

Particle Toxicology. Ken Donaldson and Paul Borm, editors. Boca Raton: CRC Press. 2007. Hard cover, illustrated, 434 pages, \$159.95.

The goal of this book is to present a state-of-the-art review of particle toxicology. Its focus is on the mechanisms of toxicity of particles at the molecular, subcellular, cellular, animal, and human levels. The main consideration is of ambient particles; that is, airborne particulate matter or particles $\leq 10 \mu\text{m}$ in diameter (PM_{10}). These are further differentiated into various size classes (eg, coarse particles [$\text{PM}_{2.5-10}$], fine particles [$\text{PM}_{2.5}$ and $\text{PM}_{1.0}$], and ultrafine particles [$\text{PM}_{0.1}$]). Briefer consideration is given to particles of industrial or occupational importance (eg, silica and asbestos fibers [particles at least 3 times longer than their width or that have an aspect ratio of $> 3:1$]). Man-made mineral fibers are only briefly alluded to, and some consideration is given to the toxic effects of diesel exhaust particles, wood smoke, and cigarette smoke. The health effects of particulates and their relevance to medicine are emphasized in nearly all of the chapters, but perhaps none more so than in the second-to-last chapter, which is about the particle of the 21st century—nanoparticles—in the chapter “Nanoparticles in Medicine,” by Borm and Muller-Schulte. Nanoparticles are particles of molecular size: $\leq 20 \text{ nm}$ in diameter. Not only do the hazards and risks of nanoparticles need to be studied, but nanoparticles also have medically useful aspects, such as drug delivery tools and as imaging and diagnostic tools. All in all, this is a book of impressive scope.

The editors, Donaldson and Borm, are well known and highly respected scientists in the field of particle toxicology and are co-editors of the journal *Particle and Fibre Toxicology*. The 2 editors are co-authors of the first chapter and contributed to 4 other chapters. In addition to the co-editors, 47 world-class scientists wrote 22 chapters for this book. Twenty-six authors are from Europe (including the 2 co-editors), 21 are from the United States, 1 is from Canada, and 1 is from India. The collaborative nature of research on this subject is demonstrated by

the fact that only one chapter has a single author.

The co-editors set the tone for the comprehensive nature of this book in Chapter 1, “An Introduction to Particle Toxicology: From Coal Mining to Nanotechnology.” Studies in the first half of the 20th century set the stage for a substantial increase in research activity in the 1970s and 1980s on the fibrotic properties of silica and coal dust and the carcinogenic effects of asbestos. Then, in the 1990s and into the 21st century, came a shift in research emphasis to the toxic effects of ambient particulate matter, and in the last 3–4 years, to the toxicology of nanoparticles. Along with the shift in research emphasis came a change in focus of the research. Aspects of this change in focus included the population of interest (from occupational groups to the population at large), the size of the particles studied (from coarse to fine, to ultrafine, and presently to nanoparticles), the target organ studied (from effects on the respiratory system to effects on other organs, particularly the cardiovascular system), and relevant exposure levels (from studying toxic effects at doses in the mg/m^3 range to doses in the $\mu\text{g}/\text{m}^3$ range).

The book's chapters are not grouped into sections, but they do follow a logical sequence. After the introductory chapter, Chapter 2 is the only nonbiological chapter, but rather has a geological focus: “Mineralogy and Structure of Pathogenic Particles,” by Jones and BéruBé. A chapter on particle dosimetry is followed by a group of chapters on toxic mechanisms, such as fibrosis and airway remodeling, oxidative and nitrosative stress, particle-cell membrane interactions (including translocation of ultrafine particles across cell membranes), inflammation and the possible role of metals, particle-associated organics, and cell-signaling pathways. Then follows a group of chapters on the various target organs (eg, immune system, cardiovascular system, including blood and endothelial cells, brain and nervous system, and genotoxic effects and the role of genetic background). An overview and conceptual framework is the subject of the final chapter.

Each chapter begins with an outline of the chapter's contents, which consist of sub-

headings and their associated page numbers. This feature, along with the entries in the index, greatly facilitates searches for specific information, such as the relevant particle variables regarding particle dosimetry (Chapter 3), the role of redox active metals (Chapter 5), and the factors that affect particle toxicity (Chapter 17).

A subject of emphasis in this book is the toxic effect of particles at the organism level. Such studies often involve histological and pathological analyses, and this book is illustrated with micrographs (either at the light or electron-microscope level of resolution) or schematic structural drawings in 12 of the 22 chapters. An 8-page color insert reproduces color illustrations otherwise shown in black-and-white in the chapters. In addition, the text is supported by a number of graphs and tables.

A great strength of this volume is as an up-to-date reference book. Each chapter has a separate references list and most chapters have a copious number of citations, including a high proportion in the 1990s and 2000s (through 2005). There are a few citations to publications in 2006, including some electronic publications available before publication in print. In total, the book has approximately 105 pages of references; I calculated an average number of 23 references per page, which yields a total of some 2,415 references (less duplicates among the various chapters).

There are a few inconsistencies in how individual chapters are organized. Most begin with an introduction or overview, but a little more than half end with a conclusion or discussion. Only 13 of the 22 chapters have both. Eight have an acknowledgments section. Most chapters cite publications in the text by author and year, with an alphabetical list of citations by author, but 4 chapters use numbered lists of citations. More diligent proofreading would have helped. Errors include the occasional use of undefined abbreviations, incorrect units (mg/m^3 vs $\mu\text{g}/\text{m}^3$) or no units given, a mention of a Chapter 23 when there are only 22 chapters in the book, and typographical errors such as “preset” when “present” was intended.

Overall, this book is highly recommended. It is a compendium of accurate information, written by scientists with ac-

tive research programs on the subject. As is stated simply in the final summary chapter, what this book is about is trying to answer 2 questions: what is it about particles that makes them harmful or not? and how do harmful particles cause harm? Though the answers remain incomplete, the contributors to this book did an excellent job of compiling the information relevant to answering those questions.

This volume would be most useful for university and medical-center physicians who are active researchers, toxicologists, pathologists, environmental health researchers, air pollution experts, government regulators, and epidemiologists who would like to understand better the toxic mechanisms and health effects of particles.

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The author of this review reports no conflict of interest.

Pulmonary Drug Delivery: Basics, Applications and Opportunities for Small Molecules and Biopharmaceuticals. Karoline Bechtold-Peters and Henrik Luessen, editors. *APV-Pharma Reflexions* series, volume 2. Aulendorf, Germany: Editio Cantor Verlag. 2007. Soft cover, illustrated, 412 pages, \$200.

In 1971, medical aerosol therapy in the hospital was largely use of drugs such as isuprel and racemic epinephrine, and our biggest choices were mainstream or side-stream jet nebulizers, with an occasional ultrasonic nebulizer thrown in the mix. Meanwhile, aerosol innovations such as the pressurized metered-dose inhaler, introduced in the mid-1950s, were left in the medicine cabinet when patients entered the acute care setting. Only after another 15 years, and as our scope of practice began to expand from the hospital to the clinic and home, did we become more active in supporting the use of the innovative dry powder inhalers and pressurized metered-dose inhalers, with the broader range of medications that they were designed to deliver.

In the hospital, respiratory therapists have been at the epicenter of the aerosol universe, even though liquid nebulization represents far less than 5% of aerosol therapy

prescribed to patients. Nonetheless, as a profession we receive far more time learning about the range of aerosol delivery devices and inhaled medications than virtually any other medical or allied health profession. This education and our involvement in therapy administration positions us to be valuable advisors on device options and their proper use for the health care team. However the 20–40 pages in the typical 1,200+ page respiratory care textbook is not sufficient to fulfill that important role. Journals such as *RESPIRATORY CARE* have been a tremendous source of more comprehensive information on aerosol, but its focus is more clinical application and differential selection than product development and characterization.

Respiratory therapists offer a unique perspective on the use and usability of aerosol devices. This has been recognized by increasing numbers of biotechnology and pharmaceutical companies that seek knowledgeable respiratory therapists to contribute in a variety of functional areas, including research and development, clinical operations, regulatory affairs, business development, marketing, and sales. The transition from the bedside to the world of biotechnology and pharmaceuticals can be both exciting and disorienting, and requires a rather steep learning curve.

Transition to aerosol device and drug development can be just as disorienting for pharmaceutical development professionals with expertise in oral and parenteral dosage forms. That is why the International Association for Pharmaceutical Technology (*Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik [APV]*) sponsored a 2-day workshop on pulmonary delivery. Over the next 5 years the core faculty, with some additional academic and industry experts, put pen to paper to create 6 chapters to bridge the most relevant topics in pulmonary research and development.

Chapter I introduces the principles of aerosol drug delivery in 2 therapist-friendly parts. "Understanding Clinical Aerosol Therapy" describes the respiratory system and the range of devices and drugs currently used in the treatment of asthma and chronic obstructive pulmonary disease. "Biophysical Parameters Determining Pulmonary Drug Delivery" is a primer on factors that affect local and systemic aerosol delivery. This is familiar territory for respiratory clinicians, with additional information not available in our standard texts.

Chapter II focuses on models used to test drugs and devices. In vitro models for pulmonary drug absorption and in vivo animal models are described in sufficient detail to provide good orientation to the processes required for clinical aerosol drug/device development. A clinician's perspective on systemic aerosol therapy focuses on the examples of insulin, heparin, and estradiol.

Aerosol application devices are the focus of Chapter III, which starts with a comprehensive review of current aerosol delivery device technology, and transitions to the role of new and emerging technologies in pulmonary drug targeting. Again, this is familiar territory for the therapist, that should add depth and breath to our standard training.

Chapter IV, "Formulation and Production," describes the science of formulating drugs for use with devices. The form and function excipients added to the active drug are described in some detail, and systems used for making and packaging dry powders are presented in a clear and readily assimilated format.

Chapter V, "Regulatory Issues and Analytics," was an unexpected pleasure. The pedantic aura surrounding regulatory affairs is dissipated with an easy-to-understand functional description of the regulatory framework of drug development, integrated with the methodologies required for device and drug testing and aerosol characterization.

The final chapter discusses new trends and opportunities for aerosol drug development. Examples of microparticles and liposomes as pulmonary delivery systems are described. The paradigm of systemic delivery through the lungs is explored, as is the use of aerosol for delivery of vaccines. This culminates in a review of market trends in pulmonary therapies.

This is an excellent, up-to-date primer ideal for practicing therapists who want to bolster their knowledge of and skills with aerosol devices and delivery systems, as well as those who might want to play a role in making new aerosol products available for meeting unmet needs of our patients by participating in the biotechnology and pharmaceutical development process.

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Nektar Therapeutics manufactures aerosol devices. The author reports no other conflicts of interest.