TOPICS IN ENVIRONMENTAL PHYSIOLOGY AND MEDICINE

W. Brendel and R.A. Zink

High Altitude Physiology and Medicine

Springer-Verlag
New York • Heidelberg • Berlin

High Altitude Physiology and Medicine

Edited by
Walter Brendel
Roman A. Zink

With 159 Figures

Springer-Verlag
New York Heidelberg Berlin

Walter Brendel, M.D.
Institute for Surgical Research of the LM-University
Klinkum Grosshadern
D-8000 Munich 70
Federal Republic of Germany

Roman A. Zink, M.D.
Documentation Center for High
Altitude Medicine
and Urological Clinic of the
LM-University
Klinkum Grosshadern
D-8000 Munich 70
Federal Republic of Germany

Library of Congress Cataloging in Publication Data
Main entry under title:
High altitude physiology and medicine.
(Topics in environmental physiology and medicine)
Bibliography: p.
Includes index.
1. Altitude, Influence of. 2. Oxygen in the body.
3. Acclimatization. I. Brendel, Walter, 1922-
II. Zink, Roman A. [DNLM: 1. Acclimatization.
2. Adaptation, Physiological. 3. Altitude. WD 710
H638]
QP82.2.A4H53 612'.0144 80-28376

Printed in the United States of America.

9 8 7 6 5 4 3 2 1

ISBN 0-387-**90482-4** Springer-Verlag New York Heidelberg Berlin
ISBN 3-540-**90482-4** Springer-Verlag Berlin Heidelberg New York

Topics in Environmental Physiology and Medicine

edited by Karl E. Schaefer

Preface

High altitude physiology and medicine has again become important. The exceptional achievements of mountaineers who have climbed nearly all peaks over 8,000 m without breathing equipment raise the question of maximal adaptation capacity of man to low oxygen pressures. More importantly, the increase in tourism in the Andes and the Himalayas brings over 10,000 people to sites at altitudes above 4,000 and 5,000 m each year. At such heights several kinds of high altitude diseases are likely to occur, and these complications require detailed medical investigations.

Medical authorities need to inform both mountaineers and tourists as to how great a physical burden can be taken in the mountain environment without risk to health. Physicians need to know what kind of prophylaxis is to be employed at high altitudes to prevent the development of diseases and what therapeutic measures should be used once high altitude diseases have occurred. Moreover, the physical condition of the indigenous population living at higher altitudes such as the Andes and the Himalayas, who are exposed continuously to the stress of high altitude, requires our attention. We have become familiar with symptoms characteristic of chronic high-altitude disease: under special conditions this population has a tendency to develop pulmonary hypertension, which is associated with pulmonary edema, pulmonary congestion, and right heart failure.

This book will provide the latest up-to-date information on the recent developments in physiology and medicine of high altitudes for the medical researcher and the physician who treat patients suffering from high altitude sickness or give advice on preventive measures to their clients. The book is also intended to provide the newest teaching material on high altitude physiology and medicine to medical schools.

This volume contains contributions from many countries: Bolivia, China, France partly with investigators from Bolivia, Holland, India, Switzerland, USA, and West Germany. The publication is organized in two parts: (A) physiology of adaptation to high altitude and (B) high altitude sickness and therapy. In the first part the majority of articles deal with basic problems of oxygen transport and respiratory and circulatory control in rest and exercise at high altitude. New aspects

of sleep at high altitude and hormonal responses and electrolyte changes at high altitude are included.

The second part is concerned with altitude sickness and therapy and contains the latest contributions towards understanding and managing the two most important pathological disturbances at high altitude: cerebral edema and eye problems, and pulmonary edema. Moreover, acute and chronic mountain sickness is treated extensively. Preventive medicine measures at high altitude are presented in two reports. An overview of accidents and diseases at high altitude (Himalaya and Andes) is given, which makes the reader aware of the new dimension which modern tourism to the Himalayas and Andes has brought to high altitude medicine. A special section contains a proposal for international standardization in high altitude research and documentation of high altitude medicine.

Medical scientists have carried out in the past laborious and extensive investigations of high altitude physiology and medicine and continue to do so at present with more sophisticated methods and broader scope, opening up new fields of knowledge.

In recent years there has been a shift in the focus and emphasis on high altitude research. Previously the main areas of interest in high altitude physiology were external respiration, in particular ventilation and gas exchange of the lungs and an exploration of the mechanisms responsible for the increased ventilation observed at high altitudes under condition of reduced partial pressure of oxygen. Mechanisms sensitizing the respiratory center were found to depend on altitude and length of sojourn at high altitudes. As a result of increased ventilation a respiratory alkalosis develops. Its influence on the O_2-dissociation curve, the Bohr effect, and cerebral blood flow has been thoroughly investigated. The increase in hematopoiesis found under conditions of oxygen deficiency at high altitudes, which results in an increased number of red cells in the circulating blood and therefore in a larger oxygen-carrying capacity, has long been considered the basic mechanism of adaptation to low oxygen pressure.

Hematopoietin was "discovered" as a hormonal factor controlling erythropoiesis, and the influence of the kidneys on the formation of hematopoietin was established. However, the significance of these findings about adaptive mechanisms to high altitude oxygen deficiency related to respiration, gas exchange, and erythropoiesis declined with the advent of equipment providing oxygen at high altitudes and in space.

In the past comparatively little attention has been given to peripheral respiration, i.e., oxygen transport in capillaries and oxygen diffusion into tissues and mitochondria within cells. This lack of knowledge was largely due to the unavailability of specific methods required for the investigation of peripheral oxygen transport processes. In recent years new methods have been developed and dramatic advances in the knowledge of microcirculation at high altitude have been made. It is now recognized that high altitude disorders and diseases such as pulmonary edema and brain edema are related to disturbances of blood flow in capillaries and impairment of oxygen transport to mitochondria. The better understanding of microcirculation has made it possible to use more effective measures for prophylaxis and therapy of high altitude disorders.

Pioneers in high altitude physiology and medicine came from many different countries. Paul Bert (1878) was the first to become interested in the effect of reduced atmospheric pressure; Mosso (1897) and Cohnheim (1903) published

books on altitude physiology. Before and after World War I significant advances in high altitude physiology were made by Barcroft (1914), Haldane and Priestly (1935), Henderson (1938), Zuntz (1906), and Loewy (1932), as well as by Dill (1938), and Keys (1938), and Fleisch (1944), von Muralt (1948), and Verzar (1945).

Before World War II, in Germany, an active group of young physiologists, as researchers in aviation medicine or as mountaineers, became very interested in high altitude physiology. This group included Balke, Benzinger, Gauer, Hartmann, Hepp, Kramer, Luft, Noell, Opitz, Schneider, and Strughold. Their work has been published in *German Aviation Medicine, World War II*. Fundamental investigations were conducted, especially on respiration during acute and chronic hypoxia, hypoxia and anoxia of the brain, survival time of the brain and hypoxia tolerance. After World War II most of these young investigators went on a temporary or permanent basis to the United States to work on space physiology.

Significant progress in establishing the limits of adaptation to high altitude were made during high altitude expeditions carried out by Pugh at Mount Cho Oyu and Mount Everest (1957, 1964, 1968) and by Houston and Riley (1947) and West (1962a,b). In the 1950s, research on problems of high altitude adaptation in Germany was limited to few investigators (Brendel, 1956). Later a group formed in Munich, associated with the Institute for Surgical Research, studied problems of oxygen supply to tissues at high altitudes. Investigations were carried out during expeditions to the Kantschen Szönga by Zink et al. (1978) and at the Lhotse by Schaffert and Zink (1979). These investigations were based on our newly acquired understanding of the physiology and pathophysiology of the microcirculation and on the method of isovolemic hemodilution developed in Munich (Messmer, 1971, 1975) to combat disturbances of the microcirculation.

The encouraging experience with this method during expeditions to the Kantschen Szönga and Lhotse was the basic reason for organizing this symposium in Murnau, West Germany, and for inviting contributions to this volume by experts on capillary oxygen transport to tissue, especially to skeletal muscle and brain. We hope that the combined knowledge of these experts, specialists in respiratory physiology and our colleagues with practical experience in high altitude medicine of mountaineers and high altitude residents, will result in a better understanding of the pathophysiological processes of high altitude-induced diseases and complications.

The International Symposium on High Altitude Physiology and Medicine was organized by the Documentation Center for High Altitude Medicine (a section of the Association for Comparative Alpine Research, Munich) and the Institute for Surgical Research, LM-University of Munich. It was supported by the Volkswagen Foundation (I135 610).

References

1. Barcroft, J. (1925): The Respiratory Function of the Blood. In: Lessons from High Altitude. Cambridge, Massachusetts: Cambridge University Press.
2. Bert, P. (1943): Barometric Pressure (English translation of Paris edition, 1877.) Columbus, Ohio: College Book Company.
3. Brendel, W. (1956): Anpassung von

Atmung, Hämoglobin, Körpertemperatur, und Kreislauf bei langfristigem Aufenthalt in grossen Höhen (Himalaya). Arch. Ges. Physiol. *263*:227.

4. Cohnheim, O. (1903): Physiologie des Alpinismus. Wiesbaden, West Germany: Bergmann.
5. Dill, P.B. (1938): Life, Heat, and Altitude. Cambridge, Massachusetts: Harvard University Press.
6. Fleisch, A. and von Muralt, A. (1949): Klimaphysiologische Untersuchungen in der Schweiz, 1944–1948. Basel, Switzerland: Benno Schwabe.
7. Haldane, J.S. and Priestley, J.G. (1935): Respiration. Oxford, Great Britain: Clarendon Press.
8. Henderson, Y. (1938): Adventures in Respiration. London, Great Britain: Balliere.
9. Houston, C.G. and Riley, R.L. (1947): Respiratory and circulatory changes during acclimatization to high altitude. Am. J. Physiol. *149*:565.
10. Keys, A. (1938): Die Wirkung des Höhenklimas. In: Ergebnisse der inneren Medizin. Berlin, West Germany: Springer.
11. Loewy, A. (1932): Physiologie des Höhenklimas. Berlin, West Germany: Springer.
12. Messmer, K. (1975): Hemodilution. Surg. Clin. North Am. *55*:659. *Also* Sunder-Plassmann, L., Klövekorn, W.P., Holper, K., Hase, U., and Messmer, K. (1971): The physiological significance of acutely induced hemodilution. In: 6th European Conference on Microcirculation. Basel, Switzerland: Karger, pp. 23–28.
13. Mosso, A. (1898): Fisiologia dell 'Uomo sulle Alpi, 1897. German translation: Der Mensch auf den Hochalpen. Veit: Leipzig.
14. Pugh, C.G. (1957): Resting ventilation and alveolar air on Mt. Everest. J. Physiol. *135*:590.
15. Pugh, C.G. (1968): muscular exercise on Mount Everest. In: Joke, Exercise and Altitude. Basel, Switzerland: Karger.
16. Pugh, C.G. (1964): Man above 5000 meters—mountain exploration. In: Handbook of Physiology. Washington, D.C.: American Physiological Society, Chap. 55.
17. Schaffert, W. and Zink, R.A. (1979): How should we manage high altitude illness? In: Proceedings of the Hypoxia Symposium. Arch. Inst. North America, Calgary.
18. Verzar, F. (1945): Höhenklima-Forschung des Baseler Physiologischen Instituts. Basel, Switzerland: Benno Schwage.
19. West, J.B. (1962): Diffusing capacity of the lung for carbon monoxide at high altitude. J. Appl. Physiol. *17*:421.
20. West, J.B., et al. (1962): Arterial oxygen saturation during exercise at high altitude. J. Appl. Physiol. *17*:617.
21. Zink, R.A., Schaffer, W., Brendel, W., Messmer, K., Schmiedt, E., and Bernett, P. (1978): Hemodilution in high altitude mountain climbing. Proced. Amer. Soc. Anesthesiologists.
22. Zuntz, N., Loewy, A., Müller, D., and Caspari, W. (1906): Höhenklima und Bergwanderungen. Berlin, West Germany: Deutsches Verlagshaus.

Contributors

G. Antezana *Chapters 11, 19, 35*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

J. Arnaud *Chapter 11*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

A. Baethman *Chapter 30*
Institute for Surgical Research
Ludwig-Maximilians Universität München
D-8000 Munich 70, Federal Republic of Germany

L. Barragan *Chapter 19*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

K. Bitter *Chapter 10*
Abteilung Sportmedizin und Arbeitsphysiologie
Medizinische Hochschule Hannover
D-3000 Hannover 61, Federal Republic of Germany

H. Bender *Chapter 10*
Abteilung Sportmedizin und Arbeitsphysiologie
Medizinische Hochschule Hannover
D-3000 Hannover 61, Federal Republic of Germany

D. Böning *Chapter 10*
Abteilung Sportmedizin und Arbeitsphysiologie
Medizinische Hochschule Hannover
D-3000 Hannover 61, Federal Republic of Germany

F. Brandt *Chapter 32*
Eye Clinic
Ludwig-Maximilians Universität München
D-8000 Munich 2, Federal Republic of Germany

K.-M. Braumann *Chapter 10*
Abteilung Sportmedizin und Arbeitsphysiologie
Medizinische Hochschule Hannover
D-3000 Hannover 61, Federal Republic of Germany

W. Brendel *Chapters 27, 29, 34, 46*
Institute for Surgical Research
of the LM-University
Klinkum Grosshadern
D-8000 Munich 70
Federal Republic of Germany

P. Cerretelli *Chapters 2, 13*
Department of Physiology
University of Geneva
CH-1211 Geneva, Switzerland

C.-H. Chou *Chapter 22*
Shanghai Institute of Physiology
Academia Sinica
Shanghai, People's Republic of China

S.-C. Chu *Chapter 5*
Shanghai Institute of Physiology
Academia Sinica
Shanghai, People's Republic of China

G. Coates *Chapters 25, 26, 37*
Department of Medicine
McMaster University
Hamilton, Ontario L8S 4K1, Canada
and
Defense Institute of Environmental Medicine
Downsview, Ontario M3J 1P3, Canada

J. Coudert *Chapters 4, 11, 19, 24, 35, 40*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

L. Coudkowicz *Chapter 19*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

J.C. Cruz *Chapter 43*
Cardiovascular Pulmonary Research Laboratory
University of Colorado Medical Center
Denver, Colorado 80208, U.S.A.

P.E. di Prampero *Chapter 12*
Department of Physiology
University of Geneva
CH-1211 Geneva, Switzerland

J. Drouet *Chapter 24*
Département de Physiologie Humaine
Faculté de Médecine Paris XI
Paris, France

J. Duhm *Chapter 8*
Physiologisches Institut
der Universität München
D-8000 Munich 2, Federal Republic of Germany

J. Durand *Chapters 11, 14, 18, 19, 21, 24, 31, 40*
Département de Physiologie Humaine
Faculté de Médecine Paris XI
Paris, France

J. Ergueta Collao *Chapters 4, 11*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

M.L. Forsling *Chapter 39*
The Middlesex Hospital School
London WIP 6DB, United Kingdom

P. Gaehtgens *Chapter 17*
Institute for Normal and Pathological Physiology
University of Cologne
Cologne, Federal Republic of Germany

F. Garmendia *Chapter 23*
Institute of Andean Biology
University of San Marcos
Lima, Peru

G.W. Gray *Chapters 1, 25, 26, 37*
Department of Medicine
McMaster University
Hamilton, Ontario L8S 4K1, Canada
and
Defense Institute of Environmental Medicine
Downsview, Ontario M3J 1P3, Canada

J.D. Guieu *Chapter 40*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

M.-C. Gung *Chapter 44*
Shanghai Instutute of Physiology
Academia Sinica
Shanghai, People's Republic of China

N. Gutierrez *Chapters 4, 11*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

A. Morales Guzman *Chapter 35*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

P.H. Hackett *Chapters 33, 39*
Cardiovascular Pulmonary Research Laboratory
University of Colorado Medical Center
Denver, Colorado 80208, U.S.A.

B. Heimhuber *Chapter 28*
Documentation Center for High Altitude
D-8000 Munich 19, Federal Republic of Germany

C.S. Houston *Chapter 1*
Department of Medicine
McMaster University
Hamilton, Ontario L8S 4K1,
Canada

S.-T. Hu *Chapters 5, 22, 44*
Shanghai Institute of Physiology
Academia Sinica
Shanghai, People's Republic of China

H.-Y. Huang *Chapters 5, 22, 44*
Department of Respiration and Circulation
Shanghai Institute of Physiology
Academia Sinica
Shanghai, People's Republic of China

C. Jacquemin *Chapter 18*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

F. Kreutz *Chapter 17*
Institute for Normal and Pathological Physiology
University of Cologne
Cologne, Federal Republic of Germany

F. Kreuzer *Chapters 9, 20*
Department of Physiology
University of Nijmegen
Nijmegen, Holland

S.K. Kwatra *Chapter 42*
Voillabhbhai Patel Chest Institute
Dehli 110007, India

N. Lassen *Chapter 41*
Department of Clinical Physiology
Bispebjerg Hospital
Copenhagen, Denmark

G. Leguia *Chapter 35*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

H.P. Lobenhoffer, *Chapters 28, 34, 48*
Documentation Center
for High Altitude
D-8000 Munich 19,
Federal Republic of Germany

A. Lockhart *Chapter 19*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

D.W. Lübbers *Chapter 7*
Max-Planck-Institut für Arbeitsphysiologie
D-3400 Göttingen, Federal Republic of Germany

O.K. Malla *Chapter 32*
Nepal Eye Hospital
Katmandu, Nepal

A. Mansell *Chapter 37*
Departments of Radiology and Medicine
McMaster University
Hamilton, Ontario L8S 4K1,
Canada

C. Marconi *Chapter 13*
Department of Physiology
University of Geneva
CH-1211 Geneva, Switzerland

J. Mensch-Dechene *Chapters 19, 21, 40*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

M.D. McFadden *Chapter 1*
Department of Medicine
McMaster University
Hamilton, Ontario L8S 4K1,
Canada

K. Messmer *Chapters 16, 46*
Institute for Surgical Research
Ludwig-Maximilians Universität München
D-8000 Munich 70,
Federal Republic of Germany

J. Milledge *Chapter 39*
Northwick Park Hospital
Harrow, Middlesex,
England

A. Mognoni *Chapter 12*
Department of Physiology
University of Geneva
CH-1211 Geneva, Switzerland

C. Nahmias *Chapters 25, 26, 37*
Department of Medicine
McMaster University
Hamilton, Ontario L8S 4K1,
Canada
and
Defense Institute of Environmental
Medicine
Downsview, Ontario M3J 1P3
Canada

H.-H. Ning *Chapters 22, 44*
Shanghai Institute of Physiology
Academia Sinica
Shanghai, China

O. Oelz *Chapter 47*
Department of Medicine
University Hospital
Zurich, Switzerland

C.-F. Pa *Chapter 5*
Shanghai Instutute of Physiology
Academia Sinica
Shanghai
People's Republic of China

M. Paz Zamora *Chapters 4, 11, 19*
Institute Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

J. Piiper *Chapter 3*
Abteilung Physiologie
Max-Planck-Institut für Experimentelle
Medizin
D-3000 Göttingen
Federal Republic of Germany

A.C. Powles *Chapters 1, 25, 26, 37*
Department of Medicine
McMaster University
Hamilton Ontario L8S 4K1
Canada
and
Defense Institute of Environmental
Medicine
Downsview, Ontario M3J 1P3
Canada

J. Raynaud *Chapters 14, 24*
Département de Physiologie Humaine
Faculté de Médecine Paris XI
Paris, France

S. Recavarren *Chapter 43*
Department of Pathology
Universidad Peruana Cayetano Heredia
Lima, Peru

D. Rennie *Chapters 33, 39*
Rush Medical Center
Chicago, Illinois, U.S.A.

E.D. Robin *Chapter 6*
Stanford University
School of Medicine
Stanford, California 95305, U.S.A.

C. Rupp *Chapters 27, 28*
Documentation Center
for High Altitude Medicine
D-8000 Munich 19,
Federal Republic of Germany

W. Schaffert *Chapters 46, 48, 49*
Documentation Center for High Altitude Medicine
D-8000 Munich 19
Federal Republic of Germany

H. Schmid-Schönbein *Chapter 15*
Institute of Physiology
Rhein-Westfälische Technische Universität
D-5100 Aachen,
Federal Republic of Germany

R. Schneider *Chapter 28*
Institute of Physiology
Rhein-Westfälische Technische Universität
D-5100 Aachen,
Federal Republic of Germany

C.-Y. Shi *Chapter 44*
Shanghai Institute of Physiology
Academia Sinica
Shanghai, People's Republic of China

H. Spielvogel *Chapters 11, 19, 35*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

N.C. Staub *Chapter 38*
Cardiovascular Research Institute
and Department of Physiology
University of California
San Francisco, California, U.S.A.

J.R. Sutton *Chapters 1, 23, 25, 26, 37, 41*
Department of Medicine
McMaster University
Hamilton, Ontario L8S 4K1,
Canada
and
Defense Institute of Environmental
Medicine
Downsview, Ontario M3J 1P3
Canada

F. Trost *Chapter 10*
Abteilung Sportmedizin und Arbeitsphysiologie
Medizinische Hochschule Hannover
D-3000 Hannover 61
Federal Republic of Germany

Z. Turek *Chapters 9, 20*
Department of Physiology
University of Nijmegen
Nijmegen, Holland

E. Vargas *Chapters 4, 11, 19*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

P. Varene *Chapter 18*
Departement de Physiologie Humaine
Faculté de Médecine Paris XI
Paris, France

A. Veicsteinas *Chapters 12, 13*
Department of Physiology
University of Geneva
CH-1211 Geneva, Switzerland

R. Viswanathan *Chapters 36, 42, 45*
Voillabhbhai Patel Chest Institute
Dehli 110007, India

C. Webber *Chapter 37*
Departments of Radiology and Medicine
McMaster University
Hamilton, Ontario L8S 4K1, Canada

H.R. Weingart *Chapter 29*
Documentation Center for High Altitude Medicine
D-8000 Munich 19
Federal Republic of Germany

M. Zelter *Chapter 19*
Instituto Boliviano de Biología de Altura
Facultad de Medicina
Universidad Mayor de San Andres
La Paz, Bolivia

R.A. Zink *Chapters 27, 28, 29, 34, 46, 48, 49*
Documentation Center for High Altitude Medicine
D-8000 Munich 19
and Urological Clinic of the LM-University
Klinkum Grosshadern
D-8000 Munich 70
Federal Republic of Germany

Contents

Oxygen Affinity and Oxygen Unloading

Hypoxia and Anaerobic Metabolism

Flow Distribution and Oxygen Transport