

In summary, **Coronary Circulation and Myocardial Ischemia** is an elegant, compact summary of the basic science and physiology, applied physiology, functional assessment, and treatment of coronary circulation and myocardial ischemia as known at the time of the initial (hard-cover) publication in 2000. Since then cardiovascular research has substantially advanced our understanding and treatment of ischemic heart disease, but those new findings were not included in the 2002 paperback edition of **Coronary Circulation and Myocardial Ischemia**. Certain of the new treatments are major advances, including the widespread use of angiotensin-converting enzyme inhibitors, statins, clopidogrel, novel anti-angina agents such as nicorandil (in Europe), and rapamycin-coated stents. These new advancements greatly benefit our patients but, unfortunately, make **Coronary Circulation and Myocardial Ischemia** dated. One additional note: the book suffers from many irritating errors in English usage, grammar, and spelling, which should have been corrected by the copy editor.

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**Inhalation Therapy for Pulmonary Hypertension: The Proceedings of a Symposium Held at the Annual Congress of The European Respiratory Society, Berlin, September 2001.** Timothy Higenbottam and Celia Emery, editors. New York: Parthenon. 2003. Soft cover, illustrated, 110 pages, \$99.95.

Twenty years ago, severe forms of pulmonary hypertension were considered a “fate”, rather than a “challenge,” by physicians, nurses, and respiratory therapists. Interest in this field of pulmonology has grown, mainly because of encouraging new therapy options, one of which is inhalation therapy, using either gases (eg, nitric oxide) or aerosolized drugs (eg, prostanoids). The enormous progress on this subject gave rea-

son for a special symposium, which was held in Berlin, Germany, in September 2001, during the Annual Congress of the European Respiratory Society. The presentations at the conference are now compiled in this soft-cover book.

Unlike usual textbooks, which try to give a complete review, this book discusses only the latest advances in inhalation therapy for pulmonary hypertension, for pharmacologists, toxicologists, physicians, respiratory physiologists, and graduate and medical students who are interested in these discipline. The editors, Timothy Higenbottam and Celia Emery, successfully maintained the logical structure of the symposium and included the transcribed post-presentation discussions between the presenters and the audiences, which is a charming way to make problems and criticisms visible that might be easily bypassed in reading the text.

Based on the table of contents, the reader might assume that this book refers exclusively to inhaled prostanoids. Actually, the book addresses many clinical questions in pharmacology, pathophysiology, and new therapeutic possibilities for severe pulmonary hypertension.

Higenbottam wrote Chapter 1, which presents the historical background and scientific rationale for the use of aerosolized prostanoids. The chapter describes the main advantages of the prostanoid substance group (vasodilation and inhibition of platelet aggregation), as well as the disadvantage of physiological prostacyclin for clinical use. The rapid hydrolyzation and inactivation of the molecule after contact with oxygenated blood fluids led to the development of similar, more stable substances. In addition, the author refers to the World Health Organization's classification of pulmonary hypertension, to demonstrate which patients are responding to inhalation therapy. This leads to the pathophysiology of pulmonary arterial hypertension, which is the topic of Chapter 2, written by Robert Naeije. The author, who is a world expert in this field, points out that the mechanisms of pulmonary hypertension development are incompletely understood. The text presents the genetic patterns of pulmonary hypertension patients as well as additional aspects of specific pathological changes (so-called “plexiform lesions”), which are speculated to be related to genetic mutations. Then the text describes inflammatory pathways of the pulmonary vasculature, with spe-

cial regard to the relationship of inflammation to coagulation, serotonin-dependent pathways, and cellular alterations of the vascular endothelium, the pulmonary artery smooth muscle, and the adventitium. Unfortunately, this chapter does not have any figures, which would help illustrate the complex pathophysiology. Nevertheless, the text's concise description makes it obvious that the crucial point is the disrupted equilibrium between endothelium-derived vasoconstrictors and vasodilators and that therapy and new approaches should be aimed at correcting those abnormalities.

In Chapter 3 Gerald Simonneau describes alternative routes of prostanoid administration. Simonneau also points out the short half-life of physiological prostacyclin, as well the problems with and adverse effects of long-term treatment of pulmonary hypertension with continuous intravenous prostacyclin infusion. Several other modes of prostanoid administration have been investigated that are less invasive, potentially less costly, and associated with fewer severe complications. First, subcutaneous treprostinol therapy is presented. Treprostinol is a much more stable prostacyclin analogue, which obviates the central intravenous catheter and thus improves patient compliance. A randomized, controlled trial demonstrated a significant improvement in patient function variables. The data are included in clear tables and figures that are of very good quality and easy to understand. That section is followed by data from another administration mode: oral administration of beraprost. Again, a randomized, controlled trial demonstrated significantly better and clinically important improvement in the treatment group. In summary, this chapter nicely demonstrates the feasibility, efficiency, and safety of stable prostacyclin analogues.

Prostanoids, however, are not the only therapeutic option for patients with severe pulmonary hypertension. Chapter 4, written by Nazzareno Galiè et al, describes non-prostacyclin modes for treating pulmonary hypertension. This section begins with another short review of the pathophysiology, to demonstrate how and why other substance groups are also effective. The disturbed equilibrium of vasoregulation includes additional metabolic abnormalities, such as thromboxane-, endothelin-, nitric oxide-, and phosphodiesterase-dependent pathways. The referring therapeutic options are

presented, supplemented by excellent graphs and figures, and completed by a final review of nonpharmacologic treatment options such as the graded balloon atrial septostomy or organ transplantation.

Unfortunately, the book has some minor typographical errors, most of which are not important but are nevertheless a bother when they appear both in the text and in the reference list; the first author of one of the most important reports on inhaled nitric oxide, Pepke-Zaba, is misspelled, which can make it difficult for the reader to find the correct reference.

Undoubtedly, the main issue in **Inhalation Therapy for Pulmonary Hypertension** is to demonstrate the benefit of the aerosolized prostacyclin analogue iloprost in patients with severe pulmonary hypertension, which is addressed in the 2 final sections. Chapter 5, written by Werner Seeger, describes the basic concept of inhaled prostanoids. The author presents the principles of inhalation therapy with regard to anatomical and physiological aspects within the lung, technical problems of correct distribution of inhaled drugs, and special problems of patients with acute respiratory distress syndrome and pulmonary hypertension. Several controlled and uncontrolled studies are mentioned and compared with other options (eg, inhaled nitric oxide). The benefits of aerosolized iloprost are convincingly demonstrated. In most cases the figures are clear and self-declaring. Some of them, however, are too complex (Figs. 7 and 8) and potentially misleading, since the author did not include legends, so it is difficult to distinguish the groups. This is a pity but only slightly diminishes the book's overall high quality.

In the final chapter (Chapter 6), Horst Olschewski presents the data from the important randomized, controlled trial on aerosolized iloprost with patients suffering primary and nonprimary pulmonary hypertension (the AIR study),<sup>1</sup> which revealed the outcome benefit of inhalation therapy among those patients, and the author clearly and concisely describes the convincing results. The figures and tables are excellent, and it is a noteworthy feature of this trial that a substantial proportion of patients from a poor functional class were included, who have hitherto been regarded as unlikely candidates for inhalation therapy. This chapter's discussion section addresses dose-response evaluation, technical limitations of nebuliz-

ers, and how to estimate the alveolar distribution of aerosolized drugs.

I think the book's editors achieved their aims. The book's overall appearance is very good; the chapters are well structured and in a logical sequence; the various aspects of the topics are put into titled paragraphs, each of which can be read as its own section, providing clear and logically sound findings and arguments. The writing is mostly clear and concise, and there are very few typographical errors. The overall quality of the figures and tables is excellent, frequently enriched by clear and ingenious schemes and cartoons. The references cited are useful and cover the material well, and the index is well-structured and contains many useful subheadings.

I think **Inhalation Therapy for Pulmonary Hypertension** could reach a broad readership of physicians and scientists, although the interest of nurses will probably be limited. It was obviously not intended to include nurses and respiratory therapists in its audience, which has to be registered as a drawback of this book, although the use of inhaled drugs outside the ICU and outside the hospital will become a relevant and economically important issue in the future.

My final criticism concerns the book's high price. In my view, approximately \$1 per page is a high threshold, maybe too high, and I hope the publisher will revisit that issue.

Nonetheless, for the clinician the book offers a good "view into the future," thus encouraging clinicians to continue clinical evaluation of inhalation therapy as a fascinating opportunity. **Inhalation Therapy for Pulmonary Hypertension** is an excellent tool that helps us to not lose reference to pathophysiology, pharmacology, and practical aspects of inhalation therapy in clinical use.

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European Respiratory Review. European Lung White Book. RespiMedia. Guidelines. Involvement of the pulmonary micro-vasculature in chronic thromboembolic pulmonary hypertension (CTEPH) S. Gáñther, O. Mercier, X. Jañs, D. Montani, S. Maitre, J.F. Paul, V. de Montprñville, E. Fadel, M. Humbert, G. Simonneau, P. Dartevelle, P. Dorfñller (Clamart, Le Plessis Robinson, Kremlin-Bicñtre, France). Belongs To categories: Adult respiratory medicine COPD, Pulmonary hypertension, Cardiac disease Paediatric respiratory medicine Paediatric respiratory medicine. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK. Abstract. Table 1 Recommendations on the therapy of acute pulmonary hypertension in the paediatric ICU. Recommendations Oxygen should be given when transcutaneous oxygen saturation <95% in children with PH and normal cardiac anatomy<sup>2</sup> Intravenous prostanoids should be considered to treat children with severe PH<sup>3</sup>. Potts shunt As an alternative to lung transplantation, creation of an aorto-pulmonary shunt (Potts shunt) in children with suprasystemic idiopathic PH has been described in a small case series.<sup>37</sup> Although these rst long-term results are promising, no recommendation can be made because of the limited experience at this stage. Pulmonary hypertension (PH), defined as an elevated mean pulmonary arterial pressure (mPAP)  $\geq 25$  mmHg, is a common complication of chronic lung disease (CLD). PH often progresses to right heart failure (RHF), with initial compensatory right ventricular (RV) hypertrophy becoming overwhelmed by increased systolic requirements, whilst left ventricular (LV) systolic function remains preserved. In fact an elevated mPAP > 25 mmHg, indicating that at least 50% of the pulmonary vascular bed has been damaged, is a late marker of lung vascular remodelling with significant impact on the RV [26]. Pulsed inhalation of mixed nitric oxide and oxygen, when compared to LTOT in stable COPD patients with PH, improved mPAP and PVR [83].