

## Book review on hypoxic respiratory failure in the newborn – from origins to clinical management

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Dear Sir/Madam,

I am writing to encourage the readers of *Pulmonary Circulation*, and others who are interested in pulmonary vascular disease in the neonatal period of life, to read a new comprehensive book on this subject entitled *Hypoxic Respiratory Failure in the Newborn – From Origins to Clinical Management* edited by Shyamala Dakshinamurti and published by Boca Raton FL: CRC Press/Taylor & Francis; Oct 2021. ISBN 9780367493998

Hypoxic respiratory failure, due to persistent pulmonary hypertension of the newborn (PPHN), has an incidence of occurring in 1–2 per 1000 live births despite access to tertiary-level obstetrical and neonatal care and is three times that rate in the developing world. Review articles on the development, diagnosis, and/or management of PPHN appear annually in many journals but are generally limited to discussion of current physiological knowledge or management strategies since no one review could fully encompass this growing field. Hence, any new book on pulmonary hypertension in the newborn has to first define its territory while capturing the subject as broadly as possible.

This book elects to follow the thread of hypoxia, as an originating etiology and defining feature of neonatal pulmonary hypertension. It is a comprehensive and thematic volume of topical articles by world-renowned authors addressing the evolutionary origins of hypoxia adaptation, the impact of oxygen on circulatory transition at birth, the biochemistry of hypoxia in the pulmonary circuit, as well as the classification, diagnosis and clinical management of hypoxic respiratory failure, and pulmonary hypertension in the neonate. This book has assembled all information pertinent to this topic in 38 chapters divided into five distinct sections, each marshalled by a dedicated co-editor. This strong interdisciplinary editorial team brings to bear complementary theoretical and practical expertise in different aspects of hypoxia and respiratory failure, and clearly a wide-ranging contact list – the book has over

80 contributing authors. Salient features of this book are helpful signaling pathway diagrams, conceptual illustrations, and synthesis figures by Satyan Lakshminrusimha.

*Section 1* on *The Origins of Hypoxia Tolerance* (co-edited by William Milsom), begins with context on the ontogeny of human fetal metabolic tolerance of hypoxia, a topic not discussed in comparable books. It then reviews human evolutionary adaptations for life and birth at altitude, before surveying the physiology of animals in extreme environments – llamas at high altitude, hibernating ground squirrels, and deep diving seals – and the impact of hypoxia on cardiorespiratory coupling across species. This section stands alone as a comparative physiology primer but also walks clinicians through the relevance of evolutionarily conserved mechanisms for coping with hypoxia that remain active in the human fetus.

*Section 2* (co-edited by Satyan Lakshminrusimha) deals with *Fetal Hypoxia*, including normative data on the human fetal environment, the impact of maternal hypoxia on the fetus (relevant to the COVID-19 pandemic during which this book was written), and the effects of postnatal oxygenation on normal circulatory and respiratory transitions.

*Section 3*, titled *Biology of Hypoxic Respiratory Failure in the Neonate* (co-edited by Steven Abman), details the physiology and biochemistry of neonatal pulmonary hypertension in all involved tissues (endothelium, smooth muscle, and myocardium), touching on structure–function relationships in pulmonary artery and heart, controversies in the development of relevant animal models, and mechanisms driving neonatal pulmonary hypertension from vasoconstrictor–vasodilator balance to reactive oxygen species,

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from remodeling and cell cycle regulation to epigenetics. This section constitutes a deep dive into pathophysiology and highlights opportunities for ongoing research.

Of course, acute perinatal hypoxia does not only impact the lung. *Section 4 on Hypoxia and Collateral Damage* (co-edited by Po-Yin Cheung) provides a targeted overview of other organs damaged by hypoxia in the neonate, and practical approaches to handle neuroprotection, pharmacokinetics, and anesthesia in the infant with hypoxic respiratory failure.

*Section 5*, the final section of the book entitled *Diagnosis and Management of Neonatal Hypoxic Respiratory Failure* (co-edited by Patrick McNamara), is the largest. It includes international epidemiologic data, detailed state-of-the-art diagnostic approaches including targeted neonatal echocardiography, management strategies for ventilation technologies and pharmacotherapies, troubleshooting tools to systematically approach the difficult-to-manage patient, and a series of scenarios where special considerations are required: the infant with diaphragmatic hernia, hypoxic ischemic encephalopathy, or prematurity. Of note, the terms hypoxic respiratory failure, neonatal pulmonary hypertension, and PPHN seem to be used interchangeably within this book; but this controversial point is addressed in

this section, by disambiguating the various pulmonary hypertension phenotypes which may present in the neonatal age group. Further work remains to be done to split up the natural histories of distinct pathophysiologies commonly lumped as PPHN.

It may be asked, why a scientist interested in reading about hypoxic llamas and a clinician keen to treat hypoxic infants pick up the same book? The book is divided and indexed in detail, so one can turn to the precise review article that suits one's current inquiry. But scanning through other sections gives one a bird's eye view of fascinating literature one might not have customarily dipped into, but which turns out to be surprisingly interesting and useful. Reading the whole volume provides a satisfying continuous narrative of hypoxia through the evolutionary and developmental timeline, and deeper insight into what might appear to be only a superficial problem solved by turning up the oxygen dial. This book is therefore recommended to practicing clinicians as much as to scholars in this field of science.

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