

# **Intermittent Hypoxia**

**From Molecular Mechanisms To Clinical Applications**

Editors

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## PREFACE

*“Science and men of science are cosmopolitans, and it seems hardly important whether a scientific truth develops at any particular spot on the globe, as long as the general diffusion of science allows all men to share in it.”*

**Claude Bernard**

(French physiologist, 1813-1878)

As inspired by the above-quoted wisdom of Claude Bernard (1813-1878), this book has gathered a tremendous global effort of 74 prominent experts from 17 countries in Asia, Europe, North America, and Oceania, focusing on the single subject – intermittent hypoxia. To our best knowledge, this is the very first and most comprehensive book (in English language) dedicated to a variety of topics on intermittent hypoxia. As the readers may extract from the Table of Contents, the 30 chapters are divided into 6 sections ranging from molecular aspects to merely clinical applications. We truly wish that this monograph could provide many valuable information to all interested scientists, researchers, sports coaches, trainers, and clinicians as well as medical and graduate students on the updated scientific basis and therapeutic regimens of intermittent hypoxia for utilizing its beneficial effects and preventing or reducing its detrimental effects. It is even more important and valuable that many contents of this book are not available or easily accessible in any of the peer-reviewed periodicals. This is mainly due to the fact that many innovative investigations and advanced applications in the field of intermittent hypoxia were originated in the former Soviet Union countries, which were severely underrepresented in the biomedical literatures in English language (also see our chapter on Historical Overview of Intermittent Hypoxia Research). One of our primary goals for this book is to provide a unified and unbiased forum for both the most renowned authorities in USA and the relatively less well-known but highly experienced investigators from a number of non-English speaking countries. We attempted to assist these groups of researchers to overcome their language barriers for effectively communicating their novel findings. This effort has proved to be rewarding as well as very time-consuming due to the excessive editing workload. We have tried our best to put the work quality first even at the cost of consequently postponing the publication timetable for several months.

In spite of our extensive efforts, the readers may still find many important research topics or clinical applications related to intermittent hypoxia that are not covered in this book. For instance, the studies on effects of intermittent hypoxia on tumor genesis and growth and the therapeutic applications of intermittent hypoxia training to treat of bronchial asthma, chronic obstructive pulmonary diseases, industrial pneumoconiosis, and gynecological diseases are not included. The effects of intermittent hypoxia on the pathogenesis and prognosis of diabetes, metabolic syndrome, and heart failure should also be of great interests in current clinical practice around the world. We therefore hope that these additional topics will be thoroughly discussed in the second edition of our book.

Finally we like to present a condensed list of acknowledgements. We first want to express our sincerest appreciation to each of the 74 contributing authors for spending their precious time to

write the outstanding chapters, which present the key value of this book. Indeed, it has been a scientifically challenging and culturally fulfilling process for us as editors to have the opportunity to interact with these distinguished scholars. We are truly honored for having a Foreword written by Prof. John B. West (University of California at San Diego, USA), one of the world-class authorities in Respiratory Physiology and Hypoxia Medicine. Many thanks to the management team and staff of Nova Science Publishers (particularly Mr. Frank Columbus, Ms. Maya Columbus, Mr. Michael Knespler, and Ms. Stephanie Gonzalez) for their encouragement, support, and extraordinary patience throughout the planning and publication process.

We also like to individually thank our academic mentors who inspired and promoted our careers. [From Lei Xi]: I like to dedicate this book to my three mentors - Prof. Paolo Cerretelli (University of Geneva, Switzerland), Prof. Jerome A. Dempsey (University of Wisconsin at Madison, USA), and Prof. Rakesh C. Kukreja (Virginia Commonwealth University, USA), who had guided me at the different stages of my academic career and made crucial impact on the formation and maintaining of my profound interests in Hypoxia Physiology and Pathophysiology since 1980s. [From Tatiana V. Serebrovskaya]: I want to dedicate this book also to three outstanding personalities who played fundamental roles in formation of my Weltanschauung and scientific knowledge. There are Prof. Platon Kostyuk and Prof. Philipp Serkov (Bogomoletz Institute of Physiology, Ukraine), my unsurpassed teachers in General Physiology, and the late Prof. John (Jack) Reeves (University of Colorado at Denver, USA) who gave me indelible lessons of selfless service to Hypoxia Science and true love to the people.

At last, we are indebted to our beloved families for tolerating the countless long hours we spent at office and home for writing and editing the book contents throughout the past two years. Without their sacrifice and moral support this book could not be completed.



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## FOREWORD

It is a pleasure and a privilege to provide a foreword for this book devoted to intermittent hypoxia. This is a topic that has attracted a great deal of attention in the last few years although its origins go back much further. An important feature of the subject is that it covers a very broad area including such diverse topics as lowlanders commuting to high altitude, training for athletic competitions, and potential applications in the prevention and treatment of a number of diseases. These subjects have been discussed in a variety of journals and professional meetings, and it is timely to have a compendium of in a single volume. Lei Xi and Tatiana Serebrovskaya can be congratulated on having the foresight to assemble 74 contributors for this first comprehensive book on the subject.

Of course humans have been intermittently exposed to hypoxia from time immemorial when travelers crossed high passes on route to some distant destination. We are reminded of the colorful reference to Acute Mountain Sickness in the classical Chinese history of the period preceding the Han Dynasty, the Ch'ien Han Shu, dating from about 30 BC. Here there is a reference to the Great Headache Mountain and the Little Headache Mountain which were reported to cause headache, vomiting, and other distressful symptoms. Subsequent ascents to high altitude such as those by Joseph de Acosta in Peru in the 16th century confirmed these problems, and they were magnified during the exploits of the early balloonists in the late 18th century, culminating in the tragic death of two balloonists in the French balloon Zenith in 1875.

However these periods of exposure to severe hypoxia were somewhat random in nature and the term "intermittent hypoxia" has come to refer more to planned repetitive events. My interest in intermittent hypoxia was first stimulated by the development of the commuting pattern of miners from sea level where they lived to mines as high as 4500 m in North Chile. This practice was introduced some 30 or so years ago, and in a typical operation such as in the Collahuasi mine, several thousand workers have taken part in this commuting pattern. Their home is at Iquique on the Chilean coast and they are bused up to the mine in a few hours where they spend the next 7 days working 12-hour shifts at altitudes of up to 4500 m, although the sleeping quarters are at the somewhat lower altitude of 3800 m. At the end of the week they return to their families at sea level for a further week. Studies of the physiology of this group show that they develop a sort of intermediate acclimatization between sea level and 4500 m.

Another group of workers who are exposed to intermittent hypoxia are astronomers who operate telescopes as high as 5050 m, also in North Chile. It is true that their exposure is not as regular as that described for the miners, but the altitude is appreciably higher. An important innovation for this group is oxygen enrichment of the room air at the telescope site because there is convincing evidence of neuropsychological impairment at this altitude. Another site with a number of telescopes is Mauna Kea in Hawaii where the summit is at about 4200 m. Interestingly however, although oxygen enrichment of room air would clearly be advantageous to improve neuropsychological function at this altitude, there has been considerable reluctance to take advantage of it.

Another extensive application of intermittent hypoxia has been in training for athletic events at sea level. There seems to be no doubt that the "sleep high-train low" regime is beneficial to some athletes, particularly as in this competitive environment a fraction of a second or so can mean the difference between a gold and silver medal. However interestingly, there still seems to be uncertainty about the precise regime that gives the most beneficial results, and also there are apparently substantial differences between individual responses. This is an area where a great deal of time and money is being spent in trying to elucidate the physiological mechanisms and to implement the most advantageous mode.

Finally there has been a great deal of research on the potential value of intermittent hypoxia in the prevention or treatment of some diseases. Much of this work was carried out in the Soviet Union before people in Western Europe and North America became interested in intermittent hypoxia. In fact one of the earliest proponents of intermittent hypoxia was Nikolai Sirotinin (1896-1977) who did much of his work in the Bogomoletz Institute of Physiology in Kiev. Sirotinin was one of the first people to describe “cross-adaptation,” that is the fact that adaptation to one particular physiologic stress, for example the hypoxia of high altitude, would improve tolerance to a different kind of physiologic stress, for example exposure to high acceleration. This area remains controversial, and indeed some of the claims from the use of intermittent hypoxia in the treatment and prevention of disease seems exaggerated to some Western scientists. Perhaps there is something of a cultural divide in this area. Nevertheless it is clear that in some instances, intermittent hypoxia does have value in the prevention and treatment of disease and further research of this area has a high priority.

It only remains for me to congratulate Lei Xi and Tatiana Serebrovskaya for their enterprise in putting together such a timely volume. I am sure it will make an important contribution.



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