficiency of these quaint, old-fashioned devices. Yet despite a flood of newly patented high-efficiency devices, nebulizers continue to be popular with practitioners and patients. The survival of nebulizers is no doubt due to their relatively low cost, versatility with a variety of medications, and simplicity and ease of use. The advent of valved holding chambers (for metered-dose inhalers) and powder inhalers has obviated nebulizers in the maintenance therapy of many patients with asthma and chronic obstructive pulmonary disease (COPD), but nebulizers continue to be useful during asthma and COPD exacerbations and with very young and elderly patients. Nebulizers are also essential for the management of cystic fibrosis, and, because of their simplicity, nebulizers are useful in the development of new and experimental therapies.

Practical Handbook of Nebulizer Therapy offers a wealth of information about nebulizers and nebulizer therapy, and the authors provide a comprehensive bibliography and literature review. It covers the subject in a forthright and logically sequential manner, with a level of detail not found in typical pulmonology and respiratory therapy texts.

This book is the brainchild of 2 pulmonary physicians and an aerosol scientist (all Europeans) who, as chief editors, assembled a diverse and talented group of contributors. Including the editors, there are a total of 20 contributors, from specialties as varied as pulmonology, aerosol science, nursing, respiratory therapy, physiotherapy, and environmental sciences. All but 2 of the contributors are European, so much of the writing has a subtle European undertone. The book emanated from a European Respiratory Society task force, chaired by the editors, which was charged to produce

guidelines for nebulizer use in Europe. The aerosol science and clinical data presented by these contributors are generally universal, but reviewing the North American experience in the delivery of respiratory care services would have enhanced the sections that focus on the implementation and costs of therapy. Had the editors included one additional chapter on the North American perspective, the audience for this book could have been much larger. Despite the book's scientific and clinical excellence, ignoring the concerns and experience of an entire profession (licensed respiratory therapists) is likely to be off-putting for many people who would otherwise benefit from this book.

The book's organization and content are quite appropriate for its subject. It is organized into 3 sections (on technical, clinical, and practical considerations) and 15 chapters. The technical section contains 3 chapters. Chapter 1, "Theory and Science of Nebulizer Use," leads off with a brief history of nebulized aerosol delivery and then includes the standard review of the mechanisms of particle deposition, which can be found in most respiratory therapy texts. The chapter explains the physical principles of nebulizer operation and invites the reader to discover that nebulization is a good deal more complex than one might initially think. The principles relating to particle generation, aerosol release, dead-space volume, and particularly the effect of evaporation on droplet size are all given appropriate coverage. The chapter ends with a brief overview of the various types of nebulizers and their differences. We would like to have seen more detail on assessment of lung deposition with various nebulizers, as well as more detailed discussion on the influence of abnormal airway anatomy on lung deposition.

Chapter 2 has the title "Quality Control and Standards in Nebulizer Performance and Use." It begins with the observation that the delivery of nebulized drugs is uncontrolled and poorly understood by the clinical community that is chiefly responsible for prescribing it. Although this pertains specifically to Europe, we can attest that the situation is similar in the United States, and we suspect that it is also similar in most other countries. Some of the reasons for this

state of affairs are briefly mentioned. The chapter discusses the need for standards and describes some of the difficulty in achieving standards, namely the enormous differences in methods of assessing nebulizer performance. Though the "device related" issues are well covered, some additional material on formulation (preservatives and excipients sterility) could have been added for completeness.

Chapter 3, "New Developments in Nebulizer Technology," provides a peek into the future of aerosolized-drug delivery. A hypothetical list of features composing the "ideal drug aerosol delivery system" is presented, along with a qualifying statement that it is probably impossible for a single device to embody all of the ideal features. The chapter goes on to review a fairly comprehensive collection of "next generation" aerosol-delivery devices that employ various microelectronics and nanotechnologies.

There are 8 chapters in the clinical section of the book. Basically these chapters describe various approaches and experience in treating specific disease states with nebulized drugs. Where appropriate, they describe the differences between various aerosolization methods, such as metered-dose inhaler, powder inhaler, and nebulizer, and especially the different outcomes that may result from a particular choice of device. Though no single chapter explores the types of drugs that can be given via the aerosol route, the interested reader can discover that information scattered in these chapters.

Chapter 4 reviews the treatment of acute asthma and exacerbations of COPD via nebulization of β_2 agonists, anticholinergics, and corticosteroids. Briefly mentioned are a few of the other nonmainstream drugs that have occasionally been used, such as epinephrine, magnesium, and furosemide.

Chapter 5 looks at nebulizer use for chronic asthma and COPD and discusses nebulization as a means of maintenance therapy and as a method to treat patients at home to prevent or reduce hospitalizations.

Chapter 6 deals with "Special Applications of Aerosol Therapy" and rightfully points out that aerosols can be useful for applications other than asthma and COPD. For example, the topical delivery of aerosolized antibiotics for the treatment and pre-

vention of pulmonary infections is gaining success now that there is a better understanding of the delivery systems and the effect of the patient's pathophysiology on aerosol delivery. Similarly, specialized aerosols (prostacyclins and phosphodiesterase inhibitors) for treating pulmonary hypertension are beginning to show promise, though most of the research is still in the experimental stages and definitive clinical applications have not yet been described. Topical delivery of cyclosporine for the prevention of acute pulmonary rejection in lung allograft recipients is also showing promise. Also being researched is nebulizer delivery of opioids for palliative care of patients dying from terminal lung cancer and end-stage COPD, though that is controversial because of the difficulty in adequately assessing outcome.

Chapter 7 covers the use of aerosolized antibiotics for cystic fibrosis (CF) and bronchiectasis. Use of nebulized antibiotics for those conditions was first described in the mid-1940s and has had variable success over the years. Currently, nebulized antibiotics are regarded as effective therapy for *Pseudomonas* infection in patients with CF. There is now good potential to improve the quality of life and survival, owing in part to our better understanding of aerosol delivery of antibiotics.

Chapter 8 describes various other drugs that can be aerosolized for patients with CF or bronchiectasis. These include various mucolytics and wetting agents, bronchodilators, steroids, amiloride, and heparin. Because CF patients are frequently prescribed a multitude of inhalation drugs, the chapter warns about the mixing of medications in the same nebulizer. Tempting though that may be, in order to cut down on treatment time, mixing drugs may result in deleterious drug-drug interactions, untoward effects on the patient, or may impair the functioning of the aerosol delivery system so that its performance is not predictable or consistent. The chapter does a very good job of reviewing the clinical use and outcomes of 2 agents that CF patients use as mucolytics: inexpensive hypertonic saline solution, and the much more expensive solution of recombinant human deoxyribonuclease (aka, rhDNase or dornase alfa). The chapter describes and provides references about the implications of using various aerosol delivery systems with rhDNase.

Chapter 9, "Diagnostic Uses of Nebulizers," is chiefly concerned with nebulization

as a means of administering an aerosol challenge test to quantify airway responsiveness. The chapter describes various test approaches and their interpretation and usefulness. A nebulizer is necessary to generate the aerosol for an airway challenge test. The physical characteristics of the aerosol (nebulizer output and particle size) and, thus, the device that creates the aerosol, are important determinants of the success of the procedure. Similarly, radioactive aerosols are widely used for lung-deposition imaging and for measurement of mucociliary clearance. The chapter mentions these in a mere 3 paragraphs; we would have preferred to see more on this topic, because radio-aerosol studies have provided valuable methods for investigating the interactions between inhaled particles and the human respiratory tract.

Pediatric patients present special challenges for nebulization therapy, although nebulization can be quite effective with children. Chapter 10 describes the anatomical and physiological differences that give rise to those challenges.

Chapter 11 covers the use of nebulizers in primary care, and the authors acknowledge that nebulizers should not be the first choice for maintenance therapy of asthma or COPD. Nevertheless, greater emphasis should have been given to the increased use of long-acting bronchodilators such as salmeterol, formoterol, and tiotropium (as well as the use of long-acting bronchodilator/steroid combination products) that do not use nebulizer technology. The change from short-acting bronchodilators to long-acting bronchodilators will probably decrease nebulizer use, and the clinical and pharmacoeconomic implications of that trend merit greater emphasis, in our view.

In conclusion, **Practical Handbook of Nebulizer Therapy** provides a valuable and detailed review of the clinical applications of nebulization, and despite its Eurocentric tendencies, it should be a valuable reference on nebulization for respiratory therapy departments and libraries.

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Acute Exacerbations in Chronic Obstructive Pulmonary Disease. Nikos M Siafakas, Nicholas R Anthonisen, and Dimitris Georgopoulos, editors. (*Lung Biology in Health and Disease* series, Volume 183, Claude Lenfant, executive editor.) New York: Marcel Dekker. 2004. Hard cover, illustrated, 603 pages, \$195.

Volume 183 of the *Lung Biology in Health and Disease* series is devoted to exacerbations of chronic obstructive pulmonary disease (COPD). This is a timely contribution and nicely complements the previous volume in this series, which was devoted to pharmacotherapy for COPD exacerbation. The editors assembled over 50 contributors, from all over the world. The book has 32 chapters and 9 parts. The reason for grouping the chapters into parts was not clear to me and did not seem to help the flow of the volume.

The first part begins with some general aspects of COPD exacerbation, including definitions, epidemiology, and the effects of exacerbations on the natural history of COPD, and it ends with a chapter on the economic burden of COPD exacerbation. The chapters in this part are quite short and probably could have been combined. The chapter on economics highlights the lack of data available on the human and economic cost of exacerbations of COPD.

Part 2 has 2 chapters that focus on the pathology and immunology of COPD exacerbation, and it gives a nice overview of the role of oxidative stress and cytokines in smoking and COPD exacerbation. Some of the pathology figures are hard to interpret because they are in black-and-white, with low resolution. This section includes a chapter that covers biomarkers of COPD, a subject of growing interest that may help us better manage COPD exacerbation.

Parts 3 and 4 are made up of chapters that cover the clinical and diagnostic aspects of COPD exacerbation. There is a discussion of how COPD exacerbation may be a systemic illness, and a comprehensive review of the infectious causes of COPD exacerbation. There is not much new in the chapter on signs and symptoms, but it is a nice review and a good update. The chapter on gas exchange is detailed and basic, but not oriented toward the clinician. There is an excellent chapter on imaging, with some very crisp radiographs and some nice computed tomograms, and this chapter was one of my favorites. Following it is a chapter on