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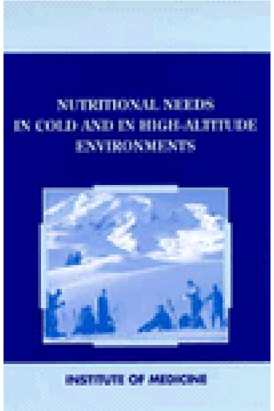

Nutritional Needs in Cold and High-Altitude Environments: Applications for Military Personnel in Field Operations

Bernadette M. Marriott and Sydne J. Carlson, Editors; Committee on Military Nutrition Research, Institute of Medicine

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THE NATIONAL ACADEMIES
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Nutritional Needs In Cold And In High-Altitude Environments

Applications for Military Personnel in Field Operations

Committee on Military Nutrition Research
Food and Nutrition Board
Institute of Medicine

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NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competencies and with regard for appropriate balance. Part I of this report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.
The Institute of Medicine was established in 1970 by the National Academy of Sciences to enlist distinguished members of the appropriate professions in the examination of policy matters pertaining to the health of the public. In this, the Institute acts under both the Academy's 1863 congressional charter responsibility to be an adviser to the federal government and its own initiative in identifying issues of medical care, research, and education. Dr. Kenneth R. Shine is president of the Institute of Medicine.
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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The image adopted as a logotype by the Institute of Medicine is based on a relief carving from ancient Greece, now held by the Staatlichemuseen in Berlin.

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Preface

This publication, *Nutritional Needs in Cold and in High-Altitude Environments*, is the most recent in a series of reports based on workshops sponsored by the Committee on Military Nutrition Research (CMNR) of the Food and Nutrition Board (FNB), Institute of Medicine, National Academy of Sciences (NAS). Other workshops or mini-symposia have included such topics as body composition and physical performance, nutrition and physical performance, cognitive testing methodology, fluid replacement and heat stress, nutritional needs in hot environments, food components to enhance performance, and strategies to overcome underconsumption. These workshops form a part of the response that the CMNR provides to the Assistant Surgeon General of the Army regarding issues brought to the committee through the Military Nutrition Division of the U.S. Army Research Institute of Environmental Medicine (USARIEM) at Natick, Massachusetts.

FOCUS OF THE REPORT

The conduct of military missions may require operations in hostile climatic environments. The success of such operations will be influenced by how well humans can perform in these extreme conditions. This report is concerned with nutrition and related factors that may influence the ability of personnel to operate in cold or high-altitude terrestrial environments. While there are differences in the stresses imposed by cold as compared to high-altitude environments, there are enough similarities to make them suitable to address at the same workshop and in the same resulting publication.

During the 1950s and 1960s, a series of symposia on Environmental Physiology in Cold and High Altitude Environments was sponsored or cosponsored by the U.S. Armed Services. These resulted in several publications (see Askew, Chapter 3 in this volume) during the period 1952–1967. While studies on working in environmental extremes continued after this time, they were largely through in-house research at various Armed Services laboratories. More recently, the scientists of USARIEM have been interested in updating information available on the impact of extreme environments and now of cold and high-altitude environments on the nutritional requirements of military personnel.

This publication follows previous CMNR studies requested through the Military Nutrition Division of USARIEM on *Fluid Replacement and Heat Stress* and *Nutritional Needs in Hot Environments*. The present report thus completes this series by summarizing the current state of knowledge about the influence of cold and high altitudes on nutrient requirements. Also identified are current programs for feeding troops in these two environments and recommendations for areas of future study.

HISTORY OF THE COMMITTEE

The Committee on Military Nutrition Research (CMNR) was established in October 1982 following a request by the Assistant Surgeon General of the Army that the Food and Nutrition Board of the National Academy of Sciences set up a committee to advise the U.S. Department of Defense on the need for and conduct of nutrition research and related issues. The committee's tasks are to identify nutritional factors that may critically influence the physical and mental performance of military personnel under all environmental extremes, to identify deficiencies in the existing data base, to recommend research that would remedy these deficiencies and approaches for studying the relationship of diet to physical and mental performance, and to review and advise on standards for military feeding systems. Within this context, the CMNR was asked to focus on nutrient requirements for performance during combat missions rather than requirements for military personnel in garrison. (The latter were judged as not significantly different from those of the civilian population.) Although the membership of the committee has changed periodically, the disciplines represented have consistently included human nutrition, nutritional biochemistry, performance physiology, food science, and psychology. For issues that require broader expertise than exists within the committee, the

CMNR has convened workshops or utilized special consultants. These workshops provide additional state-of-the-art scientific information and informed opinion for the consideration of the committee.

COMMITTEE TASK AND PROCEDURES

In early summer 1993, personnel from the USARIEM requested that the CMNR examine the current state of knowledge concerning the influence of cold and high-altitude terrestrial environments on nutrient requirements of military personnel. The task was to evaluate the latest research on energy requirements and potential changes in the requirements for other nutrients necessary to maintain military physical and mental performance in these harsh environments.

The committee was aware that the majority of the scientific work on these topics had been conducted through military research. Committee members decided that the best way to review the state of knowledge in this diverse area was through a small workshop at which knowledgeable researchers could review published research and provide an update on current knowledge. Such a workshop would enable the CMNR to review the adequacy of the current nutrient specifications for military operational rations and to identify gaps in the knowledge base that might be filled by future research.

A subgroup of the committee met in August 1993, determined the key topics for review, identified speakers with expertise in these topics, and planned the workshop for January 1994. Invited speakers were asked to prepare review papers on their assigned topics for presentation and subsequent publication and to identify gaps in the data base. The CMNR also believed that it would be beneficial to obtain the viewpoints of military commanders and training staff who worked with soldiers in cold and high-altitude environments. The planning group identified several speakers who were involved in mountain warfare training. These speakers presented informal commentary at the workshop on troop training and feeding. In addition, LTC Nancy King and CW4 Thomas Lange provided information on rations and the logistics of feeding soldiers in the cold and at high altitudes.

At the two-day workshop, the speakers gave formal presentations, which were followed by questions and a brief discussion period. The proceedings were tape-recorded and professionally transcribed. At the end of the presentations, a general discussion of the overall topic was held. On the day after the workshop, the CMNR met in executive session to review the issues, draw some tentative conclusions, and assign the preparation of draft reviews and summaries of specific topics to individual committee members. Committee members subsequently met in a series of working sessions and worked separately and together using the authored papers and additional reference material to draft the summary and recommendations. The final report was reviewed and approved by the entire group. These early working sessions included Richard Atkinson and Joël Grinker, who have since rotated off the committee.

The summary and recommendations of the Committee on Military Nutrition Research constitute Part I of this volume, and the papers presented at the workshop make up Parts II, III, IV, and V. As is part of the NAS process, Part I has been reviewed anonymously by an outside group with expertise in the topic area and experience in military issues. The authored papers in Parts II, III, IV, and V have undergone limited editorial change, have not been reviewed by the outside group, and represent the views of the individual authors. Selected questions directed toward the speakers and their responses are provided at the end of each part to give an indication of the discussion after each set of presentations. This is followed by a summary of an unpublished manuscript presented by K. K. Srivastava, "Environmental Stress Management at High Altitudes by Adaptogens," in Appendix A, brief biographical sketches of committee members and chapter authors in Appendix B, and a list of abbreviations used in this report in Appendix C. The invited speakers were also requested to submit a brief list of selected background papers prior to the workshop. These recommended readings, as well as relevant citations obtained through a computerized literature search and the citations from each chapter, are included in the Selected Bibliography (Appendix D).

ACKNOWLEDGMENTS

It is my pleasure as chairman of the CMNR to acknowledge the contributions of the FNB staff, particularly the excellent technical and organizational skills of Bernadette Marriott, the associate director for the FNB and the study director for the CMNR. Her assistance in organizing the workshop and in bringing the proceedings to the point of publication is greatly appreciated. I wish to acknowledge as well the fine contributions by the workshop speakers and their commitment to participating and preparing detailed review papers on relatively short notice. The CMNR appreciates the assistance of COL Eldon W. Askew and others from the USARIEM for their assistance in identifying issues of concern to the military and obtaining the involvement of the military personnel who participated in the workshop. COL Askew provided outstanding leadership to the Military Nutrition Research Program at USARIEM and clearly identified the issues to be reviewed by the CMNR. James Vogel, former director of the Occupational Health and Performance Directorate at USARIEM, retired in September 1995. Jim played an instrumental scientific role at USARIEM in areas that were related to a number of the CMNR reports. His expertise and leadership will be missed. The comments by FNB director Allison Yates provided helpful insight in the development of this final document. I want to thank Sydne Carlson who has recently joined the FNB staff and significantly contributed to editorial efforts on this report. The editorial efforts of Judy Grumstrup-Scott are gratefully acknowledged. The assistance of Susan Knasiak, CMNR research assistant, and Donna Allen, CMNR project assistant, in editing, proofreading, and word processing this report is greatly appreciated.

Finally, I am grateful to the members of the committee who participated significantly in the discussions at the workshop and in the preparation of the summaries of the proceedings. In particular, I wish to express my thanks to Richard Atkinson and Joël Grinker, who have completed their terms on the CMNR. Their participation in various committee activities, workshops, and reports has been very valuable in the conduct of CMNR activities. I wish also to express my appreciation to Allison Yates, whose term on the CMNR ended as she was appointed director of the FNB. We are pleased to have her continued input on our activities and her continued interest in our work. Committee members William Beisel and Gail Butterfield have been instrumental in organizing, reviewing, and writing major sections of this report. The full committee is grateful for their time and interest. I and the other members of the committee are very appreciative of liaison member Johanna Dwyer. She has been much more than a liaison to the FNB as she has actively participated in our meetings and workshops and assisted in preparing this workshop report.

The commitment of the members of this committee, past and present, who serve without compensation in participating and contributing to the successful outcomes of our activities is commendable. Any success this CMNR has had in fulfilling the committee's mission is due to their interest and diligence, and they are a real inspiration to me.

ROBERT O. NESHEIM, CHAIRMAN

COMMITTEE ON MILITARY NUTRITIONAL RESEARCH

Participants at the Workshop on Nutritional Needs in Cold and High-Altitude Environments, January 31–February 1, 1994, Washington, D.C. Back Row (Left to Right): Peter J. H. Jones, Harris R. Lieberman, Inder S. Anand, Reed W. Hoyt, André Vallerand, Thomas J. Lange, John L. Beard, Robert B. Schoene, Robert Gifford, Andrew J. Young, and Beau Freund. **Middle Row:** Irwin Taub; Robert S. Pozos; Nancy King; K. K. Srivastava; Ira Jacobs; Jacques A. LeBlanc; William D. Strauss; Russell W. Schumacher, Jr.; Robert D. Reynolds; Irene M. Simon-Schnass; Robert E. Feeney; Allen Cymerman; and Murray P. Hamlet. **Seated:** Barbara Shukitt-Hale, Orville A. Levander, Allison A. Yates, G. Richard Jansen, William R. Beisel, Robert O. Nesheim, Bernadette M. Marriott, Eldon W. Askew, Joël A. Grinker, and Gail E. Butterfield. **Not Pictured:** Richard L. Atkinson, A. J. Dinmore, Johanna T. Dwyer, John D. Fernstrom, Gilbert A. Leveille, and John E. Vanderveen.

CONTENTS

Appendixes

I

COMMITTEE SUMMARY AND RECOMMENDATIONS

PART I OUTLINES THE TASK presented to the Committee on Military Nutrition Research (CMNR) by scientists at the Military Nutrition Division (MND), U.S. Army Research Institute of Environmental Medicine (USARIEM), as part of the committee's ongoing work regarding the nutritional needs of soldiers in environmental extremes: to review research pertaining to nutrient requirements for working in cold and in high-altitude environments and to make recommendations regarding the application of this information to military operational rations. As part of the charge to the CMNR, the Army posed 15 questions in the areas of performance, health and medical aspects, thermoregulation and acclimatization, and nutritional requirements. These issues are summarized in the following two questions:

1. Aside from increased energy demands, do cold or high-altitude environments elicit an increased demand or requirement for specific nutrients?
2. Can performance be enhanced in cold or in high-altitude environments by the provision of increased amounts of specific nutrients?

In Chapter 1, the committee reviews the physiology and nutrition in cold and in high-altitude environments by using relevant background materials and the workshop proceedings from January 31–February 1, 1994. The committee presents the military's concerns for meeting energy expenditure in the cold and at high altitudes from the perspectives of both commanders and researchers. Beginning with the cold environment, the CMNR examines cold physiology and the body's countermeasures to heat loss, focusing on thermoregulation and its effects on performance. On the nutritional side, cold-induced diuresis is a concern given the effects of cold stress on fluid balance. Data on energy needs in cold environments are presented in the committee's discussion of macronutrients, vitamins, and minerals. At high altitudes, physiological responses can be detrimental to physical and cognitive performance given the debilitating impact of acute mountain sickness (AMS) and related altitude illnesses. Nutrient requirements at altitude often depend on rate of ascent and duration of stay. The combination of cold and altitude presents new considerations given the differences in physiological response and nutritional needs for these environmental extremes.

The CMNR answers the questions posed by the Army in Chapter 2 before presenting their recommendations, suggestions for future research, and conclusions. For work in cold and in high-altitude environments, the importance of water discipline and the availability of safe fluids for drinking are critical because fluid imbalance is detrimental to performance. To insure that energy intake equals energy expenditure, high energy, palatable rations must be supplied, and troops should be educated regarding changes in physical and cognitive performance at environmental extremes and their countermeasures. In an era of rapid redeployment, soldiers who have not regained lean body mass lost in previous operations should not be sent to cold or to high-altitude environments until lean body mass is regained. Future research in cold and in high-altitude environments should focus on defining water requirements and how to meet them; encouraging the maintenance of body weight and composition; and determining the best ratio of macronutrients, vitamins, and minerals.

1

A Review of the Physiology and Nutrition in Cold and in High-Altitude Environments by the Committee on Military Nutrition Research

PROJECT OVERVIEW

Military operations are frequently conducted in locations where soldiers are exposed to desert, arctic, and high-altitude environmental extremes. Gradual adaptation to these environments aids physiological acclimatization. However, military missions rarely can be planned to allow lengthy acclimatization periods. The recent Desert Storm operation is an example of an operation conducted under adverse conditions with little time initially for preparation or acclimatization.

Recreational mountain climbers, individuals whose professions involve working outdoors in seasonally cold weather, and people who live in cold or high-altitude environments have the opportunity to plan for their activities in these extreme environments. Individuals who are accustomed to the cold or high altitude learn how to adjust their apparel and activities to maintain an acceptable lifestyle in spite of the external environment.

Regardless of climatic conditions, troops must be supplied with food, weapons, housing, and other support facilities that will enable the immediate performance of their mission.

THE COMMITTEE'S TASK

For many years the Military Nutrition Division (MND) at the U.S. Army Research Institute of Environmental Medicine (USARIEM) has been reviewing the nutritional needs of soldiers in environmental extremes and conducting extensive experimentation both in experimental chambers and in the field to ascertain the changing demands placed on soldiers. The Committee on Military

Nutrition Research (CMNR) of the Food and Nutrition Board (FNB), Institute of Medicine (IOM) previously has been requested to provide reviews and recommendations through workshops and reports (IOM, 1991, 1993, 1994) on nutritional needs of soldiers in environmental extremes. These included fluid replacement and nutrient requirements in hot environments.

In 1993, the CMNR was asked by the MND to review research pertaining to nutrient requirements for working in cold and in high-altitude terrestrial environments. In addition, the committee was asked to make recommendations regarding the application of this information to military operational rations. The committee was thus asked to provide a thorough review of the literature in this area and to interpret these diverse data in terms of military applications. The CMNR was asked to address the increased energy demands of such environments and to consider whether these environments elicit an increased requirement for other specific nutrients. The MND also asked the CMNR to include in their response the answers to the questions listed in Table 1-1. This

TABLE 1-1 Questions Pertaining to Nutritional Needs in Cold and in High-Altitude Environments Posed by the MND to the CMNR

Performance
- What is the effect of cold/altitude exposure on muscle strength and endurance?
- Can diet influence these changes?
- How does cold/altitude exposure influence appetite?

Health and Medical Aspects
- Is there concern for increased cardiovascular risk when a high fat diet is consumed for intermittent (7- to 14-d) time periods in the cold?
- What nutrients prevent or lessen the signs and symptoms of acute altitude exposure?
- Is free radical formation a concern for prolonged (10- to 30-d) military operations at 10,000-15,000 ft (3,048-4,572 m) elevation?

Thermoregulation and Acclimatization
- Is cold/altitude acclimatization facilitated by prior satisfactory nutritional status or supplemental nutrients?
- What nutrients influence thermoregulation?
- Does the timing of food ingestion influence cold tolerance?
- What is the relationship between fluid intake and thermoregulation in the cold and at altitude?

Nutritional Requirements
- What are typical energy requirements for work in cold and high-altitude environments?
- What is the effect of cold and altitude exposure (at rest) on basal energy requirements?
- Does cold or altitude exposure alter the requirement for nutrients other than energy?
- What is the sodium requirement for hard physical work in a cold environment?
- What is the relationship between fluid intake and food intake in the cold/altitude?

report thus provides a parallel review to the previous CMNR report on the nutritional needs of individuals actively working in hot climates (IOM, 1993).

These specific issues were summarized by COL Eldon W. Askew (program officer designee) into two overriding questions:

1. Aside from increased energy demands, do cold or high-altitude environments elicit an increased demand or requirement for specific nutrients?
2. Can performance be enhanced in cold or high-altitude environments by the provision of increased amounts of specific nutrients?

To assist the CMNR in responding to these questions, a workshop was convened on January 31–February 1, 1994 that included presentations from individuals familiar with or having expertise in cold and in high-altitude physiology, energetics, macronutrient and micronutrient requirements, ingestive behavior, psychology, and military rations. In addition, military commanders familiar with working and training personnel in the cold and at high altitudes gave presentations and actively participated in the discussions. The invited speakers discussed their presentations with committee members at the workshop and submitted the content of their verbal presentations as written reports. The committee met after the workshop to discuss the issues raised and the information provided. The CMNR later reviewed the workshop presentations and drew on its collective expertise and the scientific literature to develop the following summary, conclusions, and recommendations that are found in the two chapters in Part I. In writing the first two chapters of this report, the CMNR has used the operational terminology included in Table 1-2.

MILITARY RESEARCH, COMMAND ISSUES, AND RATIONS FOR COLD AND FOR HIGH-ALTITUDE ENVIRONMENTS

The initial presentations at the workshop and the resulting chapters (3 though 6) in Part II of this report present a background for understanding military nutrition issues in the cold and at high altitudes.

The influence of cold and high altitudes on nutritional needs of the soldier has been a topic of interest to the military for many years. In his introduction COL Askew reviews the previous cold- and high-altitude intramural research activities of the Army, research sponsored by Army grants to academic institutions, and military-sponsored workshops or conferences (see Chapter 3 in this volume). COL Askew indicates that early work on cold and on high-altitude physiology and nutrition was typically a collaborative effort between military and civilian scientists. Since the 1970s, the overall extramural research activity supported by the military has significantly decreased, and specific research on nutritional needs in environmental extremes has been conducted largely within military research facilities.

TABLE 1-2 Terms Used in This Report

Acclimation	Adaptive changes to an environment under controlled conditions, such as an environmental chamber (indoors/in the laboratory).
Acclimatization	Adaptive changes that occur due to exposure to a natural environment (outdoors/in the field).
Altitude Designations	
At high altitudes	General term to represent altitudes of 5,280 ft (1,609 m) or more above sea level.
Moderately high altitudes	8,000 to 11,000 ft (2,438 to 3,353 m).
High altitudes	12,000 to 18,000 ft (3,658 to 5,486 m).
Extremely high altitudes	Over 18,000 ft (5,486 m) (above which acclimatization is difficult).
Cold	Temperature range within which human body has difficulty functioning. 30°F to -30°F (-1°C to -34°C).
Diuresis	Excretion of urine; commonly denotes transient production of unusually large volumes of urine.
Hypothermia*	Core body temperature significantly below 95° F (35°C). *Mild*: Body temperature of 89.6°F to 95°F (32°C to 35° C) *Moderate*: Body temperature of 82.4°F to 89.6°F (28°C to 32°C). *Severe*: Body temperature of less than 82.4°F (28°C).
Hypoxia	Below normal levels of oxygen in arterial blood or tissue, short of anoxia.
Hypohydration	Decrease in body fluids equivalent to a loss of 1% body mass or more.

SOURCE: Granberg (1991).

Clothing, equipment, state of mind, leadership, physical conditioning, mental attitude, preparation, and nutrition are considered by COL Russell W. Schumacher, Jr. in relation to success in cold and in high-altitude training and operations (see Chapter 4 in this volume). COL Schumacher suggests that the single most significant contributor to successful operations in the cold is a positive attitude. In Chapter 4 he further reviews the necessary components of developing and maintaining positive attitudes in troops in these environmental extremes. He stresses the need for unit commanders to have realistic performance expectations of their troops in the cold and at high altitudes and concludes that daily effort must be put forth to attain and maintain positive troop morale in environmental extremes.

Military operational rations are the principal source of nutrients provided for the soldier in military operations in all environments. Therefore as background for the report, a review of current rations specified for use in cold environments and the systems for preparation and use of field rations are summarized by LTC Nancy King and CW4 Thomas J. Lange (see Chapters 5 and 6 in this volume; see also IOM, 1995a). A modified table from Chapter 5 listing the nutrient contents of rations for cold-weather use has been reproduced here for clarity (Table 1-3).

The principal ration for group feeding in military field operations currently is the Tray Pack (T Ration). The T Ration is ready-to-heat and -serve, and is provided in low-profile, rectangular metal cans that can be heated quickly in hot water baths. This ration is described in more detail in Chapter 5. The standard T Ration is augmented with a cold-weather supplement module to provide 1,000 kcal per meal extra energy for cold environments. This Arctic T (T Ration supplemented with the cold-weather module) provides approximately 2,400 kcal per meal.

Frequently military missions do not permit group feeding, and individually packaged rations must be provided. The basic individually packaged ration is the Meal, Ready-to-Eat (MRE). The general composition of this ration is discussed in Chapter 5. In cold environments the basic three-ration per day provision is augmented with an additional fourth MRE or an energy supplement providing extra kcal. While the MRE can be consumed cold, individual ration heaters are provided since hot rations are more acceptable to soldiers in a cold environment.

The Ration, Cold Weather (RCW) is dehydrated and can be reconstituted with hot or cold water, or consumed dry. This ration was developed to meet some of the special needs for operating in arctic conditions. The specifics of the ration are discussed in Chapter 5, along with those of another more specialized food packet, the Long-Range Patrol, Improved (LRP I).

CW4 Lange (see Chapter 6 in this volume) summarizes some of the problems of feeding soldiers in the cold. He also discusses the issues of specialized equipment design that have been used to address the arctic and high-altitude conditions that present a very harsh environment for feeding the individual soldier. Problems of sheltering people and equipment as well as food preparation in severely cold and windy conditions are unique. These problems have required the development or improvement of mobile equipment that can function properly in such environments. Examples of these include the Mobile Kitchen Trailer and Kitchen Company Level Field Feeding equipment. These developments are important in providing food to sustain the military effectiveness of the soldier and the unit. Chapters 3 through 6 indicate the need for close coordination between the ration developer and troop support activities to ensure continued improvement in the quality and delivery of nutritionally adequate foods to soldiers operating in these environmental extremes.

THE COLD ENVIRONMENT

PHYSIOLOGICAL CHANGES IN THE COLD

Basic Physiology of Cold Exposure

When exposed to cold environments, the body loses heat through both convective and conductive heat transfer mechanisms. Heat losses are greater if the body is exposed to cold water than to cold air due to the greater heat transfer capacity of water (Gonzalez, 1988). As detailed by Andrew J. Young and colleagues (see Chapter 7 in this volume), the body possesses mechanisms to help maintain core temperature during cold exposure and to reduce heat loss, as well as to restore heat that has been lost. The mechanisms collectively are called thermoregulation.

Peripheral Vasoconstriction and Vasodilation

The principal mechanism to reduce heat loss is the neurologically induced constriction of vessels in the skin and extremities. This response diminishes heat transfer from the body core to the surfaces. As a result, body surface temperatures fall rapidly upon exposure to cold (Veicsteinas et al., 1982). These low skin and extremity temperatures can result in cold injuries, especially to the hands and fingers. A second mechanism, cold-induced vasodilation (CIVD), somewhat offsets the harmful effects of falling skin temperatures. With exposure to cold, vasoconstriction reduces skin temperatures, but then CIVD allows the temperatures to rise within about 10 minutes (Lewis, 1930). Over time the alternation of these two vascular responses results in a rhythmic (or cyclic) rise and fall of skin temperatures (Lewis, 1930).

Metabolic Heat Production

Heat production occurs as the result of voluntary muscular work, by involuntary (central nervous system [CNS]-induced) shivering, or by a combination of both mechanisms. Humans have no unique nonshivering, thermogenic mechanisms for responding to cold (Toner and McArdle, 1988). Nevertheless, as pointed out by Ira Jacobs (see Chapter 10 in this volume), every cellular metabolic process within the body has, as its byproduct, the production of heat. Even the vasoconstrictive activity of vessel walls produces some heat.

TABLE 1-3 Approximate Nutritional Content of Rations Used in Cold-Weather Operations

MRDA			T Ration[*] (3 meals)	MRE[†] (4 meals)	RCW (1 ration)	LRP I (3 meals)
Nutrient	Men	Women				
Energy, kcal	4,500	3,500	4,323[‡]	5,392	4,567	4,668
Protein, g	100	80	181	197	94	179
Carbohydrate, g	—[§]	—[§]	582	669	682	586
Fat, g	—[‖]	—[‖]	141	215	163	179
Vitamin A, IU	5,000	4,000	15,153	16,880	8,022	8,133[#]
Vitamin E, mg TE	10	8	15[#]	22[#]	21	13[#]
Vitamin C, mg	60	60	208	408	329	183
Thiamin, mg	1.6	1.2	3.5	10.8	5.7	3.7
Riboflavin, mg	1.9	1.4	3.5	4.3	2.6	2.8
Niacin, mg NE	21	16	42	52	31	541
Vitamin B_6, mg	2.2	2.0	2.2	7.6	3.9[#]	2.7
Folacin, µg	400	400	339	292[#]	141[#]	132[#]
Vitamin B_{12}, µg	3	3.0	5.3[#]	3.5[#]	0.8[#]	1.8[#]
Calcium, mg	800–1,200	800–1,200	1,687	2,052	1,379	1,149
Phosphorus, mg	800–1,200	800–1,200	2,761	3,184	2,168	2,352

MRDA			T Ration[*] (3 meals)	MRE[†] (4 meals)	RCW (1 ration)	LRP I (3 meals)
Nutrient	Men	Women				
Iron, mg	10–18	18	29	24	19	24
Sodium, mg	–[**]	–[**]	7,374	7,292	4,720	7,740
Potassium, mg	–[††]	–[††]	5,626	5,424	4,084	4,419
Magnesium, mg	350–400	300	523	556	592	489
Zinc, mg	15	15	20	13[#]	11[#]	9[#]
Cholesterol, mg	–[§]	–[§]	484[#]	476[#]	183[#]	174[#]

NOTE: MRDA, Military Recommended Dietary Allowances for moderately active military personnel ages 17 to 50 years old operating in cold weather; T Ration, Tray Pack Ration without cold-weather supplement (FY1992); MRE, Meal, Ready-to-Eat (version XII); RCW, Ration, Cold Weather; LRP I, Long-Range Patrol, Improved.

[*] The T Ration cold-weather supplement provides 148 g carbohydrate (53 percent), 29 g protein (11 percent), and 45 g fat (36 percent of total kcal) for a total of 1,110 kcal (Personal communication, M. S. Harrington, U.S. Army Research Institute of Environmental Medicine, Natick, Mass., February 1996).

[†] The MRE is reformulated annually. Values provided are for version XII. The version in current use is XVI. The relative proportions of energy provided by protein, carbohydrate, and fat vary by no more than 1 percent from year to year (Personal communication, L. D. Sherman, U.S. Army Research Institute of Environmental Medicine, Natick, Mass., February 1996).

[‡] Cold-weather supplement adds approximately 1,000 kcal.

[§] No MRDA established.

[||] Should not exceed 35 percent of total energy intake.

[#] Data missing (more than 50 percent) or inaccurate.

[**] No MRDA established. The safe and adequate levels published in the RDA are considered to be unattainable within military foodservice systems. An average of 5,500 mg for men and 4,100 mg for women is the target.

[††] NO MRDA established. The safe range is 1,875–5,625 mg, based on AR 40–25 (1985).

SOURCE: Adapted from AR 40–25 (1985). Record of nutritive values for each ration.

Skeletal muscle contractions, either during voluntary exercise or involuntary shivering, are the major source of the metabolic heat produced to protect against cold stress (Horvath, 1981). Heat production parallels an increase in oxygen uptake, the magnitude of which depends on the proportion of the muscle mass engaged in shivering or work and the duration and severity of work being done (Young et al., 1986a). Shivering alone can cause only a fourfold increase over basal rates of heat production, and even the greatest increases in heat production because of shivering alone are less than one quarter of a muscle's maximum contractile activity (Horvath, 1981).

The thermogenic response to voluntary exercise differs with the form of exercise (Toner and McArdle, 1988). Arm-only exercise causes a greater loss of body heat than does leg-only exercise (when both yield the same magnitude of heat production per unit). As a result, leg-only exercise is more efficient in maintaining body core temperatures (Toner et al., 1984). If voluntary exercise does not maintain body core temperatures during cold exposure, involuntary shivering responses are initiated, and heat production then may result from both forms of muscular work. Maximal energy expenditure by skeletal muscles may be reduced by cold exposure, if temperatures decline in muscle, body core, and/or blood. A fall in the temperature of blood reduces its delivery of oxygen to body tissues, because of temperature effects on the oxyhemoglobin dissociation curve (Young, 1990).

Cardiac Responses

The increase in oxygen uptake during shivering thermogenesis is also accompanied by an increase in cardiac output (Muza et al., 1988). This increase is due almost entirely to an increase in stroke volume, which appears to be the result of the increased central blood volume that is associated with cold-induced peripheral vasoconstriction. Resting heart rate remains unchanged (Muza et al., 1988).

Effect of Gender

Almost all studies of physiological responses to cold stress have been conducted in men. However, there is no evidence to suggest that basic mechanisms for peripheral vasoconstriction, cardiovascular responsiveness, and metabolic heat production in the cold are different in men and women. Metabolic changes during the menstrual cycle have not been studied during cold exposure, but basal body temperature is known to vary in response to hormone secretions (Stephenson and Kolka, 1993). Differences in body composition also may play a role, with the higher content of body fat in women and their smaller body surface areas providing some degree of protection from heat loss. Current knowledge of physiological responses to cold is largely based on studies of healthy young adult males. With the growing numbers of women in the military, they should not be neglected in future studies (IOM, 1995b).

Effect of Age

As reviewed by Young et al. (see Chapter 7 in this volume), general medical knowledge, backed by older physiological studies, suggests that older individuals may respond poorly to severe cold stress. The typical loss of muscle mass that accompanies the aging process undoubtedly plays a role by reducing the capacity for production of heat from metabolic processes. On the other hand, the accumulation of body fat with aging may provide additional protection against heat loss in mid- to late mid-life, but this protection is most likely lost or may change as aging continues. Extremely old individuals are often characterized by a gradual loss of body fat, especially subcutaneous fat. The increase in body surface area in comparison to body mass combines to reduce the mechanisms used to protect against heat loss (Young, 1991). Similar problems would arise in malnourished subjects who have lost both body fat and muscle mass.

Other Factors

Cold acclimatization can occur in humans but it is minimal. Probably the most important modifying factor on the thermoregulatory response to cold is the individual's endowment of subcutaneous fat since fat reduces thermal conductance from the core to body surfaces (Toner and McArdle, 1988). Physical fitness has mixed effects: the fittest individuals show the greatest heat production, but they are also the leanest, and that combined with their higher skin temperatures (from increased heat production) causes them to lose heat more quickly. Older individuals tend to maintain lower body temperatures (Mathew et al., 1986) and have less efficient vasoconstrictive mechanisms, so they are at greater risk for heat loss in cold environments. Generalized malnutrition may also impair thermoregulation. Severe losses of body weight associated with the complex stresses of prolonged military operations could also complicate the normal physiological responses to cold. Emphasis on maintaining an adequate intake of operational rations to prevent excessive weight loss in severe operational environments is important to sustain normal physiological responses to cold (IOM, 1995a). A discussion of nutrient requirements in the cold begins on page 15.

The most important modifying factors for thermoregulation, however, are the behavioral strategies employed in cold environments. Humans don warm, protective clothing, seek shelter whenever possible, and create or move to warmer environments.

Central Nervous System Function and Sleep

The Role of the Central Nervous System and Sleep during Cold Stress

Central nervous system (CNS) responses are of fundamental importance in body responses to cold stress. Hot and cold sensors in skin, body tissues, and the brain itself continually send signals via afferent nerves to the CNS for monitoring and response, if needed.

As a result, the CNS produces and responds to numerous neurotransmitters, such as catecholamines and serotonin. Both the temperature regulating and sleep regulating functions of the CNS respond to similar neurochemical stimuli. Further, sleep regulating functions of the CNS appear to be linked to those employed in temperature regulation (for discussion, see R. S. Pozos et al., Chapter 8 in this volume).

Stages of Sleep

Sleep consists of a series of repeating cycles of physical and brain wave activity. The sleep cycle may be divided into two main phases. The first phase, referred to as nonrapid eye movement sleep (NREM sleep), can be subdivided further into 4 stages. These are Stage 1, or the transition from the waking to the sleeping state; Stage 2, which is marked by a change in the electroencephalographic (EEG) pattern and the true beginning of NREM sleep; Stage 3, characterized by the onset of Slow Wave (or delta) Sleep (SWS), so-called because of the pattern of EEG activity; and Stage 4 in which SWS continues and begins to display hypersynchronization (Gregory, 1987). The second, deeper, phase of sleep is called REM or Paradoxical Sleep, and is characterized by rapid eye movement, a paradoxical increase in brain wave activity to the level of the waking state, and an increase in physical activity. All stages of sleep are considered necessary for maintenance of normal bodily and mental functions. While NREM sleep ordinarily precedes REM sleep, a sleep-deprived individual can progress almost immediately into REM sleep (Kandel et al., 1991). For this discussion of cold stress, it is important to note that the CNS fails to maintain its temperature regulating functions during REM sleep (Jennings et al., 1993).

Interrelation of Sleep and Temperature Regulation

During REM sleep, neither the cold-sensing nor the warm-sensing neurons fire: the CNS basically shuts down with respect to temperature regulation. In slow wave, NREM sleep, some information on temperature sensation is still received. Sleeping animals exposed to cold will still shiver during NREM sleep, but cease shivering as sleep deepens. Extreme degrees of cold or heat will cause sleeping animals to rouse.

Because temperature regulation ceases during deep REM sleep, a decrease in body temperature usually occurs. This phenomenon appears similar to changes seen in animals in deep hibernation. The sleep-induced decrease in body temperatures spare metabolic activity, and thereby reduce nutritional needs (Jennings et al., 1993).

Sleep and Temperature Regulation in Humans

In humans, the sleep-induced fall in body temperature is reversed on, or shortly before, waking. However, if a sleeping person (in either REM or NREM sleep) is aroused momentarily, core temperatures will fall further each time sleep is interrupted. Prior exercise, prior food intake, and the menstrual cycle all influence core body temperatures during sleep. Giving meals on a precise time schedule appears to help synchronize the temperature regulating clock. On the other hand, if the temperature regulating and sleep inducing clocks become desynchronized, as during military operations for example, appetite and food intake may be adversely affected (Jennings et al., 1993).

In summary, the neural mechanisms involved in sleep regulation appear to interact with those that regulate body temperature. The ability of the CNS to sense and respond to incoming information of a thermal nature is affected by both time of day and stage of sleep. Hence, during REM sleep, the CNS thermoregulatory response is dampened, resulting in a decrease in body temperature similar to that observed in hibernating animals. Extremes in temperature cause arousal in animals. In humans, repeated arousal results in a progressive decrease in core body temperature during subsequent sleep. Temperature in the sleeping human is also influenced by nutritional status, physical activity, hormones, and sleep schedule.

Thermoregulation and Physical Performance

If humans can regulate their core body temperatures properly during periods of physical work, their performance should not be significantly impaired. On the other hand, when physiological temperature-regulating responses cannot cope with environmental (or other) stressors, performance will decline. Depressed core temperatures can reduce maximal oxygen uptake and maximal cardiac output, and interfere with muscle energy metabolism by accelerating muscle glycolysis and lactate production. Differences in body size, configuration, and composition also influence the ability to maintain body temperatures during stress (see Young et al., Chapter 7 in this volume). Humans can use such external factors as shelter and clothing to help maintain core temperatures.

Drug-Induced Delay of Hypothermia

While most of this report deals with nutritional and physiological aspects of cold exposure, André L. Vallerand (see Chapter 15 in this volume) presents a useful discussion of drug-mediated delay in hypothermia during cold exposure. Earlier work in animals had demonstrated that a variety of drugs can delay the onset of hypothermia, but the relevance to humans was not clear (LeBlanc, 1975). For example, it was well known that dinitrophenol uncouples oxidative phosphorylation and increases substrate oxidation and heat production (Sellers, 1972). However, observations of side effects in obese subjects precluded use of dinitrophenol in humans (Hall et al., 1948).

Recent research by Vallerand and his colleagues (Vallerand et al., 1993) has centered on the evaluation of a commercially available, theobromine-containing "sports bar" purported to delay hypothermia during cold exposure in humans (see discussion in Chapter 15 in this volume). Comparison of the product with either an isocaloric mixture of carbohydrates or with an unspecified placebo revealed no significant differences in either rectal temperature or body heat debt of cold-exposed volunteers.

The inability to confirm claims made for the commercial sports bar prompted Vallerand and colleagues to study combinations of β-adrenergic agonists with methylxanthines. When compared to a placebo, a mixture of ephedrine (1 mg/kg) and caffeine (2.5 mg/kg) significantly increased metabolic heat production by 19 percent in cold exposed humans (Vallerand et al., 1989). The increase in heat production was derived from a large increase in whole body carbohydrate oxidation. The treatment also reduced the fall in rectal and skin temperature. Additional studies confirmed the value of mixtures of ephedrine with caffeine or theophylline in increasing heat production, decreasing heat debt, and reducing the lowering of body temperature in cold exposed individuals (Astrup et al., 1985, 1992; Dulloo and Miller, 1986; Dulloo et al., 1990).

These interesting results warrant additional studies to define further the benefits and disadvantages of the proposed treatment in improving the cold tolerance of human subjects, including further refinement of the most effective treatment modality. These initial results have significant promise for providing protection to individuals during cold exposure and therefore have potential military application in specific settings.

CHANGES IN NUTRIENT REQUIREMENTS FOR COLD ENVIRONMENTS

Fluid Balance

Body fluid balance is normally held within a fairly narrow range by a wide range of control measures. Exposure to cold stress, however, typically leads to dehydration, with a cold-induced diuresis (CID) as a major, long recognized contributing factor that is accompanied by reduced blood and plasma volumes (see review by Freund and Sawka, Chapter 9 in this volume). Other contributing causes to dehydration in the cold include losses of body water through respiration and through sweating, as well as through a diminished intake of fluids.

Mechanisms of Cold-Induced Diuresis

The mechanisms of origin of cold-induced diuresis (CID) are not yet entirely clear. It is known that CID can be blocked by administration of antidiuretic hormone (ADH or vasopressin) (Bader et al., 1952; Eliot et al., 1949). Despite early evidence for lowered concentrations of this hormone in plasma of individuals exposed to cold, subsequent research failed to confirm its suspected etiologic role in CID (Lennquist et al., 1974). Later, cold-induced increases in blood pressure, leading to a diminished renal tubular reabsorption of sodium and water became a popular mechanistic explanation for CID (Wallenberg and Granberg, 1976). More recently, studies in humans have shown that repeated immersions in cold water produced an equal diuretic response each time; however, the hypertensive component was lost with the acclimation to cold water immersion (Muza et al., 1988; Young et al., 1987). Currently, the movement of water to the body core caused by cold-induced peripheral vasoconstriction is the most attractive explanation for CID. Hydration status and body posture (Wallenberg and Granberg, 1976) also appear to be confounding factors.

Other Causes of Cold-Induced Losses of Body Water

Losses of respiratory water may also contribute to cold-induced dehydration. Water vapor pressure of cold air is considerably less than under thermoneutral conditions, so additional water can be lost when exhaling fully saturated warm alveolar air (Brebbia et al., 1957; Mitchell et al., 1972). Exercise-induced hyperventilation also will add to the amounts of water being lost via expired air. In fact, exercise-induced respiratory water losses are probably greater than cold-induced losses.

Exercise-induced sweating is another source of water loss, and is obviously related to the severity and duration of exercise performed as well as the types of clothing worn (Gonzalez et al., 1988; see Freund and Sawka, Chapter 9 in this volume). Some military clothing systems allow for little evaporation, causing large amounts of water from sweating to accumulate near the skin. Such water accumulation can pose additional problems in cold environments.

Performance Decrements Caused by Cold-Induced Dehydration

Although many studies have focused on dehydration in hot environments, few studies have investigated effects of hypohydration on performance in extremely cold conditions. The contributions of hypohydration to observed, cold-induced decrements in maximal aerobic power ($\dot{V}_{o2}^{max}$), muscular strength and endurance, and/or manual dexterity are also not well understood. $\dot{V}_{o2}^{max}$ and physical work capacity are reduced by hypohydration (Sawka and Pandolf, 1990). Small amounts of dehydration can produce alterations in thermal regulation, and higher ratings of perceived exertion during exercise tests (Greenleaf and Harrison, 1986; Montain and Coyle, 1992; Sawka, 1992). Cold-induced dehydration also is accompanied by changes in disposition, leading to sullenness, loss of appetite, breakdown in military discipline, failing physical exertion, and finally exhaustion (Orth, 1949). Such dehydration, therefore, may also contribute to cold injury.

In summary, in cold environments, dehydration compounded by CID is a significant factor that is often not given necessary consideration. The mechanisms of CID are not well understood, but overall hydration status appears to play a role. Exercise-induced respiratory water losses and sweating are additional contributors to dehydration in the cold. The changes in performance, appetite, and emotions that are well documented with heat-related dehydration also occur in cold-induced dehydration and can lead to cold injury.

The obvious countermeasure to dehydration is to drink fluids, but this practice is not always possible. Major problems can arise from the logistical constraints in delivery of drinking fluids during military operations in cold environments. In cold weather, fluids for drinking will freeze unless they are held in warm environments or have their solute concentration raised to lower the freezing point. The logistical problem would not be altered appreciably by attempting to meet fluid requirements by melting snow or ice due to the additional weight of heat-producing units. Hyperhydration before cold exposure is a useful strategy if cold stress will be of short duration.

Macronutrients

Energy Sources

The energy requirements of an individual in the cold are discussed in Chapters 11 and 12 in this volume by Peter J. H. Jones and Ian K. K. Lee and by Jacques A. LeBlanc, respectively. Total energy requirement is the sum of (1) the energy expended to maintain body functions (basal energy needs[1]), (2) the energy expended in processing meals (the thermic effect of food), and (3) the energy expended by physical activities (see Jones and Lee, Chapter 11 in this volume). Exposure to cold environments has been shown to increase the basal energy needs relative to the basal energy requirements measured under thermoneutral conditions (BMR[1]), which has been attributed to the increased energy demands of thermoregulation in the cold. In addition, activity-related energy expenditure is increased by the cold, due to the increased difficulty of locomotion over snow-covered terrain and the hobbling effect of multi-layered clothing, heavy boots, and packs filled with cold-weather gear.

Until recently, attempts to determine the magnitude of the increase in energy requirements in the cold focused on estimation of food intake, under the assumption that in healthy, weight-stable individuals, intake represents need (Kark et al., 1948).

Studies of energy needs of troops living in cold environments, based on food intake, have suggested that energy needs range from 3,100 to 3,900 kcal/d, (41 to 52 kcal/kg/d for a 75 kg man) depending on the activity performed and the extent of cold exposure (both ambient temperature and duration of exposure) (King et al., 1993; LeBlanc, 1957; Rodahl, 1954). More recent studies in which measures of energy expenditure (based on the doubly labeled water [DLW] method) rather than intake were used as a means of estimating energy need indicate that energy requirements in the cold may vary from 3,400 kcal/d to 4,300 kcal/d (45 to 57 kcal/kg/d for a 75 kg man), depending again on the degree of exposure to the external environment and activity levels (DeLany et al., 1989; Hoyt et al., 1991; King et al., 1993). The difference in estimates of energy requirement as determined by the DLW method compared to food intake estimates may reflect the frequently encountered bias of underreporting in self-reports of food intake found in other research studies (Schoeller, 1990; see Jones and Lee, Chapter 11 in this volume).

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[1] The basal metabolic rate (BMR) is the metabolic rate determined at rest at a comfortable temperature in a thermoneutral zone, after 12 hours of fasting. Thus, the determination of resting metabolic rates in cold environments does not meet the criteria for BMR. The term "basal energy needs" is used here to indicate the energy requirements of individuals in the cold, unrelated to exercise or the thermic effects of food.

Some disagreement exists among data based on self-reported food intake concerning the adequacy of energy intake by military personnel engaged in cold-weather field exercises. While data reviewed by Baker-Fulco (1995) suggests evidence of chronic underconsumption of energy and loss of weight in the cold, evidence presented by LeBlanc (see Chapter 12 in this volume) show that soldiers deployed to cold environments as well as members of arctic expeditions tended to gain weight, at least initially. Enhanced appetite may account for the 1 kg/month gain in weight observed during some studies of subjects experiencing prolonged stays in Antarctica (Milan and Rodahl, 1961). The estimates of energy intake reported by Baker-Fulco as well as by LeBlanc were based on dietary records, which, as mentioned above, tend to underreport caloric intake. In the case of the studies reviewed by Baker-Fulco, the reported caloric deficits were at times too large to account for the reported weight losses. In neither case was it possible to ascertain the activity levels of the subjects. The answer to the question of whether undernutrition is a problem in the cold may hinge upon the activity levels of the personnel in question as well as the amount of rations consumed.

In summary, energy requirements of 41 to 57 kcal/kg/d have been estimated for troops operating under conditions of arctic cold. The Military Recommended Dietary Allowance (MRDA) for energy used in rations designed for consumption in the cold is 4,500 kcal/d (60 kcal/kg/d for a 75 kg man) (AR 40-25, 1985). These present policies on nutrient density for energy needs of troops in the cold thus appear to be sufficient, even when not all the rations provided are consumed.

Determination of the optimal macronutrient ratio. Determination of the optimal macronutrient ratio for provision of energy in the cold must take into consideration a number of factors. These include the caloric density of fat as compared to carbohydrate (or protein); the enhancement of thermogenesis associated with the digestion, absorption, and storage of a particular nutrient (thermic effect of food or TEF); the preferential metabolism in the cold of one nutrient over another; and the preference of a particular nutrient in the diet.

- *Relative caloric density and TEF of energy sources.* In terms of caloric density, fat provides more than twice the amount of energy per unit mass compared to carbohydrate or protein, so that a ration providing a specific level of calories but higher in fat would be lighter, and easier to transport. Early concepts, largely based on the dietary practices of primitive Eskimos, suggested that an Eskimo-like diet, composed of half fat and half protein, was necessary to survive in chronic conditions of extreme cold (Hoygarrd, 1941). These concepts were compatible with scientific knowledge that high fat intake provides dietary energy with the greatest caloric density. While a high fat ration would have the advantage of light weight and easy portability, a fat-based diet has a number of disadvantages in the field and particularly in the cold. A sudden change to a high fat diet has the potential to cause adverse gastric (heartburn) and metabolic effects, the symptoms of which can be difficult to distinguish from a heart attack (IOM, 1992). An additional factor that must be considered in cold environments includes the TEF, which is lower for fat than for either carbohydrates or protein.

- *Preferential metabolism of one nutrient over another.* The question of whether one macronutrient is preferentially metabolized over another to satisfy energy needs in the cold has been addressed by several groups of investigators. As discussed above, the increase in energy requirements in the cold is attributable to thermoregulation and to increased physical activity. In Chapter 7 of this volume, Young and colleagues review the energy requirements for thermogenesis, which occurs as a result of increased voluntary muscular activity, or in the absence of voluntary activity, involuntary muscle activity (shivering). For over 60 years, evidence has pointed to voluntary physical activity in the cold as well as in thermoneutral conditions being fueled preferentially by carbohydrate, which provides 8 percent more energy per unit of oxygen consumed than does fat (Lusk, 1928). Adequate stores of muscle glycogen are required for provision of energy during periods of intense, prolonged exercise. At a workshop held by the CMNR in 1987 to consider the possible benefits of a calorie-dense ration, Gollnick (Unpublished paper, "Energy production during exercise; influence of diet and training," P. D. Gollnick, Washington State University, Pullman, Wash., 1987) reported the average muscle glycogen content of an 80 kg man to be 480 g (Gollnick 1985) and cited evidence from a study by Edwards and coworkers (1932) reporting that during 6 hours of moderately intense exercise, approximately 415 g carbohydrate was utilized. The ability of muscles to replenish depleted glycogen stores is a function of dietary carbohydrate intake. Also cited by Gollnick was a study by McDougall and colleagues (1977) which showed that, following exercise-induced muscle-glycogen depletion, 80 percent repletion was achieved in 24 hours by feeding either 625 g carbohydrate or a diet containing 50 percent (378 g) carbohydrate. Thus, it has been estimated (IOM, 1992) that a minimum of 400 g of carbohydrate is required per day for glycogen resynthesis. Underconsumption of carbohydrate leads to a depletion of reserves which necessitates reliance upon body fat stores for fuel (Costill, 1988). Although it has been estimated that a typical person's reserve of fat energy is sufficient to meet a 2000 kcal/d energy deficit for over a month, the switch to fat as a primary metabolic fuel (without an adequate period for adaptation) results in decreased physical (and mental) performance (Phinney et al., 1983) and loss of lean body mass (Askew et al., 1987). Thus, while the amount of carbohydrate that should be provided has not been precisely determined, it is the consensus of the CMNR that a minimum of 400 g should be provided. Further research is necessary to define more precisely the carbohydrate intake required to replace glycogen at various exercise intensities in cold (and in high-altitude) environments.

The amount of energy required for shivering is proportional to the degree of cold exposure due to changes in intensity with need for heat generation. According to Toner and McArdle (1988), this can contribute to an increase in basal energy requirement of two- to fivefold over the resting metabolic rate in thermoneutral conditions (RMR). A study of men briefly exposed to the cold while at rest, showed an increase in metabolic rate of 2.5-fold over that of RMR. Carbohydrate oxidation rose sixfold while fat oxidation rose by less than twofold (Vallerand and Jacobs, 1989). These authors also reported that in the cold, 51 percent of calories were derived from carbohydrate and 39 percent from fat. (Energy from protein catabolism plays a relatively small role.) This suggests that insofar as shivering contributes to the cold-related energy requirements, these requirements are met by both carbohydrate and fat, with a strong preferential utilization of carbohydrate.

The source of carbohydrate utilized by shivering muscle is discussed by both Young et al. and Jacobs in Chapters 7 and 10 in this volume. The question of whether shivering thermogenesis, like voluntary muscle activity, is dependent upon glucose derived from glycogen and can be enhanced by increasing dietary carbohydrate has attracted a great deal of interest since the discovery of the crucial role of muscle glycogen in voluntary muscle activity and the effect of dietary carbohydrate loading in improving physical performance. Contradictory findings have emerged concerning the contribution of blood glucose versus muscle glycogen stores as energy sources for involuntary shivering (Jacobs, 1993; Martineau and Jacobs, 1989; Young et al., 1989).

Young and colleagues contend that muscle glycogen stores do not seem to be a particularly important substrate for shivering work (see Chapter 7 in this volume for further review). They reported on their study in which muscle biopsies were obtained from volunteers whose muscle glycogen stores had been purposefully expanded or depleted prior to cold exposure. No differences were found in muscle glycogen utilization or thermogenesis during cold-induced shivering in nonexercising volunteers, despite the pre-exposure differences in their stores of muscle glycogen (Young et al., 1989).

In contrast, Jacobs (see Chapter 10 in this volume) reports on studies with a virtually identical experimental design, which showed that the muscular work of shivering in cold water-exposed, nonexercising volunteers was fueled, in part, by muscle glycogen (Martineau and Jacobs, 1988, 1989). These data were in agreement with findings in experimental animals. In addition, the subjects in Jacobs' study who had depleted pre-exposure stores of muscle glycogen showed a small but significant increase in the rate of body cooling compared to subjects with normal or high glycogen stores. Both Young and Jacobs have hypothesized that the difference in results may have stemmed from Jacobs' selection of extremely lean subjects, while Young et al. had used subjects with more body fat; however, no mechanism has been postulated to explain how this might have brought about the difference in results.

Studies that have been completed since the workshop show that carbohydrate supplementation during brief periods of cold exposure has no influence on cold-induced (shivering) thermogenesis, suggesting that at least in the short-term, energy-substrate mobilization is not a limiting factor in thermogenesis (Glickman-Weiss et al., 1994; Vallerand et al., 1993). An additional study has shown that during brief periods of cold exposure, blood glucose is the primary source of fuel for shivering, with smaller contributions from glycogen and lactate (Vallerand et al., 1995).

In summary, energy is needed in the cold to fuel both voluntary physical activity and involuntary shivering. As in thermoneutral conditions, voluntary muscular activity is fueled primarily by carbohydrate, and at high levels of activity, a minimum of 400 g carbohydrate is recommended per day to replace depleted glycogen stores. The energy requirements of shivering are supplied primarily by carbohydrate, with fat contributing to a lesser degree. It would appear that the carbohydrate utilized as fuel for shivering muscle derives from both blood glucose and the glycogen stored in the muscle itself; however, further investigations with longer cold-exposures may be warranted. The current recommendation of providing 4,600 kcal/d for troops operating in the cold appears to be sufficient to meet the needs for carbohydrate for shivering and voluntary muscle activity.

- *Preferential macronutrient distribution.* Preference for macronutrient distribution of energy does not appear to change in the cold; the usually chosen distribution is 13 to 16 percent protein, 37 to 38 percent fat, and 48 to 49 percent carbohydrate (Hoyt et al., 1991; King et al., 1993; Swain et al., 1949), which is essentially the same as the choices made under conditions of moderate ambient temperature (Swain et al., 1949) and does not substantiate information about dietary practices of the early Eskimos (which were probably based upon the foods available rather than being an adaptation to energy needs in the cold). The amount of fat being consumed by troops studied under arctic conditions is within the range currently consumed by a large portion of the American population, with the most recent review placing the average intake by young Americans at 34 percent dietary fat (CDC, 1994). While this level of dietary fat is higher than the current dietary recommendations for the general population, which call for a fat intake of no more than 30 percent of total calories (USDA, 1995), these recommendations do not take into consideration the significant increases in caloric requirements under circumstances that may be encountered in the cold.

In summary, there appears to be no change in the preference for one macronutrient over another in the cold. The fat content of the diet, which is higher than current dietary recommendations, may be justified by the higher activity level and circumstances encountered in the cold.

Protein

The protein requirements of individuals working in the cold are mentioned briefly in Chapters 11 and 12, by Jones and Lee and by LeBlanc, respectively. Jones and Lee cite an early study by Issekutz et al. (1962) that reported significant increases in urea production during full-day cold exposures. They interpreted this finding as an indication of an increased use of protein for energy in the cold. Other studies by Rodahl et al. (1962), Jones et al. (1993), and Vallerand and Jacobs (1989) failed to demonstrate any effects of brief cold exposure on fasting protein oxidation. Similarly there was no effect of prolonged cold exposure on fat free mass. In all studies however, dietary records were not maintained so protein intake was not measured.

The MRDAs do not include a higher protein allowance for cold weather (AR 40-25, 1985); the protein allowance of 100 g/d recommended for moderately active males in temperate climates is the same as that recommended for cold. In fact, since the recommended energy allowance is significantly higher for cold (4,500 kcal vs. 3,200 kcal), the percentage of calories to be contributed by protein is significantly lower (9 percent vs. 12.5 percent).

The nutrient contents of military rations employed in the cold are reviewed and compared by LTC King in Chapter 5. The protein content of the Ration, Cold Weather (RCW) (94 g protein per 4,500 kcal or 8 percent of energy intake) is significantly lower than that of the Meal, Ready to Eat (MRE) (197 g per 5,200 kcal or 15 percent of intake in 4 MREs). Thus, the protein content of the RCW is significantly closer to MRDA levels for the cold than is the recommended allotment of MREs. Comparison of the two rations in cold-weather field trials by Edwards et al. (1992) revealed inconsistent effects of the diets on measures of serum protein and albumin as well as blood urea nitrogen (BUN). In addition both groups underconsumed calories and protein and lost body weight, so it is difficult to draw conclusions about the adequacy of protein intake. The authors commented, however, that the protein content of an MRE plan is too high for cold weather consumption. This is because the increase in urea excretion that would result from metabolism of the extra protein would increase the requirement for water, and the availability of drinking water is often restricted in cold environments. The authors therefore recommended limiting protein intake to the level of the RCW. Based on early experiments by Keeton et al. (1946), Askew (1989) recommends a daily intake of 100 g of protein per 4,650 kcal as an optimal level for work in the cold.

The question of whether protein consumption increases during prolonged cold exposure has no definitive answer. While anecdotal evidence has suggested that Eskimos consume diets that derive approximately half of their calories from fat and the rest from protein (see Jones and Lee, Chapter 11 in this volume) (and soldiers participating in an 8-d cold-weather trial voluntarily increased consumption of foods high in protein when offered a mixed diet [Edwards et al., 1992]), several other studies reported no change in relative protein consumption in the cold. Nevertheless, an increase in protein intake in the cold appears to have a beneficial thermic effect. The thermic effect of feeding (TEF) for protein is higher than that for both carbohydrates and fat, resulting in an increase in body warmth for the 5 to 6 hours following ingestion of a high protein meal (Jéquier, 1993). LeBlanc (see Chapter 12 in this volume) suggests that ingestion of protein late in the day may serve to increase warmth throughout the night and prevent cold-induced waking.

In summary, while there is no evidence for an increased requirement for protein in the cold, if an additional MRE were consumed, protein intake would increase. When water supplies are scarce, there is good reason to maintain protein intake at the MRDA level. The use of the lower protein RCW or supplementation of the MRE with primarily fat-and carbohydrate-containing supplements would be beneficial in minimizing the increase in protein in the face of scarce water supplies.

A protein snack prior to retiring to sleep could provide some benefit from the thermic effect of protein in cold environments.

Vitamins

The influence of cold exposure on the need for vitamins is reviewed by Robert D. Reynolds in Chapter 13 in this volume. Given the extended period of time required for a nutritionally-replete individual to develop vitamin A deficiency and the relatively short duration of most expeditions and field maneuvers, there appears to be little justification for increasing the recommended intake of vitamin A. Likewise, there appears to be little rationale for increasing the recommendations for vitamins D or K. Although Reynolds proposes that increased consumption of vitamin E could possibly increase the oxygen supply for such purposes as energy production, the scientific support for this hypothesis is limited to a few studies (see Chapter 13 in this volume).

Thiamin, niacin, riboflavin, and pantothenic acid play a central role in the production of sufficient energy for thermogenesis. However, there are no experimental data indicating that increased consumption of any of these water-soluble vitamins above MRDA levels (AR 40-25, 1985) (which are always based on energy intake) provides any benefit to the cold-exposed individual (see Reynolds, Chapter 13 in this volume). Therefore, the CMNR does not recommend an increase in the dietary intake of these nutrients beyond MRDA levels. Similarly, there appears to be little justification for increasing the recommendation for vitamin B6, vitamin B12, biotin, or folic acid. Although it has been proposed that vitamin C might play some role in maintaining core and body surface temperatures, the 45-yr old study on which this concept is based has never been confirmed (Thérien et al., 1949).

In summary, there are very few studies that have investigated the influence of vitamin supplementation on resistance to hypothermia. Therefore, there is little evidence upon which to base recommendations to increase vitamin intake above MRDA levels to help cope with cold stress.

Minerals

Reynolds (see Chapter 13 in this volume) did not identify any scientific basis to justify increased dietary intakes of calcium, phosphorus, or magnesium beyond MRDA levels as a consequence of cold exposure.

The possible effect of micromineral deficiencies on thermoregulation in the cold is discussed by John L. Beard in Chapter 14 in this volume. Chronic deficiency of a number of different trace elements, including iron, zinc, or copper, may lead to defective thermoregulation (Lukaski and Smith, in press). Iron deficiency could be a concern because of its importance in maintaining core body temperature. However, there is no evidence at this time to indicate an increased requirement for iron in cold conditions. Thus, MRDA levels should be sufficient to prevent deficiency of this element.

Trauma and various types of stress are known to increase the urinary excretion of zinc, and increased urinary losses of this trace element have been observed during certain mountaineering expeditions (Rupp et al., 1978). The effect of cold per se on zinc requirements has apparently not been studied. Therefore, it is not possible to draw any conclusions regarding additional requirements for zinc due to cold exposure.

There is no information regarding the effect of cold on dietary copper needs.

Animal studies suggest that selenium deficiency may impair the cold-stimulated thermogenic response. However, as with the other trace elements, deprivation over the several week time span typical of field exercises is not likely to result in deficiencies of microminerals unless tissue reserves were already in a depleted state. Consumption of diets providing MRDA levels of microminerals should provide sufficient nutrients to allow for normal thermoregulatory processes in the cold.

In summary, there appears to be no scientific basis at this time for altering the dietary recommendations for any of the mineral nutrients discussed in this report due to exposure to cold climates; however, additional research is warranted.

APPETITE AND BEHAVIOR CHANGES IN THE COLD

In several long-term studies in cold environments, significant body weight gains were observed (see LeBlanc Chapter 12 in this volume). It is unclear if these weight gains can be attributed to an increase in appetite induced by the cold exposure or if the gains in weight are due to other changes in the environment and activity patterns of the subjects. Among the other changes common to all the studies described by LeBlanc in Chapter 12 were diet, season of the year, emotional factors caused by isolation, and changes in physical activity (Kark et al., 1948; Lewis et al., 1960; Milan and Rodahl, 1961). Changes in diet alone seem unlikely to be the cause of the weight gain since the foods used in some of the studies were reported to be less palatable than foods consumed before the study. It is well known that a reduction in food intake does not simultaneously occur with a reduction in physical activity. However, it is not clear from these studies that changes in physical activity could account for all of the weight gain. Likewise there is no clear evidence that the weight gain observed in cold environment studies is due to season of the year or emotional factors caused by isolation. LeBlanc suggests in Chapter 12 that cold exposure per se is not a likely cause of the energy imbalance which leads to the weight gains, because weight gains were not observed for individuals during the coldest months of the year. In addition, the weight gains recorded in these studies (see LeBlanc's review in Chapter 12 in this volume) could have resulted from the sudden change in exposure to a cold environment, i.e., lack of acclimatization. Perhaps the subjects would have reached a new stable weight if the study had continued for a longer time. Clearly the study results tend to indicate that exposure to a cold environment does not depress appetite.

THE HIGH-ALTITUDE ENVIRONMENT

PHYSIOLOGICAL CHANGES AT HIGH ALTITUDES

Basic Physiology of High-Altitude Exposure

A variety of physiological and mental responses are initiated by the unique physical and environmental factors which characterize the Earth's high altitudes. As reviewed by Allen Cymerman, Robert B. Schoene, and Inder S. Anand and Y. Chandrashekhar (see Chapters 16, 17, and 18 in this volume, respectively), many of these responses have adverse, mission-threatening impacts on military performance, both in the short-term, as exemplified by acute mountain sickness (AMS)[2], and in the long term through diminished physical capacity because of decreased muscle mass and the other effects of the environmental stress on the body. Some of these adverse responses may

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[2] AMS is a syndrome noted in susceptible individuals that is associated with the rapid ascent to (and short stays at) altitudes over 10,000 ft (3,048 m); AMS is characterized by headache, nausea, vomiting, malaise, and ataxia.

progress to pathophysiological, life-threatening conditions such as high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE)[3].

An impressive number of studies has been conducted on mountain climbers, military personnel, and acclimatized individuals residing at or transiently exposed to moderately high altitudes, i.e., 10,000 to 15,000 ft (3,048 to 4,572 m). Far fewer studies have been conducted at extremely high altitudes, i.e., 16,500 ft (5,029 m) and over. Integration of these various studies can be difficult due to:

- numerous confounding variables (e.g., duration and severity of any coexisting physical activity, harsh environmental conditions and temperatures, and/or variations in fluid and food intake);
- interpersonal differences;
- speed of ascent;
- final altitude reached;
- duration of stay at altitude;
- relatively small number of subjects studied at extreme altitudes; and
- methodological difficulties and differences, especially in studies involving salt and water balances and body fluid compartment volumes.

Available data thus are at times conflicting, and are generally difficult to interpret.

Although some of the biophysical stresses of high altitude also can be duplicated and studied in laboratory altitude chambers, difficulties in interpreting field data typically have not been resolved by subsequent testing in altitude chambers. Further, although excellent studies have been done with laboratory animals or livestock exposed to high-altitude environments, their applicability to the human situation remains uncertain.

Biophysical Realities of High Altitudes

High altitude presents an adverse environment that challenges the physiological processes in the body. An individual can adapt (acclimatize) somewhat to these environmental conditions, provided the altitude encountered is not too high (for example, greater than 18,000 ft [5,486 m], which is considered an extremely high altitude). Failure to acclimatize may result in

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[3] HACE is a syndrome associated with the rapid ascent of susceptible individuals to high altitudes and stays of prolonged duration; HACE is characterized by a progression of the neurological symptoms of AMS. HAPE is a clinical complex caused by the rapid ascent of unacclimatized individuals to altitudes greater than 8,202 ft (2,500 m); HAPE is characterized by fatigue, weakness, dyspnea (without exertion), and tachycardia. The pulmonary edema may be neurogenic in origin (Hackett et al., 1989).

minor medical illnesses, known collectively as acute mountain sickness (AMS) or major life threatening illnesses (i.e., HAPE or HACE) (see Cymerman, Chapter 16 in this volume).

The challenging environmental conditions at high altitudes include hypobaric hypoxia, dry air, and extreme variations in external temperature. Each of these conditions elicits physiological responses that appear to allow the individual to remain conscious and functional during the first hours and days at high altitude (Cymerman and Rock, 1994).

The governing biophysical factor at high altitudes is the decreasing barometric pressure that characterizes increasing altitude (Cymerman and Rock, 1994). Although the atmospheric concentration of oxygen remains at a constant 20.93 percent at all terrestrial altitudes, the partial pressure of oxygen (pO_2 = 0.2093 × barometric pressure) falls along with the decline in barometric pressure. As altitude increases, the lowered oxygen pressure (pO_2) in pulmonary alveolae causes a declining saturation of hemoglobin in arterial blood, and a lower oxygen pressure gradient throughout the body, especially at the level of the capillaries, where the pO_2 may be close to zero. With low pO_2 the blood flow is too rapid to allow appropriate gaseous exchange, resulting in unfavorable conditions for oxyhemoglobin dissociation. Exercise of any kind becomes difficult. Respiratory rate and heart rate increase in response to chemoreceptor activity with resultant modest improvement in oxygen delivery.

The dry air found in high environments adds to the problem of oxygen delivery at altitude. Because air must be moistened to protect the respiratory epithelium, water is added to the air inspired at each breath. As a result, alveolar pO_2 is further reduced. This process adds about 47 mm Hg of water vapor pressure to the alveolar gasses. Further exacerbating the alveolar "crowding" is expired CO_2, which contributes 40 mm Hg with normal breathing and increases transiently at altitude. With the higher respiratory rates characteristic of high altitudes, the concentration (and thus partial pressure) of alveolar CO_2 declines somewhat with time, allowing alveolar pO_2 to increase somewhat with length of exposure (Milledge, 1992; Buskirk and Mendez, 1967). The increased rate of respiration increases fluid loss through the lungs, creating the potential for dehydration if fluid intake is not maintained.

The oxygen dissociation curve for hemoglobin is another important physiological factor at high altitudes. The curve "breaks" at about 14,110 ft (4,300 m), at which point hemoglobin saturation is already decreased to 85 percent of that seen at sea level. At even higher altitudes, small declines in the pO_2 of alveolar air result in large declines in arterial blood and hemoglobin saturation, making even the act of breathing hard work.

As altitude increases, ambient temperature decreases at a rate of approximately 3.6°F/984 ft (2°C/300 m) rise in elevation. However, work at high altitudes has the potential for creating extremes of temperature for the individual, with sweating one minute as a result of strenuous work in heavy clothing, and shivering the next because of cessation of effort. These vacillations as well as the decreased ambient temperature provide further stress to the cardiovascular system. Plasma volume falls, and heart rate increases. Basal energy requirements are elevated in individuals living at altitude, and total energy requirements are elevated in those performing work at altitude.

Physiological Responses at High Altitudes

Many factors contribute to the impaired ability of soldiers to perform at high altitudes. Acclimatization of the various physiological processes occurs at varying rates as cardiovascular, respiratory, and biochemical responses all adapt to maintain a normal hemoglobin saturation.

Within the first 7 days of high-altitude exposure, respiratory rate increases (when pO_2 drops below 122 mm Hg) in response to central and peripheral chemoreceptor input to the respiratory centers in the brain. This response is countered by an exaggerated loss of CO_2, leading to central respiratory depression (Bender et al., 1989). The system comes to an equilibrium after about 20 days at high altitudes (Bender et al., 1989).

A rise in cardiac output at rest also occurs at high altitudes, because of an increase in heart rate in the face of a constant stroke volume (Hannon and Vogel, 1977). Plasma volume declines, concentrating the available hemoglobin, and venous return decreases, thus finally depressing stroke volume after the first 3 to 5 days at high altitudes (Hannon and Vogel, 1977). Cardiovascular responses also reduce peripheral blood flow, with a shunting of blood to the heart, lungs and brain. These responses are influenced by an increased secretion of norepinephrine, as evidenced by increases in both plasma and urinary norepinephrine values (Brooks et al., 1991; Cruz et al., 1976; Cunningham et al., 1965; Hoon et al., 1976; Kotchen et al., 1973; Mazzeo et al., 1991; Moncloa et al., 1965; Reeves et al., 1992; Young et al., 1989).

Cardiovascular responses are also influenced by alterations in body salt and water balances. Diuresis upon acute exposure to high altitudes is reported frequently, and is thought to contribute to the concentration of available hemoglobin. Red cell mass increases over time in response to secretion of erythropoietin, providing a more permanent mechanism for maintaining oxygen saturation. Exercise at high altitudes worsens hypoxia, but there is no change in the energy cost of performing a given task. At very high altitudes (18,000 ft [5,486 m]), there is a linear decrease in O_2 consumption and exercise performance, and the work of breathing becomes a major factor in itself. The combination of stress, physical activity, and hazardous terrains often leads to physical injuries.

Water Balance at High Altitudes

As reviewed by Anand and Chandrashekhar (see Chapter 18 in this volume), data from more than 50 studies on fluid shifts at high altitudes are conflicting and controversial. Many studies show that diuresis occurs upon acute exposure to high altitudes (for example, Phillips et al., 1969), but an equal number show anti-diuresis (for example, Singh et al., 1990). Few studies have had adequate experimental controls for the insufficient dietary intake observed. This dietary insufficiency could result in diuresis from the excretion of breakdown products of lean and fat tissues. Conversely, water retention is most common at extremely high altitudes, and contributes to AMS as well as to both HAPE and HACE (Anand and Chandrashekhar, 1992; Anand et al., 1990). Exercise also stimulates an accumulation of body electrolytes and water, and may cause the plasma volume to increase (Withey et al., 1983).

Changes in water excretion are influenced by a number of regulatory hormones. Hypoxic subjects, at rest, generally show decreased plasma concentration of aldosterone, which results in a decrease in sodium retention and thus in water retention (Bouissou et al., 1989; Colice and Ramirez, 1985, 1986; Heyes et al., 1982; Hogan et al., 1973; Maher et al., 1975; Maresh et al., 1985; Milledge et al., 1983; Olsen et al., 1992; Raff et al., 1986; Ramirez et al., 1992; Shigeoka et al., 1985; Slater et al., 1969a, b; Sutton et al., 1977). Hypoxia also blunts the normal increase in aldosterone associated with exercise even when the same amount of exercise is done (Maher et al., 1975; Milledge et al., 1983; Olsen et al., 1993; Shigeoka et al., 1985). A decrease in renin activity seems to follow similar patterns. The function of renin is to convert the prohormone angiotensinogen to the active hormone angiotensin. Angiotensin is a potent peripheral vasoconstrictor that promotes renal sodium retention and stimulates secretion of aldosterone by the adrenals. Thus, with hypoxia the renin-angiotensin-aldosterone relationship becomes uncoupled. Responses of antidiuretic hormone (ADH) also differ with the degrees of hypoxia and exercise. ADH secretion decreases when hypoxia is moderate and exercise is light, thus resulting in decreased fluid retention, and increases with extremely high altitudes and/or severe exercise stress, which would increase fluid retention (Bärtsch et al., 1991).

Increases in the stress-related hormones, cortisol and norepinephrine, are associated with both high altitude and exercise and may affect fluid balance. Subjects who are prone to develop AMS have an atypical ADH and aldosterone response, which increases fluid retention (i.e., both hormones tend to increase in concentration in the blood at high altitudes, rather than decrease, with the increases being exaggerated by exercise).

Relatively few data exist on renal function at high altitudes; the small amount of information available suggests that high altitudes lead to a decrease in effective renal plasma flow (ERPF), although glomerular filtration rates are maintained (Olsen et al., 1993). Undoubtedly, the magnitude of these changes varies, depending on the conditions under which they are measured.

Cymerman (see Chapter 16 in this volume) emphasizes that dehydration is a militarily important factor, especially when exposure to moderately high altitudes is abrupt and accompanied by strenuous exercise. With moderate-altitude exposure, diuresis is an important component of the initial physiological response, anti-diuresis being associated with AMS (Anand et al., 1990). However, fluid losses because of high altitude and exercise may be exacerbated by fluid loss associated with inadequate energy intake. Dehydration is exaggerated by a reduced sensation of thirst with an accompanying reduction in fluid intake (Adolph et al., 1947). The dehydrated state may be further exacerbated by both sensible and insensible water losses. Exercise in bulky clothing induces significant sweating, at a rate as high as 2 liter/h. Insensible losses through skin (minor) and respiratory epithelium may reach 1 to 2 liter/d even without exercise (Milledge, 1992). This respiratory fluid loss also carries with it significant heat losses, which increase the maintenance energy requirement by as much as 1.6 times that at sea level (Gonzalez et al., 1985). At moderately high altitudes, losses of body fluids are proportional to losses in body weight, and there are significant decreases in plasma volume (Jain et al., 1980, 1981; Singh et al., 1986, 1988, 1990). In addition, there are uncontrolled shifts of fluid out of the vascular compartment, which, along with the initial fall in total body water, help lower the stroke volume. Some studies show intracellular dehydration as well. Fluid losses thus contribute to the observed losses of body weight. Dehydration may engender symptoms comparable to those of AMS. Body water must be maintained at high altitudes, but should not be by the ingestion of bacterially-contaminated fluids or snow.

In marked contrast, an accumulation of body salt and water occurs in individuals who remain at extremely high altitudes (over 18,000 ft [5,486 m)] for many weeks. Anand's studies, in 10 asymptomatic soldiers who lived at 22,000 ft (6,706 m) for at least 10 weeks, showed a 20 percent increase in total body water. There was also an 80 percent increase in circulating blood volume because of sizable increases in both plasma volume and red cell volume. Fluid accumulations were accompanied by an 18 percent increase in body sodium, a reduced renal blood flow, and increased circulating concentrations of norepinephrine, cortisol, and aldosterone (Anand and Chandrashekhar, 1992).

Acclimatization to High Altitudes

Acclimatization to moderately high and high altitudes depends upon the swiftness of ascent, as well as the duration of the stay. Individual physiological systems acclimatize at different rates, some taking as little as a few days, others as long as a month to years to fully adjust (see Figure 1-1 below). With acclimatization there is a continuing hyperventilation over the first 14 days at high altitude, with a slow rise in O_2 saturation of hemoglobin. The kidney corrects the respiratory alkalosis, and after a month or so there is an increase in the number of circulating red blood cells in response to increased erythropoietin secretion (see above under "Physiological Responses to High Altitudes"). As a rule acclimatization will occur at elevations up to 17,000 ft (5,182 m), but full acclimatization rarely occurs at extremely high altitudes.

Altitude-Induced Illness

Failure to acclimatize results in a continuum of symptoms. AMS may vary from a minor problem to a militarily incapacitating illness. AMS is characterized by mild to severe headaches, mild to severe nausea and vomiting, and a general lethargy with possible personality changes (Bahrke and Shukitt-Hale, 1993; Hackett et al., 1989). Further, more severe illnesses include an accumulation of fluid in the lungs (HAPE), because of leaking of the endothelial membranes, and in the brain (HACE), possibly because of a similar mechanism. HAPE is characterized by inability to perform, or even to walk, and often includes the production of foamy sputum (Hackett et al., 1989). The

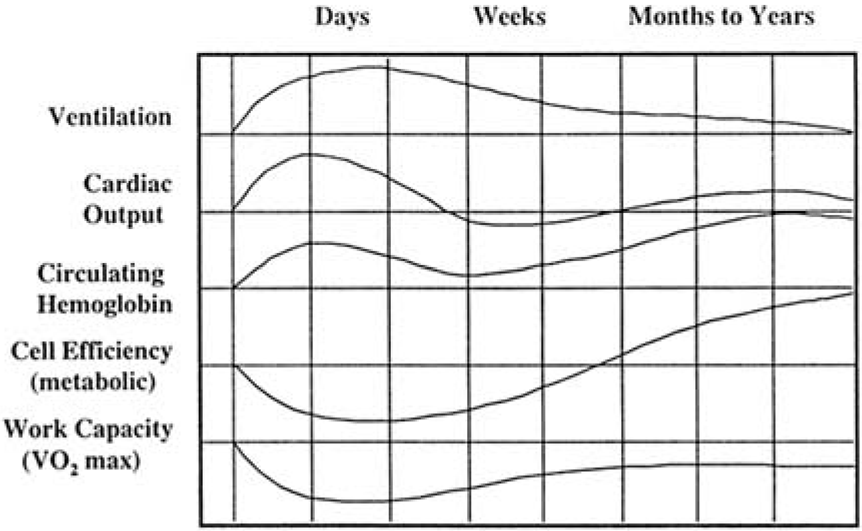

FIGURE 1-1 Approximate size, direction, and temporal changes that occur during acclimatization to 14,000 to 15,000 ft (4,267 to 4,572 m). SOURCE: Adapted from Houston (1982).

accumulation of fluid in the interstitial space increases the distance across which oxygen must diffuse to reach the cells and thus further compromises performance ability.

Acute Mountain Sickness (AMS)

Acute mountain sickness (AMS) has been recognized for centuries, and occurs in most individuals to some degree at altitudes of 11,500 ft (3,505 m) or more. About 25 percent of tourists develop signs of AMS at elevations of only 8,900 to 10,000 ft (2,712 to 3,048 m), the severity and incidence depending upon the rate of ascent (Hackett et al., 1989). A severe bilateral headache is the primary symptom, but AMS also produces extreme fatigue, shortness of breath, and sleep disturbances. The headaches are accompanied by sharp increases in cerebral blood flow velocities, as measured by Doppler techniques. Cerebral symptoms of AMS may be secondary to an initiation of brain edema (Hackett et al., 1989).

Intestinal disturbances, with vomiting, are aggravated by expanding intestinal gas, and gas trapped in nasal sinuses can be particularly painful. AMS severely reduces appetite. The ability to carry out various functions is markedly impaired. AMS is usually self-limiting within 3 to 7 days of exposure.

Strangely, some individuals show no symptoms of AMS, whereas those who suffer AMS once are likely to experience it every time they go to high altitudes. Freedom from AMS seems to be linked to the ability to diurese quickly, and diuretics have been used as therapy. The drugs most widely used to treat AMS are acetazolamide (Diamox), a carbonic anhydrase inhibitor, and adrenocorticoids (especially Decadron) (Hackett et al., 1989). Acetazolamide stimulates breathing and prevents nocturnal periodic respiration; it also stimulates renal bicarbonate excretion to balance the respiratory alkalosis caused by hyperventilation. Acetazolamide is effective at 125 mg given up to twice daily, beginning with the onset of symptoms (Hackett et al., 1989). Adrenocorticoid therapy should be reserved for those seriously ill with AMS due to its failure to promote acclimatization.

Subacute Mountain Sickness

A new syndrome, termed subacute mountain sickness, was observed in healthy young soldiers who had spent several months at extremely high altitudes of approximately 22,000 ft (6,706 m) (Anand et al., 1990). As described by Anand and Chandrashekhar (see Chapter 18 in this volume), the syndrome appeared to be one of severe systemic and congestive heart failure without pulmonary hypertension. About 20 percent of the group developed shortness of breath, puffiness of the face and eyelids, anasarca (generalized pitting edema), and pericardial fluid accumulation, with a normal heart size and normal pericardium. Left ventricular function was also normal on cardiac catheterization. These accumulations of fluid all disappeared in a few weeks at sea level with no additional therapy.

High-Altitude Cerebral Edema (HACE)

Severe AMS can precede or predispose to cerebral edema, which is termed high-altitude cerebral edema (HACE) (see Cymerman, Chapter 16 in this volume). This edema of the brain tissue is accompanied by engorged cerebral and retinal arteries, extremely high cerebrospinal fluid pressures, and sometimes small cranial and retinal hemorrhages. The edema can be progressive, and even lethal, unless treated rapidly by oxygen administration, by moving the patient quickly to a lower altitude, and/or by using a hyperbaric bag (Hackett et al., 1989).

High-Altitude Pulmonary Edema (HAPE)

An acute build up of fluid transudate in the alveolae and the bronchial tree, associated with pulmonary artery hypertension, is another potential problem of high altitudes (see Cymerman, Chapter 16 in this volume). This high-altitude pulmonary edema (HAPE) is complicated by bronchial secretions that are extremely thick and viscid due to leakage of protein into the alveolar and bronchial fluids. These fluids block gas exchange within the lung. This potentially lethal condition may develop quite quickly, and it requires immediate therapeutic measures, such as oxygen administration and removal of the patient to lower altitudes, which usually correct the problem.

Weight Loss at High Altitudes

Sojourns at high altitudes result in weight loss in most individuals allowed to eat ad libitum (see discussion by Gail E. Butterfield, Chapter 19 in this volume). As pointed out above, some of this weight loss may be a result of diuresis, other contributing factors include a decline in appetite, which accounts for a deficit of almost 200 kcal/d in most studies, and an increase in basal energy needs, which accounts for almost 300 kcal/d. Thus, even a sedentary visitor to high altitudes may experience an energy deficit of at least 500 kcal/d. There is little data to suggest that this deficit is further exacerbated by malabsorption of fat, carbohydrate, or protein.

However, the loss of body weight is often accompanied by negative nitrogen balance, with associated losses of muscle mass, which may significantly impact on performance. The inevitability of this weight loss has been debated, but recent studies by Butterfield and colleagues suggest that strict attention to adequacy of energy intake can essentially eliminate this problem, as well as diminish some of the diuresis of acute exposure (see Chapter 19 in this volume).

The provision of sufficient energy intake to meet energy expenditure needs in experiments where individuals visit high altitudes also ensures the study of true metabolic responses to hypoxia, not malnutrition. Under circumstances of energy balance, Butterfield reports in Chapter 19 in this volume that the primary metabolic fuel at rest and during exercise after acclimatization to high altitudes is carbohydrate (Roberts et al., in press a), with the utilization of fat falling to very low levels (Roberts et al., in press b). Thus, enforced consumption of carbohydrate foods to ensure adequate energy intake is important. In field situations, sufficient time must be allowed for preparation and consumption of adequate energy and carbohydrate to maximize troop productivity and decrease morbidity.

Effects of Age and Gender on Response to Altitude

Little information is available concerning the effects of age and gender on physiologic response to high altitudes. Some investigators claim that women acclimatize better than men (Hannon et al., 1976) in that basal metabolic rates and appetite appeared to return toward sea level values more rapidly in women studied at high altitudes than in men. However, very few studies of women have been conducted, and the impact of menstrual cycle phase on the process of acclimatization is completely unknown, although sex hormones have been shown to influence the key physiologic processes involved in acclimatization (Tatsumi et al., 1995).

In addition, several aspects of energy metabolism known to be affected by altitude in men are also affected by phase of the menstrual cycle at sea level in women. These include food intake (Lyons et al., 1989), basal metabolic rate (Meijer et al., 1992; Webb, 1986), nitrogen balance (Calloway and Kurzer, 1982), and fat utilization (Hackney et al., 1991). Thus, the investigation of the interaction of these factors with altitude and menstrual cycle would be important for understanding the needs of female troops.

The issue of age and high-altitude acclimatization is also not adequately investigated at the present time.

CHANGES IN NUTRIENT REQUIREMENTS AT HIGH ALTITUDES

Macronutrients

Energy Sources

Total dietary energy requirements at altitude are discussed by Reed W. Hoyt and Arnold Honig (see Chapter 20 in this volume). These needs are determined by the type and duration of physical activity, preexisting body energy stores, and environmental conditions. The macronutrient composition used to provide dietary energy depends upon the intensity and duration of the exercise performed, the macronutrients available from body stores and the diet, and environmental conditions.

Troops in the field at high altitudes frequently experience energy deficits as a natural consequence of high energy outputs and limited intakes. Under training circumstances, strenuous exercise (greater than 75 percent of maximum oxygen consumption, $\dot{V}_{o2}{}^{max}$) may be performed for as many as 17 to 18 hours each day. Work expenditures as measured by the DLW technique may reach 4 to 7 times basal metabolic rate (BMR) (Forbes-Ewan et al., 1989; Hoyt et al., 1991). Hoyt and Honig report on a study of 781 soldiers engaged in field maneuvers at altitudes of 7,000 to 11,000 ft (2,134 to 3,353 m), for 3 to 34 days who demonstrated a mean energy expenditure of 3,500 kcal/d, or about 2.2 × BMR (Jones et al., 1990).

Military operations at high altitudes may require even greater increases in energy expenditure. Basal metabolic rates at altitude may initially be elevated 20 to 30 percent above those at sea level. After 2 to 3 days, BMR falls and may be maintained at 15 to 16 percent above sea level values. The time course of this elevation varies among studies. Some studies show these acute (20 to 30 percent) increases to be sustained for 1 to 2 weeks while other studies show the elevation to be maintained throughout a 3-wk stay (Butterfield et al., 1992; Meda, 1955; Nair et al., 1971; Stock et al., 1978; Terzioglu and Aykut, 1954). The decline in BMR with acclimatization seems to be the result of inadequate energy intake. Individuals native to high altitudes demonstrate elevated BMRs as compared to individuals at sea level of similar body size, and individuals required to consume the energy at a level equivalent to their need will maintain an elevated BMR throughout altitude exposure.

Although altitude acclimatization increases endurance capacity, there is little change in energy expended at submaximal work loads between altitude and sea level, either acutely or with chronic exposure. Thus, energy expenditure for specific tasks is no different at high altitudes than at sea level (Fulco and Cymerman, 1988; Grover et al., 1986; Young and Young, 1988).

The high energy requirements of training are usually not countered by increased intakes. Rather, dietary intake in field situations is frequently inadequate to meet needs due to decreased palatability of foods provided, boredom in menus, reluctance to work on a full stomach, lack of fluid availability, odd meal times, anxiety, or self-imposed dieting. In Chapter 20 of this volume, Hoyt and Honig present a review of 11 recent field studies. In these studies the reported energy intakes using dietary records were about 2,400 kcal/d, although approximately 3,600 kcal/d were provided. This intake represented a consumption of only about two-thirds of the rations provided, which created a theoretical energy deficit of almost 1,000 kcal/d.

The anorexia commonly experienced at high altitudes may contribute to this difficult situation. There is some speculation that the anorexia of altitude may serve to limit sodium and water intake with the teleologic consequence of adjusting body stores for better acclimatization (Hoyt and Honig, 1996). However, no research in human subjects has been able to attribute the anorexia of acute mountain sickness to a possible physiological mechanism.

The metabolic fuels used to supply energy requirements during military operations at high altitudes are derived from both dietary sources and preexisting body stores. Most troops have fat stores sufficient to cover an energy deficit of 1,000 kcal/d for 1 to 2 months (fat stores equivalent to about 30,000 to 60,000 kcal, or about 9 kg of fat mass) (Sahlin, 1986). However, glycogen stores, which determine to some extent the endurance capacity of the individual, are more limited. Carbohydrate needs, based on a mean Respiratory Exchange Ratio (R) of 0.85, which represents a carbohydrate contribution to energy supply of about 70 percent (Kleiber, 1961), would need to be at least 400 g/d. Normal rations available to troops supply 580 to 680 g carbohydrate per day (AR 40-25, 1985; see Table 1-3); however, data presented by Hoyt and Honig (see Chapter 20 in this volume) suggest actual carbohydrate intakes of less than 300 g/d. Thus, inadequate carbohydrate intake may exist in troops working at high altitudes, a state which might contribute to diminished performance.

The failure to match dietary fuel supply with physiological need results in a shift in metabolic fuel use toward fat. Increased energy needs at high altitudes may increase the use of body fat under these circumstances of energy deficit. Acclimatization results in a decrease in muscle glycogen utilization (Young et al., 1982) and a decrease in muscle lactate (Green et al., 1989) in individuals functioning under an energy deficit, suggesting to Hoyt and Honig that acclimatization leads to an increase in fat utilization. However, in individuals maintaining adequate energy intake, the situation may be reversed (Roberts et al., in press a).

Estimation of energy requirement in the field is difficult. Hoyt and Honig (see Chapter 20 in this volume) describe a new ambulatory monitor and method that involves estimation of energy expenditure based on body weight, the time during each stride that a single foot contacts the ground (foot contact time), and the nature of the terrain being covered. The resulting estimate is based on the energy cost of supporting body weight and the rate at which this force is generated. The rate of force generation can be estimated as total body weight divided by the time during each stride that a single foot was in contact with the ground. One relevant finding was that soldiers performing similar tasks in mountainous terrain had energy expenditures proportional to their total weights (Hoyt et al., 1994). This method is currently being tested and still requires validation against other methods, such as the use of doubly labeled water.

In summary, soldiers in field training exercises, particularly those in mountainous, high-altitude terrain, are characteristically in negative energy balance. This deficit is largely attributable to the amount of time spent in physical activity, the weight of work loads, the elevation in basal energy requirements at high altitudes, and the limited consumption of field rations. Food and salt intakes appear to be reduced during the periods of adaptation to altitude. Carbohydrate intakes should be encouraged during such periods of adaptation to altitude.

Protein

A major observation of many of the studies reviewed by Butterfield and by Hoyt and Honig (see Chapters 19 and 20 in this volume, respectively) was the significant loss of lean body mass (LBM) among most of the subjects. The question raised was whether the protein requirement was increased in high-altitude environments or whether this loss in LBM was due only to a negative energy balance. Butterfield points out that the LBM losses were accompanied by losses of both total body weight and fat mass, which indicated that a negative energy balance was a more likely explanation for the LBM loss rather than an increased protein requirement. She further reasons that negative energy balance was likely caused by anorexia coupled with an increased metabolic rate induced by altitude exposure. In studies designed to increase energy intake during high-altitude exposure, Butterfield et al. (1992) demonstrated that if subjects were encouraged to consume sufficient energy to achieve energy balance, body weight losses were corrected and nitrogen balance could be achieved. The implication of these data is that the loss of lean body mass and resulting negative nitrogen balance are due entirely to the negative energy balance caused by anorexia and increased metabolic rate and not to an increase in protein requirements per se. Butterfield et al. (1992) further report that in a study where energy needs were adequately met throughout a 21-d stay at 14,000 ft (4,267 m), both body weight and nitrogen balance were maintained. It should be noted that these studies involved only moderately active, untrained individuals. Further studies involving strenuous exercise such as those performed by military troops on maneuvers, should be conducted using continuous nitrogen balance to define protein requirements in military type activities at high altitudes.

In summary, based on the available data, there is no apparent scientific rationale for increasing the recommended protein allowance for work at high altitudes above the existing MRDA value as provided to soldiers in cold weather rations. Strategies described in previous reports (IOM, 1995a) should be employed to encourage soldiers to eat their rations and thereby meet their energy needs and avoid negative nitrogen balance.

Vitamins

As in the case of cold exposure, no scientific basis was found to recommend increasing dietary recommendations for vitamins A, D, or K for individuals working at high altitudes (see Reynolds, Chapter 13 in this volume). However, the provocative data of I. Simon-Schnass (see Chapter 21 in this volume) showing that high doses (400 mg/d) of vitamin E decreased the exhalation of pentane and the production of thiobarbituric acid-reacting substances (TBARS) by erythrocytes of subjects at high altitudes, suggest that tocopherol may have a role in inhibiting increased lipid peroxidation under such conditions. Furthermore, a high dose of vitamin E appeared to improve the rheological characteristics of blood of subjects at high altitudes (see Reynolds, Chapter 13 in this volume). However, no attempt was made to titrate the dose of vitamin E between the dietary levels typically ingested on such expeditions (17-19 mg/d) and the large intervention dose (400 mg/d), nor was dietary vitamin E controlled. Since no dose-response was observed, it is not possible to arrive at a precise dietary recommendation based on this research. Nonetheless, the committee believes that the data were sufficiently intriguing that additional research along these lines should be encouraged.

As with cold exposure, concern was expressed regarding the adequacy of current dietary recommendations for the water-soluble vitamins essential for energy production (thiamin, niacin, riboflavin, and pantothenic acid) for individuals at high altitudes (see Reynolds, Chapter 13 in this volume). However, the influence of high altitudes on the requirement for these vitamins appears not to have been studied, so there is no basis for modifying these recommendations, which are already related to the levels of energy expended. Also, no data were found regarding the effect of altitude on requirements for vitamin B_6, vitamin B_{12}, biotin, or folic acid. Although some altitude simulation studies conducted during the early 1950s indicated that such treatment decreased tissue concentrations of vitamin C in guinea pigs and urinary excretion of ascorbic acid by humans (Boutwell et al., 1950; Mitchell and Edman, 1951), this suggestive research does not permit any quantitative expression of increased vitamin C requirements at high altitudes.

In summary, with the possible exceptions of vitamins E and C, there is little indication that increased vitamin intake is of any benefit to persons exposed to high altitudes. Further research is needed before the recommended allowances for vitamins E and C could be increased to levels above the current MRDA.

Minerals

No scientific justification could be identified for increasing the dietary intake of calcium, phosphorus, or magnesium beyond MRDA levels because of exposure to high altitudes (see Reynolds, Chapter 13 in this volume). However, adequate iron nutriture is important for individuals working at higher elevations, because of the well-known phenomenon of altitude-induced polycythemia. For example, iron-deficient individuals living at altitudes of 11,800 to 13,500 ft (3,597 to 4,115 m) had a lower maximal workload and voluntary V_{o2}^{max} than controls with adequate iron status (Beard et al., 1988). Transiently increased iron absorption has been observed following exposure to 15,000 ft (4,572 m) altitude, so that any temporarily increased need for iron was presumably compensated for by this mechanism (Reynafarje and Ramos, 1961). Therefore, there appears to be no reason to advocate dietary intakes of iron greater than MRDA levels because of high-altitude exposure. Urinary excretion of zinc was not increased during an expedition carried out at moderate altitudes (8,000-14,000 ft [2,438-4,267 m]) but urinary zinc losses were significantly elevated during exposure to the very high altitude of 27,726 ft (8,450 m) altitudes (Deuster et al., 1992; Rupp et al., 1978). Urinary losses of zinc averaged between 0.5 and 0.9 mg/d during an expedition to Mt. Everest, with a peak excretion of 3.2 mg/d (Rose et al., 1987). Since the maximum excretion appeared to coincide with periods of greatest physical exertion, these abnormally high urinary losses were thought to be due to muscle breakdown. Losses of body zinc generally accompany negative balances of energy and/or nitrogen. An increased gastrointestinal absorption of the element could compensate for these increased excretory losses of zinc, but further research into the possibility of increased dietary zinc needs at high altitudes is warranted. With regard to copper, there is insufficient information to determine whether dietary copper needs are increased as a result of high-altitude exposure.

In summary, although physiological needs for iron appear to be increased at high altitudes, enhanced compensatory absorption may obviate the need for increased dietary intake. Additional research is warranted to clarify this point. Similarly, the increased zinc losses seen at very high altitudes may be partially compensated by increased absorption.

APPETITE AND BEHAVIOR CHANGES AT HIGH ALTITUDES

Mental Response to High Altitudes

A hypoxic person often experiences personality changes, beginning with euphoria and then depression, with compromised ability to make decisions, especially when severe cold is a confounding factor (Nelson, 1982; Shukitt and Banderet, 1988; Tune, 1964). As noted by Schoene (see Chapter 17 in this volume), high altitudes "dull the spirit and engender a loss of spontaneity." He also noted, "the higher you go, the slower you go." As hypoxia worsens, there is increasing sensory and mental impairment, with the potential for paranoia and hostility. Patterns of mental response differ with individuals and the time course of acclimatization. Affect and emotions are altered at 14,000 ft (4,267 m) and above to the extent that cohesive groups, such as small military units, may experience a social breakup or dysfunction (Nelson, 1982; Shukitt and Banderet, 1988; Tune, 1964). There may also be decreased ability to perform small motor tasks which may persist after acclimatization.

Sleep is disturbed at altitudes of 14,000 ft (4,267 m) and above. Sleep becomes periodic, often with Cheyne-Stokes breathing[4] and periodic awakening accompanied by gasping for breath. There may be as much as a 50 percent reduction in total sleeping time, and a decrease in REM sleep (Anholm et al., 1992; Goldenberg et al., 1992; Normand et al., 1990; Sutton et al., 1979; Weil, 1985; White et al., 1987). This disturbed sleep pattern usually corrects within 3 to 5 days, but in some individuals may last for weeks. The general and REM sleep deprivation may contribute to personality changes.

The Effect of Altitude on Cognitive Performance and Mood States

Physiological changes associated with exposure to altitudes above 10,000 ft (3,048 m) are often accompanied by changes in mood, performance, and appetite (see Chapters 17 and 22 in this volume). The limited available data are based on self-evaluation and suggest that there is mood impairment at high altitudes, including unfriendliness, impaired thinking, and dizziness (Bahrke and Shukitt-Hale, 1993; Van Liere and Stickney, 1963). Other data indicated fatigue, which may have been exacerbated by physical exertion and increased oxygen demand (Shukitt and Banderet, 1988; Shukitt-Hale et al., 1990). In an

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[4] Cheyne-Stokes breathing is characterized by a gradual increase in depth and sometimes in rate to a maximum of inhalation and exhalation. This pattern is followed by an overall decrease in breathing rate, resulting in apnea. The cycles ordinarily are 30 seconds to 2 minutes in duration, with 5 to 30 seconds of apnea. This is characteristically seen in patients who may be in a comatose state or those who have experienced an injury to the brain centers that control respiration.

altitude chamber, subjects exhibited significant mood deterioration with increases in hypoxic conditions and duration of exposure (Lieberman et al., 1991). Available data thus are suggestive of mood deficits, but more studies are needed.

Data on cognitive performance under hypoxic conditions are also limited. Some results indicate impairment at high altitudes (10,000 ft [3,048 m]), including deficits in reaction time, vigilance, memory, and reasoning ability (Lieberman et al., 1991). Complex task performance also deteriorates, with increased error rate and slowing of performance (Lieberman et al., 1991). Simulation studies in altitude chambers (hypoxic conditions) suggest that such adverse changes increase in severity with greater hypoxia and duration of exposure (Lieberman et al., 1991). There appears to be individual variability in susceptibility to these effects of altitude/hypoxia. Moreover, rate of ascent (onset of hypoxia) influences onset and severity of symptoms (Hansen et al., 1967; Shukitt-Hale et al., 1991a).

In general, mood symptoms of altitude "sickness" develop over about 2 days, with maximal severity at 30 to 40 hours (Carson et al., 1969). Performance decrements occur more quickly and individuals accommodate well before mood changes are maximal. Thus, the temporal development and resolution of behavioral manifestations of hypoxia/high altitude are not simple or uniform (see Barbara Shukitt-Hale and Harris R. Lieberman, Chapter 22 in this volume), or directly tied to decreases in performance.

The underlying mechanisms in the brain responsible for mood and performance deficits at high altitudes are unknown. Some data allow speculation that alterations in certain neurotransmitters might be involved, namely those whose synthesis requires oxygen (catecholamines, serotonin) (Gibson and Duffy, 1981). Recently, more focused behavioral studies in animals point toward changes in acetylcholine formation and release (Shukitt-Hale et al., 1991b, 1993a, b). In addition, the reduced food intake and body weight loss associated with hypoxia at high altitudes may exacerbate direct chemical effects of high altitudes on brain chemistry and function.

Food Components that May Enhance Mental Performance at High Altitudes and in the Cold

Exposure to hypobaric hypoxia and to extreme cold at high altitudes can cause deficits in mental performance. Acclimatization eventually occurs, but only partly corrects cognitive deficits. Performance decrements caused by these and other environmental stressors and the attendant sleep loss can compromise combat operations. Effective countermeasures would be highly desirable, but their development requires an understanding of the specific underlying brain mechanisms causing the decline in mental function in adverse environmental settings (see discussion by Harris R. Lieberman and Barbara Shukitt-Hale, Chapter 23 in this volume).

For example, one important causal relationship may be the changes in brain catecholamine neurons that accompany stress. During stressful situations, catecholamine neurons increase their firing rate. Over time, the rise in firing rate may deplete the neuron's stores of transmitter, thereby compromising its ability to perform its required functions. Replenishment of transmitter might help to restore normal neuronal function, and overall cognitive function as well. One method for replenishing catecholamine involves administering tyrosine, the catecholamine precursor, to stimulate transmitter production (see Lieberman and Shukitt-Hale, Chapter 23 in this volume; for a more detailed discussion, see Ahlers et al., 1994; Lieberman, 1994; Wurtman and Lieberman, 1989). Indeed, in laboratory studies, increases in catecholamine production and release by neurons occur when tyrosine is administered to animals in a stressful setting (Luo et al., 1993; see Lieberman and Shukitt-Hale, Chapter 23 in this volume). Such tyrosine treatment improved performance in rats in these experimental situations (Ahlers et al., 1994; Luo et al., 1992; Rauch and Lieberman, 1990; Shurtleff et al., 1993). In limited field tests to date, consistent with the results of animal studies, tyrosine treatment maintained some aspects of cognitive performance in soldiers exposed to stressful situations (Ahlers et al., 1994; Banderet and Lieberman, 1989; Lieberman et al., 1990; Shurtleff et al., 1994).

A second causal relationship may be the changes in brain acetylcholine neurons that accompany stress. Acetylcholine neurons, particularly in the hippocampus, are important for normal learning and memory. Stress diminishes the functioning of these cholinergic neurons, with attendant decrements in performance. Preventing acetylcholine depletion during stress might therefore help prevent the loss of cognitive function under stressful conditions.

A variety of plant and animal extracts have been used by Asian practitioners since ancient times to manage stress and increase endurance, as presented by K. K. Srivastava at the workshop (see summary of his unpublished manuscript in Appendix A in this volume). These extracts have been termed *adaptogens*, and their chemical composition is relatively poorly defined. Careful studies in human subjects to evaluate the true efficacy of adaptogens are lacking. Because of the lack of information on composition and limited data on human or animal trials using these compounds, the CMNR concluded that they could not evaluate these materials or this concept.

Military Considerations

As described in this report, the many adverse physiological reactions, physical, or cognitive performance difficulties, and mood changes at high altitudes, when combined with increased risks for mountain illnesses, trauma, and malnutrition, create obvious difficulties for military operations. Some of these difficulties can be minimized by appropriate military planning, policies, and training. Troops conducting military operations at high altitudes, as they currently do in several mountainous regions of the world, have unique needs for special training and support. To prevent severe dehydration, water discipline is as essential at high altitudes as it is in the desert, and potable water must be supplied, whatever the logistical problems. Despite the tendencies for high-altitude and AMS-induced anorexia, discipline in food intake must also be enforced and military field feeding doctrines (IOM, 1995a) should include specific mention of environmental extremes. Energy and carbohydrate-rich foods must be provided, as outlined earlier in this chapter. Time to prepare and consume adequate energy must also be allowed. Increased energy needs at high altitudes result from an increase in basal energy needs as well as from strenuous activity. In order to prevent loss of body weight and muscle mass, the foods required to supply these needs must be provided, and they must also be compatible with logistical constraints. Palatability also must be considered; for example, provision of an easily consumed, preferred high energy "finger" food or beverage could be important in maintaining body weight and muscle mass.

Because gradual ascent to altitude and gradual acclimatization are not often compatible with military missions, a high incidence of AMS and breakdown in military unit cohesiveness must be anticipated. Military missions must be planned with the expectation that more than half of the troops will suffer from some degree of AMS, and that up to 25 percent may be transiently incapacitated (Hackett et al., 1989). Additional medical problems must be anticipated in troops who remain at altitudes above 18,000 ft (5,486 m) for many weeks (see Butterfield, Chapter 19 in this volume). Acclimatization to moderately high altitudes (8,000-12,000 ft [2,438-3,658 m]) may be accomplished within a week (many physiological systems adapt in this time, but some take far longer). However, full acclimatization to extremely high altitudes may not occur, and accumulations of body salt and water may become a consistent problem (see Cymerman, Chapter 16 in this volume).

All personnel must be trained to recognize the early symptoms of acute pulmonary edema or cerebral edema. These life-threatening problems are most likely to be observed in those individuals who have experienced difficulty in keeping up the pace and lag behind. Troops assigned to high altitudes should also be trained to master the difficulties in treating and evacuating patients with these altitude-induced conditions, as well as the task of dealing with soldiers who fall victim to the inevitable mountain climbing injuries.

INTERACTIONS OF COLD AND HIGH ALTITUDES

When considering nutritional and physiological aspects of cold and high-altitude environments, it is important to keep in mind that while there are similarities between the two in that high altitudes are frequently cold, there are also important differences. For example, as outlined by COL Askew (see Chapter 3 in this volume), these environments are similar in such characteristics as low ambient temperature, limited available water (mostly from snow and ice), and problems in food preparation. In both, diuresis occurs at least initially, energy requirements for work are increased, carbohydrate is well tolerated, and there appears to be no advantage of extra protein over the usual requirement.

Cold exposure tends to increase appetite and, over time, body weight may increase, whereas at high altitudes, appetite tends to be depressed, and body weight may decrease. Studies done in the cold at elevations above 11,500 ft (3,505 m) have shown further increases in energy need over those in the cold to more than 5,000 kcal/d (Jones et al., 1993; Swain et al., 1949). The dissimilarities also include lower oxygen tension and greater anorexia at high altitudes. Fat as a source of energy is well tolerated in the cold, but carbohydrate is the fuel of choice in low oxygen environments. These factors need to be considered when evaluating potential physiological responses of troops operating in these environments.

SUMMARY

Predictable medical problems can arise when military operations must be conducted in arctic cold, at high altitudes, or during combinations of both stressful conditions. Cold-induced injuries, altitude-induced illnesses, and psychological changes are described in this report. In addition, a great deal is known about the physiological responses used by the body during exposure to extreme cold, and the types of clothing and shelters that are militarily effective. Physiological adjustments, however, cannot mitigate the biophysical reality of declining availability of atmospheric oxygen as altitude increases. Much less is known about nutrient requirements for working in the cold and in extremely high environments.

A number of additional nutritional questions arose and were discussed during the workshop. These focused on possibly altered nutrient requirements for optimal or enhanced performance during operations in cold and/or high altitudes, and for assisting in thermoregulation, acclimatization, and prevention of medical problems. During the workshop, current military rations also were exhibited.

Physiological responses to cold and altitude were reviewed in depth, as were central nervous system functions and the interrelations between sleep and body temperature regulation. Dangers of acute mountain sickness and high-altitude cerebral and pulmonary edema were considered, as were the effects of cold and of high altitudes on appetite, mood, and both physical and mental performance. A review of available knowledge about altered nutrient requirements at cold and altitude extremes included presentations on fluid balance, energy costs, body weight changes, specific needs for various macro- and micronutrients, and the effects of appetite, gender, and age on these requirements. Discussion of these topics set the stage for the recommendations and conclusions concerning the questions under consideration, some immediately available military approaches, and future research needs, all of which are found in the next chapter.

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Committee on Military Nutrition Research Recommendations and Conclusions

As stated in Chapter 1, the Committee on Military Nutrition Research (CMNR) was asked to respond to 15 specific questions that address factors affecting nutrient requirements and food intake for work in cold and in high-altitude environments. The committee's responses to these questions appear below.

ANSWERS TO QUESTIONS POSED BY THE ARMY

Performance

1. What is the effect of cold or altitude exposure on muscle strength and endurance?

Cold and high-altitude exposure affects muscle strength and endurance through changes in cardiac output and oxygen uptake. Very cold environments that lower body temperature by more than 0.9°F (0.5°C) may limit maximal cardiac output and result in reduced maximum oxygen uptake. Because moderately cold environments lower muscle temperature, endurance of moderate physical activity actually can be theoretically increased if body core temperature can be maintained. There are conflicting data on the effects of cold exposure on muscle strength, and more research is needed to determine this relationship.

High altitudes can also affect physical performance because they decrease maximum oxygen uptake by approximately 10 percent for every 3,280 ft (1,000 m) increase in altitude. Endurance is also significantly reduced at high altitudes (see Chapter 1 in this volume). While acclimatization to high altitudes does not improve maximum oxygen capacity, endurance does improve (often as much as 50 percent or more) (see Chapter 1 in this volume).

2. Can diet influence these changes?

Maintenance of muscle structure and function over the long term depends on muscle strength and exercise. Muscle strength and endurance are influenced by diet through maintenance of muscle mass and the availability of appropriate substrates for muscle activity. Provision of adequate dietary energy under circumstances of either cold or high-altitude exposure will maximize the possibility of maintenance of muscle mass, and thus muscle strength. Conversely, inadequate energy intake will result in loss of muscle tissue with a concomitant decrease in strength and endurance.

Macronutrient composition of dietary intake may influence this process. In the cold or at high altitudes, protein requirements are not elevated above the needs of the individual at ambient temperature or at sea level performing the same level of activity. Nevertheless, dietary protein should be adequate to maintain the muscle mass that supports the strenuous physical activity performed. Fat as a source of energy is well tolerated in the cold, but provision of adequate carbohydrate is important because it is the major fuel needed for shivering, an important method for maintaining body temperature, and thus indirectly affects endurance. At high altitudes, carbohydrate becomes the predominant fuel at rest and during exercise. Failure to supply sufficient energy as carbohydrate (at least 400 g/d) at high altitudes can result in loss of muscle mass and decreased endurance.

3. How does cold or altitude exposure influence appetite?

The term appetite in this context is defined as a desire for food or drink. The traditional wisdom has been that cold climatic conditions lead to an increase in appetite. The evidence for this conclusion is derived from changes in body weight, self-scored questionnaires, and food intake records in cold environments at sea level. However, the reported increase in appetite is also associated with changes in other aspects of the subjects' environment such as altered activity levels, isolation, reduced social interaction, and modifications in diet. Nonetheless, it does appear that food intake is generally increased with cold exposure.

With ascent to altitudes above 10,000 to 12,000 ft (3,048 to 3,658 m), food consumption is reduced regardless of temperature. Body weight loss is common among subjects during the first few weeks at high altitudes, and such weight loss can be avoided only with successful efforts to consume food.

Although some studies have reported weight gain in cold environments, other investigations have found that soldiers operating in cold climates may not consume military rations in amounts adequate to meet energy expenditure. Reports from field training exercises have shown decreased intake of energy relative to need in both cold and high-altitude environments. The factors that influence ration consumption discussed in the CMNR's report on *Not Eating Enough* (IOM, 1995) may be even more significant for operations in the cold and in high altitudes. Encouragement of food discipline through a field feeding doctrine (IOM, 1995) would help soldiers maintain an appropriate level of food intake. With adaptation to altitude, appetite increases but generally food intake is insufficient to regain lost weight or even to maintain the lower weight.

Health and Medical Aspects

4. Is there concern for increased cardiovascular risk when a high fat diet is consumed for intermittent (7- to 14-d) time periods in the cold?

Although this question was not addressed specifically by any participant in the workshop, all available evidence indicates that there should be no concern with higher fat diets for these short periods of time. A major nutritional problem during military operations in the cold is meeting the added requirements for water and food to prevent both dehydration and weight loss. King et al. (1993) reported that in arctic field tests, the Army's 18-Man Arctic Tray Pack Ration Module [1] (29 percent of calories from fat), in combination with either a wet-pack (Meal, Ready-to-Eat[1] [MRE, 36 percent of calories from fat]) or a dehydrated (Long-Range Patrol, Improved[1] [LRP I, 35 percent of calories from fat]) individual ration, met the full daily nutritional recommendations for protein and micronutrients. However, energy needs were not met, and soldiers consistently lost body weight.

The easiest way for military feeding systems to provide for increased caloric needs during cold-weather operations is to include additional dietary fats. Such an increase in dietary fat is also most expedient, logistically. However, some tested supplements, containing only a modestly higher fat content, did not result in sufficient energy intake to prevent weight loss (Edwards and Roberts, 1991). Cold-weather operations probably require a total energy intake ranging from 45 to 62 kcal/kg body weight/d, but earlier military studies in the Arctic suggested that 4,000 kcal/d or less were actually being consumed (LeBlanc, 1957). Current projections for energy needs in arctic conditions focus on 58 kcal/kg body weight/d (see Chapter 1 in this volume).

Controversial questions about the relationships between dietary intakes of fat and cholesterol and the pathogenesis of atherosclerosis, strokes, and coronary heart disease have fueled important clinical research studies for several decades. Although recent estimations indicate that the average total fat intake in the United States has declined to 34 percent of total calories (CDC, 1994), the most recent review of national dietary guidelines recommends that an individual consume no more than 30 percent, with an increased intake of complex carbohydrates to provide total energy needs (USDA, 1995). Increased consumption of fruits and vegetables, which would increase the intake of complex carbohydrates, is also recommended.

However, these recommendations for the diet of the general population may not be appropriate for the military and logistical requirements for conducting either short- or long-term field operations in arctic climates. Fresh fruits and vegetables would be impossible to supply. Although diets supplying 58 kcal/kg body weight/d can be formulated with only 30 percent fat, they may prove operationally difficult to provide and the CMNR believes that this guideline is too restrictive for military operational rations. Diets containing more of the high density fat fuels may become an operational necessity. In addition, as pointed out by Edwards et al. (1992), the choice of ration must consider water availability, size and volume of load, resupply schedule,

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[1] See Table 1-3 in Chapter 1 for total nutrient composition.

logistics, and the task at hand. Although a higher fat diet is clearly not a nutritional necessity in the Arctic, it may prove to be a logistical need.

From a metabolic point of view, it is probable that the additional fat calories will be metabolized promptly, to satisfy immediate energy needs, rather than being stored in body fat depots. If extra dietary fat is consumed primarily to meet high daily energy requirements and to prevent weight loss during military operations in cold climates, it will not necessarily have important long-term consequences.

Current national dietary recommendations have been in effect for only a few years, and there is no available research evidence to suggest that a temporary deviation from a low fat diet, eaten in order to meet unusually high energy demands, would have a long-term effect on slowly developing cardiovascular pathology.

If this question is viewed from a risk/benefit perspective, the short-term risks to a soldier who must participate in a dangerous military operation in arctic cold are high, and nutritional assistance must be given to help the soldier function at an optimal level. Clearly, inadequate energy intakes and progressive weight losses are not desirable. The immediate benefits of an adequate energy intake far outweigh the possibility that a short-term intake of extra fat calories (eaten to meet the energy demands of cold, arctic climates) might contribute to deleterious health effects several decades later.

5. What nutrients prevent or lessen the symptoms of acute altitude exposure?

Two nutrients have the reputation of being protective against acute mountain sickness (AMS): water and carbohydrate. Because acute altitude exposure is accompanied by diuresis in most individuals, replacement of water lost through diuresis has been reputed to be important in minimizing the symptoms of mountain sickness. Scientific data on this question are minimal. More careful studies have been done on the effect of carbohydrate feeding during acute exposure to altitude, and the general consensus from those studies is that carbohydrate is of benefit in minimizing the symptoms of acute exposure (Consolazio et al., 1969). Because carbohydrate is the primary metabolic fuel at rest and during exercise (Brooks et al., 1991; Roberts et al., in press a, b), and because it provides slightly more energy for the oxygen consumed than does fat (Kleiber, 1961), provision of ample amounts of this macronutrient could be expected to overcome the 500 kcal/d deficit created by exposure to hypobaric hypoxia, maintain body glycogen stores, and assist in the maintenance of muscle mass.

6. Is free radical formation a concern for prolonged (10- to 30-d) military operations at 10,000–15,000 ft (3,048–4,572 m) elevation?

Free radical formation, the consequence of oxidative stress, might be expected to increase in cold or in high altitude environments, due to (1) the elevation in metabolic rate that results from an increased energy expenditure; (2) the stress of hypoxia at altitude; and (3) the increased exposure to ultraviolet radiation at altitude or on snow-covered ground. As recently reviewed by Askew (1995), some limited evidence does suggest an increase in oxidative stress in high altitude environments. During a 6-wk polar expedition, an increase in production of malonaldehyde, a product of lipid peroxidation believed to be a marker for oxidative stress, was measured in erythrocytes and plasma, followed by decreased blood concentrations of vitamin E (Panin et al., 1992 as reported by Askew, 1995). Simon-Schnass (see Chapter 21 in this volume) also reported increased exhalation of pentane, another marker for oxidative stress, with prolonged stays at high altitudes. Further research is needed to assess the physiological significance of such markers in terms of actual oxidative tissue damage as well as the potential long-term consequence of such damage, and the likelihood for significant oxidative damage during the timeframe of typical military deployments to high-altitude areas. Thus, there appears to be a potential for increased oxidative stress at high altitudes. However, the possible long-term consequences as well as the extent to which any ensuing damage would be decreased or prevented by providing additional antioxidant nutrients are not known at this time, but this is an important area for future research.

Thermoregulation and Acclimatization

7. Is cold/altitude acclimatization facilitated by prior nutritional status or supplemental nutrients?

There are few data on this topic. Prior nutritional status may affect acclimatization to cold/altitude in that an individual in poor nutritional status may have difficulty in adapting. Nutrients of particular concern would be iron, because of its relationship to hemoglobin and hemoglobin synthesis, and vitamin E, because of its relationship to oxidative stress.

In addition to prior nutritional status, the body composition, recent losses of body weight or lean body mass, and recent health and training history of individual soldiers should be considered prior to their participation in missions or training in cold and in high-altitude environments. In particular, the extreme losses of lean body mass described for some individuals who participated in U.S. Army Ranger Training would need to be regained prior to working in environmental extremes.

8. What nutrients influence thermoregulation?

Thermoregulation involves cardiovascular measures to reduce heat loss (nonshivering thermogenesis), an increase in metabolic heat production through shivering and an increase in voluntary muscular activity.

In short-term studies, shivering thermogenesis, like voluntary muscular activity, has been found to be fueled by carbohydrate and, to a lesser extent, fat. There is no evidence for a role for protein in shivering thermogenesis at this time; however, more research is needed to establish whether a specific proportion of nutrients has any advantage in maintaining thermoregulation under field conditions.

Thiamin, niacin, riboflavin, and pantothenic acid all play a critical role in thermogenesis due to their involvement in energy metabolism; however, there is no evidence at this time to support increased intake in the cold of any of these nutrients above MRDA (AR 40-25, 1985) levels. Evidence from studies conducted primarily in laboratory animals has suggested a role for the micronutrients iron, copper, and zinc in nonshivering thermogenesis. There is no evidence at this time to indicate that short-term depletion of any of these micronutrients interferes with thermoregulation in humans; however, more research is needed.

The macronutrient sources of energy (carbohydrate, protein, and fat) also have thermogenic effects. Fat is absorbed slowly but has the lowest postprandial thermogenic effect. Carbohydrates are absorbed most rapidly, but their thermogenic effect is higher and may last for 2 to 3 hours. Protein digestion gives rise to amino acids, which are absorbed more slowly than carbohydrates, but have the highest thermogenic effect, lasting up to 5 to 6 hours after absorption. The use of a high protein snack prior to retiring to sleep has been recommended to aid in thermoregulation.

9. Does the timing of food ingestion influence cold tolerance?

Postprandially induced thermogenesis can be a significant source of heat production within the body. Consumption of a substantial meal high in protein may provide necessary heat during periods of low activity or during sleep (see LeBlanc, Chapter 12 in this volume and the answer to Question 8 above). The consumption of small meals or snacks at intervals throughout periods of moderate activity is useful for maintaining body heat and work performance.

10. What is the relationship between fluid intake and thermoregulation in the cold and at altitude?

With acute exposure to both cold and high altitudes, fluid losses may result in a hypohydrated state. Diuresis is a common consequence of acute exposure to both conditions. Additional water is lost to the dry air through respiration, especially with the hyperventilation of exercise. Body water loss is also increased through sweating, especially if the individual is wearing excess clothing and engages in physical activity. Finally, fluid intake is often limited under these circumstances because of the response to stress, lack of fluid availability, or desire to control urine formation. The resulting reduction in body water, including blood and plasma volume, will decrease the ability to sweat. Thermoregulation is also affected by a decrease in body water due to the decrease in body heat transfer to the periphery with the decrease in blood volume because it is the blood that carries the body heat to the periphery, where it is given up to the environment through evaporative heat loss. Body fluid losses of greater than 10 percent of total body water are life threatening.

Some of this lost water will be replaced with metabolic water which is produced in greatest amounts with the burning of carbohydrate, the fuel of choice at altitude, and a fuel of significance in the cold. In spite of this, water balance is difficult to attain at altitude or in the cold due to the excessive losses, and the difficulties in supply.

11. What is the effect of cold and altitude exposure (at rest) on basal energy requirements?

Exposure to either cold or high altitudes significantly increases the energy needs of the body. In both cases, basal energy needs[2] (BMR) are elevated by as much as 15 percent after acclimatization. In the cold, this elevation in energy requirements is consequent to the need to maintain body temperature. The cause of the increase at altitude is not as clearly defined but may be associated with the increased respiratory rate and difficulty in sleeping.

During acute exposure to high altitudes, both the magnitude and time frame of changes in the BMR will vary with total energy intake and environmental conditions. Generally, the BMR increases by 20 to 40 percent over

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[2] Basal metabolic rate (BMR) refers to a parameter measured under strict circumstances of temperature, time at rest, and nutritional status. Consequently the determination of metabolic rate in cold environments does not meet the definition of BMR. The term "basal energy needs" is used here to indicate the energy requirements of individuals in the cold, unrelated to exercise or the thermic effects of food. Determination of basal energy needs at altitude met the criteria for measurement of BMR.

BMR during the first days at high altitudes, and then falls somewhat over the ensuing 3 to 10 days. There may be some loss of lean body mass during this time period, occurring simultaneously with inadequate energy intake, as BMR begins to decline toward the level that existed prior to altitude exposure. In experiments where energy intake has been matched to increased needs, basal needs remain elevated throughout the time spent at high altitudes. Individuals who are native to high-altitude environments show an elevated basal energy requirement in comparison to low-altitude natives of similar body size. The basal energy needs of soldiers can, therefore, be expected to be elevated in cold, high-altitude environments.

Nutritional Requirements

12. What are typical energy requirements for work in cold and in high-altitude environments?

Work in the cold or at high altitudes may result in very high energy requirements. When doubly labeled water techniques were used to determine energy expenditures, mean total energy requirements of 3,400 to 4,300 kcal/d (or 2.5 to 3 times BMR) were recorded in sedentary male military personnel in the cold or at high altitudes. Under training conditions, the energy requirements increased to as much as 5,000 kcal/d. The individual requirement will depend on body size, clothing, and activity level, but energy requirements of 54 to 62/ kcal/kg/d are recommended for these environments. Individual requirements may reach as much as 4 to 7 times BMR for short periods of time, especially when activities are being performed in clothing that restricts movement. No available studies define the total energy requirements during military operations under conditions of both intense cold and high altitudes. It should be noted, however, that there is no evidence that the actual energy expenditure of the work done is increased under the conditions of altitude exposure, although the hobbling effect of working in protective gear in the cold may increase appreciably the energy expended in given activities.

13. Does cold or altitude exposure alter the requirement for nutrients other than energy?

With the possible exception of vitamin E, there appears to be little scientific basis at this time to indicate that cold or altitude exposure changes the nutritional requirements for any vitamins or minerals. Questions have been raised about increased needs for vitamin C, iron, zinc, and copper in cold and in high-altitude environments. The MRDAs for operational rations (AR 40-25, 1985) supply generous amounts of nutrients over the requirements in normal conditions and should be adequate to meet any small increases in requirements due to cold or altitude.

14. What is the sodium requirement for hard physical work in a cold environment?

Sodium requirements in the cold have not been the subject of specific investigation. Although there has been monitoring of sodium status in individuals participating in metabolic research in cold environments, the focus of these studies was not to determine sodium requirements, and thus dietary intake of sodium was not controlled.

There is good reason to conduct research on sodium requirements in cold environments especially where hard physical work is required. Excessively high sodium intake can lead to increased diuresis, which is a major concern in cold environments. On the other hand, it is well known that significant sodium loss can occur during heavy physical activity. This loss of sodium through sweating occurs in cold-weather conditions when body heat is allowed to build up in heavy clothing. The loss will likely be reduced after acclimatization occurs. In the absence of more data, it is recommended that sodium intake be maintained as recommended in the MRDAs with no additional amounts given for hard physical activity. It is unlikely that electrolyte complications will occur, such as those associated with hard physical work in hot environments.

15. What is the relationship between fluid intake and food intake in the cold or at altitude?

Requirements for food are clearly distinct and separate from requirements for water, even though some foods may partially satisfy water requirements and generate metabolic water after they are consumed. The distinction between needs for water and food is most evident in hot, arid desert-like conditions, where water needs are greatly increased because much body water is lost by physiological mechanisms used to maintain normal body temperatures. This distinction is equally necessary for working in cold and in high-altitude environments.

Extremes of both cold and high-altitude environments have independent effects upon the nutritional and physiological requirements for food and water. As detailed in several chapters (for example, see Chapters 7, 10, and 11 in this volume), physiological responses to extreme cold induce metabolic heat production, which in turn increases the need for an adequate intake of dietary energy. Cold stress also leads to dehydration because of cold-induced diuresis, a phenomenon stimulated by several possible physiologic mechanisms (see review in Chapter 1 in this volume). Body water losses are also increased in the cold because of increased losses of respiratory water as well as losses induced by sweating. Cold conditions tend to reduce fluid intake because of logistical difficulties in supplying water and in preventing it from freezing. Water discipline is as important during cold stress as it is during heat stress.

The pair of problems created in meeting food and fluid needs is exaggerated when high-altitude stress is superimposed upon cold stress. Fluid needs become complicated by physiologic processes and hormonal effects that induce an antidiuretic effect in some individuals (see Anand and Chandrashekhar, Chapter 18 in this volume). This effect can contribute to AMS as well as to high-altitude pulmonary edema. More commonly, however, dehydration may become a potential military problem. Dehydration can result from several causes (see Cymerman, Chapter 16 in this volume), including reduced thirst, inadequate fluid intakes (from both water and foods), and increased sensible and insensible water losses associated with exercise. Again, water discipline is a military necessity.

Increased energy needs are also a separate but important issue at high altitudes. Weight loss is a common reality that must be met by increasing fuel intakes to meet additional energy needs (see Butterfield, Chapter 19 in this volume). Dehydration may also result in anorectic symptoms and lowered food intake. The provision of high calorie, energy dense snack-type foods was recommended by several participants in this workshop and by the CMNR in a previous report (IOM, 1995) as a potential means of providing extra food energy. Thus, the needs for supplying fluids and for supplying food must each be approached as equally important, and logistical support for cold and high-altitude work in the military must take into consideration the distinct differences in effort that are required for the adequate provision of each.

These issues can be summarized in two general questions:

1. Aside from increased energy demands, do cold or high-altitude environments elicit an increased demand or requirement for specific nutrients?

Cold and/or high-altitude environments can increase the needs for two important nutrients, water and carbohydrate (see answers to Questions 2, 5, 8, 10, and 15 in this chapter). Additional fat may sometimes be required to supply energy needs under certain circumstances (see reply to Question 4). While preliminary studies of increasing vitamin E intake to 400 mg/d show research promise in providing protective effects at high altitudes, considerable additional research is needed before questions regarding efficacy and effective doses are fully addressed and before implementing a supplement policy (see reply to Question 6). The needs for certain other single nutrients, i.e., vitamin C, iron, zinc, copper, and sodium, may also be increased (see comments on

Questions 7, 13, and 14), but because currently available data are inadequate, additional research will be needed to identify and define any increased needs for these nutrients. There is no evidence at this point to indicate a need for any of the nutrients to be provided at levels beyond that included in the MRDAs. For further elaboration see Chapter 1.

2. Can performance be enhanced in cold or high-altitude environments by the provision of increased amounts of specific nutrients?

Very little research is available to support any need to administer single nutrient dietary supplements in cold or high-altitude environments. As noted in an earlier CMNR report on *Food Components to Enhance Performance* (IOM, 1994), a number of nutrients have been investigated for these purposes but rarely under environmental conditions of cold or high altitudes. Harris R. Lieberman and his colleagues at the U.S. Army Research Institute of Environmental Medicine (USARIEM) have investigated single dose tyrosine pretreatment (100 mg/kg) in humans subjected to a 4.5-h exposure to cold and hypoxia. In a single controlled study, this large supplement significantly decreased symptoms, adverse moods, and performance impairments (Banderet and Lieberman, 1989). This work has been further expanded in several studies by the Naval Research group (Ahlers et al., 1994; Shurtleff et al., 1994). In rats, tyrosine pretreatment (400 mg/kg) reversed the behavioral depression caused by a forced swim in cold water, although it had no influence on deep body cooling (Rauch and Lieberman, 1990). These preliminary findings are worthy of additional future studies.

RECOMMENDATIONS

On the basis of the papers presented by the invited speakers, discussion at the workshop, and subsequent committee deliberations, the Committee on Military Nutrition Research offers the following recommendations regarding nutrient requirements for work in cold and in high-altitude environments.

Water and Dehydration

- Because cold-induced dehydration can cause serious performance decrements, it must be anticipated. The **training of military personnel assigned to cold-weather operations must include water discipline, safe fluid sources because snow or ice are generally unsafe, and the protection of drinking fluids from freezing**.

- Water discipline is as important during military operations in intense cold and at high altitudes as it is during desert heat. **Training should include water discipline measures following guidelines in military doctrines and means for their enforcement**.

Energy and Specific Nutrients

- Because of increased energy demands of cold operations, **dietary energy sources must be adequate to meet actual or anticipated needs** , including the needs for adequate carbohydrate foods. A field feeding doctrine, as previously recommended (IOM, 1995), should be considered. Pre-exposure diets should insure that muscle glycogen stores become optimized. **Meal times should be standardized whenever possible in order to encourage increased food intake**.
- **Carbohydrate intake should be promoted** during military operations conducted in the cold or at high altitudes. The inclusion of a liquid or solid carbohydrate supplement in the rations of troops may be useful in maintaining macronutrient balance and performance over time. **Carbohydrate intake should be at least 400g/d** under these conditions. When energy expenditures are high and total caloric intake is increased, the CMNR recommends that carbohydrate intake be increased to maintain calories from carbohydrate in the range of at least 40 percent of total caloric intake. This will help provide a palatable diet that is not excessive in fat content.

  The Ration, Cold Weather (RCW), MRE, and LRP I as currently prescribed for cold-weather operations all provide a minimum of 4,300 kcal and 582 g carbohydrate per day (see Table 1-4). The percentages of calories in these rations that are contributed by carbohydrate are 49 percent for the MRE, 60 percent for the RCW, and 50 percent for the LRP I. Thus these all meet the recommended criteria.
- **Restriction of fat calories to only 30 percent**, as recommended for the American civilian population, **is not appropriate for some military operational rations** where caloric density, ration bulk, and palatability are of concern. This is particularly the case for rations designed for use in cold and in high-altitude environments. The percentages of calories in currently available rations that are contributed by fat are 36 percent for the MRE, 32 percent for the RCW, and 35 percent for the LRP I. These levels appear appropriate, given the situational requirements.
- Sharing of food rations is encouraged as a means of meeting the higher than average caloric needs of some individuals in the field.
- In the absence of more data concerning sodium requirements during heavy exercise in conditions of arctic cold, **normal sodium intakes should be maintained**.

Education and Logistics

- Because **physiologic responses and adaptations differ importantly between moderately high altitudes** (8,00$1$2$32,000 ft [2,43$1$2 $3,658 m]) **and extremely high altitudes** (greater than 18,000 ft [5,486 m]), **planning for military training or military missions at high altitudes should take these differences into account**.
- **Individuals who have not yet regained lean body mass lost in prior field operations should not be deployed to cold or high-altitude environments until lean body mass is regained**.
- **Military troops, leaders, and medical personnel being assigned to high-altitude training or missions should be fully instructed on the symptoms and signs of AMS**, subacute mountain sickness, high-altitude pulmonary edema **(HAPE), and** high-altitude cerebral edema (**HACE**). In addition, they should be trained in the use of appropriate countermeasures and therapy.

  Because about 25 percent of people seem to be "immune" to AMS, **military personnel who have successfully completed a tour at altitude should be the ones selected for assignment to altitude missions of unique military importance**. Conversely, those who have developed AMS during training at high altitudes should be excluded in advance from participating in such unique military missions whenever possible.
- **Information about possible changes in physical performance, alertness, and emotional stability associated with hypoxia should be provided** to all levels of command so that soldiers and their leaders will not be surprised when they occur. Breakdown in troop cohesion should be anticipated.
- Because weight loss is common during military operations at high altitudes, command and logistical practices should attempt to ensure, whenever possible, that **the availability of palatable foods and fluids, as well as the social setting at mealtimes, are optimized to insure adequate dietary intakes** (see IOM, 1995).
- Logistical measures for cold-weather operations must put primary emphasis on the delivery and maintenance of sufficient food stores and unfrozen dietary fluids.
- Military rations are the fuel for the soldier and emphasis should be placed on adequate availability and consumption of operational rations to maintain performance in these harsh environments.

AREAS FOR FUTURE RESEARCH

The Committee on Military Nutrition Research suggests a number of areas for future research within the military related to nutrition for soldiers working in cold and in high-altitude environments. The CMNR believes that the military services, through their pool of volunteer personnel, offer an excellent and often unique opportunity to generate research data and statistics on the nutrition, health, and well-being of service personnel. It is important that future studies include men and women representative of the full range of ages in the active duty military. These findings can be directly applied to improve both the health of military personnel and that of the general U.S. population.

Water and Dehydration

Further research is needed:

- to define the best strategies (including pharmacological ones) to avoid cold-induced dehydration.
- to define the water needs of the body during the early phases of exposure to high altitudes, along with its relationship to the diuresis experienced by many subjects, and importantly, to the development of acute mountain illnesses.
- to define the potential "value" of dehydration in association with long-term stays at moderate altitudes and to define the limits whereby such dehydration might be preventable, beneficial, or detrimental.

Energy

Further research is needed:

- to assess the applicability to the military, both men and women, of the finding that it may be possible to maintain body weight, nitrogen balance, and muscle protein mass at optimal values during high-altitude missions.
- to define energy requirements during military operations in which simultaneous exposures to intense cold and high altitudes occur, by validation of the "free-living" estimation of energy requirement based on Hoyt and Honig's proposed use of body weight, foot strike, and terrain (see Chapter 20 in this volume).
- to understand the metabolic aspects of shivering.

Specific Nutrients

Further research is needed:

- to define more precisely the carbohydrate intake required to maintain body glycogen stores and to replenish stores depleted by exercise in the cold and at high altitudes.
- to establish whether a specific proportion of calories from fat, carbohydrate, or protein has a clear-cut advantage in maintaining thermoregulation in cold environments.
- to determine the optimum intake of micronutrients for improving performance in the cold. Such studies must control for nutrient status prior to and at the time of testing, the training level of subjects, and intensity and duration of any exercise to be tested.
- to determine sodium requirements during heavy exercise in intensely cold conditions and the possible advantages of restricting sodium during the first few days at altitude.
- to determine the possible beneficial effects of anorexia at altitude.
- to determine whether supplemental doses of vitamin E have any protective effects on humans exposed to oxidative stress.
- to determine if supplements of vitamin C, iron, zinc, copper, and/or other nutrients could improve performance during the stresses of extreme cold and high altitudes.

Performance and Medical Conditions

Further research is needed:

- to explore the merits of some potentially useful pharmacological compounds such as theophylline, caffeine, and ephedrine, as well as the potential value of prestress tyrosine administration.
- to evaluate possible pharmacological, physiological, and nutritional methods, either in the field or in altitude chambers, to predict, prevent, and/or treat AMS.
- to consider the pathophysiological problems of salt and water balance and the intercompartmental shifts in body fluids at altitude. Physiological mechanisms requiring additional study include cardiovascular, renal, endocrine, metabolic, and biochemical responses.
- to resolve conflicting data on possible effects of cold exposure on muscle strength and endurance.
- to examine the relationship between the aging process and acclimatization. Research in this area would not only be beneficial to the military but the general American population.

- to improve the understanding of mood and performance changes over time in subjects exposed to high altitudes and hypoxia, using animal models for the purpose of identifying the neurochemical cause(s) of those changes.
- to develop follow-up drug and nutrient intervention strategies for ameliorating chemical changes, and thus, ideally mood and performance decrements at high altitudes.
- to develop and evaluate diet-focused pharmacologic countermeasures (e.g., tyrosine and caffeine), with the ultimate goal of applying such countermeasures in field situations to stem the decline in cognitive function that accompanies the exposure to adverse environmental conditions.
- to define the effects of acclimatization to high altitudes in terms of altered performance measures and to optimize nutrition for more rapid acclimatization.
- to address the impact of preexisting malnutrition on the performance of soldiers at environmental extremes of cold and altitude, possibly through the use of key nutrient deficiency screening procedures to be administered to individuals prior to their participation in unique military missions or training in the cold and at high altitudes.

Military Ration Development and Guidance

Further research is needed:

- to insure that consumption of rations specially developed by the Army for use in cold-weather conditions provides intakes of energy, protein, and micronutrients that fully meet the increased requirements of troops operating in the field.
- to optimize packaging, delivery, and serving of these rations to insure that adequate amounts are consumed.

CONCLUSIONS

In conclusion, the CMNR wants to emphasize the critical importance of water discipline, availability of safe fluids for drinking, and a clear understanding on the part of all troops involved in operations or training in cold and in high-altitude environments. High energy, palatable rations supplying at least 400 g carbohydrate per day must be provided to insure that energy intake matches energy expenditure. Restriction of fat calories to only 30 percent is not appropriate in these operational rations. All military personnel who participate in cold and in high-altitude operations or training must be well informed about the symptoms and signs of AMS, HAPE, HACE, and possible changes in physical and cognitive performance, and trained in appropriate countermeasures. The logistics of troop supply and the composition of cold and high-altitude military units should be carefully screened regarding their previous experiences in these environments and their current nutritional and overall health status. Individuals who have not yet regained lean body mass lost in prior field operations should not be deployed to cold or high-altitude environments until lean body mass is regained.

An impressive body of evidence has already been generated to define the nutritional needs of troops required to engage in military operations under environmental conditions of extreme cold and/or high altitudes. The chapters in this report have addressed a number of specific nutritional areas and unanswered questions that need additional research study. The preceding series of research recommendations stem from these apparent gaps in knowledge. These informational gaps or uncertainties must be resolved in order to help define nutritional needs and military logistic strategies most appropriate for operations under these environmental extremes.

The primary nutritional considerations for soldiers operating in the cold or at high altitudes are:

- Fluid intake must be encouraged to prevent dehydration. Water discipline as practiced in hot, dry environments should be applied to operations in the cold and at high altitudes.
- Individuals who have not yet regained lean body mass lost in prior field operations should not be deployed to cold or high-altitude environments until lean body mass is regained.
- Energy intake of soldiers is usually inadequate when operating in the cold or at high altitudes. The deficit in intake frequently observed at moderate climates may be increased due to the greater energy needs when operating in these environments. Encouragement of food intake, use of supplemental rations, and alteration of energy composition through modest increases in fat content (to no more than 40 percent of total caloric intake) may aid but not fully overcome the deficit in intake usually observed in these environments.
- Increased carbohydrate intake (to at least 400 g/d) when functioning at higher altitudes is recommended to help maintain soldier performance.
- There appears to be little scientific evidence to indicate that cold or altitude exposure should change the nutritional allowances for any vitamins or minerals, with the possible exception of increased needs for vitamin E at high altitudes beyond that recommended for military rations. Further studies may be required to evaluate the suggestion that the needs for iron, zinc, copper, and vitamin C are influenced by cold temperatures. Carefully controlled studies are needed to evaluate whether or not supplemental doses of vitamin E have any protective function at high altitudes.
- Several areas for additional research have been identified that may offer future benefits in improving performance under the environmental extremes of cold or high altitudes. Among those most critical to military

operations are (1) the need to define further the water requirements in cold and in high-altitude environments, and how best to meet them; (2) the need to apply to military personnel the recent findings concerning maintenance of body weight and composition at altitude by encouraging the intake of a minimum level of dietary carbohydrate and total calories; (3) the need to determine the optimal ratio of energy sources, micronutrients, and sodium in the cold; (4) the need to develop better methods to predict, prevent, and treat altitude-related illnesses; and finally (5) the need to obtain a better understanding of the causes, ramifications, and treatments of altitude-related changes in mood and performance.

The Committee on Military Nutrition Research is pleased to participate with the Military Nutrition Division, U.S. Army Research Institute of Environmental Medicine and U.S. Army Medical Research and Materiel Command in programs related to the nutrition and health of American military personnel. The CMNR hopes that this information will be useful and helpful to the Department of Defense in developing programs that continue to improve the lifetime health and well-being of service personnel.

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II

BACKGROUND AND INTRODUCTION TO THE TOPIC

IN PARTS II THROUGH V THE PAPERS from the workshop appear in the in which they were presented. The chapters have undergone limited editorial change, have not been reviewed by an outside group, and represent the views of the individual authors. Selected questions and the speakers' responses are included at the end of each section to provide the flavor of the workshop discussion.

Part II includes four chapters based on the introductory presentations by current and former Army scientists and personnel to provide the background for understanding military nutrition issues in the cold and at high altitudes and to highlight the importance of coordinating research and logistical considerations. Chapter 3 presents the purpose of the workshop and an overview of cold and high-altitude research conducted or sponsored by the Army. Research efforts were largely a civilian-military collaboration until the 1970s, and now much of the research on soldiers' nutritional needs in environmental extremes are conducted by the military. This chapter puts this report into historical perspective.

The influence of a positive attitude at environmental extremes should not be underestimated. In Chapter 4, the performance expectations of unit commanders are discussed as being essential to developing and maintaining their troops' positive attitude.

Chapters 5 and 6 summarize the preparation and use of military operational rations in cold environments, an important topic given that rations are the principal source of nutrients for soldiers in the field. In Chapter 5, the options for group and individual field feeding are reviewed, as is the composition of the rations in relation to the cold. The problems of feeding soldiers in harsh environments are discussed in Chapter 6. The development and improvement of mobile kitchen equipment requires attention because the unique conditions of cold and wind affect the sheltering of personnel and the preparation of food.

3

Cold-Weather and High-Altitude Nutrition: Overview of the Issues

Eldon W. Askew[1]

INTRODUCTION

Climatic extremes can exert profound influences on human physiology (Figure 3-1). How well humans adapt to these environmental stresses ultimately determines the degree of success they achieve in these difficult and often hostile environments. Success or failure may be influenced by how well the body responds to the challenges of maintaining homeothermia and work output. The body's metabolic response to cold and hypoxia can be either augmented by proper nutrition or impaired by inadequate nutrition (Askew, 1994).

The many similarities between cold and high-altitude environments (Table 3-1) make them suitable to address in the same workshop and book. This is not without precedent. The Arctic Aeromedical Laboratory held a symposium,

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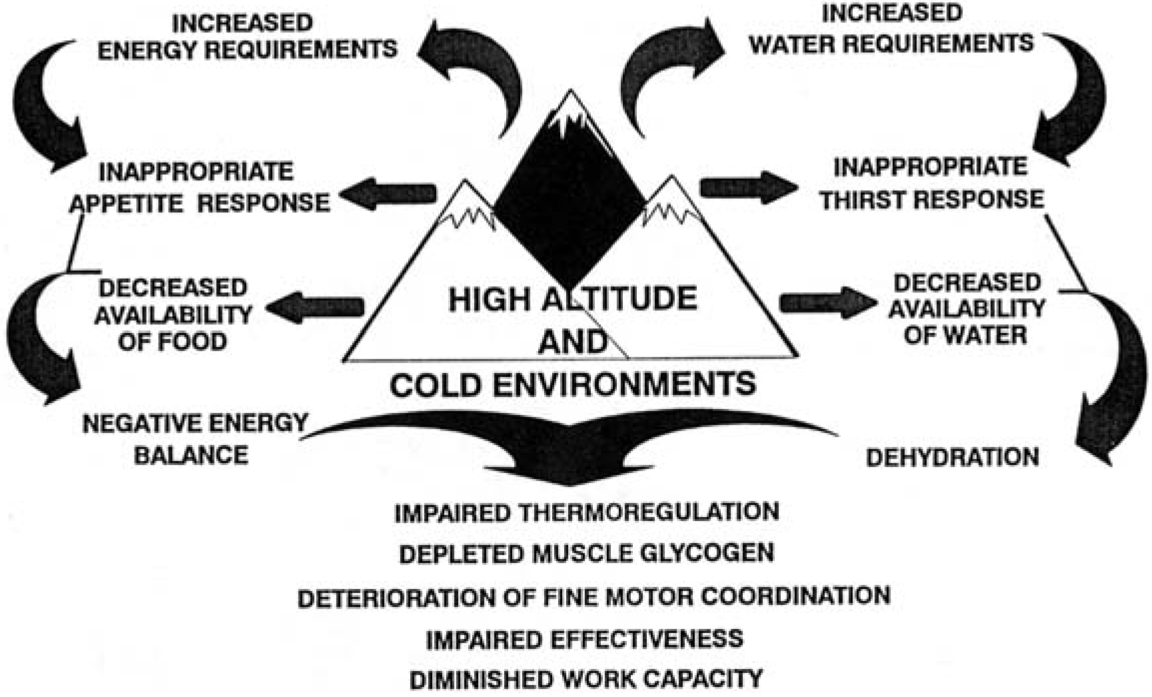

FIGURE 3-1 Schematic representation of the influence of cold and high-altitude environments on energy and fluid balances and the resulting physiological consequences. SOURCE: Adapted from Askew (1994).

Arctic Biology and Medicine: The Physiology of Work in Cold and High Altitude, at Fort Wainwright, Alaska (Helfferich, 1966). General Ross, the Yukon Commander, gave the welcoming address at this 1966 meeting of environmental physiologists, and his words regarding the military relevancy of cold and high-altitude research are as appropriate now, as then:

TABLE 3-1 Similarities and Dissimilarities Between Cold and High-Altitude Environments

Similarities	Dissimilarities
Low ambient temperatures	Lower atmospheric oxygen tension at high altitude
Diuresis, at least initially	Usually greater anorexia and hypophagia at high altitude
Increased energy requirements for work	Fat tolerated well in the cold
Lack of water except for ice and snow	Fat not tolerated well at high altitude
Difficult to prepare food	
Carbohydrate is tolerated well	
Protein not particularly advantageous	

> Military interest is expanding to areas that were once considered uninhabitable and forbidding, such as the Arctic. The geopolitical importance of the Arctic basin and the Arctic mountainous area necessitates much greater knowledge and special understanding of these areas…In light of the constantly changing military requirements, it is singularly important for us to understand the physiological responses and limits of man to these unusual stresses in order to utilize human capabilities maximally in the accomplishment of our military mission. It is also necessary for us to understand what measures can be taken to improve the functional capacity of military personnel in these adverse and hostile environments…(Helfferich, 1966, p. 1).

PREVIOUS SYMPOSIA

During the 1950s and 1960s there were a number of symposia or conferences on environmental physiology, usually sponsored or cosponsored by the U.S. Armed Services (Table 3-2). These excellent reviews of environmental medicine came to an end after the mid 1960s, perhaps due to a lack of military sponsorship. Their end also coincided with a gradual decline in the amount of contract funds available from the Armed Forces to support extramural research of this nature.

Historically, a significant proportion of environmental medicine research during the World War II and Korean War eras was conducted in government-supported civilian research institutions such as the Universities of Illinois, Minnesota, Washington, California, Hawaii, Colorado, and Alaska, and in the Fatigue Laboratory at Harvard University. In the 1970s and 1980s the emphasis began to shift from extramural to intramural research, and the Armed

Forces' laboratories began to conduct the majority of their environmental research in military facilities. The establishment of the U.S. Army's altitude research facility at the summit of Pike's Peak, Colorado in 1966 and the acquisition of the mission for cold research from the Air Force's Arctic Aeromedical Laboratory by the U.S. Army Research Institute of Environmental Medicine (USARIEM) in 1968 contributed to the trend toward intramural research. Whether this change in emphasis away from extramural research funding was due to a shift in military research strategies, a constrained military research budget because of the Vietnam conflict, or a decline in academic institution research interest in environmental nutrition and medicine, is not entirely clear. Ancel Keys, Director of the Laboratory of Environmental Hygiene at the University of Minnesota, commented on what may have been the beginning of the schism between academia and the military regarding scientific interest in nutrition research at a symposium held at the National Academy of Sciences in 1952:

TABLE 3-2 Conferences and Symposia on Environmental Physiology in Cold and/or High-Altitude Environments

Conference/ Symposium Title	Year	Location	Reference
Nutrition Under Climatic Stress	1952	Washington, DC	Spector and Peterson, 1952
Cold Injury	1958	U.S. Army Medical Research Laboratory, Ft. Knox, KY	Horvath, 1960
Man Living in the Arctic	1960	U.S. Army Quartermaster Research and Engineering Center, Natick, MA	Fisher, 1961
Nutritional Requirements for Survival in the Cold and at High Altitude	1965	Arctic Aeromedical Laboratory, Ft. Wainwright, AK	Vaughn, 1965
The Physiology of Work in Cold and High Altitude	1966	Arctic Aeromedical Laboratory, Ft. Wainwright, AK	Helfferich, 1966
Biomedicine Problems of High Terrestrial Elevations	1967	U.S. Army Research Institute of Environmental Medicine, Natick, MA	Hegnauer, 1969

> It is appropriate to ask why, in general, the scientists of our country have been rather reluctant to engage in research directed toward problems of military subsistence. For it is a fact that many nutritionists may be willing, occasionally, to act on advisory boards and committees and to attend meetings like this symposium, but the amount of research they are carrying out is small.

> Most scientists of real ability and worth are such because they are irresistibly attracted to gaining knowledge of a permanent nature…he feeds his vanity on the thought that his research has universal meaning…and that he is at grips with something more durable than this year's specifications for a combat ration…This means writing articles that he hopes will be applauded, commanding the attention of his fellows…a succession of purely practical researches directed toward changing problems of military subsistence, no matter how good, will not serve these ends…The answer is that every research program and project must carry with it the prospect of some real scientific advance…there must be provided opportunities for enlarging the scientific horizon of the field, for testing basic theories, for formulating new truths of general application (Keys, 1954, p. 199).

The "writings on subsistence" of those talented and dedicated scientists of the not-so-distant past should be applauded. Their credit is long overdue. In retrospect, their ideas have lived on and formed the origins of the 1993 *Workshop on Nutrient Requirements for Work in Cold and High-Altitude Environments*, on which this book is based. The work of such university-affiliated scientists as Adolf, Keys, Mitchell, Horvath, Johnson, Sargent, Belding, Buskirk, and other civilian academic scientists too numerous to name, has achieved an important place in the nutrition literature.

Although it is difficult to explain the rather abrupt cessation of environmental medicine symposia sponsored by the Armed Forces, it is worthwhile to note that USARIEM in Natick, Massachusetts has begun to resume meetings of this nature in the form of workshops hosted by the Committee on Military Nutrition Research (CMNR) of the Food and Nutrition Board, Institute of Medicine, National Academy of Sciences. These workshops are narrow in focus and limited to a small group of civilian and military scientists who have expertise that can be focused on relevant practical scientific problems from a military standpoint. Publications of the National Academy Press provide the Department of Defense Food Program and the Surgeon General of the U.S. Army with comprehensive summaries of recent scientific literature, advice on specific scientific questions of military application and importance, and recommendations for future research in military nutrition. They also contribute to the preparation of U.S. Armed Forces environmental medicine "pocket guide deployment manuals," which are prepared by the USARIEM to assist soldiers and their commanders in conducting field operations in hot, cold, and high-altitude environments (Glenn et al., 1990; Thomas et al., 1993; Young et al., 1992).

The most recent workshop that focused on environmental extremes, *Nutritional Needs in Hot Environments*, was held during Operation Desert Storm in 1991. The resulting report (IOM, 1993) provided the Armed Forces with a comprehensive review of nutritional requirements in hot environments. Fluid requirements for work in the heat were addressed at a previous workshop sponsored by the CMNR in 1990 (IOM, 1991).

This book summarizes the advancement (or lack thereof) of knowledge of specific nutrient requirements as influenced by cold and high altitude, particularly since the mid 1960s. The ultimate goal is to contribute to the design of rations and ration supplements that will permit more efficient soldier performance in cold and high-altitude environments.

Much of the scientific literature on cold and high-altitude nutrition has come from observations made by explorers. Although many of these reports are reliable and carefully conducted, their direct application to military operations may not be warranted. Soldiers are not necessarily of the same ilk as explorers. Sir George Hubert Wilkins, famed explorer of the Arctic and Antarctica, who made the first air flight over the North Pole and the first submarine voyage under the arctic ice, remarked:

> Food problems to be met by explorers differ widely from those of the Armed Forces…men on an arctic expedition have been selected because of their interest in the area and in the work they must do. They are generally the type of men who eat to live rather than those who live to eat. They are not greatly concerned about their food except that it must give them the nourishment they require (Wilkins, 1954, p. 102).

PREVIOUS MILITARY RESEARCH: THE POLE MOUNTAIN WYOMING WINTER PROJECT

Because humans inhabit all the climatic regions of the Earth, there has always been considerable interest in both human genetic adaptations and cultural traditions that enhance survival, particularly in environmental extremes. The diet of humans living in different climates varies greatly, which raises the question whether the diet varies primarily due to the availability of food in the area, or because certain foods impart unique advantages to life in that climate.

For years, scientists have been intrigued with the possibility that humans select foods and acquire food habits that will help them adapt to their environment and combat climatic stress (Mitchell and Edman, 1949). Interest in foods and nutrients to combat environmental climatic stress peaked during World War II and continued into the postwar years.

Following World War II, scientific understanding of the roles of vitamins in the regulation of metabolism was clarified, and there was considerable research interest in these relatively new "glamour nutrients." The concept of vitamin supplementation to combat climatic stress arose and became the subject of much scientific debate. Some preliminary evidence suggested that when severe demands or stresses are placed on individuals (such as soldiers), their ability to withstand such stress might be improved by the administration of very large amounts of certain vitamins, particularly the water-soluble vitamins (Dugal, 1954; Ralli, 1954). Although not all investigators believed that excess vitamin intakes would improve human tolerance to cold (Glickman et al., 1946), by 1952, the body of evidence supporting this view was "…impressive enough to cause the Research and Development Board of the

Surgeon General's office and its consultants to pose the question of whether the concept might be applicable in certain military situations" (Medical Nutrition Laboratory, 1953, p. 1).

Following this recommendation, the staff of the Medical Nutrition Laboratory (located then in Chicago) drew up a protocol for a cold-weather field study. It was quite an undertaking and became known as the *Medical Nutrition Laboratory Army Winter Project: Vitamin Supplementation of Army Rations Under Stress Conditions in a Cold Environment—The Pole Mountain, Wyoming Study* (Medical Nutrition Laboratory, 1953). The study was designed to answer the basic question: Will the functional abilities of the soldier in a cold environment be significantly improved by supplementation with large amounts of vitamin C and B-complex? The specific objective of the 2-month cold-weather field study was to determine the effect of supplementation with large amounts of ascorbic acid and B-complex vitamins on the physical performance of soldiers engaged in a high-activity program in a cold environment, both with and without caloric restriction. The study was conducted at Pole Mountain, Wyoming (elevation 8,300 ft [2,532 m]), from 2 January 1953 to 10 March 1953 with 86 military personnel as study participants. The control group (42 men) received a capsule containing 6 mg of ascorbic acid four times a day. The supplemented group (44 men) received four capsules that appeared to be identical to the control capsules, each containing: 10 mg thiamin, 10 mg riboflavin, 100 mg niacinamide, 80 mg calcium pantothenate, 40 mg pyridoxine, 2.5 mg folic acid, 4 µg of vitamin B_{12}, and 300 mg ascorbic acid. The average daily temperature was 26°F (-3°C), with the wind chill making it much colder. To enhance the effect of cold, the outdoor clothing was restricted to "less than the amount required for comfort when inactive under the prevailing weather conditions" (Medical Nutrition Laboratory, 1953, p. 23).

The subjects maintained a program of high-level outdoor physical activity. Physical performance measurements were taken, including the Harvard step test, handgrip strength test, Army Physical Fitness Test, and forced marches. The decline in rectal temperatures during indoor and outdoor cold exposure was measured, and a group of psychological tests were administered.

Major findings of the Pole Mountain study showed no significant differences between groups for physical performance measures or psychological tests. There was, however, a significantly greater loss of body weight in the supplemented group, perhaps related to a significantly smaller decline in their rectal temperatures upon cold exposure. The conclusions from this study were as follows:

> Under the conditions of this experiment, supplementation of an adequate diet with large amounts of ascorbic acid B-complex vitamins in men subjected to the stresses of high physical activity,…cold,…and caloric deficit did not result in significantly better physical performance than that of unsupplemented men (Medical Nutrition Laboratory, 1953, summary, p. 2).

This report recommended that Army rations used in cold weather did not need to be supplemented (beyond the then current values in the Recommended Dietary Allowances, NRC, 1948) with ascorbic acid and B-complex vitamins, and this basic recommendation has stood for 41 years since the study. However, it was also recommended that further studies be made on the effect of vitamin supplementation on the physiological and pathological response of human subjects to cold exposure. This recommendation has not been pursued to a significant degree by military or civilian scientists. Only a small amount of subsequent research has taken place between 1952 and 1993 on the topic of vitamin supplementation and thermoregulation.

GOALS OF THE 1993 WORKSHOP AND THIS BOOK

The 1952 workshop on *Nutrition Under Climatic Stress* proposed that the participants address six topics:

1. practical problems of service operations under climatic stress,
2. physiological responses of men to heat and cold,
3. animal experimentation,
4. human experimentation,
5. summary of present knowledge, and
6. survey of areas in which more research is needed.

This was a reasonable format in 1952 and also served the 1993 workshop on *Nutrient Requirements for Work in Cold and High-Altitude Environments* (on which this book is based). Speakers for the 1993 workshop addressed one or more of these topics in their presentations, but animal and human work were not treated as separate topics.

Speakers for the 1993 workshop also received the list of questions that were of particular interest to the Army and that were presented and addressed by the CMNR in Chapters 1 and 2 of this volume.

AUTHOR'S CONCLUSIONS

This brief historical review of cold and high-altitude issues relative to military operations illustrates that the Armed Forces traditionally have been aware of and keenly interested in the impact of these extreme environments on human performance. Nutrition has been viewed as a key factor for enhancing both physiological performance and morale during operations in these environments. Military interest in research on nutrition and human physiology in cold and high-altitude environments peaked during and after World War II and the Korean conflict, probably due to the extensive cold weather operations that were conducted in these wars and the doctrinal and equipment shortfalls that were perceived. During the 1950s and 1960s civilian and military scientists jointly participated in several excellent environmental medicine conferences that were sponsored by the Armed Forces. It is apparent that many of the same concerns regarding physiological limitations to human performance in cold and high-altitude environments that were expressed by civilian and military scientists 30 to 40 years ago still exist today. Advances in technology, doctrine, and equipment have not eliminated the need for a better understanding of human physiology and nutritional needs in these environments that are still critical to current military operations. It is hoped that this conference and report will help document and update the advances that have been made in establishing nutrient requirements for work in cold and high-altitude environments and give direction to future research.

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4

Leadership Insights for Military Operations in Cold Weather and at High Altitudes

Russell W. Schumacher, Jr.[1]

INTRODUCTION

Soldiers, scholars, and military historians have always marveled at Hannibal overwhelming the Italian Peninsula by way of the Alps. This classic historical feat was successful primarily because he planned his campaign in detail and was prepared for any known eventuality. This early military operation, which was conducted in the cold at high altitude, is one of many that lends credibility to the need to know how to operate in these areas of the world.

Cold and high altitude have always been enemies of military planners as well as their troops, and most large armies of the world have training centers where they maintain an expertise in cold-weather operations. The human body, which functions normally at 98.6°F (37°C), faces difficulty when the temperature ranges from –30°F to 30°F (–34°F to –1°C). The question is, how

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can the military operate in this environment? Is it clothing, equipment, state of mind, leadership, physical condition, medical knowledge, or proper nutrition that allows soldiers to function in a cold, high place? The truth of the matter is, it can be all of these factors or just a few, depending on the individual and the circumstances. However, when dealing with large military forces, the initial planning must include all of the above factors, and probably more, and they must be consistently addressed throughout an operation.

THE MIND AND LEADERSHIP

The single most important factor for successful military operations in cold and at high altitudes is the development of a state of mind that allows soldiers to survive and actually thrive, if they are familiarized, oriented, and led properly. The philosophy of simply "surviving the cold" has no place in U.S. military operations. Troops must be convinced that the cold is manageable, and that it is not something to be intimidated by, but rather something to respect and conquer. This task is not easy to accomplish. Consider the young Marine who declared that he could not ski or adapt to the cold because he was from Oklahoma. To follow that logic, the great Carthaginian Hannibal should never have crossed the Alps because he was from sunny North Africa. Many people believe that they are not capable of dealing with the cold or that they should not have to. Therefore, cold is a daily challenge to field commanders, and military leaders must be masterful psychologists with regard to planning for cold and high-altitude operations. They must be aware that exceptional physical fitness and proper equipment and its proper use contribute much to building the soldiers' confidence in a cold environment. The expectations of soldiers' performance must also be reexamined. This issue can cause difficulties for leaders. How a unit performs at sea level on a 75°F (24°C) day has no relationship to what the same unit can do at 9,000 ft (2,745 m) when the temperature is 20°F (-7°C), when it is snowing and the wind is blowing off and on at 20 knots, or even when the sun is shining. High altitude is a major hindrance, and if leaders do not recognize this fact and adjust their expectations for their troops and mission accordingly, they are in for a long day and probably eventual disaster. Simply put, the best equipment and physical condition will not in itself create success. The commander, as well as each small-unit leader and the individual, is responsible for developing a positive attitude toward the situation. If possible, this training must take place weeks and months in advance of any military operation. If not, then the commander and all the subordinate leadership must work daily to maintain a positive attitude among the troops. Adaptation and flexibility are key to success in cold and high-altitude environments.

DIET

The diet of an average soldier is much like that of an average American. It is not always the best. However, one cannot function for long on a poor diet in the cold and certainly not above 6,000 or 7,000 ft (1,830 or 2,135 m) for any extended period of time. The caloric intake required in this environment, as well as the kind of food received from those calories, is very important. Soldiers can survive on Snickers bars and Top Ramen soup for a few days (which is often the case in short-term military exercises), but for long campaigns troops need to eat a proper diet to avoid early casualties. The rations provided by the U.S. Department of Defense are most adequate, as long as variation for troop morale and the proper daily intake of calories are maintained.

MEDICAL CASUALTIES

A commander must be aware of the potential medical problems that soldiers face in the cold and at higher elevations. These problems are not hypothetical; they are real casualty producers and killers. History reveals that the cold and high altitude (above 7,000 ft [2,135 m]) produce far more casualties than bullets or any other single cause. Acute mountain sickness, high-altitude cerebral edema, high-altitude pulmonary edema, and frostbite are all potential casualties that are the price of doing business in cold, high places. All medical personnel need to be trained to deal with them, and battalion, regimental, and division surgeons must know how to treat these ailments and conditions. Small-unit leaders and personnel need to know the proper way to recognize symptoms and to react so that they can assist their fellow soldiers and prevent death. Excellent leadership, clothing, equipment, and diet do not in themselves prevent these medically related problems. Specific awareness and treatment of potential medical problems must be maintained by all personnel and planned for well in advance of an operation.

TRAINING TROOPS

Just as troops can be trained to attack a fortified position (which logic warns against), troops can be trained to become acclimatized and to operate in the cold. However, such training requires masterful and consistent leadership and education. Of the many battalions that have come through the Marine Corps Mountain Warfare Training Center, the good ones all had strong, knowledgeable, flexible commanders who had plenty of common sense. These commanders took a deliberate, planned approach to unit training. The took care of their personnel and did not exhaust them early in the training cycle. To train troops to operate in cold and high-altitude environments, military leaders must provide specific training and reemphasize all aspects of it on a daily basis.

PHYSICAL CONDITION OF TROOPS

Peak physical condition of soldiers is critical for operations in cold and high-altitude environments. Some of the physical challenges in cold, high places include the weight of the pack, size of the lungs, and natural fatigue caused by the cold. Soldiers must be in superb physical condition to compensate for these challenges. Generally, the body will adjust to a higher altitude over a period of time (80+ percent in 90 days) and physical performance levels will return to approximately 80 percent of sea-level performance levels within 90 days. However, even though the body adapts, the soldier must also deal with fatigue, the much heavier pack (more clothing and equipment), and less oxygen in the alpine environment. This combination of challenges is devastating to soldiers who are in poor physical condition and who then become a burden to their units. Of the many kinds of units that have trained in the mountains, those that focused part of their training on exceptional physical conditioning for the most part had a great advantage over those who did not.

CLOTHING AND EQUIPMENT

Probably nothing has affected cold-weather military operations more positively in recent years than the public's exploding interest in challenging outdoor activities and the necessary clothing and equipment to pursue them. Clothing and equipment manufacturers have responded by creating superb lightweight clothing and equipment, and the U.S. military has taken advantage of this trend by obtaining an entirely new inventory of cold-weather clothing and equipment. However, much of this equipment is complex and sophisticated. Soldiers must know its proper use; otherwise, they are better off in the old wool and cotton used at the Bastogne in World War II. For example, with the old gear, there was only one way to wear a heavy, olive-drab wool sock. With the new synthetic and wool three-sock system, there are many combinations, and soldiers can freeze their feet if the socks are not worn properly. Training and small-unit leadership, if consistent, can address these problems.

AUTHOR'S CONCLUSIONS

The effects of cold and high altitude on the U.S. soldier are, by nature, negative. Military leadership must take into consideration the specific elements discussed above to compensate for the challenges presented by this unique environment. Soldiering generally is not difficult as long as individuals can adjust to the situation presented. Cold, high environments require great adaptation and knowledge by all personnel involved. A failure to recognize this fact can spell disaster. Unlike Hannibal, who did not have Gore, the U.S. military has a broad range of equipment and knowledge of how to operate effectively in the cold and at high altitudes. Military leaders must make sure that it is used with all the skill and energy required.

5

Cold-Weather Field Feeding: Military Rations

Nancy King[1]

INTRODUCTION

The U.S. Army Field Feeding System can be tailored to the tactical situation and unit mission in both training and combat environments (AR 30-21, 1990). The cornerstone of field feeding is the military ration. Generally, a ration is the nutritionally adequate food necessary to subsist one person for 1 day. A meal is a specific quantity of food provided for one person during one scheduled serving period. Military rations used for cold-weather field feeding are nutritionally adequate in accordance with the Military Recommended Dietary Allowances (MRDA) (AR 40-25, 1985). Military rations may be wet packed, i.e., they do not required additional water during preparation, or dehydrated and are divided into group feeding rations and individually packaged rations. Although any military ration may be provided to the soldier

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while operating in cold environments, some rations may be more suitable than others.

MILITARY RECOMMENDED DIETARY ALLOWANCES FOR COLD WEATHER

Military Recommended Dietary Allowances (MRDAs) are the recommended daily nutrient intake levels that should meet the nutritional and physiological requirements of practically all healthy 17- to 50-year old, moderately active military personnel (AR 40-25, 1985) (Table 5-1). The MRDAs are established jointly by all military services, in concurrence with the Food and Nutrition Board of the National Research Council. The 1985 MRDAs are based on the 1980 Recommended Dietary Allowances (RDAs) (NRC, 1980), with the increased requirement of certain nutrients due to the increased physical activity and, therefore, increased energy requirement of military personnel compared to their more sedentary civilian counterparts. The MRDAs are used for evaluating the nutritional adequacy of military rations, ensuring that military

TABLE 5-1 Military Recommended Dietary Allowances

		Dietary Allowance[*]	
Nutrient	Unit	Temperate Climate	Cold Climate[†]
Energy	kcal	3,200 (2,800–3,600)	4,500
Protein	g	100	100
Vitamin A	IU	5,000	5,000
Vitamin D	mcg	10	10
Vitamin E	mg TE	10	10
Ascorbic Acid	mg	60	60
Thiamin	mg	1.6	1.6
Riboflavin	mg	1.9	1.9
Niacin	mg NE	21	21
Vitamin B_6	mg	2.2	2.2
Folacin	mcg	400	400
Vitamin B_{12}	mcg	3	3
Calcium	mg	800–1,200	800–1,200
Phosphorus	mg	800–1,200	800–1,200
Magnesium	mg	350–400	350–400
Iron	mg	10–18	10–18
Zinc	mg	15	15
Sodium[‡]	mg	5,500	5,500

[*] MRDA for males ≥ 17 years old.

[†] Dietary allowance for cold environment (< 57.2°F [14°C]).

[‡] Maximum amount allowed.

SOURCE: Adapted from AR 40-25 (1985).

personnel maintain their nutritional status, health, and performance in extreme as well as temperate environments. The MRDA are currently being revised to reflect the 1989 RDAs (NRC, 1989).

The increased energy requirement during cold-weather operations is due to the heavy cold-weather clothing and footgear (the hobbling effect), and increased effort needed for locomotion on snow- or ice-covered terrain (Gray et al 1957; Johnson and Kark, 1947; see Jones and Lee, Chapter 11 in this volume). Energy requirement increases in proportion to the amount of time spent working in the cold; thus, it is dependent on mission. The increased energy allowance does not apply to military personnel stationed in cold climates who are not engaged in field operations.

Even though the MRDAs recommend a minimum of 4,500 kcal/d for military personnel working in the cold, energy requirements for cold-weather field operations are variable and difficult to predict. Studies in which energy expenditure of military personnel working in the cold was measured using stable isotopes showed mean energy expenditures of 4,253 kcal/d (King et al., 1992) and 4,919 kcal/d (Hoyt et al., 1991).

MILITARY RATIONS USED IN COLD WEATHER

Military rations may be wet packed, i.e., they do not required additional water during preparation, or dehydrated and are divided into group feeding rations and individually packaged rations. Although any military ration may be provided to the soldier while operating in cold environments, some rations may be more suitable than others. Freezing of rations and water, and difficulties associated with preparing and serving hot foods, are inherent problems of cold-weather field feeding.

Group Feeding Rations

Group feeding rations are used whenever the opportunity to eat together as a unit is possible. The meals are prepared and served hot to military personnel. Among the group feeding rations, the Tray Pack (T Ration) is the ration most commonly used for cold-weather field feeding because it does not require refrigeration or cooking. The other group feeding rations are: (1) A Ration, which consists of both shelf-stable and perishable food items requiring refrigeration and cooking, and (2) B Ration, which consists of canned and dehydrated food items requiring cooking but no refrigeration. Because of the effects of extreme cold temperatures on the equipment required to maintain and prepare the A and B Rations, these rations are not commonly served during cold-weather field operations.

Tray Pack

The Tray Pack (T Ration) is ready to heat and serve. The ration is thermally processed, pre-prepared, shelf-stable food, packaged in hermetically sealed half-size steamtable metal containers. The containers serve as the package, heating pan, and serving tray. The containers can be heated, unopened, in boiling water for 15–50 minutes (depending on the product) or opened and heated in an oven to an internal temperature of 165°F (74°C). A special hand-held or table-mounted can opener is required to open the T Ration food containers.

The ration consists of 10 breakfast and 10 lunch-dinner menus including an entree, starch, vegetable, and dessert (Table 5-2). The T Ration is augmented with a cold-weather supplement module (Arctic T), which provides additional calories to meet cold-weather energy requirements. The supplement module consists of oatmeal, soup, candies, cookie bars, bread, and additional hot beverages. The Arctic T also contains styrofoam clamshell trays and hot cups with lids to maintain food temperature during serving. The Arctic T Ration provides approximately 2,400 kcal per meal (including approximately 1,000 kcal supplied by the cold-weather supplement module) (NRDEC, 1992).

Individually Packaged Rations

Individually packaged rations are used when the mission or tactical scenario prevents group feeding. These rations provide singular meals that can be consumed hot or cold, but they are more palatable when they are hot. Therefore, individual flameless ration heaters are provided to the soldiers so that the rations can be heated. The chemicals in the heater pad (magnesium and iron) are activated by 2 oz (59.2 ml) of water, and it takes only 10 to 12 minutes for the entree to reach an optimal serving temperature of 140°F (60°C).

Meal, Ready-to-Eat

The standard military operational ration is the Meal, Ready-to-Eat (MRE), which is wet packed. It consists of heat-processed, shelf-stable food components that require no preparation. Twelve menus are available, each containing an entree, crackers, a spread (cheese, peanut butter, or jelly), dessert, candy, and beverage powder (Table 5-2). The water requirement is approximately 23 oz to rehydrate all beverages in one MRE; thus, the water requirement for an entire day subsisting on MREs could be 92 oz. One meal provides 1,300 kcal (15 percent protein, 49 percent carbohydrate, and 36 percent fat) and 1.8 g sodium (NRDEC, 1992). Thus, to meet the cold-weather energy requirement,

TABLE 5-2 Menus of Military Rations Used in Cold-Weather Operations

	T Ration[*]				
	Breakfast[†]	Lunch-Dinner[‡]	MRE[§]	RCW[‖]	LRP I[#]
Menu 1	Western omelet; Pot w/bacon; Peaches	Chic breast w/gvy; Sweet pot; Mixed veg; Pound cake	Pork w/rice in BBQ sce; Applesauce; Jelly	Chicken stew	Chicken stew; Cornflake bar; Oatmeal cookie bar; Tootsie Rolls; Apple cider
Menu 2	Omelet w/ sausage and pot; Crm grd beef; Spice cake	Lasagna; Green beans; Frt cocktail	Corned beef hash; Fruit; Oatmeal cookie bar; Jelly	Beef stew	Beef stew; Granola bar; Choc-covered cookie; Caramels; Cocoa
Menu 3	Bread pudding w/ham; Maple syrup; Ham slices; Frt cocktail; Coffee cake	Beef pot rst; White rice; Mixed veg; Choc cake	Chicken stew; Fruit; Peanut but	Chili con carne	Escalloped pot & Pork; Cornflake & rice bar; Fig bar; Choc bars w/toffee; Apple cider
Menu 4	Omelet w/ bacon; Pork sausage; Applesauce; Spice cake	BBQ pork; Mac & cheese; Peas/carrots; Applesauce; Spice cake	Omelet w/ ham; Pot augratin; Oatmeal cookie bar; Cheese spread	Chicken a la king	Chicken w/ wh sce & veg; Cornflake bar; Choc-covered cookie; Chuckles
Menu 5	Omelet w/ bacon & cheese; Corned beef hash; Pears	Beef strips w/peppers; Pot w/butter; Carrots; Marble cake	Spaghetti meat sce; Maple nut cake; Cheese spread	Chicken & rice	Chicken & rice; Granola bar; Choc-covered brownie; Chuckles

	T Ration[*]				
	Breakfast[†]	Lunch-Dinner[‡]	MRE[§]	RCW	LRP I[#]
Menu 6	Western omelet; Pork sausage; Peaches; Bluebry cake	Chicken cacciatore; Pot w/ butter; Green beans; Choc pudding	Chicken a la king; Fruit; Peanut but	Spaghetti w/meat sce	Spaghetti w/meat sce; Cornflake & rice bar; Tootsie Rolls
Menu 7	Omelet w/ sausage & potato; Ham slices; Frt cocktail	Hamburger w/roll; Beans w/ bacon; Frt cocktail; Cheese spread	Beef stew; Cherry nut cake; Peanut but		Chili con carne; Granola bar; Choc-covered brownie Charms
Menu 8	Crm grd beef; Pot w/ bacon; Pineapple	Chili con carne; White rice; Corn; Marble cake	Ham slices; Pot augratin; Brownie; Jelly		Beef & rice; Cornflake bar; Fig bar; M&M's
Menu 9	Western omelet; Ham slices; Peaches	Turkey w/ gvy; Pot w/ butter; Mixed veg; Pound cake/ bluebry topping	Meatballs & rice w/tom sce; Fruit; Cookie; Peanut but		
Menu 10	Egg w/ ham; Pork sausage; Bluebry cake	Beef tips w/ gvy; White rice; Peas/ carrots; Choc pudding	Tuna w/ noodles; Choc nut cake; Cheese spread		
Menu 11			Chix w/rice; Cookie; Cheese spread		
Menu 12			Escalloped pot w/ham; Applesauce; Brownie; Jelly		

NOTE: T Ration, Tray Pack Ration (FY1992); MRE, Meal, Ready-to-Eat (Version XII); RCW, Ration, Cold Weather; LRP I, Long-Range Patrol, Improved. [*] Includes bread, milk, coffee, peanut butter, and jelly. Cold-weather T Ration supplement includes MRE pouch bread, candy, oatmeal cookie bars, soup, extra hot beverages, nondairy creamers, clamshell trays, and hot cups with lids. [†] Includes fruit juice and cocoa. Menus 1, 2, 5, 7, 8, and 10 include assorted oatmeal. [‡] Includes beverage powder. [§] Includes crackers, cocoa beverage power, and hot sauce. Menus 1–6, 10, and 11 include candies. Accessory packet contains coffee, cream, sugar, salt, chewing gum, matches, toilet paper, and towelette. Includes assorted oatmeal, nut-raisin mix, cocoa beverage powder, apple cider mix, chicken noodle soup, fruit bar (fig or blueberry), crackers, granola bars, oatmeal cookie bars, chocolate-covered cookie or brownie, orange beverage powder, Tootsie Rolls, M&M's, and lemon tea. Accessory packet contains coffee, cream, sugar, chewing gum, toilet paper, matches, and closure devices. [#] Accessory packet contains coffee, cream, sugar, chewing gum, toilet paper, matches, and salt.
SOURCE: NRDEC (1992).

the soldier requires four MREs (Table 5-3) or three MREs with an energy supplement. An example of an energy supplement commonly provided to soldiers working in the cold is granola bar, beverage powder, pouch bread (shelf-stable, water-activity controlled bread in a pouch), and trail mix.

Ration, Cold Weather

The Ration, Cold Weather (RCW) is a dehydrated ration that can be reconstituted with hot or cold water or consumed dry. This ration was developed to satisfy a Marine Corps requirement in 1983 for their annual deployment of units to Norway for cold-weather training. Subsistence items and rations available at that time were unsatisfactory for three reasons: (1) they were too bulky or heavy; (2) they contained amounts of sodium and protein that were in excess of requirements and added to the metabolic water burden; or (3) their high water content made them susceptible to freezing.

The RCW consists of six menus and contains freeze-dried, cooked entrees and other low-moisture foods, such as granola bars, oatmeal, nut-raisin mix, chicken noodle soup, fruit bars, and crackers (Table 5-2). Several beverage mixes and soup are included in each menu to encourage water consumption. The water requirement is 90 oz per ration, if all components are consumed hydrated; thus the water requirement for an entire day subsisting on RCW could be 90 oz. The ration is lightweight and will not freeze. There are 2 meal bags per ration which provide food for 24 hours. The protein and sodium contents are adequate but are reduced to conserve metabolic water requirements. One ration (two meals) provides 4,500 kcal (8 percent protein, 60 percent carbohydrate, and 32 percent fat) and 5 g sodium, enough food to meet energy and nutrient requirements in cold-weather operations (Table 5-3).

Long-Range Patrol, Improved

The Long-Range Patrol, Improved (LRP I) is a dehydrated, lightweight, freeze-resistant ration which occasionally is used during cold-weather operations. This ration was designed to sustain personnel during initial assault and special operations (one ration per day). When used in cold weather, this ration can be used as a meal (e.g., one per day in conjunction with two group ration meals) or as one complete day's ration (three LRP I meals per day). The LRP I has eight menus, each consisting of an entree, cereal bar, cookie, candy component, and beverage (Table 5-2). The water requirement is 10 to 12 oz for the entree and 16 oz for the beverages; thus, the water requirement for an entire day subsisting on LRP Is could be 84 oz. One ration provides 1,500 kcal (15 percent protein, 50 percent carbohydrate, and 35 percent fat) and 2.5 g sodium (NRDEC, 1992). Three LRP Is would provide enough food to meet cold-weather energy requirements (Table 5-3).

SELECTING A MILITARY RATION FOR COLD-WEATHER OPERATIONS

The selection of military rations for cold-weather operations is influenced by the tactical situation, mission, and logistical support. These factors determine length of operations, how feasible it is to carry the rations, how often resupply would occur, how much water would be available, etc. Thus, ration weight, size, and amount of water required for reconstitution are important considerations. Table 5-4 illustrates how some military rations may be more suitable than others during cold-weather operations. For instance, a daily supply of MREs weighs approximately twice as much as a daily supply of RCW or LRP Is. This difference becomes critical when, due to length of mission, military personnel are required to carry several days' supplies.

The macronutrient distribution of these rations is similar, except for the percent energy provided by protein. Where most of the rations provide approximately 15 percent of total calories from protein, the RCW provides only 8 percent (NRDEC, 1992). The RCW was designed to be lower in protein than other rations to conserve metabolic water in the cold. Still, the RCW is adequate in protein, providing over 90 percent of its MRDA. Studies conducted by scientists from the U.S. Army Research Institute of Environmental Medicine (USARIEM) have shown similarities among the nutritional intake of soldiers consuming MREs, RCWs, LRP Is, and Arctic Ts during cold-weather field training exercises (Edwards et al., 1991, 1992; King et al., 1992). These studies also showed that even though the soldiers were provided with an adequate supply of rations, they did not consume enough food to meet their energy requirements. Overall ration acceptability was reported at or above "neutral" score for MREs, RCWs, LRP Is, and Arctic Ts, suggesting that the low intake was not caused by poor acceptability (Edwards et al., 1991, 1992; King et al., 1992).

AUTHOR'S CONCLUSIONS

The Army Field Feeding System provides commanders with a variety of alternatives for cold-weather field feeding; thus, the system can be tailored to tactical situation and unit mission (AR 30-21, 1990). Each feeding modality and ration has intrinsic advantages and disadvantages. For instance, whereas group feeding promotes socialization that increases morale and food intake, it may interfere with military operations. Further, group feeding rations require

TABLE 5-3 Approximate Nutritional Content of Rations Used in Cold-Weather Operations

MRDA			T Ration (3 meals)	MRE (4 meals)	RCW (1 ration)	LRP I (3 meals)
Nutrient	Men	Women				
Energy, kcal	4,500	3,500	4,323[*]	5,392	4,567	4,668
Protein, g	100	80	180.9	196.7	93.9	179.2
Carbohydrate, g	—[†]	—[†]	582	669	682	586
Fat, g	—[‡]	—[‡]	141	215	163	179
Vitamin A, IU	5,000	4,000	15,153	16,880	8,022	8,133[§]
Vitamin E, mg TE	10	8	15[§]	22[§]	21	13[§]
Vitamin C, mg	60	60	208	408	329	183
Thiamin, mg	1.6	1.2	3.5	10.8	5.7	3.7
Riboflavin, mg	1.9	1.4	3.5	4.3	2.6	2.8
Niacin, mg NE	21	16	42	52	31	54
Vitamin B_6, mg	2.2	2	2.2	7.6	3.9[§]	2.7
Folacin, µg	400	400	339	292[§]	141[§]	132[§]
Vitamin B_{12}, µg	3	3	5.3[§]	3.5[§]	0.8[§]	1.8[§]
Calcium, mg	800–1,200	800–1,200	1,687	2,052	1,379	1,149

MRDA			T Ration (3 meals)	MRE (4 meals)	RCW (1 ration)	LRP I (3 meals)
Nutrient	Men	Women				
Phosphorus, mg	800–1,200	800–1,200	2,761	3,184	2,168	2,352
Iron, mg	10–18	18	29	24	19	24
Sodium, mg	—[‖]	—[‖]	7,374	7,292	4,720	7,740
Potassium, mg	—	—	5,626	5,424	4,084	4,419
Magnesium, mg	350–400	300	523	556	592	489
Zinc, mg	15	15	20.2	13.4[§]	10.8[§]	8.9[§]
Cholesterol, mg	—[†]	—[†]	484[§]	476[§]	183[§]	174[§]

NOTE: MRDA, Military Recommended Dietary Allowances for moderately active military personnel ages 17 to 50 years old operating in cold weather; T Ration, Tray Pack Ration without cold-weather supplement (FY1992); MRE, Meal, Ready-to-Eat (version XII); RCW, Ration, Cold Weather; LRP I, Long-Range Patrol, Improved.

[*] Cold-weather supplement adds approximately 1,000 kcal.

[†] No MRDA established.

[‡] Should not exceed 35 percent of total energy intake.

[§] Data missing (more than 50 percent) or inaccurate.

[‖] No MRDA established. The safe and adequate levels published in the RDA are considered to be unattainable within military foodservice systems. An average of 5,500 mg for men and 4,100 mg for women is the target.

[#] No MRDA established. The safe range is 1,875-5,625 mg.

SOURCE: Adapted from AR 40-25 (1985). Record of nutritive values for each ration.

kitchen equipment and utensils. While wet packed rations are more convenient to use than dehydrated ones, they are heavier, bulkier, and prone to freezing. On the other hand, the dehydrated rations require additional hot water to make them more palatable and increase their consumption.

TABLE 5-4 Characteristics of Individually Packaged Rations Used in Cold-Weather Operations

	MRE	RCW	LRP I
Type	Wet Pack	Dehydrated	Dehydrated
Number required per day to meet cold-weather requirements (each)	4	1*	3
Weight per daily supply (kg)	2.7	1.3	1.4
Water required to reconstitute entree and/or beverages (ml)	2,760	2,700	2,430
Energy provided in 1-day supply (kcal)	5,200	4,500	4,500
Sodium provided in 1-day supply (g)	7.3	5	7.5

NOTE: MRE, Meal, Ready-to-Eat; RCW, Ration, Cold Weather; LRP I, Long-Range Patrol, Improved.

* One RCW consists of 2 bags.

SOURCE: Adapted from King et al. (1994).

While the provision of adequate nutrition and hydration to military personnel remains a major problem during cold-weather operations, the commander must consider ration characteristics together with the environmental conditions, unit tactical situation, mission, and logistical support. The final decision should be made carefully to optimize mission accomplishment and military performance. The consequences of poor nutritional intake and dehydration are increased medical problems and decreased unit effectiveness. Command leadership and enforcement of ration consumption and water discipline are crucial to prevent these consequences. Most often, a combination of rations, such as Arctic T breakfast, LRP I lunch, and Arctic T dinner, provides maximum flexibility for the commander and increases ration consumption.

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6

Feeding the U.S. Army Sixth Infantry Division (Light) in the Cold

Thomas J. Lange[1]

INTRODUCTION

For generations cold weather and extreme cold weather have altered the outcome of the best laid military plans. Conflicts between nations that took years to resolve involved sustaining armies during the winter months. Commanders of the past moved forward utilizing instinct, persistence, and the undying drive to succeed. Often, the logistics of resupply and keeping the Army fed and warm were the greatest threat, not the enemy.

Decades of extensive research and development have greatly improved commanders' ability to accomplish their missions. Due to the fall of the Soviet Union as a threat and the current philosophy of downsizing U.S. forces, today's commanders are required to accomplish their missions with less

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equipment and personnel. Military personnel today are highly trained, and equipment is state of the art.

The instruments of death have been developed and utilized with great success. Instruments to sustain the life support systems of U.S. soldiers on the modern battlefield must keep pace with these changes. Following World War II great strides were made through the development of a doctrine to improve the "Quality of Life" of U.S. soldiers. Since that time, there has been a continued emphasis on improving food, apparel, and other supplies and logistics for the soldier.

Harsh winter environments require detailed planning, coordination, and troops that are physically hardened and trained. Flexibility, maneuverability, and the use of equipment are all reduced in the cold, while logistic, engineering, subsistence, and medical problems increase dramatically. Winter creates physiological stress on the individual, and the additional weight of winter clothing, sleeping bags, and rations combine to reduce individual and unit mobility. "Survive, move, fight!" is the moxie of winter warfare.

THE U.S. ARMY FAMILY OF RATIONS

Foodservice equipment to support and service a family of rations has been developed under the auspices of the U.S. Army. Examples of this equipment include the Mobile Kitchen Trailer (MKT) and Kitchen Company Level Field Feeding equipment (KCLFF). Rations supported through these kitchen units include menus of A Rations; B Rations; Meal, Ready-to- Eat (MRE); Ration, Cold Weather (RCW); and Food Packet, Long-Range Patrol II (LRP[II]).

Feeding the right meal, at the right place, and at the right time is the ultimate goal of the Army feeding program. The U.S. Army has had a field feeding standard of providing all soldiers with one MRE and two hot meals per day (U.S. Department of the Army, 1991a). The hot meal has been primarily the T Ration. This standard has also allowed for two A Ration meals in a 7-d period. The standard was regarded by field commanders as a prescription that dictated the contents and timing of meals, rather than as a policy or guideline for overall nutrition. They felt that the standard failed to offer them the flexibility they needed to modify feeding schedules within their own commands in response to the demands of particular situations.

At that same time, the U.S. Army Quartermaster Center and School was aggressively pursuing a revised feeding standard that would provide the commander with the flexibility needed to ensure that all soldiers on the battlefield were provided the right meal, at the right place, and at the right time (U.S. Department of the Army, 1991a). A revised feeding policy was written, which simply states that field commanders have the responsibility for providing their soldiers with three quality meals per day. This revised feeding policy (U.S. Department of the Army, 1990) was approved for implementation in November 1990 and was successfully executed.

To support the revised feeding policy of three quality meals per day, the commander has available to him a family of rations that is built on individual and group rations. The primary individual ration is the MRE, and the group rations include unitized T Rations, unitized B Rations, and A Rations.

The RCW is a unique individual ration that is used in arctic environments and that includes six menus containing three entrees, several snacks, and numerous hot drinks (U.S. Department of the Army, 1989). Little preparation of the ration is required by the soldier. The RCW is lighter and smaller than three MREs and contains approximately 4,500 kcal per daily ration menu with a nutrient content designed to conserve body water. The packaging cannot be damaged by temperatures below freezing, and it is flat, flexible, and waterproof. Although the RCW was designed to be totally self-contained, there have been training exercises in which additional food items have been included (primarily prepared soup and coffee). MREs have also been used as a daily ration in arctic environments; they must be supplemented with additional ration items to be nutritionally adequate.

Soldiers with the Alaska Army National Guard ("scouts")[2] who operate out of the most remote villages have experienced problems feeding their troops. Past generations of Alaskan scouts were hardened veterans of extreme cold weather, and they ate off the land. Their diet consisted of seal and polar bear. As these older scouts retired and were replaced by younger scouts, it was found that the replacements could not sustain themselves as had their predecessors, who had more of the skills needed to live off of the land. To update the scouts' diet to Army standards that would be supported with the state-of-the-art "family of rations," the Alaska Army National Guard's suggested immediate solution was to use the RCW. Two problems occurred with its use, however, which made replacement of the RCW necessary. First, the RCW was still a dramatic diet change for the younger troops. Most scouts had been exposed to MREs and preferred the MRE to the RCW. Second, the RCW required more water for consumption because all components are dehydrated or vacuum packed. Today, scouts in Alaska consume MREs with supplements, and additional bottled water is air dropped at predetermined locations.

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[2] The soldiers of the Alaska Army National Guard are called scouts because their mission is primarily accomplished on foot, and they serve as forward observers who support themselves without major logistical support.

EQUIPMENT PROBLEMS: THE MOBILE KITCHEN TRAILER

Under U.S. Army doctrine (FM 10-23, 1991), the Mobile Kitchen Trailer (MKT) is used in all areas and under all climatic environments for military operations in the field. The MKT provides a standard, efficient, vehicular-mounted operating unit that eliminates the need to improvise kitchen facilities. The MKT can withstand frequent movement over unimproved surfaces, and it can be moved with relative ease over great distances in daylight, darkness, and under blackout conditions. The kitchen is engineered to provide three hot meals per day for a company-sized unit and requires no major overhaul or replacement of major components for 180 days.

The MKT is issued as basic equipment to battalions, companies, batteries, and detachments as authorized in the Table of Organization and Equipment (TO&E) for mess, personnel, and equipment (CTA 50-909, Field and Garrison Furnishings and Equipment). MKTs can be pooled when the tactical or logistical situation dictates the desirability of centralized food preparation. One kitchen is issued per company or equivalent unit. The kitchen requires a 5-soldier team to set it up in 1 hour.

The MKT and its component equipment can be used to produce all families of rations and additional supplements. However, during extreme cold weather the MKT, as originally designed for tropical environments, is not suitable; the temperature is inadequate for the proper functioning of the equipment as well as for the personnel. A product improvement test involving two different models of the MKT was conducted in 1988 at the U.S. Army Cold Regions Test Center (CRTC), Fort Greely, Alaska (Sargent, 1988). The two models tested were the NRDEC-MKT-85 and the MKT-85 with winterization kit from the Sixth Infantry Division (Light) (sixth ID [L] improved MKT). The test was designed to determine if adequate protection could be provided in a cold environment without an external, heated shelter and to develop modifications that would allow the MKT to be transported without damage by rotary wing aircraft.

During 33 actual and simulated feeding missions conducted in ambient temperatures ranging from -38° to 11°F (-39° to -12°C), both MKTs were instrumented using 10 thermocouplers to monitor temperatures. The thermocouplers were positioned at head, hand, and foot levels centered at the front and rear of the center work area and at the hand level on the interior side walls. Four M-2 burner units were operated in each MKT with one-half of the roof vents open 6 to 12 inches (15.2 to 30.5 cm) for an average of 4.5 hours during each instrumented mission. Instrumented missions that were conducted at temperatures of -9° to -7°F (-23° to -22°C); -17° to -15°F (-27° to -26°C); and -38° to -36°F (-39° to -38°C) were grouped, and mean stabilized temperatures were calculated. Average interior warm-up time for the NRDEC-MKT trailer temperature was 25 minutes compared to 45 minutes for the sixth

ID (L) improved MKT. Temperatures at the head and hand level were slightly warmer in the NRDEC-MKT.

Little difference in foot-level temperature was noted between the two MKTs. Because of extremely low foot temperatures monitored throughout the testing in the MKTs, operating personnel were required to wear vapor barrier boots. Additionally, adequate cleaning of the MKT could not be performed during testing due to low foot-level temperatures. This caused food and grease buildup on the floor insulators and resulted in unsanitary and slippery conditions. The cold floor temperatures and slippery conditions are considered significant problems.

During the test period, an attempt was made to determine an effective means to increase the temperature of the floor area in both MKTs. A 400,000-BTU space heater (Herman-Nelson) was vented under the MKTs with positive results. However, the 400,000-BTU space heater is not a recommended solution for heating the MKT floor. The heater starts poorly and is unreliable in the cold. In addition, it has a high fuel consumption rate and frequently requires maintenance from operator and crew.

A heating trial was also performed using two M-2 burner units placed under the floor of the MKTs. This method was effective in elevating the floor temperature but constituted a safety hazard to operating personnel in the MKT. In addition, minor damage was caused to the wiring harness of the MKT because of excessive heat, even though M-2 burners were set at low levels. This method also removed one-third of the kitchen's cooking capabilities because after using two of the six M-2 burner units provided in the MKT to heat the floor, only four units were available for heating and cooking food.

After one actual heating mission in each MKT, it was determined that excessive amounts of air entered both MKTs, and as a result, all cover assembly panels were extended 6 inches. After performance of two additional actual feeding missions in each MKT, it was noted that the doors on the end cover assemblies could not be closed properly due to fabric contraction in the cold.

During testing of both MKTs in temperatures below -5°F (-21°C), the fabric of the roof canopy assemblies and the cover assemblies became extremely stiff. Failure of the fabric to stretch during installation of the upright poles during setup resulted in frequent damage to the roof canopy sections and made assembly of the cover tedious.[3] Both MKTs had to have cover

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[3] The MKT canopy assemblies, made of heavy canvas and plastic, became unduly stiff when exposed to extreme cold. When a unit reached the training area, the stored, folded canvas was so stiff that it could not be stretched and laid flat for proper assembly. While the fabric did not tear, it did not stretch for complete assembly, which is designed so that zippers are connected to complete a sealed kitchen. Problems were also noted with placing the poles upright. Poles fit into slots in the floor, then connect with horizontal hand rails, and finally attach to the roof canopy.

Since the canvas would not stretch correctly, there were open air spaces throughout the trailer's canopy assemblies.

assemblies heated in a building before installation. These problems are significant as mobility of the MKT was greatly reduced.

After testing both MKTs, it was determined that neither met the standards required for use in an extreme cold-weather environment. The Sixth Infantry Division (Light) therefore implemented other policies and procedures to ensure that soldiers are adequately fed in a field environment under extreme cold. This test encouraged the present Army doctrine that MKTs and A Rations are not to be used within the Sixth Infantry Division (Light) during the period 15 October through 15 April (U.S. Department of the Army, 1993a, b).

AN EQUIPMENT SOLUTION: THE KITCHEN COMPANY LEVEL FIELD FEEDING EQUIPMENT

The Kitchen Company Level Field Feeding equipment (KCLFF) with tentage and a Yukon stove is the current U.S. Army solution to heating rations in cold environments. The tentage is a modified M-577 TOC (Tactical Operations Center) extension. The KCLFF and M-577 TOC extensions have been issued and used with great success. As the M-577 TOC extensions are phased out, the Tent, Expendable, Modular, Personnel (TEMPER) and extendable, modular frame-supported shelter consisting of a collapsible aluminum frame covered with polyester fabric is the best solution to the Sixth Infantry Division (Light) tentage problem. Both are easily set up and taken down, which meets the requirement for quick mobility. The tentage fabric shrinks slightly in cold weather, but it does not create open areas to allow the entry or escape of cold winds or heat, as was the problem with the trailer. All equipment can be transported in a Small Unit Support Vehicle (SUSV) over a variety of terrain.

THE U.S. ARMY FIELD FEEDING SYSTEM

Commanders and unit leaders must understand the U.S. Army Field Feeding System (AFFS) (FM 10-23, 1991) to ensure that the system benefits their soldiers in training and on the battlefield. Command involvement in training and planning for field training and contingency operations must be detailed and comprehensive. They must know ration availability, equipment requirement, logistics support, enhancement requisitioning, and accountability. They must understand the capabilities and limitations of their personnel, both cooks and subsistence handlers.

To standardize requests for ration support, the following procedure is used:

1. Ninety days prior to an exercise, the requesting unit is responsible for submitting Class I forecasts[4] to the Division Support Command element (DISCOM). The forecast will then be forwarded through the Division Class I Officer (DCI) to the supporting Troop Issue Subsistence Activity (TISA). The request will contain the unit's exercise dates, personnel strength, and desired ration schedule.
2. Sixty days prior to the start of the exercise, the unit will update the forecast.
3. Forty-five days prior to the exercise start date, the supporting TISA and DCI will publish a ration issue schedule, which includes issue dates for T Ration menus.
4. Thirty days prior to an exercise, the DCI section will publish a preprinted issue schedule and menu.
5. Twenty days prior to the exercise, the requiring units will submit ration requests for the first 10 days of the exercise.
6. Fourteen days prior to the exercise, the DISCOM Division Support Area (DSA) element will submit all ordering documents for the first 10 days to the supporting TISA.

The Sixth Infantry Division (Light) uses the KCLFF with M-577 TOC extension for foodservice operations in the field and to provide remote feeding capabilities to forward areas. Tray rations currently are the preferred hot operational ration for Cold-Weather Feeding Doctrine (U.S. Department of the Army, 1993a). The Arctic T Ration (18-Man Module) and the MRE will be used in the ration cycle T-MRE-T.

The Sixth Infantry Division (Light) established Standard Operation Procedures (U.S. Department of the Army, 1993b) that allowed units close to home station (not more than 30-min travel) to have the option of providing A Rations from a dining facility for their soldiers. The lunch meal will be MREs with warming beverages. RCWs will be utilized only for long-range patrols, mountain-glacier training, and in areas where resupply is extremely difficult.

SUMMARY

During the past 4 to 5 years, the Sixth Infantry Division (Light) tested, modified, and invented equipment to withstand arctic conditions in order to

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[4] The Army has nine classifications of supply, and Class I is food or subsistence. Class I forecasts determine the food and water requirements for a unit in a field environment for a specific period of time.

provide the best and safest means of Class I ration support (U.S. Department of the Army, 1990). The KCLFF meets the requirement of providing two hot Arctic T Rations daily in temperatures as low as -70°F (-57°C).

Soldiers in extreme cold environments are being offered the KCLFF, M-577 TOC extension, the Arctic T Ration, MREs, and the RCW. They are therefore provided with the right meal, at the right place, and at the right time.

AUTHOR'S RECOMMENDATIONS

The following recommendations are made regarding field feeding of U.S. soldiers in the cold:

- Sources of heat to prepare and serve hot meals under arctic conditions must improve. The dependency on liquid or gas fuels creates safety hazards, and a dry heat source must be developed. The use of electricity, microwave, or solar power should be considered.
- When heating water, condensation causes tremendous problems with tentage and camouflage netting. A system to vent steam out and away from kitchen preparation areas should be developed.
- Research and testing to improve the Arctic T Ration, MRE, and RCW should continue in order to increase troop acceptability.

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II

Discussion

ALLISON YATES: Is pouch bread consumed at high altitudes or in cold weather?

RUSSELL SCHUMACHER: We never use it, but that does not mean we would not if we had it. The reason is supply rather than lack of demand. Crackers and some kind of bread are what the troops want at high altitudes.

ROBERT REYNOLDS: A quick question. You have given us the nutrition profile of the T Ration; Meal, Ready-to-Eat [MRE]; Ration, Cold Weather; and Long-Range Patrol Rations. This would be the intake if they consumed everything in the ration. What percentage or what fraction of these rations is actually consumed by the troops?

RUSSELL SCHUMACHER: The Marine Corps is the only Service Branch that uses the Ration, Cold Weather to any extent. With all operational rations, the first thing soldiers do is take the package and discard everything they do not want; then they make smaller packages. Overall, I would say 75 to 80 percent is consumed.

But you only have two packages in the Ration, Cold Weather and that is it for the whole day. So with the Ration, Cold Weather, more may be consumed, but still no more than about 80 percent.

ALLISON YATES: In our other workshop earlier this year, we had a demonstration of the KCLFF [Kitchen Company Level Field Feeding equipment] and the kitchen company. I understood that it would prepare more than just T Rations; one could prepare A and B Rations as well. Do you have access to the KCLFF?

THOMAS LANGE: They are trying to modify the KCLFF now so it has the ability to prepare some limited A Rations. We do not utilize it to prepare A or B Rations; it is strictly for T Rations. Soup and coffee would probably be the closest we get to an A Ration.

ANDRÉ VALLERAND: I have a question for LTC King. I am interested in the MRE heater. Could you give us more information about how much heat it produces or maybe the temperature that it can achieve, how long it will work, and its cost?

NANCY KING: It takes between 10 and 12 minutes to heat up an MRE entree, to 140°F (60°C). Currently they are issuing two heaters per ration because troops often want to thaw the ration first, if necessary, and use the second heater to warm the food. I do not know the cost.

Since we have some extra heaters and COL Schumacher has some rations, we can actually try one and you can see how it works.

RUSSELL SCHUMACHER: From practical experience, the heater should be in every ration.

NANCY KING: The MRE-13 and subsequent versions will have a ration heater included in each of meal pack.

III

THE COLD ENVIRONMENT

CHANGES IN PHYSIOLOGY AND NUTRIENT requirements due to the cold environment are considered in Part III. The mechanisms to maintain core body temperature and to reduce and restore heat loss during cold exposure are collectively termed thermoregulation. Chapter 7 discusses physiological thermoregulation, or the way in which dry heat loss is reduced through vasomotor responses and replaced through metabolic responses, in relation to physical performance. While involuntary shivering contributes to body-temperature regulation, voluntary physical activity can do more to increase heat production. Individual characteristics, such as body composition and physical fitness, also contribute to the regulation of the rise and fall of body temperature.

Biological clocks control various physiological processes and often conflict with military schedules. Chapter 8 explains the behavioral and physiological responses that the body utilizes to manage these changes and focuses on the physiological process of sleep and how it is disrupted by military operations. To enhance physical and cognitive performance in extreme environments, it may be possible to develop biological and pharmacological agents that may alter circadian rhythms and other biological clocks.

As Chapter 9 explains, environmental extremes can cause disruption in fluid balance, and dehydration is a possibility in cold environments as well as hot environments. The most significant factors associated with dehydration during cold exposure include cold-induced diuresis, respiratory water losses, the metabolic cost of movement, and reduced fluid intake, with the most the metabolic cost of movement, and reduced fluid intake, with the most significant being the increased fluid loss associated with high metabolic work rates. Dehydration negatively influences physical and cognitive performance and thermoregulation, and increases possible susceptibility to injury.

Chapter 10 briefly summarizes some recent research on how skeletal muscle fuels shivering. Understanding shivering can be useful in a survival situation to enhance thermogenesis and delay the onset of life-threatening hypothermia.

Chapters 11 and 12 focus on energy requirements in the cold. To determine the optimal macronutrient ratio, several factors must be considered, including the caloric density of fat as compared to carbohydrate or protein, the enhancement of thermogenesis associated with the thermic effect of food, and the preference for a particular nutrient in the diet. As an example of environmental influence on appetite, cold exposure increases energy expenditure which may stimulate appetite to allow an enhanced intake of energy. The thermic effects of food, of cold, and of exercise are important considerations in understanding appetite and weight maintenance in the cold.

Using the Military Recommended Dietary Allowances (MRDAs) as a frame of reference, the influence of cold exposure on the need for vitamins and minerals is reviewed in Chapter 13. There is little scientific justification for supplementation above the MRDAs to cope with cold stress and exposure. In Chapter 14, the possible effects of iron, copper, and zinc deficiencies on thermoregulation are discussed. Major emphasis is placed on iron's role in maintaining core body temperature, although the MRDA for iron appears to be sufficient to prevent deficiency. For the most part, any short-term deficiency that may occur during a military operation is not likely to lead to micronutrient deprivation unless there is a preexisting reserve depletion.

Finally, this section on the cold environment concludes with a discussion in Chapter 15 of the possibility of a drug-mediated delay of hypothermia during cold exposure. The author is unable to verify the claims of a commercial sports bar and its ability to delay hypothermia, but does find that ephedrine-xanthine mixtures represent a safe agent to enhance cold tolerance in humans.

7

Physiology of Cold Exposure

Andrew J. Young[1] *Michael N. Sawka and Kent B. Pandolf*

INTRODUCTION

Understanding and ameliorating the effects of cold is an important military concern. Throughout history, there are many examples of the terrible effects experienced by soldiers during military operations conducted during cold weather. Over 90,000 U.S. Army and Army Air Force casualties during World War II were attributable to cold injury. German Army cold-injury casualties were at least as high. Another 10,000 casualties resulting from cold injury occurred during the Korean War. Currently, cold injury prevention is an area of major command emphasis for Army units operating in cold climates.

Humans tend to rely on behavioral thermoregulation to protect themselves against the cold. That is, they wear clothing, remain in shelters, and use various heat-generating devices. However, when behavioral strategies are inadequate to defend body temperature homeostasis, physiological responses are elicited. Besides protecting against cold effects and playing a role in the

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etiology of cold injuries, these physiological responses may alter the metabolism of persons living and working in cold climates. This chapter reviews the human physiological responses elicited by cold exposure and then considers some factors accounting for differences in response among individuals. The purpose is to provide a basis for considering how physiological responses influence performance and nutritional requirements of soldiers exposed to cold.

HUMAN HEAT BALANCE IN THE COLD

Biophysical Factors

Body temperature reflects the summated effects of internal heart production and heat transfers between the body and ambient environment. The heat balance equation describes the relationship:

$$S = M - (\pm W_k) \pm E \pm R \pm C \pm K \quad [W/\mathrm{m}^2],$$

where M represents metabolic heat production, and W_k represents energy leaving (positive for concentric work) or entering (negative for eccentric work) the body as external work.[2] Heat exchange between the body and environment occurs via evaporation (E), radiation (R), convection (C), and conduction (K), with W/m^2 being watts per square meter. The sum of these processes is heat storage (S), which represents heat gain by the body if positive or heat loss from the body if negative. The biophysics of human thermal balance is considered in detail elsewhere (Santee and Gonzalez, 1988).

In humans exposed to environments colder than body temperature, heat flows from the body core toward the environment, primarily via dry (i.e., conductive and convective) heat-loss mechanisms. Wind increases convective heat loss from the body surface (Santee and Gonzalez, 1988), thus providing the basis for the concept of wind chill (Siple and Passel, 1945). Because water has a much higher thermal capacity than air, convective heat transfer is greater (perhaps 70-fold) during immersion in water than in air of the same temperature (Gonzalez, 1988). Clothing provides insulation between the body and the environment, thus limiting convective and conductive heat loss, but wet clothing provides considerably less insulation than dry. Thus, environmental characteristics besides temperature influence the potential for heat loss and the resulting physiological strain of defending body temperature.

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[2] During concentric work, the muscle shortens as it develops tension; during eccentric work, the muscle lengthens as it develops tension.

Physiological Responses

Humans have two general types of responses to cold. Vasomotor responses reduce dry heat loss to the environment. Metabolic responses act to replace heat lost to the environment.

Vasomotor Responses

Peripheral vasoconstriction is one important physiological response exhibited by humans exposed to cold. Blood flow decreases as water temperature becomes colder, as shown in Figure 7-1, which depicts blood flow in the hand decreasing in response to immersion in water of decreasing temperature. During whole-body cold exposure, the vasoconstrictor response is not limited to the hands, but is widespread throughout the peripheral shell. The decrease in peripheral blood flow reduces convective heat transfer between the body's core and shell (skin, subcutaneous fat, and skeletal muscle) and increases insulation. Heat is lost from the body surface faster than it is replaced. As a result, whole-body cold exposure causes skin temperature over the entire body surface to decline (Figure 7-2). Insulation begins to increase when skin temperature falls below about 95°F (35°C), and becomes maximal

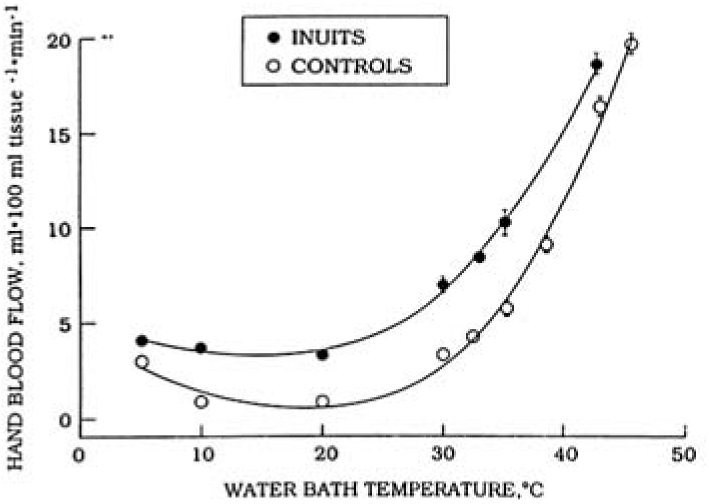

FIGURE 7-1 Steady-state blood flow (mean ± SE) to the hand of male Inuit and caucasian control subjects during immersion of the hand in water of various temperatures.
SOURCE: Adapted from data of Brown and Page (1952).

when skin temperature is about 89°F (31°C) or less (Veicsteinas et al., 1982). Thus, during cold exposure, central core temperature defense occurs at the expense of a decline in skin temperature.

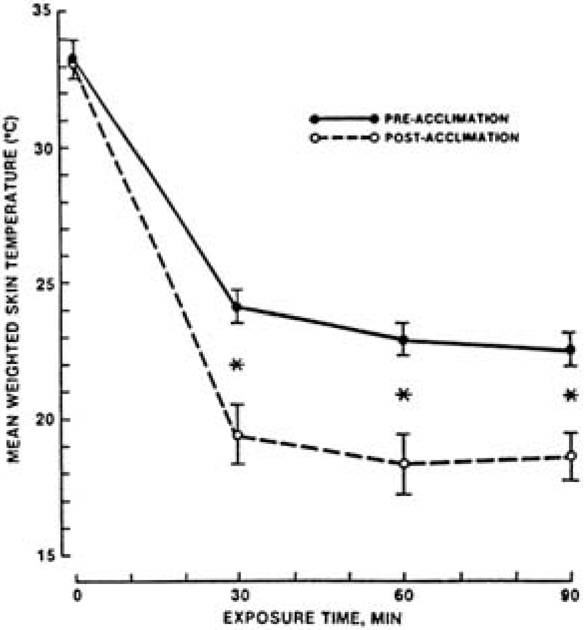

FIGURE 7-2 Mean weighted skin temperature before and during a 90-min resting cold-air exposure. Values are means ± SE of measurements in seven young caucasian men. *, Significant (P 8 0.01) difference between pre- and postacclimation. SOURCE: Young et al. (1986), used with permission.

The reduction in blood flow and consequent fall in skin temperature contribute to the etiology of cold injuries (Purdue and Hunt, 1986). The hands and fingers are particularly susceptible to cold injury (Boswick et al., 1979) and to a loss of manual dexterity due to cold-induced vasoconstriction (Gaydos, 1958). In these areas of the body, another vasomotor response to cold, cold-induced vasodilation, modulates the effects of vasoconstriction. Figure 7-3 illustrates this response, first described by Lewis (1930), who termed the response the *hunting reaction*. Periodic oscillations (rise and fall) of skin temperature follow the initial decline in skin temperature during prolonged cold exposure. These skin temperature oscillations are the result of transient increases in blood flow to the cooled finger. Originally thought to be a local effect of cooling (Burton and Edholm, 1955), recent evidence suggests the hunting reaction may involve a centrally-mediated mechanism (Lindblad et al., 1990). A similar cold-induced vasodilation occurs in the forearm (Clarke et al., 1957; Ducharme et al., 1991). This effect may reflect the operation of a different physiological mechanism, since the forearm response appears to be the result of vasodilation in muscle vasculature rather than in skin (Ducharme et al., 1991).

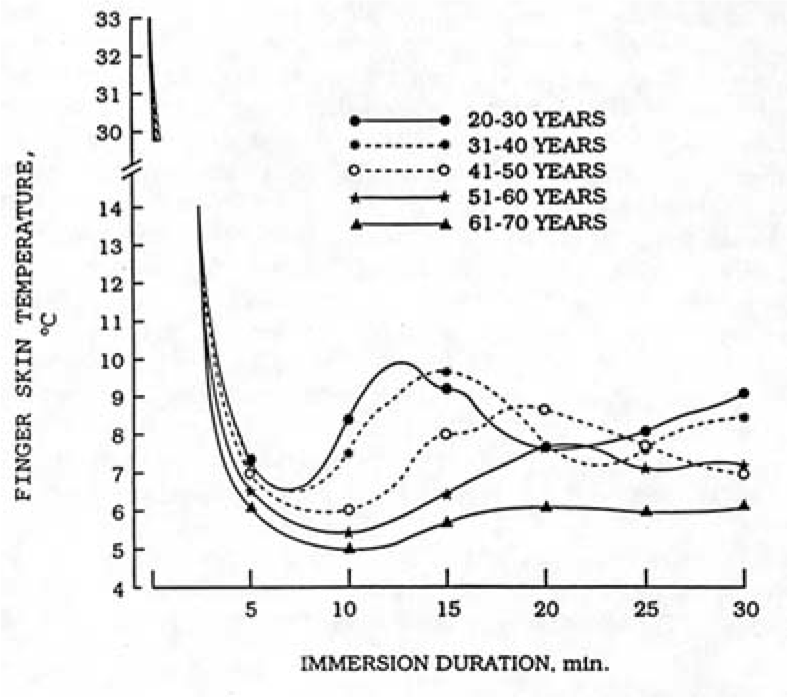

FIGURE 7-3 Finger skin temperature measurements from young and older men immersing their hands in 39°F (4°C) water. SOURCE: Adapted from Mathew et al. (1986).

Metabolic Responses

In addition to those mechanisms that limit heat loss, humans employ other means to defend body temperature. Metabolic heat production can increase in order to replace heat lost during cold exposure. Muscle is generally considered the source of the increased metabolic heat production. Besides generating external force, muscle contractions also result in the liberation of considerable heat (approximately 70 percent of total energy expended). Thus, voluntary physical activity during work or exercise increases metabolic heat production (exercise in the cold will be considered later in the chapter). In the absence of an increase in voluntary muscle activity, shivering begins. Certain animals respond to cold exposure with an increase in metabolic heat production by noncontracting tissue, a process referred to as nonshivering thermogenesis (LeBlanc et al., 1967). However, there is no clear evidence that humans share this mechanism (Toner and McArdle, 1988).

Shivering is an involuntary pattern of repetitive, rhythmic muscle contractions. Horvath (1981) referred to shivering as a "quasiexercising" state, since the muscles contract but do no external work. Shivering may begin immediately or within several minutes after the onset of cold exposure, usually in torso muscles, followed by a spread to the limbs (Horvath, 1981). The electromyographic measurement in individual shivering muscles can be analyzed to quantify shivering activity (Muza et al., 1986). More commonly, however, shivering thermogenesis is quantified by measuring the increase in whole-body oxygen uptake ($\dot{V}_{o2}$). By assuming that the respiratory exchange ratio represents a nonprotein respiratory quotient, calculation of the thermal equivalent (i.e., metabolic heat production) of the $\dot{V}_{o2}$ is possible (McArdle et al., 1991).

The increased $\dot{V}_{o2}$ associated with the onset of shivering in the cold requires an increased systemic oxygen transport. Cardiac output increases with cold exposure. Figure 7-4 depicts this increase in terms of heart rate, stroke

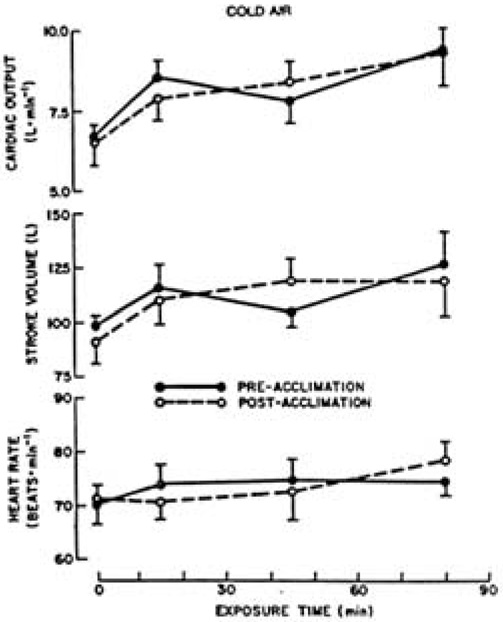

FIGURE 7-4 Resting heart rate, stroke volume, and cardiac output (mean ± SE) of seven young caucasian men before and during 90-min exposure to cold air (41°F [5°C]). SOURCE: Muza et al. (1988), used with permission.

volume, and cardiac output for men resting in thermoneutral and cold air. The cardiac output increases primarily because of an increase in stroke volume, with little change in resting heart rate during cold exposure (Muza et al., 1988).

As shivering intensity increases and more muscles become involved, the $\dot{V}_{O_2}$ increases. For example, $\dot{V}_{O_2}$ of young men resting in 41°F (5°C) air with a 1 m/s wind averaged 600 to 700 ml/min, which corresponded to about 15 percent of their $\dot{V}_{O_2}$ max (Young et al., 1986). Immersion in cold water can elicit even more intense shivering, as reflected by higher $\dot{V}_{O_2}$. Inactive men immersed in 64°F (18°C) water exhibited $\dot{V}_{O_2}$ of about 1 liter/min, which corresponded to 25 to 30 percent of their $\dot{V}_{O_2}$ max (Young et al., 1989). Investigators have attempted to define maximal shivering capacity in terms of $\dot{V}_{O_2}$. Iampietro et al. (1960) observed $\dot{V}_{O_2}$ to be about 1,500 ml/min in inactive men exposed nude to -1°F (-18°C) with a 4.5 m/s wind. The highest reported $\dot{V}_{O_2}$ during shivering in cold water is 2.2 liter/min in 54°F (12°C) water (Golden et al., 1979) corresponding to 46 percent $\dot{V}_{O_2}$ max. Thus, shivering intensity varies with the severity of cold stress.

Energy Substrate Utilization

Shivering, like all muscular activity, depends on an adequate supply of substrate for the metabolic processes producing energy for the contractions. Metabolic rate can increase two- to fivefold (Horvath, 1981; Toner and McArdle, 1988; Young, 1990), depending on intensity of shivering, as discussed above. This increase has nutritional implications for persons who live and work in cold conditions. Persons adequately clothed or sheltered from the environment do not shiver much, and thus nutritional requirements are not significantly affected. Those who are not adequately protected from the cold by clothing and shelter will shiver, and their nutritional energy requirements will be greater than in warmer climates. While it is obvious that the increment in nutritional energy requirement will be proportional to the duration and severity of cold exposure, accurate predictions of individual requirements are difficult.

Attempts have been made to determine whether the increased metabolic rate of shivering muscle causes preferential use of a particular substrate. Vallerand and Jacobs (1989) used indirect calorimetry to quantify the relative contribution of carbohydrate and fat metabolism to the total energy requirements of inactive men shivering for 2 hours in cold air. In that study, shivering metabolism increased to about 2.5 times the resting metabolic rate measured in thermoneutral conditions (Vallerand and Jacobs, 1989). The increased metabolism caused almost a sevenfold increase (588 percent) in carbohydrate oxidation while fat oxidation rose less than twofold (63 percent) compared to resting in thermoneutral conditions (Vallerand and Jacobs, 1989). Further, carbohydrate and fat oxidation provided 18 percent and 59 percent respectively of the total energy expenditure in the neutral condition compared to 51 percent and 39 percent in the cold condition (Vallerand and Jacobs, 1989). These findings indicate that both fat and carbohydrate metabolism sustain shivering, but that carbohydrate is the dominant energy source.

Either blood glucose, muscle glycogen stores, or both may provide the source of carbohydrate for shivering thermogenesis. The importance of maintaining adequate blood glucose concentrations to sustain shivering activity is clear. Young men exposed to cold air stopped shivering, and their metabolic rate and core temperature declined when blood glucose concentration dropped below 2.5 mmol/liter (Gale et al., 1981). However, intravenous glucose infusion restored shivering in both an arterially occluded and an unoccluded leg (Gale et al., 1981). This finding suggests that glucose exerts a centrally-mediated effect on shivering; however, a role for blood glucose as a substrate for shivering muscle is not precluded, particularly since cold exposure enhances insulin-stimulated glucose uptake in peripheral tissues (Vallerand et al., 1988).

The importance of muscle glycogen for shivering thermogenesis remains controversial. Young et al. (1989) attempted to determine whether shivering depletes muscle glycogen stores and whether muscle glycogen depletion limits shivering or compromises thermoregulation in the cold. Changes in muscle glycogen concentration and core temperature were measured in eight young men during 1 to 3 hours of immersion in 64°F (18°C) water preceded either by 3 days of heavy exercise and a low-carbohydrate diet or by 3 days of rest and a high-carbohydrate diet. The exercise and low carbohydrate diet resulted in very low preimmersion muscle glycogen levels, while rest and a high-carbohydrate diet produced very high glycogen levels; blood glucose concentrations were not significantly different between trials. Despite different preimmersion muscle glycogen levels, there were no significant differences in metabolic rate or in the fall in core temperature during immersion (Young et al., 1989). As shown in Figure 7-5, no significant change in muscle glycogen levels occurred during either trial immersion (Young et al., 1989). This result suggests that shivering does not deplete muscle glycogen, perhaps because of availability of blood glucose. Furthermore, muscle glycogen depletion does not compromise metabolic heat production or core temperature defense during cold exposure.

Using a similar experimental design, also using eight young male subjects, but with shorter immersions, Martineau and Jacobs (1989) arrived at a different conclusion. Figure 7-5 compares their data with the findings of Young et al. (1989). Martineau and Jacobs (1989) reported that muscle glycogen levels decreased during a high-glycogen immersion trial but not during a low-glycogen trial. Initial metabolic rate was significantly lower in the low muscle glycogen trial, although eventually it achieved the level of the high-glycogen trial. Furthermore, body temperature declined slightly faster during the low-glycogen trial (34.5°F/h [1.5°C/h]) than during the high-glycogen trial (34.25°F [1.25°C/h]) (Martineau and Jacobs, 1989). Martineau and Jacobs (1989) concluded that muscle glycogen served as a substrate during shivering and that muscle glycogen depletion impaired thermoregulation in the cold.

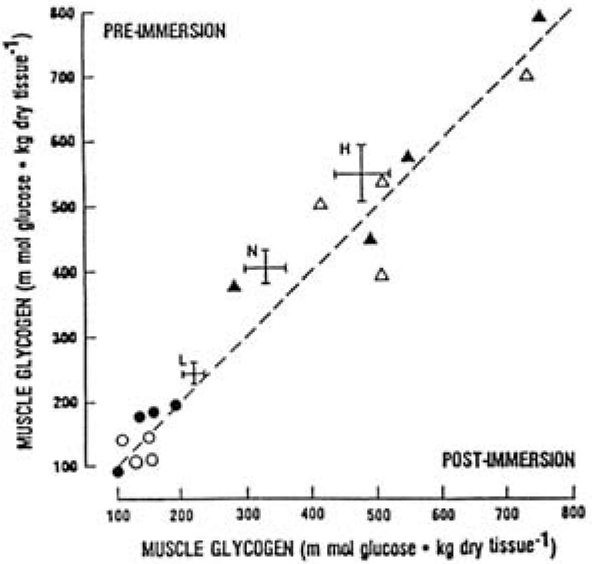

FIGURE 7-5 Effect of 1- to 3-h immersion in 65°F (18°C) water on muscle glycogen concentration. Dashed line represents line of identity (no change). Individual data from trials in which initial glycogen levels were high (triangles) or low (circles) are from Young et al. (1989). Mean ± SE of subjects studied at high (H), normal (N), and low (L) glycogen levels by Martineau and Jacobs (1989) are also depicted for comparison. Both studies employed eight young male subjects.

The discrepancies between the findings of the two studies are not readily explained. The subjects studied by Martineau and Jacobs (1989) were extremely lean compared to those studied by Young et al. (1989). However, the leaner subjects did not shiver more intensely than the fatter subjects. In both studies, metabolic rates were similar, corresponding to about 25 to 30 percent $\dot{V}_{O2}$ max. Steady-state exercise at such a low intensity would not deplete muscle glycogen. Furthermore, the fatter subjects in the study of Young et al. (1989) were immersed and shivered longer (2 to 3 hours versus 1 hour), yet they did not exhibit muscle glycogen depletion. Lastly, the changes in muscle glycogen that Martineau and Jacobs (1989) observed during immersion (see Figure 7-5), and the effect of low muscle glycogen on body cooling were small. Thus, muscle glycogen is probably not an obligatory substrate for shivering, at least at sea level. When alternate substrates, such as blood glucose, are available, muscle glycogen can be spared or resynthesized at a rate equal to its use.

At high altitudes, muscle glycogen may be an important substrate for sustaining shivering in the cold. Ascent to high altitude decreases $\dot{V}_{o2}$ max. A $\dot{V}_{o2}$ corresponding to 25 to 30 percent of $\dot{V}_{o2}$ max at sea level would require 60 to 70 percent $\dot{V}_{o2}$ max at 5,000 m. Exercise at that intensity would significantly deplete muscle glycogen, and muscle glycogenolysis during exercise is faster at high altitude than at sea level (Young, 1990). Whether altitude affects muscle glycogenolysis the same during shivering as during exercise remains to be determined experimentally.

Effects of Exercise on Thermoregulation in the Cold

Voluntary physical activity can increase metabolic heat production more than shivering. Whereas maximal shivering can elevate $\dot{V}_{o2}$ to about 2 liter/min, exercise can increase $\dot{V}_{o2}$ to 5 liter/min or even higher. However, the effect of exercise on thermal balance depends on a complex interaction among factors related to exercise intensity, environmental conditions, and mode of activity. While exercise increases metabolic heat production, it also facilitates heat loss from the body by increasing blood flow to the skin and active muscles. This flow enhances convective heat transfer from the central core to peripheral shell. Thus, while metabolic heat production increases progressively as exercise intensity increases, so too does heat loss due to increasing blood flow to muscle and skin. Also, limb movement increases convective heat loss from the body surface by disrupting the stationary boundary layer of air or water that develops at the skin surface in a still environment.

The arms have a greater surface area-to-mass ratio and a thinner subcutaneous fat layer than the legs (Toner and McArdle, 1988). Thus the increased blood flow to the muscles and skin of the arms resulting from upper body exercise has a greater effect on convective heat transfer than does that which results from lower body exercise. In fact, Toner et al. (1984) observed that heat loss is more pronounced and core temperature falls more during arm exercise than during leg exercise at the same absolute metabolic rate. These effects are magnified by the greater convective heat transfer coefficient of water as compared to air. In cold air, metabolic heat production during exercise can be high enough to compensate for increased heat loss and allow core temperature to be maintained even when ambient temperature is extremely cold (Toner and McArdle, 1988). In contrast, increased heat loss during exercise in cold water can be so great that metabolic heat production, even during intense exercise, is insufficient to defend core temperature (Toner and McArdle, 1988).

During submaximal exercise in the cold, $\dot{V}_{o2}$ can be higher than, or the same as in temperate conditions, depending on the exercise intensity (Young, 1990). Figure 7-6 schematically depicts the effect of cold exposure on $\dot{V}_{o2}$ during exercise over a range of submaximal intensities. At low intensities, $\dot{V}_{o2}$

is higher in cold than in temperate conditions, since metabolic heat production during low-intensity exercise is insufficient to maintain core and skin temperatures high enough to prevent the afferent stimulus for shivering. Thus, the increased $\dot{V}_{o2}$ represents the added oxygen requirement for shivering activity. As metabolic heat production rises with increasing exercise intensity, the afferent stimulus for shivering declines, and at some point, exercise metabolism is high enough to prevent shivering completely. At this intensity and higher, $\dot{V}_{o2}$ during exercise is the same in cold and temperate conditions. The exercise intensity at which metabolic heat production is sufficient to prevent shivering will depend on the severity of cold stress. Furthermore, that intensity will not necessarily be the same for all persons exposed to the same cold stress, because of individual characteristics that will be discussed later.

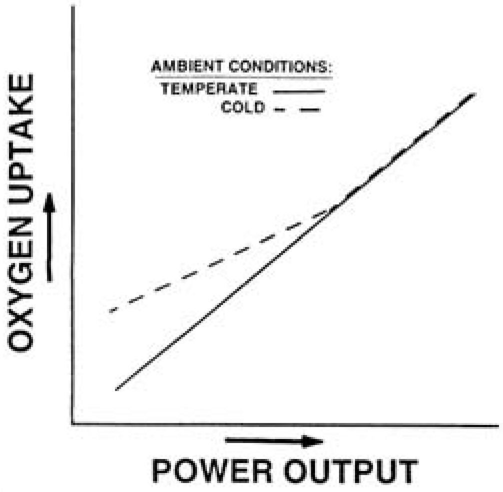

FIGURE 7-6 Effect of cold on $\dot{V}_{o2}$ during steady-state exercise at different intensities.

Cold exposure can reduce maximal oxygen uptake, but may not always do so (Young, 1990). Exposure conditions must be severe enough to reduce core or muscle temperature markedly (> 0.5°C [> 0.9°F]) before Vo_{2max} is reduced (Bergh and Ekblom, 1979; Fortney and Senay, 1979; Horvath, 1981; McArdle et al., 1976). Exposure to (cold) conditions that lower core temperature 0.5°C (0.9°F) or less does not significantly reduce Vo_{2max} (Schmidt and Bruck, 1981). Potential mechanisms explaining how cold exposure could reduce Vo_{2max} include that a low body temperature may impair myocardial contractility (Bergh and Ekblom, 1979) and limit maximal heart rate (Bergh and Ekblom, 1979; Fortney and Senay, 1979; Horvath, 1981; McArdle et al., 1976) sufficiently to limit maximal cardiac output.

Cardiovascular Responses to Exercise in the Cold

Cold exposure can also affect cardiovascular responses to submaximal exercise. Obviously, cardiac output must increase to satisfy the requirement for increased systemic oxygen transport when cold exposure stimulates shivering during low-intensity exercise in the cold. For a given $\dot{V}_{o2}$, cardiac output is the same during exercise in cold and temperate conditions (McArdle et al., 1976). However, cold exposure can alter the way that cardiac output is achieved. Heart rate is usually lower and stroke volume higher during exercise in cold air or cold water compared to exercise at the same $\dot{V}_{o2}$ in temperate conditions (Doubt, 1991; McArdle et al., 1976). This phenomenon probably reflects the effect of increased cardiac preload due to the increased central blood volume that is associated with cold-induced peripheral vasoconstriction.

Influence of Cold on Muscle Energy Metabolism

Cold exposure may affect muscle energy metabolism during exercise. Some, but not all, investigators have observed an increase in blood lactate concentration during exercise in cold over that observed in temperate conditions (Young, 1990). When core temperature and $\dot{V}_{o2}$ are similar during exercise in cold and temperate conditions, blood lactate is unaffected by cold. Studies in which cold exposure increased blood lactate concentrations during exercise also recorded lower core temperatures and higher $\dot{V}_{o2}$ during exercise in cold than in temperate conditions (Young, 1990). Furthermore, animal experiments employing radioactively labeled lactate infusions to measure lactate turnover rates during exercise show that cold exposure can increase both the appearance and removal of blood lactate compared to neutral conditions with no net increase in concentration (Minaire et al., 1971).

The effects of cold exposure on lactate metabolism during exercise raise the possibility that cold exposure may accelerate muscle glycolysis during exercise. During steady-state exercise at higher intensities, muscle glycogen utilization is the same in cold and temperate conditions (Jacobs et al., 1985; Young et al., 1995). However, during low-intensity steady-state exercise, glycogen use in the active muscle is more pronounced in cold than in temperate conditions (Jacobs et al., 1985). The increased glycogen use during low-intensity exercise has been attributed to the added metabolic cost of shivering, but in fact $\dot{V}_{o2}$ was the same during exercise in cold and temperate conditions, which suggests that shivering may not explain the increased use of glycogen (Jacobs et al., 1985). Blomstrand and Essen-Gustavson (1987) and Blomstrand et al. (1986) demonstrated that dramatically lowering muscle temperature (to about 82°F [28°C]) accelerates muscle glycolysis during short, very intense exercise. No clear experimental explanation for that observation is available, but decreased muscle temperature may reduce mechanical or biochemical efficiency of the muscle (Young, 1990). Whatever the mechanism, it seems that reduced muscle and core temperatures, rather than cold exposure, are responsible for alterations in muscle energy metabolism during exercise.

INDIVIDUAL CHARACTERISTICS MODIFYING HUMAN HEAT BALANCE IN THE COLD

Anthropometry

Differences in body size, configuration, and composition can explain much of the variability between individuals in their capability to defend body temperature during cold exposure (Toner and McArdle, 1988). These body characteristics modify the stress of a given environmental condition. Therefore, different persons exposed to the same environment do not experience the same stress or exhibit responses of the same magnitude. Effects attributed to acclimatization, aging, gender, and physical fitness on thermoregulatory response to cold are in large part due to differences in anthropometric factors that co-vary with those other factors (LeBlanc et al., 1978; Young, 1991; Young et al., 1995).

Body shape and mass contribute significantly to an individual's tendency to lose heat in cold environments. Because the principal heat loss vector in humans exposed to cold is convective heat transfer at the skin surface, a large surface area favors greater heat loss than a smaller surface area. In contrast, a large body mass favors maintenance of a constant temperature by virtue of a greater heat content when compared to a small body mass. Gonzalez (1988) explains the biophysical basis for the interaction between the two factors in detail elsewhere. Here, it suffices to point out that it is the ratio of surface area to body mass that influences heat loss. All other factors being equal (which is rarely the case), persons with a large surface area-to-mass ratio experience greater declines in body temperature during cold exposure than those with smaller surface area-to-mass ratios (Burton and Edholm, 1955; Toner and McArdle, 1988). This concept also applies when considering regional heat loss patterns. Thus, as discussed earlier, Toner et al. (1984) observed that heat loss and the decline in body temperature in cold water were greater during arm than during leg exercise at the same metabolic rate because of the greater surface area-to-mass ratio of the arms.

Body fat is one of the most important characteristics modifying the stress of cold exposure. All body tissues provide thermal resistance to heat conduction from within the body, but thermal resistivity of fat is greater than that of either skin or muscle (Toner and McArdle, 1988). Subcutaneous fat provides significant insulation against heat loss in the cold. Figure 7-7 depicts whole-body heat loss measured in young male Inuits (Native Americans residing in the Arctic) and caucasians residing in temperate regions of North

America. Heat loss was measured under conditions in which peripheral blood flow was minimal (immersion in water cool enough to induce maximal vasoconstriction without eliciting shivering). These conditions minimize heat convection so that heat flow reflects thermal conductance reasonably accurately. As shown, thermal conductance—or its inverse relationship, insulation—is closely correlated with subcutaneous fat thickness. Thus, thermal conductance decreases and insulation increases as the layer of subcutaneous fat thickens. As a result, as many studies have confirmed, fat persons shiver less and experience smaller declines in body temperature during cold exposure than do lean persons (Toner and McArdle, 1988). Nutritional strategies during cold weather should aim to prevent body fat loss in soldiers, especially during long-duration operations.

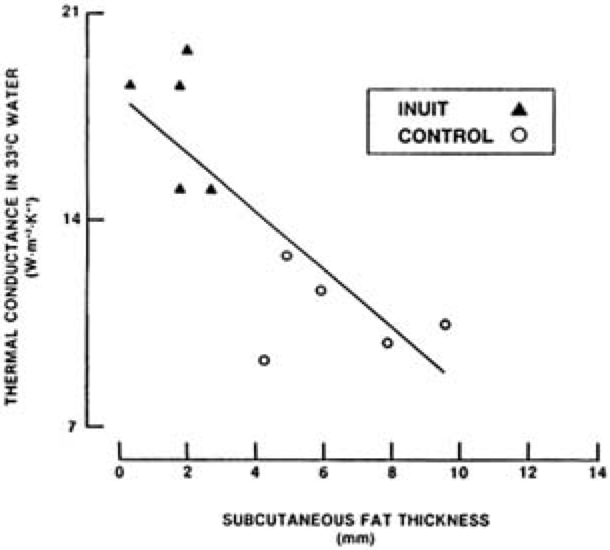

FIGURE 7-7 Relationship between subcutaneous body fat and thermal conductance measured under conditions that elicited maximal peripheral vasoconstriction without causing shivering or increased metabolism. Under these conditions, convective heat flux is minimized, and body heat loss is primarily occurring via conduction. SOURCE: Adapted from Rennie et al. (1962b).

Physical Fitness

There is no consensus concerning the influence of physical fitness, particularly aerobic capacity, on thermoregulatory response to cold. Some investigations have employed a cross-sectional experimental design to evaluate aerobic fitness effects on responses to cold. Bittel et al. (1988) reported that fit persons maintained warmer skin temperatures than did less fit persons during rest in cold air. However, the effect appeared to be due to thinner subcutaneous fat thickness and higher metabolic heat production in fit compared to less fit subjects, rather than to a fitness effect, per se, on vasoconstriction (Bittel et al., 1988). Budd et al. (1991) found no relationship between $\dot{V}_{o2}$ ^{max} and skin temperature during rest in cold air but conceded that their subjects' $\dot{V}_{o2}$ ^{max} encompassed a range too narrow to evaluate fitness effects effectively.

Endurance training effects are not addressed well by cross-sectional studies since factors in addition to training contribute to a high $\dot{V}_{o2}$ ^{max}. Longitudinal studies indicate that endurance training strengthens cutaneous vasoconstrictor response to cold. Young et al. (1995) reported that after 8 weeks of endurance training, which increased $\dot{V}_{o2}$ ^{max} by 13 percent, subjects exhibited a faster decline in skin temperature during exercise in cold water than before training. Similarly, Kollias and Buskirk (1972), reported that after 9 weeks of aerobic training, there was a faster decline in skin temperature during resting exposure to cold air than before training. Therefore, endurance training provides a thermoregulatory advantage for persons exposed to cold.

Age and Gender

Aging is widely though to compromise body temperature defense during cold exposure. A recent review of the relevant scientific literature (Young, 1991), however, suggests that this belief may not be entirely justified. The incidence of hypothermia on admission to hospitals appears greater for older (60 years or more) than for younger persons (LeBlanc et al., 1978). However, the overall incidence of hypothermia admission is low compared to other ailments resulting in hospital admission, and coexisting conditions such as injury, illness, and alcohol or drug intoxication may confound these data (Coleshaw et al., 1986; Keatinge, 1986). Epidemiological surveys of body temperature of older persons taken while in their own homes do not indicate a large incidence of hypothermia (Collins et al., 1977; Fox et al., 1973). Nevertheless, controlled laboratory comparisons show that older men may be less able than younger men to defend core temperature during cold exposures. The cutaneous vasoconstrictor response to cold may be slower and cold-induced vasodilation may be blunted (see Figure 7-3) in older as compared to younger men (Mathew et al., 1986). Shivering thermogenesis may also be less in older than younger men (Young, 1991). The latter effect is probably the result of a loss of muscle mass, rather than an effect of aging on thermoregulation (Mathew et al., 1986). These aging effects begin to be apparent after about 45 years of age in men (Young, 1991). Data from one study, however, indicated that older women defend core temperature during cold exposure as well as, or better than, younger women (Wagner and Horvath, 1985). Here again, body composition changes with aging (the older women were much fatter than the younger women) probably accounted for the difference attributed to aging. It is possible that preventable changes in body composition and physical fitness rather than aging may account for impaired (as well as improved) thermoregulatory responses to cold.

Gender-related differences in body size, body shape and composition, and hormonal effects associated with the menstrual cycle affect heat balance and thermoregulatory response to cold (Stephenson and Kolka, 1993). These differences contribute to a disparity in cold tolerance between men and women, which is particularly apparent in cold water. Most women have greater fat content and subcutaneous fat thickness than men of comparable age. A thicker subcutaneous fat layer accounts for the greater maximal tissue insulation and lower critical water temperature (coldest water tolerated without shivering) observed in women as compared with men (Rennie et al., 1962a). Despite this difference, however, greater fat content may not provide women with a thermoregulatory advantage over men.

When women and men of equivalent subcutaneous fat thickness are compared, the women have a greater surface area and smaller total body mass. Although insulation is equivalent, women's total heat loss is greater due to the larger surface area for convective heat flux. Because of their smaller body mass, body heat content is less in the women. Therefore body temperature falls more rapidly for any given thermal gradient and metabolic rate. The mathematical basis for this concept is explained elsewhere (Gonzalez, 1988). The findings of McArdle et al. (1984a, b) provide experimental demonstration of the concept. They reported that women's core temperatures fall more rapidly during cold-water immersion with resting than those of men with equal subcutaneous fat thickness (McArdle et al., 1984a). When men and women of equivalent subcutaneous fat thickness exercised in cold water at the same metabolic rate per unit surface area, both experienced similar core temperature changes (McArdle et al., 1984b).

Comparison of men and women with equivalent total body masses shows that women still seem to be at a disadvantage in the cold. In this case, women's greater fat content enhances insulation, and surface area differences between the genders are not as pronounced. Nevertheless, a smaller lean body mass, the source of metabolic heat production, limits women's capacity for heat production, compared to men of comparable total body mass. This disparity may be inconsequential under conditions where metabolism is low and does not differ much between men and women (i.e., when resting in mildly cool conditions such as those used to assess maximal tissue insulation) (Rennie et al., 1962a). However, under colder conditions that stimulate shivering—especially maximal shivering—the limited thermogenic capacity of women will result in a more rapid decline in their core temperature than in men of equivalent total body mass.

Acclimatization

Persons chronically exposed to cold experience adjustments in thermoregulation (Young, 1988). Habituation is, by far, the most commonly observed adjustment to chronic cold exposure. Blunting of both shivering and cold-induced vasoconstriction are the hallmarks of habituation (Young, 1988). These adjustments enable skin to be kept warmer during cold exposure, but they can contribute to a greater heat loss and more pronounced fall in core temperature.

Besides habituation, cold acclimatization and cold acclimation can heighten responses to cold or induce responses not apparent in the unacclimatized state. These adjustments follow two patterns. First, metabolic acclimatization-acclimation is characterized by a more pronounced thermogenic response to cold (Young, 1988). An exaggerated shivering response may develop because of chronic cold exposure, and the possibility that humans develop a nonshivering thermogenesis cannot be completely ruled out. In contrast, enhanced heat conservation mechanisms characterize the insulative acclimatization-acclimation pattern (Young, 1988). More rapid cutaneous vasoconstriction develops in some chronically cold-exposed persons, an adjustment that may reflect an enhanced sympathetic nervous response (Young, 1988).

Compared to chronic heat stress, physiological adjustments to chronic cold exposure appear less practical in terms of relieving thermal strain, defending body temperature, and preventing thermal illness and injury. Nonetheless, changes in shivering response to cold resulting from habituation or metabolic acclimatization may have some nutritional implications.

AUTHORS' CONCLUSIONS AND RECOMMENDATIONS

Humans exhibit two major physiological responses to cold exposure. Peripheral vasoconstriction limits heat loss. Shivering, physical activity, or both increase heat production. Thus, heat balance in the cold and the requirement for shivering are dependent on the severity of environmental stress and the effectiveness of the vasoconstriction for conserving heat, as well as the intensity and mode of activity or exercise. There are nutritional implications of the physiological responses, particularly the thermogenic response. Increasing metabolic heat production requires increased energy intake. Carbohydrate metabolism may contribute more to total energy metabolism in cold than in temperate environments. Gender, aging, and acclimatization all affect thermoregulatory responses to cold, but these effects probably have little nutritional significance. Body composition is probably the most important physiological determinant of thermoregulatory tolerance in cold environments. Behavioral responses, such as taking shelter from the cold and wearing adequate protective clothing, can greatly reduce the physiological strain of cold exposure and obviate the need for nutritional interventions.

Some general recommendations can be made:

- Research should resolve discrepant findings concerning effects of muscle glycogen depletion on thermogenesis and heat balance in the cold, with emphasis on effects of body fat differences.
- The effects of hypoxia on cold-induced thermogenesis and substrate utilization should be studied.
- Novel techniques for stimulating thermogenesis should be developed, particularly for emergency or rescue situations in cold weather.
- The possibility that physiological responses to an acute cold challenge might be used reliably to predict susceptibility to cold injury should be studied.
- The possibility that age- and gender-related differences in heat balance and thermoregulatory responses to cold can be minimized by physical training and nutritional strategies should be investigated.

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8

Military Schedules vs. Biological Clocks

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INTRODUCTION

During military operations, there is an inherent conflict between the internal body clock and operational schedules. Military operations require military personnel to dramatically change their daily schedules to accommodate prolonged activity at night and enforced inactivity during the day. Due to logistical challenges, food may not be delivered on a scheduled basis. Dehydration may be a constant concern. Military history is replete with reports of military personnel who were both sleep deprived, and malnourished and in very hostile thermal environments as they engaged hostile forces for prolonged periods of time.

Coexisting with this military schedule are the inborn biological "clocks" that coordinate various physiological processes such as sleeping, eating, endocrine release, and motor activity. Long-term desynchronization of various physiological processes could result in disruption in the overall physiological

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or mental performance of military personnel during military operations (Folkard et al., 1988).

Sleep is the physiological process that is most easily disrupted by military operations (Naitoh and Kelly, 1992). Transporting persons at night over various time zones is a classic way to affect the quality of sleep. The behavioral changes associated with sleep deprivation have been known since historical times. However the accompanying changes in core and skin temperature are still being elucidated. The focus of this paper will be to discuss the role that sleep has on thermal balance in a cold environment.

BIOLOGICAL CLOCKS: FROM MINUTES TO YEARS

Biological clocks have two major components: duration and activity. The manifestation of the clock is best demonstrated as a sine wave, which has amplitude, frequency characteristics, and duration. A biological clock for one physiological process may be synchronized with another clock resulting in two sine waves that may have the frequency, amplitude, or duration correlated with each other. Thus, a biological clock that controls body temperature will cause a variation in core temperature over a period of time. The oscillatory variation in core temperature of ± 1.5°C (2.7°F) results in a sine wave amplitude over that period of time. Biological clocks can range from minutes to years. The *ultradian clocks* are those that control physiological events that have a duration of a few minutes to several hours (Dean and Aschoff, 1981). An example of the expression of an ultradian clock is the release pattern of luteinizing hormone (Soper and Weick, 1980). *Infradian cycles* may range from 14 to 15 days and from 28 to 30 days and have been termed semilunar and lunar respectively (Neumann, 1989). In addition, there are rhythms that are regulated on an annual basis and have been called *circannual*. The best example of a circannual clock is the reproductive cycle of animals and associated activities such as milk production (Hastings, 1991).

The biological clocks that have received the most attention are the *circadian* oscillators which regulate and coordinate physiological processes on an approximately 24-h basis (Refinetti and Menaker, 1992). The expressions of these biological clocks in such behaviors as feeding, body temperature, and motor activity are independent of environmental cues and can be considered as independent oscillators (Inouye and Kawamura, 1979). However, under normal conditions the activity of the circadian oscillator is entrained or synchronized by various environmental cues. Of these external cues, the light/darkness cycle is the primary synchronizer for the circadian oscillators. This relationship between the light/darkness cycle and the 24-h circadian clock is very powerful since alteration in the light/darkness cycle influences multiple physiological processes that vary during a 24-h cycle. It was initially reported that the light/dark cycle was a poor synchronizer in humans; however, more recent studies suggest that light is able to alter the sleep/wakefulness cycle if the intensity of the light is strong enough (Czeisler and Allen, 1980; Czeisler et al., 1986). In addition to the light/darkness cycle being a potent external signal, motor activity is another external cue that influences the circadian cycle. Recent studies in animals suggest that an increase in locomotive activity can shift the phase of the circadian cycle (Reebs and Mrolsovsky, 1989). The converse seems to hold as well in that induced inactivity can also induce phase shifts in the circadian cycle (Van Reeth et al., 1991).

While the light/darkness cycle and motor activity are just a few of many external cues that can alter circadian cycle, social factors may also play a role in synchronizing the clocks. Man is the only animal that habitually does not respond to his biological clocks. For example, during a military night operation, soldiers must be awake and may possibly engage in vigorous physical activity when normally they would be asleep.

DIFFERENT CIRCADIAN CLOCKS: SLEEP/WAKEFULNESS AND BODY TEMPERATURE

Both the sleep/wakefulness and body temperature systems have certain common features: (1) there are certain select areas (biological clock) of the central nervous system that control their expression, (2) sensory signals influence their activity, and (3) motor or effector signals are an expression of the biological clock. Each clock is controlled by a different area of the central nervous system; however, they interact with each other and influence other physiological systems.

Sleep/Wakefulness

The complex activity of sleep/wakefulness varies so that on average there is approximately 8 hours of sleep and 16 hours of activity per day. However, this ratio varies depending on age, activity, and other factors. As is commonly observed, the sleep phase is associated with a decrease in activity which results in a decrease in metabolism and core temperature. This state of inactivity is further characterized by specific changes which can be measured by electroencephalogram (EEG), electromyogram (EMG), and electrooculogram (EOG), as well as endocrine changes. Based on these criteria, sleep can be divided into two distinct phases, nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. During NREM sleep, there is an alteration in thermoregulation, which causes a decrease in core temperature (Glotzbach and Heller, 1993). During REM sleep, thermoregulation is further attenuated (Glotzbach and Heller, 1984). The neuroanatomical site for the sleep/wakefulness clock is the suprachiasmatic nuclei (SCN) of the hypothalamus (Meijer and Rietveld, 1989). When the SCN is lesioned, sleep and wakefulness are distributed equally throughout the day (Ibuka and Kawamura, 1975), but normal oscillations of core temperature persist (Fuller et al., 1981). These data, reported from a number of different experiments, have led to the present model that states that the circadian clocks controlling sleep/wakefulness are separate from those that control body temperature.

The responses of the circadian clocks are dampened with aging. Numerous reports have demonstrated an alteration in both thermal and motor activity in aging animals (Martin et al., 1985).

The effect of sleep deprivation is of great concern to the military. Numerous studies have shown that sleep deprivation leads to impaired psychomotor performance, although physiological response to the cold is maintained (Fiorica et al., 1968). Sleep-deprived subjects experience periods of visual hallucinations, reduced vigilance, impaired balance, and impaired coordination (Opstad et al., 1978).

Thermal Regulation in the Cold

Normally, core body temperature varies no more than 1°C (0.9°F) per day (Guyton and Hall, 1996). Core temperature is controlled by nuclei in the preoptic anterior hypothalamus (POAH) (Boulant and Hardy, 1974; Wit and Wang, 1968). The POAH acts as a thermostat and maintains the core temperature at 37°C (98.6°F). Thermal sensory signals from both the periphery and the core are transmitted to the POAH. If there is a difference in temperatures between the periphery and the core, there will be an increase in motor tone, vasoconstriction, release of catecholamines, thyroid hormones, and other factors, resulting in a maintenance of core temperature. Hypothermia is clinically defined as a core body temperature of 35°C (95°F) or lower and is classified as either accidental (primary) or secondary. Primary hypothermia refers to a decrease in core temperature that is induced by an overwhelming environmental stress. Secondary hypothermia refers to a decrease in core temperature that is due to the fact that there is an underlying pathology which does not allow the thermally stressed individual to respond physiologically to the cold environment. The effects of a decrease in core temperature have been reported elsewhere but it should be noted that hypothermia has major effects on a person's cognition and higher mental functions, resulting in amnesia, apathy, dysarthria, impaired judgment, and maladaptive behavior (Danzl and Pozos, 1994). In contrast to the chronic exposure to cold that causes these changes, even acute exposure to cold environments will cause hallucinations without any other signs of hypothermia (Lloyd, 1983).

Sleep and Core Temperature

The interaction of sleep and the ambient environment can be considered from two points of view: (1) what are the changes in core temperature that occur during the REM and NREM sleep, and (2) what is the effect of ambient temperature on the subject during REM and NREM sleep. It has been commonly reported that changes in body temperature and metabolic rate at sleep onset in humans suggest a "decrease" in the regulation of core temperature. Decreases in brain temperature accompany the transition from wakefulness to NREM sleep (Glotzbach and Heller, 1993). The significance of this phenomenon is still debated. Among the more interesting hypotheses is that NREM sleep may be associated with a cooling of the brain. Experimental data do not support this contention since small animals in cold climates sleep as much as large animals in warm climates do.

During REM sleep, thermoregulation is inhibited in experimental animals. Parmeggiani and Rabini (1967) reported that cats who slept at low ambient temperatures ceased shivering at the onset of REM sleep. REM sleep is thought to be associated with brain warming, however since there is a decrease in thermoregulation during this period of time, this theory is also not well supported. Whatever the effect the various cycles of sleep have on thermoregulation, there is agreement that these various stages of sleep may play some role in possibly conserving energy as the animal sleeps.

It is commonly observed that when individuals have a prolonged period of sleeplessness they complain of being cold. The explanation for this phenomenon may be that the sleep wake cycle has a 33-h period whereas core temperature has a 24-h period and the two may become desynchronized. The physiological mechanisms for maintaining normal core temperatures can be divided into two major categories: *heat dissipating* such as peripheral vasodilation and *heat productive* such as increase in metabolism. In humans in whom the sleep/wake cycle and core temperature have been desynchronized (loss of coupling), control of the peripheral vasculature is coupled with the sleep/wake cycle and is independent of the core body temperature (Czeisler et al., 1980). As a result, the sleep deprived individual may experience peripheral vascular constriction during the day, giving the sensation of peripheral coolness.

External Temperatures and Sleep

It is commonly observed that individuals can adapt to sleeping in various thermal environments. Initially, a person who is not accustomed to sleeping in the cold will experience a decrease in the amount of total sleeping time. However, once the individual has become acclimated to the cold there will be no decrease in the time spent in REM sleep (Palca et al., 1986). Although high intensity exercise has been reported to increase delta sleep, a component of NREM sleep, and to have no effect on REM sleep (Horne and Moore, 1985), additional studies suggest that such a definitive effect of exercise on various components of sleep may not exist (Horne and Staff, 1983). Due to the complexity of the interaction between sleep and the thermoregulatory response to environmental temperatures, there is no model that is able to coalesce the data from various experiments.

Sleep and Nutrition

The interaction between sleep and nutrition should be addressed since sleep may play a role in altering the rate of metabolism. In experimental animals, it has been shown that the amount and type of food ingested and the duration of subsequent sleep are highly correlated (Danguir et al., 1979). A number of studies suggest that ingestion of carbohydrates, which triggers the release of insulin, is associated with an increase in the duration of NREM, whereas ingestion of protein triggers the release of somatostatin to cause an increase in REM sleep (Danguir, 1996). The importance of these studies is that they suggest that sleep is not merely a process that is regulated by various levels of light and darkness or exercise, but that nutrition may also play a role in modifying the sleep cycle. Complicating this picture is the fact that diet-induced thermogenesis is dependent on the time at which the food is ingested. In a study in which human subjects were fed the same diet during different phases of the sleep/wakefulness cycle, the authors reported different thermogenic responses (Romon et al., 1993).

THE REAL WORLD: MILITARY OPERATIONS AND TRAINING

The above studies demonstrate that there is a complex relationship between sleep/wakefulness and thermoregulation. These data should not be construed to suggest that persons who are sleeping in cold environments might inadvertently slip into hypothermia. Individuals who are physically fit and who are not suffering from some disease or taking medication are able to react to the environmental stressors that occur during a cold night. In the event that the subject is: (1) physically exhausted; (2) energy depleted (malnourished); (3) sleep deprived; and (4) in constant exposure to a cold environment, it is very probable that he/she will suffer a drop in core temperature leading to secondary hypothermia and death (Pugh, 1966). It should be emphasized that, before this point is reached, the higher mental dysfunctions that are associated with sleep deprivation and/or cold stress will be evident. The actual cause of death of a hypothermic person is usually lack of sleep, insufficient food, and improper clothing which leads to a drop in core temperature. This triggers lapses in judgment that lead to further drops in core temperature and ultimately to death (Pugh, 1966). A classical historical example of the interplay between sleep deprivation, exhaustion, and constant exposure to the cold is the Finnish Campaign against the Russians in World War II. The Finnish Army did not let the Russians sleep, interrupted their supply of food and water, and patiently waited while the cold sapped the physical and mental stamina of the Russians. When the Finns attacked, the Russians were unable to mount an effective counterattack (Jarvinen, 1944). This same tactic was basically applied by the Russians when they repulsed the German invasion in World War II (Jarvinen, 1944).

A key factor in any instance of hypothermia is not only sleep deprivation but also body weight loss. Without the metabolic substrates that are required to maintain normal core temperature, the elaborate circadian cycles will not be able to maintain normal human performance in a cold environment. In a recent study, Hackney et al. (1995) studied the changes in lean body mass of military personnel engaging in mountain operations. Fifteen U.S. Navy and Marine Corps personnel were part of a Marine Corps expedition to climb Mount Denali, Alaska. The total expedition took 13.5 days during which time the subjects were able to eat and drink rations ad libitum. The subjects carried their own equipment (backpacks [23 to 28 kg] and sleds [33 to 50 kg]). Weather conditions varied from -30° to 17°C (-22° to 63°F). During the ascent, the group was caught in a snow storm and became separated. Four men were able to make the ascent successfully. Body weight was significantly less following the expedition (post = 76.6 ± 1.5 kg vs. pre = 81 ± 1.5 kg). Those who were able to complete the climb had lost more weight than those who were forced to stay in their tents due to climatic conditions. The men reported that they slept when they could. This example is used to emphasize that many times during training or real military operations, the challenges facing the personnel are multiple: lack of food, unanticipated events, and sleep deprivation (Hackney et al., 1995). Sleep deprivation by itself would not be lethal; however, when combined with a decrease in body fat, and thus, the body's inability to resist the cold challenge—then hypothermia and frost bite can occur.

In military situations, men have slept on the cold ground and have not died from hypothermia. The classic studies by Hammel (1964) demonstrate that "primitive men" are able to sleep nude in cold environments that would be unacceptable to European men accustomed to sleeping in a warm microenvironment. He studied groups living in various parts of the world and noted that when the subjects were sleeping there were diverse physiological responses to the cold environment. His subjects included Australian aborigines, bushmen of the Kalahari Desert, Alacaluf Indians of Tierra del Fuego, Arctic Indians, Andean Indians, Eskimos, and Lapps. In addition, he was able to show that Europeans were able to adjust to the cold after being exposed for a few weeks and becoming cold "hardy" (Hammel, 1964). This practice continues in that modern explorers who are attempting to cross the South or North Pole sleep outdoors during the winter months in northern Minnesota to get their bodies adjusted to the anticipated cold (Personal communication, W. Steger, Steger Inc., Duluth, Minn., 1990).

Technology to the Rescue: Antiquity to the Present

Man's ability to withstand the challenges of a cold environment have ultimately evolved into modifications of the immediate environment. Although physiological adjustments have been reported by Hammel and many others, mankind is ingenious in finding ways to survive and sleep in cold environments. Initially, mankind was able to modify the environment by living in caves, discovering fire, and using animal furs for protection. Presently, sleeping bags have become a key component in the military's ability to conduct cold weather operations. In a recent study, Roberts et al. (Unpublished manuscript, "Physiological evaluation of sleeping bag cover," D. E. Roberts, J. E. Reading, S. J. Feith, and R. S. Pozos, Naval Health Research Center, San Diego, 1995) studied the rectal and peripheral temperatures of Marines who slept at -29°C (-20°F) in a variety of sleeping bags that were lightweight and constructed of synthetic material. Subjects were outfitted with skin and rectal thermocouples while they slept in a cold chamber. Subjects wore "long underwear," caps, and socks. Rectal temperatures fell approximately 1°C (1.8° F) over the duration of the entire night (Figure 8-1). Weighted skin temperatures also fell approximately 1°C (1.8°F), but this figure is misleading since it does not reflect the actual digit temperatures (Figure 8-2). Thus, as new advances in textiles continue, the military and recreational communities can continue to have adequate protection while sleeping in cold climates that otherwise might be lethal.

The Challenge: Field Studies in Bosnia

Although a large amount of data has been accumulated from studies that investigate various complex interrelationships among sleep, nutrition, physical activity, and skin and core temperature, most of these studies occur in laboratory settings. Although helpful, these studies do not shed light on the overall physiological adjustments that occur during field conditions. With the advent of miniaturized recording equipment, it should be possible to record skin temperatures and physical activity from NATO military forces in Bosnia. In addition, as more women enter the military, it is imperative to study their responses in cold operations. Most studies that have been conducted on human subjects have evaluated male responses primarily. There is a paucity of information about the physiological responses of female personnel who have

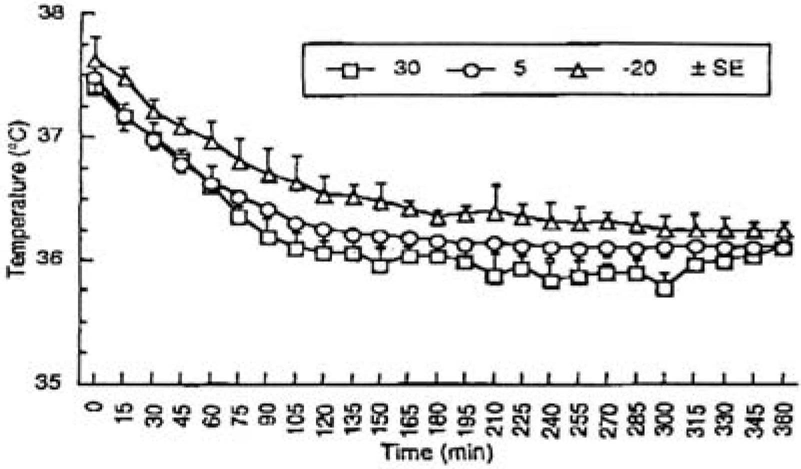

FIGURE 8-1 Rectal temperature (± SE) for 14 male subjects sleeping in military sleeping bags for 6 hours. Sleeping bags are temperature specific for temperatures: 30°, 5°, and -20°C (86°, 41°, and -4°F). SOURCE: Roberts et al. (Unpublished manuscript, "Physiological evaluation of sleeping bag cover," D. E. Roberts, J. E. Reading, S. J. Feith, and R. S. Pozos, Naval Health Research Center, San Diego, 1995).

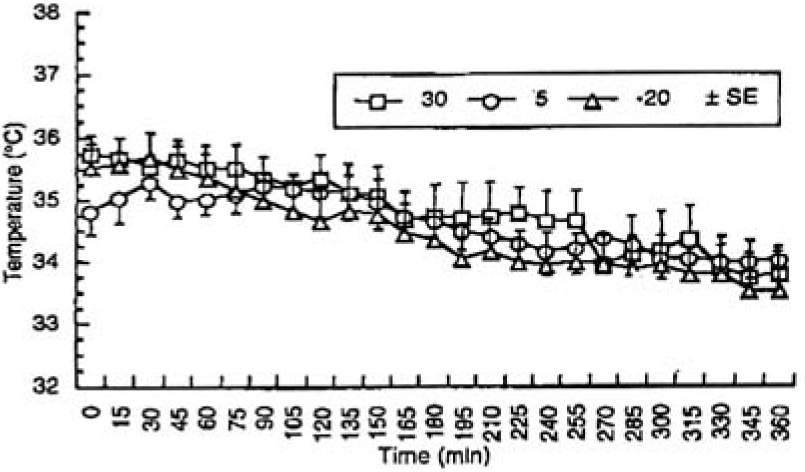

FIGURE 8-2 Mean-weighted skin temperature (± SE) for 14 male subjects sleeping in military sleeping bags for 6 hours. Sleeping bags are temperature specific for temperatures: 30°, 5°, and -20°C (86°, 41°, and -4°F). SOURCE: Roberts et al. (Unpublished manuscript, "Physiological evaluation of sleeping bag cover," D. E. Roberts, J. E. Reading, S. J. Feith, and R. S. Pozos, Naval Health Research Center, San Diego, 1995).

been sleep deprived and are participating in cold weather operations. Although gathering data in the field is a challenging situation, these data could assist in the development of the appropriate boots, tents, food, etc., to minimize cold stress and cold injury.

AUTHORS' CONCLUSION

There will always be a conflict between the demands of military operations and the biological clocks that coordinate various physiological functioning in military personnel. In general, the human body is robust enough to handle these challenging changes by utilizing behavioral and physiological responses. Research results from strictly controlled laboratory settings will assist in the development of possible biological/pharmacological agents that may alter circadian and other biological clocks to enhance human performance in adverse environmental settings. Until that time, modifications of man's immediate environment such as clothing and sleeping bags will be the major way the military will be able to conduct long-term cold weather operations. The evaluation of such gear in the field is required to quantitate the effects of the interplay of various biological clocks on human performance.

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9

Influence of Cold Stress on Human Fluid Balance

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INTRODUCTION

Water is probably the body's most important nutrient, accounting for nearly 70 percent of body weight in a normal adult. During rest in temperate climates, total body water is maintained within a narrow range, approximately ±0.2 percent of total body weight (Greenleaf, 1992). This tight balance is achieved through fluid ingestion associated with eating and drinking coupled with metabolic water released and physiological systems that regulate fluid loss (e.g., renal, cardiovascular, and hormonal).

During physical work, mental stress, and/or exposure to climatic extremes, marked disruptions of body fluid balance can occur. This is as true in cold climates as in hot. For example, soldiers conducting cold-weather operations are often dehydrated by 3 to 8 percent of their body weight (Bly et al., 1950;

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Rogers et al., 1964). These dehydration levels are similar in magnitude to those reported for persons in hot climates. Importantly, marked body water loss, if not replaced, will have a significant impact on the health and performance of soldiers.

Although the importance of hydration on work performance in hot climates has been recognized for years, considerably less is known with regard to hydration effects of cold climates. Few studies have specifically assessed the effects of cold-induced dehydration on physical work, thermoregulation, or susceptibility to cold injuries. In fact, neither of two major review articles that address fluid balance in the cold specifically discuss the military aspects, implications, or concerns (Bass and Henschel, 1956; Fregly, 1991).

Forty-five years ago, a U.S. Army physician described what he felt were the nutritional problems and concerns associated with conducting military operations in arctic climates. He concluded that "the most important problem yet to be solved is that of man's water balance" (Orth, 1949, p. 205). One might argue that the statement is as true today as it was then.

Military Situation Regarding Fluid Balance in the Cold

Sixty percent of the earth's land mass has January temperature lows below 32°F (0°C), and over 25 percent of the earth's land mass experiences January temperature lows below 0°F (-18°C) (Bates and Bilello, 1966). Furthermore, many national borders of military significance are located in mountainous regions that are not only at considerable altitude but also extreme cold. Thus, it is critical that the understanding of the effects of cold on body fluid balance be improved if the health and performance of soldiers deployed to these harsh environments is to be optimized.

This chapter reviews three areas: (1) factors that increase fluid loss and reduce fluid intake in cold climates, (2) the military impact or significance of dehydration in the cold, and (3) possible countermeasures to minimize dehydration in the cold.

Body Fluid States

Figure 9-1 clarifies the terminology used in this chapter (Greenleaf, 1992). The terms *euhydration, hypohydration,* and *hyperhydration* refer to a total body water that is normal, below normal, and greater than normal, respectively. The terms *dehydration, rehydration,* and *overhydration* refer to processes by which total body water is either decreased relative to normal, increased toward normal, or increased above normal, respectively.

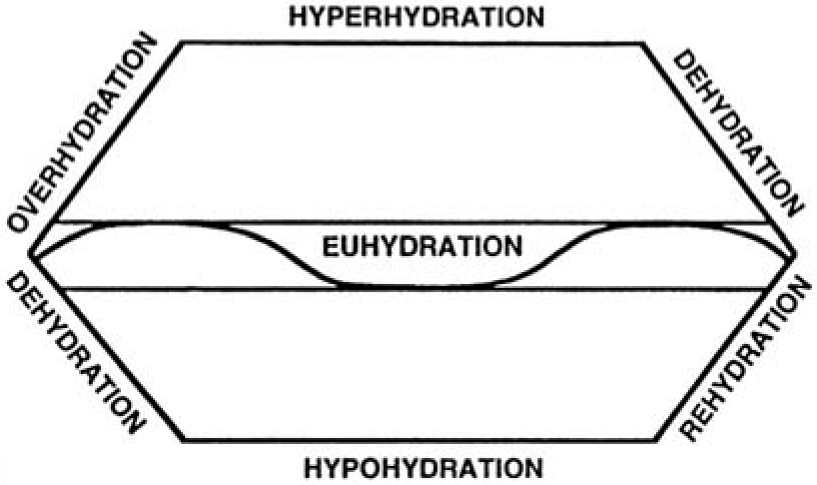

FIGURE 9-1 Body hydration terminology and variability. SOURCE: Adapted from Greenleaf (1992).

FACTORS CAUSING DEHYDRATION

Several factors are associated with dehydration during cold exposure. Some of these factors are associated with increases in fluid loss, while others are related to reductions in fluid intake. The most significant factors are cold-induced diuresis, respiratory water losses, cold-weather clothing, metabolic cost of movement, and reduced fluid intake.

Cold-Induced Diuresis

Cold-induced diuresis (CID) is one aspect of fluid balance in cold that has received considerable attention. Debate exists with regard to (1) the significance or impact of CID; (2) the nature of the diuresis; that is, whether it is free water diuresis or osmotic diuresis; and (3) the physiological mechanism(s) responsible for CID (see Table 9-1 for references). The failure by investigators to control extraneous variables is partially responsible for the discrepancies in findings. Table 9-1 summarizes some of the key studies regarding CID in humans.

CID was first observed over 200 years ago by Sutherland (1764), who reported an increase in urine flow following cold-water bathing. Sutherland, however, made no mention or speculation about the relative influence of water

TABLE 9-1 Significant Studies Regarding Cold-Induced Diuresis

Reference	Environment/Situation	Findings
Sutherland, 1764*	Cold-water bathing	↑ Urine losses
Gibson, 1909*	Cold air (39°-50°F [4°-10°C])	↑ Urine flow with ↓ temperature
Bazett et al., 1940*	2 weeks in cold climate	↑ Urine flow, ↓ BV, ↓ PV
Eliot et al., 1949	Cold air (59°F [15°C])	↑ Urine flow blocked by ADH
Bader et al., 1952	Cold air (59°F [15°C])	Demonstrated that confounding factors influence CID
Segar et al., 1968	Cold air (55°F [13°C])	↑ Urine flow and ↓ ADH
Lennquist et al., 1974*	Cold air (59°F [15°C])	Examined mechanisms for CID; concluded not ADH mechanism
Wallenberg et al., 1976	Cold air (59° [15°C])	Evidence that CID is pressure natriuresis
Young et al., 1987	Cold water (64°F [18°C]) with cold-acclimated subjects	Evidence that CID is not pressure diuresis
Various authors, 1985–present	Cold air and cold water	Conflicting findings regarding whether hormonally- mediated ADH vs. ANF vs. pressure

NOTE: * indicates field studies or observations; all others are laboratory experiments. ↑, increase; ↓, decrease; BV, blood volume; PV, plasma volume; ADH, antidiuretic hormone; CID, cold-induced diuresis; ANF, atrial natriuretic factor.

immersion versus that of cold exposure per se. It was not until 1909 that Gibson (1909) demonstrated an increase in urine flow to be the direct result of cold exposure. In 1940 Bazett and associates published a field study that confirmed that an increase in urine flow occurred with cold exposure, but also demonstrated commensurate reductions in plasma and blood volume.

Bader et al. (1952) demonstrated that confounding factors could influence the magnitude of CID and determined whether or not a diuresis occurred during cold exposure. They found that CID could be avoided if moderate exercise was performed during the exposure to cold. Subsequent investigations demonstrated that CID can be influenced by other factors such as: (1) the intensity and (2) duration of cold exposure, (3) hydration status, (4) body posture during cold exposure, (5) performance of exercise, (6) diet, (7) gender, (8) age, (9) body composition, and (10) the time of day.

Lennquist et al. (1974) attempted to determine the mechanism(s) responsible for CID. They hypothesized that CID was not the result of a fall in antidiuretic hormone (ADH) as was previously suggested (Bader et al., 1952; Eliot et al., 1949) and commonly believed. During this decade, the notion reemerged that CID was simply a pressure diuresis, the logic being that the increased systemic arterial blood pressure would increase renal blood pressure and thereby reduce tubular reabsorption of both water and solute (i.e., electrolytes). Wallenberg and Granberg (1976) demonstrated that increases in blood pressure during cold exposure were correlated to sodium excretion ($r \sim 0.60$). Hence, they speculated that the mechanism for CID was, at least in part, the result of an increase in blood pressure. The hypothesis that CID is a pressure diuresis is still favored by many investigators today, and little direct evidence has suggested otherwise.

Combined data in two publications from a study conducted at the U.S. Army Research Institute of Environmental Medicine (Muza et al., 1988; Young et al., 1987), however, suggest that CID may not be a pressure diuresis. Data for the two papers came from the same experiments in which subjects were immersed in cold water prior to and following a 5-wk cold-water acclimation program. Young and colleagues (1987) reported that the CID response to cold-water immersion was not affected by the cold-water acclimation regime. That is, the magnitude of diuresis was the same during the initial pretest as it was during the posttest. When reporting the cardiovascular data, Muza et al. (1988) showed that while mean arterial blood pressure was markedly increased during the initial cold-water exposure (pretest), it did not increase during the posttest. Together, these data provide evidence that CID and blood pressure responses can be disassociated and, hence, raise questions about the pressure diuresis hypothesis.

With regard to CID, the following conclusions can be made:

- Although there is disagreement regarding the mechanism(s), the central movement of fluid caused by peripheral vasoconstriction is likely to be involved.
- If studies are to be meaningful, confounding factors must be controlled or specifically examined.
- CID appears to be self-limiting, in that, as dehydration occurs, CID is reduced or eliminated.

Respiratory Water Losses

Although cold, dry air is often credited with being a contributor to fluid losses in cold environments, the magnitude of these losses has not been reported. The extent of fluid loss via respiration is dependent on both the ventilatory volume and the water vapor in the ambient air (Brebbia et al., 1957). Respiratory water losses can be estimated from metabolic rate and from ambient air conditions (i.e., air temperature and relative humidity). Using predictive models (Brebbia et al., 1957; Mitchell et al., 1972), respiratory fluid losses were estimated for both rest and exercise conditions at three ambient temperatures and water vapor pressures (Table 9-2). Despite high relative humidities (100 percent used for demonstration), cold air contains significantly less water vapor than does warmer air of even lower relative humidity. The difference in water vapor pressure between the saturated air in the lung (water vapor 44 mm Hg) and ambient air determines the amount of respiratory water lost with each breath. Hence, the lower the water vapor pressure in ambient air, the greater the respiratory water loss.

Respiratory water loss increases with increasing metabolic rate. To compare the effect of cold air and metabolic rate on respiratory water loss, this laboratory predicted respiratory water losses (Brebbia et al., 1957; Mitchell et al., 1972) for a 24-h scenario in which a person rested for 8 hours, performed moderate activity for 12 hours, and performed strenuous work for 4 hours (Table 9-2). Respiratory losses approximately doubled at -4°F (-20°C) versus 77°F (25°C) (0.68 versus 1.02 liters/24 hr) (Table 9-2). This 0.34-liter difference probably plays a relatively minor role in the 3 to 8 percent body weight loss reported during military operations conducted in cold climates. However, respiratory water losses do contribute to dehydration in the cold. As shown in Table 9-2, metabolic rate has a far greater impact than ambient temperature on respiratory fluid losses and, hence, on fluid requirements.

TABLE 9-2 Estimates of Ambient Temperature and Metabolic Rate Effects on Respiratory Water Loss

Temperature (°F [°C])	Relative Humidity (%)	Water Vapor (mm Hg)	Metabolic Rate (watts)	Respiratory Water (ml/h)
77 (25)	65	15	Rest (100)	~ 10
32 (0)	100	5	Rest (100)	~ 13
-4 (-20)	100	1	Rest (100)	~ 15
77 (25)	65	15	Light–moderate (300)	~ 30
32 (0)	100	5	Light–moderate (300)	~ 40
-4 (-20)	100	1	Light–moderate (300)	~ 45
77 (25)	65	15	Moderate–heavy (600)	~ 60
32 (0)	100	5	Moderate–heavy (600)	~ 80
-4 (-20)	100	1	Moderate–heavy (600)	~ 90
Total respiratory loss following 8-h rest, 12-h light–moderate activity, and 4-h moderate–heavy activity:				
77 (25)	65	~ 680 ml/24 h		
32 (0)	100	~ 905 ml/24 h		
-4 (-20)	100	~ 1,020 ml/24 h		

NOTE: Effect of cold air itself could account for increased respiratory water losses as great as 340 ml/24 h, i.e., 50 percent increase.

Cold-Weather Clothing

A potentially important factor in cold-induced water losses is the effect of heavy and cumbersome clothing. Significant metabolic heat can be generated and can result in significant sweating even in cold climates. Figure 9-2 demonstrates the relationship of total insulation and metabolic rate to the thermal comfort of individuals exposed to different ambient temperatures (Gonzalez, 1988). The total insulation required to keep a resting person warm is considerably more than that required to keep a person warm who is performing moderate-to-heavy work or exercise. (1 Clo unit is equivalent to the insulation of a business suit.)

If clothing is not carefully matched to metabolic rate, significant heat storage and sweating can occur. Table 9-3 provides one such example. Note that a person dressed in the U.S. Army Extended-Cold-Weather Clothing System (insulation ~ 4.0 Clo) produces little sweat while resting in the cold. However, if this person performed moderate or heavy exercise in that uniform, it is estimated that nearly 2.0 liters of sweat per hour would be lost. Because this clothing system allows for little evaporation, the uniform might become soaked. A wet uniform has serious implications for heat loss and subsequent cold-injury susceptibility. If the cold-weather clothing system is altered to reduce

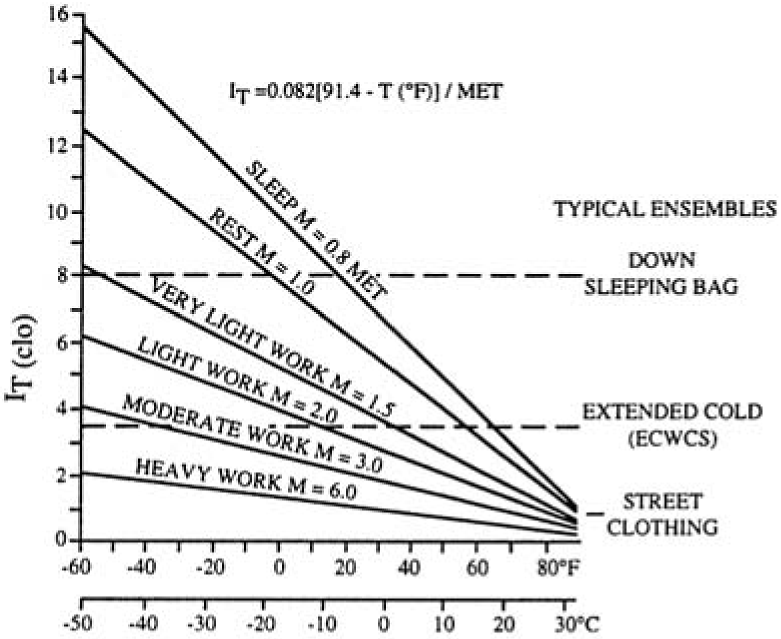

FIGURE 9-2 Total insulation (I_T, Clo) of clothing plus air necessary for comfort at various metabolic rates. (1 Clo unit is equivalent to the insulation of a business suit, and 1 MET equals 100 watts.) ECWCS, U.S. Army ExtendedCold-Weather Clothing System. SOURCE: Adapted from Gonzalez (1988).

TABLE 9-3 Estimates of Work and Clothing Effects on Sweat Loss

Temperature (°F [°C])	Clo[*]	Metabolic Rate (watts)	Sweat Loss (ml/h)
32 (0)	4.0[†]	Rest (100)	100
-4(-20)	4.0	Rest (100)	100
32 (0)	4.0	Light–moderate (300)	1,100
-4(-20)	4.0	Light–moderate (300)	800
32 (0)	4.0	Moderate–heavy (600)	1,900
-4(-20)	4.0	Moderate–heavy (600)	1,900
32 (0)	1.9[‡]	Moderate–heavy (600)	900
-4(-20)	1.9	Moderate–heavy (600)	400

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[*] Clo units. One Clo unit is equivalent to the insulation of a business suit.

[†] Approximate Clo for U.S. Army Extended-Cold-Weather Clothing System (ECWCS).

[‡] Approximate Clo for ECWCS parka with field coat liner over woodland battle dress uniform.

total insulation to a Clo of 1.9, sweating will be reduced fivefold to only approximately 0.4 liter/h (Table 9-3). Therefore, it is important that persons in cold climates dress in layers to allow insulation to be matched to their metabolic rate. Clothing can be added when work rates decrease or removed when work rates and metabolic heat production increase.

Metabolic Cost of Movement in Cold Terrain

Figure 9-3 illustrates the effects of terrain associated with cold climates (e.g., snow) on the metabolic cost of movement (Pandolf et al., 1977). Note that the metabolic cost of walking (2.5 mph) on a blacktop surface is ~ 150 watts, while movement in deep snow increases metabolic rate by three- to fourfold. The higher the metabolic rate, the greater the sweating requirement and, hence, fluid replacement requirement. The cumbersome and hobbling effects of cold-weather clothing can increase the metabolic rate during physical activity by an additional 10 to 20 percent (Amor et al., 1973; Teitlebaum and Goldman, 1972). The magnitude of this increase in metabolic rate depends on the number of clothing layers as well as the exercise or work intensity (Amor et al., 1973; Teitlebaum and Goldman, 1972).

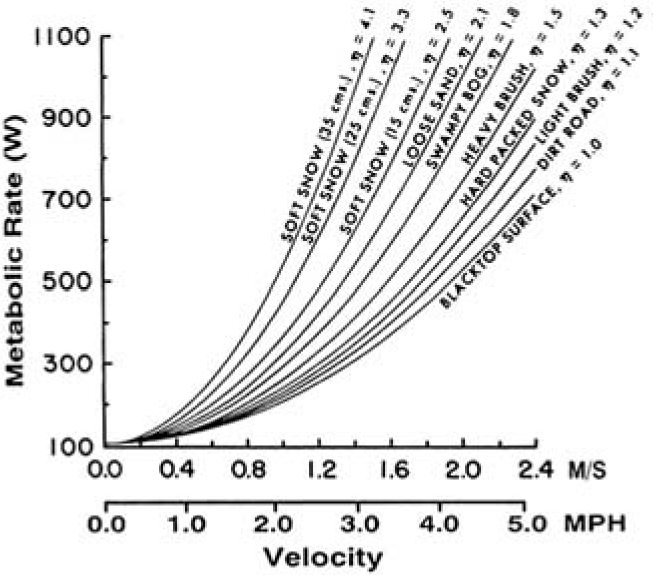

FIGURE 9-3 Predicted energy expenditure for walking at various speeds considering the type of terrain.
SOURCE: Adapted from Pandolf et al. (1977).

Reduced Fluid Intake

Fluid Delivery

The most important factor regarding fluid intake in the cold is the logistical constraint of fluid delivery. If drinking water or other fluids cannot be provided to the troops, dehydration will undoubtedly result. Although water in the form of snow or ice might be available, relying on such resources for drinking water is unrealistic. Orth (1949) demonstrated this fact when he wrote, "In experiments conducted last winter, it was found that at -50°F [-45.5°C] and an altitude of approximately 600 feet [183 m], using a Coleman stove it took 200 ml of fuel (gasoline) and 30–45 minutes to melt enough snow to give 600 ml of water" (p. 205). Orth went on to conclude, "It was determined it would take more than six hours per day and a half a gallon of gasoline to get sufficient water for one man" (p. 205).

The resources (time and fuel) required to utilize snow and ice as a major source for drinking water during military operations are prohibitive. Therefore, drinking water must be supplied to the field at regular intervals.

Frozen Drinking Water

Cold weather will often freeze drinking water, and it can take several hours to thaw a frozen 5-gallon (18.8-liter) container. Care must be taken to ensure that sufficient water is protected from the cold. For example, water supplies should be moved into warm vehicles or tents and canteens should be worn close to the body (i.e., inside the uniform or sleeping bag).

Inadequate Drinking

An inappropriate or reduced sensation of thirst can also contribute to reduced fluid intake (Adolph et al., 1947), an observation termed *voluntary dehydration* (Greenleaf and Sargent, 1965). Voluntary dehydration occurs whenever humans undergo severe stress (Greenleaf, 1992). It occurs in hot climates and may be even more pronounced in cold climates (Rogers et al., 1964; Wyant and Caron, 1983). Rogers and associates (1964) reported that despite marked dehydration during survival experiments in the subarctic, thirst was not displayed or mentioned until individuals were brought inside and warmed. This observation raises the possibility that cold skin or reduced body core temperature might provide important input that modifies thirst sensation.

In addition, persons in cold climates often voluntarily restrict fluid intake (Wyant and Caron, 1983). This behavior occurs late in the day to prevent the necessity of leaving a warm tent or sleeping bag in order to urinate outdoors during the night.

Fluid in Cold-Weather Rations

Another factor that leads to reduced fluid intake by military personnel in cold climates is that cold-weather rations, as issued, contain little fluid. The low water content of cold-weather rations is demonstrated by the fact that although one Ration, Cold Weather (RCW) provides 4,500 kcal of energy per day, 2.9 liters of fluid are required to rehydrate all of its components. In addition, unlike garrison feeding, high-moisture food items such as fruits and vegetables are not provided during cold operations as they would likely freeze. Thus, if water delivery is not adequate, problems of dehydration may be accompanied by problems of malnutrition.

Summary

Although several factors contribute to both increased fluid losses and reduced fluid intake, the relative contribution of each—as well as the sum of their effect on body fluid balance—is difficult to predict. Fluid balance in cold weather depends on a combination of many determining factors. For example, cold-induced diuresis and logistical constraints in water delivery may be the most significant factors for soldiers conducting sentry duty well forward of the main body troops. However, the increased fluid loss associated with high metabolic work rates is likely to be the most significant factor for soldiers on the move over cold terrain.

MILITARY IMPACT AND SIGNIFICANCE OF DEHYDRATION IN THE COLD

It is clear that military operations conducted in cold climates can have a significant effect on body fluid balance. The impact of this dehydration and/or the direct effects that cold exposure can have on physical and cognitive performance, thermoregulation, and the susceptibility to cold injury are discussed below.

Dehydration Effects on Physical and Cognitive Performance

Numerous studies report physical performance decrements during cold exposure, including reductions in manual dexterity and coordination (Meese et al., 1981; Wyon et al., 1982); muscular strength (Coppin et al., 1978; Horvath and Freedman, 1947; Johnson and Leider, 1977); maximal power output, jumping, and sprint performance (Bergh and Ekblom, 1979); submaximal and maximal exercise performance (Adolph and Molnar, 1946; Faulkner et al., 1981; Patton and Vogel, 1984); and maximal aerobic work capacity (Craig and Cummings, 1966; Lennquist et al., 1974). However, other studies report no reduction in submaximal performance (Roberts et al., 1984) or maximal aerobic power (Patton and Vogel, 1984; Rodahl et al., 1962; Saltin, 1966).

Upon close examination of these studies, the apparent discrepancy among them can be explained by a consideration of the effects of the cold environment on body core and/or muscle temperature. Maximal tension exerted during voluntary sustained contractions, as well as peak power output, is significantly reduced when muscle temperature is lowered (Clarke et al., 1958; Davies and Young, 1983). In Saltin's study (1966), subjects were exposed to the cold for only 30 minutes, while in Patton and Vogel's study (1984), subjects wore arctic clothing. Muscle temperatures were probably not markedly reduced, and the finding that performance was unaffected in these studies might have been expected. Therefore, both maximal and submaximal physical performance are reduced with cold exposure only when muscle temperatures are markedly lowered.

The preceding studies did not evaluate whether dehydration further affects physical performance in the cold. Lennquist et al. (1974) speculated that cold diuresis and resulting negative water balance are responsible for a reduction in physical work capacity. However, it could be argued that subjects' performance reduction resulted from muscle cooling. Without a control group for comparison (i.e., those exposed to cold but maintained in a euhydrated state), it is difficult to determine the direct effects of hypohydration per se. Roberts et al. (1984) examined the effects of dehydration on physical performance in the cold, and in this study, hydration status was controlled. In one group of subjects, euhydration was maintained, while in a second group, subjects were dehydrated by 3.5 percent of their body weight (by fluid restriction and exercise). Subjects performed two endurance exercise tests (30 minutes of cycle ergometry at approximately 75 percent of maximal oxygen consumption). One endurance test was performed in a temperate environment (65°–70°F [18°–21°C]) and one during cold-air exposure (32°F [0°C]). There was no significant effect of cold or hypohydration on submaximal exercise performance. However, exercise duration and/or intensity might have been too short or too low to accentuate differences among trials.

Although many studies report that cold exposure reduces cognitive performance, only one study actually examined the effects of dehydration on cognitive performance in the cold. Banderet et al. (1986) studied 2 groups of 18 subjects. In one group, euhydration was maintained while the second group was dehydrated by 2.5 percent body weight (prior fluid restriction and exercise). Hypohydration negatively influenced cognitive performance as assessed by performance measures of coding, number comparison, computer interaction, pattern comparison, and grammatical reasoning.

Because there are limited data on dehydration and performance in the cold, and because a soldier in the cold need not be a "cold soldier," one might estimate the effects of dehydration on performance in the cold by examining numerous well-controlled studies of dehydration in temperate or hot environments.

Sawka and Pandolf (1990) reviewed studies examining effects of dehydration on physical performance. From their summary tables, it appears that dehydration representing as little as 2 percent loss of body weight can result in significant reductions in muscular strength, muscular endurance, and anaerobic work capacity, although some studies report no significant changes in the above parameters. Likewise, dehydration seems to cause a significant reduction in maximal aerobic power and maximal work capacity with decrements following a body weight loss of as little as 2 percent. The magnitude of performance decrement is directly related to the magnitude of dehydration and is accentuated by heat stress (Sawka, 1992).

Clearly, further study is needed regarding the direct effects of dehydration on physical and cognitive performance during cold exposure.

Dehydration and Thermoregulation

Dehydration has negative effects on thermoregulation. A fluid loss representing as little as 1 percent body weight can alter exercise thermoregulation (Greenleaf and Harrison, 1986), and dehydrated persons will be more susceptible to heat exhaustion (Sawka, 1992). Furthermore, Adolph and associates (1947) indicated that body fluid losses can become life threatening when they exceed 10 percent.

A variety of mechanisms are responsible for the effects of dehydration on thermoregulation. Sawka (1992) demonstrated that when individuals were hypohydrated, the onset of sweating was delayed. That is, body core temperature needed to rise significantly higher to initiate sweating when subjects were hypohydrated compared to when they were euhydrated. For any given rectal temperature, sweating rate was significantly lower when subjects were hypohydrated compared to when euhydrated (Sawka, 1992). Recently, Montain et al. (1995) demonstrated that this hypohydration delay of sweating occurs at equal amounts across light- to heavy-intensity exercise. With reduced rates of sweating during hypohydration, less evaporative heat loss occurs. This reduction in heat loss will result in additional heat storage and potentially a greater rise in body core temperature. The greater rise in body core temperature has important implications for physical performance as well as for thermal injury and illness.

The overall effect of dehydration on thermoregulation is dependent on a combination of factors that determine whether an overall gain or loss in body heat storage will occur. For example, in moderately cold climates when individuals are wearing heavy clothing and are performing heavy work or exercise, it is conceivable that dehydration will exacerbate the core temperature rise and increase heat strain. In contrast, in severe cold or when work rates are low and body heat losses exceed heat production, dehydration probably has little effect on core temperature but may accentuate peripheral cooling (see below). In addition, dehydration appears to affect a person's perception of effort. Montain and Coyle (1992) demonstrated significantly higher ratings of perceived exertion during exercise when little or no water was ingested compared to trials in which large or moderate amounts of fluid were ingested.

Dehydration and Cold-Injury Susceptibility

It is often suggested that dehydration increases a person's susceptibility to peripheral cold injuries (Gamble, 1994). Numerous case reports indicate that patients suffering from peripheral cold injury are often dehydrated. However, the direct evidence demonstrating that dehydration itself significantly increases the risk for peripheral cold injury is limited.

Roberts and Berberich (1988) conducted a study that assessed dehydration effects on peripheral and central body cooling during cold exposure. Two groups of subjects, one maintained in a state of euhydration and the other dehydrated by 4.6 percent of body weight (by exercise and fluid restriction), were exposed to cold air on 4 separate occasions (2 days prior to dehydration and 2 days following dehydration). Subjects wore standard military cold-weather clothing, and after 15 minutes their gloves and glove liners were removed. Although rectal temperature responses were similar, dehydrated subjects exhibited greater vasoconstriction to the hand as evidenced by greater finger cooling. These data indicate that dehydration might blunt cold-induced vasodilation and increase the susceptibility to cold injury. However, considerable variability in the peripheral cooling responses existed, and the groups appeared dissimilar for this response even before being dehydrated.

Another study on the effects of dehydration on thermoregulation during cold exposure was conducted by Roberts and colleagues (1984). They reported that during 90-min exposure to 32°F (0°C) air, greater hand cooling occurred in persons dehydrated by 3.5 percent of their body weight. Although the above data suggest that dehydration might increase one's susceptibility to peripheral cold injury, additional study is clearly merited.

Summary Comments

Orth (1949) provides a summary of the potential effects of dehydration on soldiers' health and performance in cold environments: "The lack of sufficient fluids in the diet to maintain a positive water balance causes at first a change in disposition, sullenness, loss of appetite, chronic thirst, discipline begins to suffer…and finally failing physical efficiency. The final step is dehydration exhaustion, this can take place in 3–4 hours in the desert, but it also can take place in as little as two days in the Arctic where solid water abounds" (p. 205).

COUNTERMEASURES TO DEHYDRATION

The best way to prevent dehydration is to ensure that adequate fluids are ingested. However, because of various factors that cause dehydration in cold environments, dehydration is not an easily solved problem. Recent efforts have investigated potential countermeasures to prevent or to blunt cold-induced dehydration and hence the related decrements to performance and health.

Glycerol, a nontoxic, naturally occurring metabolic byproduct and food additive, has been shown to improve fluid retention over standard electrolyte beverages or water alone. Freund and colleagues (1995) demonstrated in a temperate environment that drinking approximately 1.75 liters of water in an attempt to achieve hyperhydration, resulted in only 32 percent of the fluid being retained after 3 hours (the remainder was eliminated by the kidney). However, if the same volume of water contained approximately 70 g of added glycerol, nearly a doubling in fluid retention occurred, that is, 60 percent. These experiments were duplicated during cold-air exposure. Again greater fluid retention was found following the ingestion of glycerol and water versus water alone (35 percent vs. 18 percent 4 hours post ingestion) (Freund et al., 1994). In addition to improving fluid retention and adding calories to water, glycerol also reduces the freezing point (e.g., a 30 percent glycerol solution reduces the freezing point 48°F (9°C) below the freezing point of water). Hence, the addition of glycerol might also be effective in reducing the problem of the freezing of drinking water.

Experiments in this laboratory demonstrated that differences in fluid retention with glycerol were the result of a blunted increase in urine flow. Importantly, the differences in urine flow were entirely accounted for by differences in free water and not osmotic clearance (Freund et al., 1994, 1995). Although further study is required, these studies provide evidence that differences in antidiuretic hormone response may be the mechanism responsible for improved fluid retention with glycerol. Alternatively, glycerol may directly affect the kidney's concentration gradients and hence water reabsorption.

Future countermeasures for dehydration in the cold could include pharmacological interventions, such as the administration of antidiuretic hormone analogs or perhaps even combined treatments (e.g., glycerol and antidiuretic hormone). Through innovative experimentation, the health and performance of soldiers deployed to harsh environments can be optimized.

AUTHORS' CONCLUSIONS AND RECOMMENDATIONS

In cold climates body fluid losses can be similar to those in hot environments and can result from sweating and increased respiratory water losses as well as cold-induced diuresis. Fluid intake in cold environments can also be reduced as a result of logistical constraints in fluid delivery, problems with the freezing of water, reduced thirst sensation, and voluntary fluid restriction. The resultant dehydration that occurs negatively influences physical and cognitive performance, as well as thermoregulation and possible susceptibility to peripheral cold injury. Ingestion of glycerol in drinking water might be an effective countermeasure to reduce or delay cold-induced dehydration and the associated decrements to performance.

The following recommendations regarding human fluid balance in cold environments are made:

- Additional field studies are needed to document further the magnitude of cold-induced dehydration as well as the specific distribution of these losses throughout various body water compartments.
- Both laboratory and field studies are needed to determine the direct effects of cold-induced dehydration on performance, mission accomplishment, and susceptibility to peripheral cold injury.
- Countermeasures to cold-induced dehydration, such as glycerol ingestion, should be studied in field environments to determine efficacy and effectiveness.
- Additional countermeasures and ergogenic aids, including pharmaceutical intervention where appropriate, should be explored further.

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10

Muscle Metabolism and Shivering During Cold Stress[1]

Ira Jacobs[2]

INTRODUCTION

Two English explorers recently completed an unsupported coast-to-coast crossing of the Antarctic by foot, dragging a few hundred pounds with them on sleds for 95 days; they experienced temperatures as low as -85°C (-121°F) (Stroud, 1993). A small group of Norwegians completed a similar unsupported 1,400-km trek in the Arctic lasting 100 days, with temperatures down to -54°C (-65°F) (Gautvik et al., 1993). These expeditions demonstrated that it is possible to perform hard physical work for months on end in cold environments, provided adequate planning enables appropriate preparation of food rations and protective clothing and equipment. These expeditions and others suggest there are probably no particular nutritional considerations specific to long-term operations in the cold other than the requirement for sufficient energy consumption to balance energy expenditure.

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Contrasting with such situations, the premise directing the research interests of this laboratory is the possibility that emergency survival situations can arise when military personnel cannot be adequately protected from the cold by available clothing and/or shelter. The Canadian Forces recently experienced just such an event when a C130 aircraft crashed north of the magnetic North Pole in October 1991 (de Groot, 1993). Weather complicated rescue attempts until 32 hours after the crash. During this time the survivors had to deal with temperatures ranging from -20° to -60°C (-4° to -76°F) considering the windchill factor. In such situations, hypothermia is delayed in direct proportion to the capacity for, and intensity of, metabolic heat production (i.e., shivering).

By measuring the electrical activity of many muscle groups simultaneously during cold-induced shivering, it is now known that several large muscle groups are recruited and contract at relatively low intensities that are less than 20 percent of their maximum force-generating capabilities (Bell et al., 1992). Because so many muscle groups are involved in shivering, the sum total of their contractile activities can result in a four- or fivefold increase in metabolic rate and in heat production. Much of the attention of Jacobs and coworkers has been directed toward the substrates that are used by skeletal muscle to increase heat production during shivering. Until about a decade ago there was very little empirically based information available in this regard for human subjects. Therefore, some fundamental experiments were carried out in an attempt to fill this knowledge gap. (The reader is referred to Jacobs et al. [1994] for a more detailed review of thermoregulatory thermogenesis during cold stress.)

For example, Vallerand et al. (1988) administered a clinical glucose tolerance test to subjects who were sitting in either cold air or at a comfortable temperature for 2 hours. These data were the first to show in humans that glucose is eliminated more rapidly from the circulation during cold exposure, presumably to provide more available substrate to fuel the increase in metabolic rate. It is also noteworthy that this more rapid uptake of glucose during cold exposure occurs with lower insulin levels in the cold compared to warm temperatures.

Subsequently attempts were made to quantify the rates of substrate oxidation of fat, carbohydrate, and protein in humans during cold exposure with indirect calorimetric techniques. As one might presume, the increase in metabolic rate during shivering is caused by increases in oxidation of both fat and carbohydrate, but the relative increase in the rate of substrate oxidation caused by shivering is greatest for carbohydrates (Vallerand and Jacobs, 1989). In resting subjects exposed to either cold air or cold water, carbohydrates and fat contribute approximately equally to heat production (Martineau and Jacobs, 1989a, b; Vallerand and Jacobs, 1989). From a strategic point of view, this finding seems unfortunate because the body's availability of carbohydrates is quite limited compared to the abundant fat and protein stores. Aware of the well-established positive relationship between muscle glycogen concentration and endurance exercise performance of skeletal muscle, this research group speculated that there may be a similar detrimental effect caused by muscle glycogen depletion on another form of muscle contraction, that is, shivering and the associated heat production.

CARBOHYDRATE AVAILABILITY AND COLD TOLERANCE

This laboratory has used the needle biopsy technique to measure muscle glycogen changes in the cold. This technique is relatively innocuous and enables biochemical quantification of metabolic events within the muscle cell. Cold-water immersion at 18°C (64°F) was used for experiments because it is a way to very rapidly overwhelm the body's ability to compensate for heat loss by increasing metabolism. Subjects were removed from the water when their rectal temperature reached 35.5°C (95.9°F). Biopsies were taken from the thigh muscle under local anesthetic before and after the immersion to evaluate the changes in glycogen as a result of the water immersion (Martineau and Jacobs, 1988). A series of studies were also carried out in which the muscle glycogen concentrations were manipulated prior to water immersion by appropriate dietary and exercise protocols (Martineau and Jacobs, 1989a); the purpose of these studies was to evaluate the effects of very low and very high glycogen levels on metabolic heat production during the water immersion.

Metabolic rate during cold-water immersion, expressed as oxygen consumption, increases to values that are usually around four or five times the normal resting metabolic rate. Infrequently scientists in this laboratory have observed individuals who exhibit somewhat higher values, six or seven times the resting values. Initial studies suggested that part of this increase in metabolic rate is fueled by muscle glycogen, as all of the subjects demonstrated a decrease in leg glycogen concentration after the water immersion (Martineau and Jacobs, 1988). The second objective of these experiments was to evaluate the effects of manipulating the preimmersion glycogen levels on heat production during cold-water immersion. The manipulations did result in the subjects entering the water during one trial with muscle glycogen levels that were only about 50 percent of normal and during another trial when they were about 150 percent of normal (Martineau and Jacobs, 1989a). Oxygen consumption during the water immersion was about the same on each trial. The respiratory exchange ratio (RER), which is the ratio of carbon dioxide produced divided by the oxygen consumption, differed between trials as expected. An increase in the RER is interpreted as reflecting an increase in the proportion of energy that is transduced from the oxidation of carbohydrates; a decrease in the RER reflects an increase in the proportion of energy transduced from fat oxidation. Metabolic heat production is calculated based on the combination of RER and oxygen consumption. Significantly less metabolic heat production per unit time was observed when the body's carbohydrate stores were depleted compared to the other trials (Martineau and

Jacobs, 1989a). There was also a significantly more rapid body cooling rate, as reflected by the changes in rectal temperature, when the body had little glycogen stored in its muscles and presumably also in the liver (Martineau and Jacobs, 1989a). If one were to take these observations on body temperature cooling rate and try to translate the effects into how long a downed pilot, for example, would last in cold water before becoming severely hypothermic, the results suggest that in the glycogen-depleted state, the individual would cool to a potentially critical temperature significantly more rapidly. Based on the efficiency with which search and rescue activities are coordinated today with the aid of the Search and Rescue Satellite, this time interval is indeed significant.

These initial studies were conducted with subjects resting in cold air or cold water. Based on these results, this research group hypothesized that the requirement to do physical work superimposed on the experimental cold stress might induce a more rapid breakdown of muscle glycogen than if the same work were done at a comfortable temperature. Therefore subjects were asked to perform either light or heavy exercise, once at 9°C (48°F) air temperature and again on a separate day at 21°C (70°F) (Jacobs et al., 1985). Lean subjects were intentionally recruited so that they would begin shivering quickly during their cold-air exposure. Results showed that significantly more glycogen was in fact utilized to do the light exercise in the cold compared to doing the same work at 21°C (70°F). There was no difference in glycogen depletion rates, however, for the higher exercise intensities. This result is consistent with earlier observations that the heat production associated with hard exercise is sufficient to offset heat loss to the environment, thus obviating the need for shivering.

FAT UTILIZATION AND SHIVERING

Investigations also have been conducted on the effects of manipulating the body's circulating fat pools on heat production during cold-water immersion. Vallerand and Jacobs (1990) reported that triglycerides infused into a vein were not eliminated more rapidly from the circulation during cold-air exposure than during warm-air exposure, contrasting with the results for glucose infusion (Vallerand et al., 1988). In another series of experiments, the circulating free-fatty-acid concentration was manipulated by having subjects ingest nicotinic acid in the form of niacin pills prior to and during the water immersion (Martineau and Jacobs, 1989b). Nicotinic acid blocks lipolysis. This effect was demonstrated by the dramatic reduction in plasma free fatty acids and glycerol levels prior to and during the water immersion. Again contrasting with the effects of manipulating the carbohydrate stores, metabolic heat production was virtually unaffected; the proportion of total heat production that could be attributed to fat oxidation was significantly reduced, but there was compensation by simply increasing carbohydrate oxidation.

THE PREFERRED FUEL

For reasons that are still unclear, carbohydrates seem to be a somewhat preferred substrate during shivering thermogenesis. The effect of hard physical exertion is somewhat similar to shivering thermogenesis in that the body is not able to maintain the same intensity of exertion when carbohydrate stores are depleted, that is, a shift to a greater reliance on fat oxidation to fuel muscle contraction is not sufficient for the musculature to be able to maintain a high level of exertion, just as body temperature could not be maintained as well when carbohydrate stores were depleted (Martineau and Jacobs, 1989a). Interestingly, similar experiments were carried out at the U.S. Army Research Institute of Environmental Medicine (USARIEM), and they did not detect any significant muscle glycogen utilization during cold-water immersion (Young et al., 1989). Discrepancies between USARIEM's studies and those from this laboratory cannot be explained other than to suggest that subjects in this laboratory's experiments were much leaner than those of Young et al. (1989).

AUTHOR'S CONCLUSIONS AND RECOMMENDATIONS

The above brief summary of some of the recent work from this laboratory describes fundamental research that was required to understand how skeletal muscle fuels shivering. Only after such an understanding is achieved can one then consider the development of a substance or procedure that could be applied in an acute survival situation, that is, to enhance thermogenesis during shivering and, by doing so, delay the time to onset of life-threatening hypothermia. Such applications have in fact been developed and are described in the chapter by Andre L. Vallerand (see Chapter 15 in this volume).

- Aside from increased energy demands, does a cold environment elicit an increased demand or requirement for specific nutrients? This author's opinion is that the primary requirement is to balance the increased energy expenditure associated with shivering and exercising in the cold, with a commensurate increase in energy consumption.
- Can performance be enhanced in a cold environment by providing increased amounts of specific nutrients? Studies from this lab suggest that depletion of the body's carbohydrate reserves impairs metabolic heat production during shivering and may thus accelerate the onset of hypothermia. The well-established relationship between aerobic exercise performance and

carbohydrate availability is therefore much more important in a cold environment.

- Field studies are required to evaluate the effects of nutritional energy deficits on body temperature regulation and work capacity under simulated survival conditions.

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11

Macronutrient Requirements for Work in Cold Environments

Peter J. H. Jones[1] *and Ian K. K. Lee*

INTRODUCTION

There is an important need to characterize accurately the energy and macronutrient requirements of individuals living and working in cold climates. In addition, this information is necessary to ensure optimal performance in military field settings where sizable effort is required to transport required food supplies and associated materiel. During field exercises, either excessive or inadequate food supplies will hamper unit performance capacities.

Several previous studies have suggested that caloric needs in military personnel should be increased in the cold; however, estimates range considerably (Johnson and Kark, 1947; King et al., 1993; LeBlanc, 1957; Rodahl, 1954; Swain et al., 1949). The current U.S. Military Recommended Dietary Allowance (MRDA) for males in environments that are colder than 57° F (14°C) is 4,500 kcal/d (AR 40-25, 1985). Knowledge of the impact of cold on energy and macronutrient utilization by military personnel both at rest and

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during physical exertion is of great value in establishing energy and macronutrient contents for rations in cold environments.

The objective of this chapter was to reassess the older literature and review the most recent literature dealing with energy and macronutrient requirements in the cold, focusing particularly on data obtained in trails that measured energy expenditure levels. Older estimates of requirements based on food intake data may be unreliable due to underestimation of energy consumption. The overall goal was to answer two questions. First, are caloric requirements elevated in the cold, and if so, by how much? As part of this question, mechanisms for any such increase were examined. Second, what is the dietary consumption ratio of protein, carbohydrates, and fat that optimizes performance in cold environments?

ENERGY BALANCE AND REQUIREMENT IN THE COLD

The energy balance of an individual can be determined using the following equation:

$$EE = EI \pm \Delta S,$$

where *EE* is energy expenditure, *EI* is intake, and Δ*S* is change in body energy stores over the period of measurement. For individuals maintaining body composition, *EE* = *EI*; thus *EE*, and, therefore, the energy requirement, can be determined using an estimate of metabolizable *EI*. In situations where individuals change body energy stores, as is the case in many studies to be discussed, *EE* can still be calculated from *EI*; however, Δ*S* needs to be established accurately, which is often difficult using current techniques. Past studies that examined energy needs in military personnel in cold environments have used both *EI* and *EE* to estimate these needs.

Studies Showing Increased Requirements Using Energy Intake Data

Historically, reports concerning effects of environmental temperature on energy needs began shortly after the Second World War when Johnson and Kark (1947) demonstrated a relationship between climate and reported food intake in several groups of military personnel given unlimited access to food rations. These authors suggested an inverse correlation between local mean temperature and energy reported to be consumed per man per day. Intakes ranged from 3,100 kcal/d in the desert (91°F [33°C]) to 4,900 kcal/d in arctic conditions (-29°F [-34°C]). Other earlier studies similarly indicated higher caloric needs of troops in arctic settings. Swain et al. (1949) showed that troops in garrison at Fort Churchill, Northwest Territory, Canada over two successive winters required caloric intakes of over 5,000 kcal/d. About 100 men participated in these studies, with each man spending about 3 hours each day outside. Food and beverages issued and food waste returned were recorded in the canteen daily for 10 days for each man. However, uniform records of activity were not obtained, which precluded precise assessment of movement or exercise. Weight records were kept for 16 individuals during one of these trials. It was found that over a 20-wk time period, body weight increased by an average of 1.55 kg. If this weight gain represented an increase in fat mass alone, it would account for, at most, approximately 100 kcal excess per day. Therefore, the majority of calories consumed would have been expended as energy.

Overall, studies that determined caloric needs using estimates of *EI* have demonstrated an increase in energy requirement for individuals working in cold climates as just described. However, these studies are not without exception as described below.

Studies Showing Minimal Effects of Cold Environments on Energy Requirement Determined by Energy Intake

Not all studies of caloric requirements in the cold have found an increase. LeBlanc (1957) suggested that food intakes of groups of persons living in the cold and taking part in military exercises were about 3,900 kcal/d. Similarly, Rodahl (1954) examined the nutritional requirements of a group of airmen and infantrymen in garrison in Alaska. These individuals had resided in Alaska for about a year prior to the study. Men slept in warm quarters, with outdoor temperatures ranging from -14° to 32°F (-26° to 0°C), and had low activity levels. Food was carefully weighed, and intake data were collected at mealtime, with subjects recording additional snack items separately. Mean caloric intake ranged between 3,100 and 3,400 kcal/d, with a mean of 3,200 kcal/d and no overall body weight change. Similar intakes were observed in native Eskimos. Rodahl concluded that previous studies probably overestimated caloric needs for troops in arctic conditions. He mentioned that these troops were accustomed to the terrain and operations in the Arctic. However, it cannot be ruled out that energy intakes were underestimated; thus, caloric consumption data erred on the low side. At least some of the food consumption data were self-reported, which cannot be considered reliable, as will be demonstrated.

More recently, King et al. (1993) reported that troops living in Alaska in tents during the winter, with temperatures as low as -18°F (-28°C), recorded intakes of 3,000 to 3,300 kcal/d (Table 11-1). In contrast, the energy expenditures in a subgroup of these individuals averaged 4,253 kcal/d as measured by the technique of doubly labeled water (DLW) described below.

TABLE 11-1 Military Recommended Dietary Allowances and Reported Intakes of Subjects Consuming the Meal, Ready-to-Eat and Long-Life Ration Packet

Nutrient	MRDA*	MRE†	LLRP‡
Energy, kcal	4,500	3,271	3,035
Protein, g	100	134	111
Carbohydrate, g	619§	375	376
Fat, g	175§	138	123

* Military Recommended Dietary Allowance for males ≥ 17 years old for a cold environment (<57°F [<14°C]) (AR 40-25, 1985).

† Meal, Ready-to-Eat subgroup (provided ad libitum).

‡ Long-Life Ration Packet subgroup (provided ad libitum).

§ Military feeding guidelines suggest energy intake to be 50 to 55 percent from carbohydrate and 35 to 40 percent from fats (AR 40-25, 1985).

SOURCE: Adapted from King et al. (1993).

The difference in calories consumed versus those expended in the subgroup appeared to be made up by calories lost as fat (1.4 kg over 10 days). However, once again, under rugged living conditions, it is difficult to determine accurately the quantity of food consumed. Inaccuracies in self-reported food and beverage intake may be a significant factor in explaining the results of this and other studies that suggest lower food intake, and thus food requirements, in the cold. Discrepancies in these results may be due to this important factor that has emerged only recently.

Underreporting of Energy Intakes

Results of considerable numbers of recent studies suggest that underreporting of energy intake is an important limitation of nutrient intake assessment as obtained by self-reported food intake instruments. Underreporting has been shown both in civilian and military populations. Schoeller et al. (1990) have demonstrated that overweight individuals, in particular, significantly underreport their food intake. For instance middle-aged women (29 percent body fat) who were maintaining body weight reported energy intakes (as determined by self-reported food consumption instruments) that were 25 percent lower than values derived from DLW (Martin et al., in press) (Figure 11-1). In this study, individuals were carefully instructed and repeatedly reminded to be thorough in the self-reporting of food intakes. Military personnel who were training for jungle warfare similarly reported caloric intakes that were about 85 percent of expenditure levels as determined using DLW (Forbes et al., 1989).

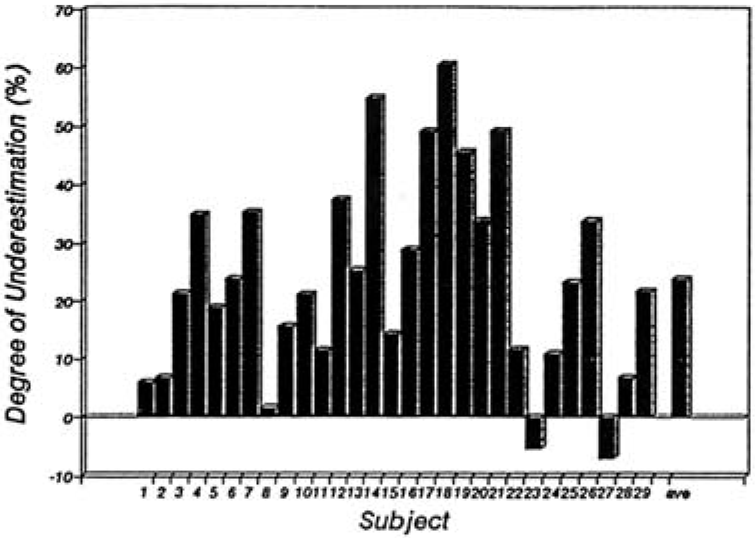

FIGURE 11-1 Degree of underreporting in middle-aged women where energy expenditure was determined by doubly labeled water, and energy intake was determined by self-reported food intake record analysis. SOURCE: Adapted from Martin et al. (in press).

Findings of a study by the authors have shown significant underreporting in subjects who maintained relatively constant body weight over a 10-d period in the Arctic (Jones et al., 1993). Subjects were instructed to record each evening all food and drink consumed throughout the day and were prompted to be thorough in their recollection at each occasion. Compared with mean expenditure levels of about 4,300 kcal/d, self-reported caloric intakes derived from food records averaged only 61 percent of expenditure (Figure 11-2). Some of this difference might be attributable to small changes in body composition. However, because body composition remained reasonably stable, most of the discrepancy was attributable to underreporting. Thus, particularly for experiments conducted in harsh environments, individual energy requirements are better determined using approaches based on energy expenditure, rather than those based on intake and balance.

Underreporting of actual food intakes may occur for several reasons in hostile environments. First, subjects are exposed to stress, which may cause them to forget to record certain items. Second, scheduling of operations may disrupt the routine of camp or garrison life in such a way that reporting opportunities are less frequent. Third, at some stage during the test, individuals may have consumed foods or beverages that they did not reveal to authorities. Military troops during intensive training are often not highly motivated study participants.

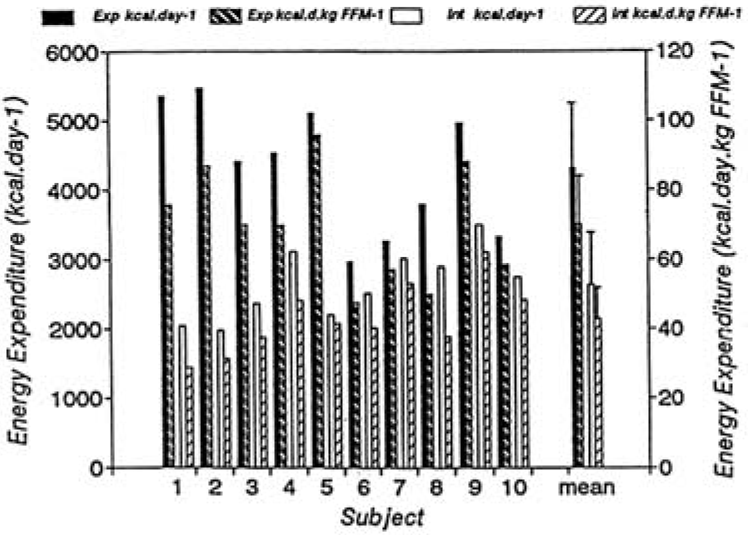

FIGURE 11-2 Comparison of energy expenditure (Exp.) calculated by doubly labeled water (DLW) with self-reported energy intake (Int.) in DLW group (infantrymen during a cold-weather field exercise on Baffin Island, Northwest Territory, Canada). Values are mean ± SD per total body weight and per kg FFM. FFM, fat-free mass. SOURCE: Jones et al. (1993), used with permission.

Studies Measuring Energy Requirements Using Energy Expenditure Data

To determine with accuracy the overall caloric needs of military troops in the cold, methods are required that provide integrative, accurate measures of energy expenditure over a representative time period. One such method is DLW, which is well suited to such field studies in that it is noninvasive, does not involve use of radio tracers, and requires minimal subject compliance. The procedure utilizes the difference in rate of elimination from the body between oxygen and hydrogen, measured following administration of water, isotopically labeled with a heavy isotope of oxygen (^{18}O) and hydrogen (deuterium) (D), to calculate the rate of carbon dioxide production of an individual. Caloric expenditure can be determined from carbon dioxide production, given knowledge of the food quotient or respiratory quotient of the subject. This technique has been validated against the methods of respiratory gas exchange (Ravussin et al., 1991; Schoeller and Webb, 1984; Westerterp et al., 1988) and caloric intake balance (Jones and Leitch, 1993; Schoeller et al., 1986) in a number of laboratories. The DLW technique was found to be accurate to within 2 to 6 percent.

At least four experiments have determined total integrated energy expenditure in troops exposed to cold conditions. First, DeLany et al. (1989)

used DLW to determine energy expenditure in relatively sedentary troops exposed to outdoor temperatures ranging from 30° to 61°F (-1° to 16°C). Expenditure levels averaged 3,400 kcal/d, or about 45 kcal per kg body weight per day.

In another experiment in a more severe cold setting, Hoyt et al. (1991) reported energy expenditure for 23 Marines during strenuous exercise in a higher-altitude operation in Bridgeport, California (7,218 ft [2,200 m]). Ambient temperatures ranged from 5° to 55°F (-15° to 13°C). Energy expenditure measured by DLW over the entire 10-d period averaged 4,919 kcal/d, with a peak level of over 7,000 kcal/d during the initial highly strenuous portion of the study. During less extreme activities, energy expenditure averaged 3,632 kcal/d. Over the entire study these subjects' caloric requirements were 62 kcal per kg body weight per day as measured using DLW. The subjects also lost an average of 2.5 kg of body weight, with 1.7 kg loss as fat.

Third, in a more severely cold environment, troops at Fort Greely, Alaska were observed to have expended 4,253 kcal/d as measured by DLW during a 10-d trial period where the average temperature was -18°F (-28°C) (King et al., 1993). Troops were fairly active over the test period. This result represents an expenditure level of 54 kcal per kg body weight per day. Subjects lost about 1 kg of fat mass on this training exercise.

Studies in this laboratory have determined caloric expenditure and requirements at temperatures colder or similar to those of the Fort Greely experiment (Jones et al., 1993). Energy expenditure and requirements were determined in a group of Canadian infantrymen during a cold-weather field exercise on Baffin Island, Northwest Territory, Canada. During most of the experiment the outdoor temperature rarely exceeded -13°F (-25°C), with the average temperature remaining below -22°F (-30°C). Subjects slept in tents where the temperature ranged from below freezing to 59°F (15°C) and on one or two nights slept in unheated igloos. The subjects performed outdoor exercises during this period which ranged in severity (Table 11-2); however, most of these activities were not highly strenuous. Mean caloric expenditure level was 4,317 kcal/d or 57 kcal per kg body weight per day. This expenditure was about equivalent to that provided in a single day's standard-issue individual meal pack (IMP) rations (4,350 kcal/d) if all foods were consumed.

In this trial a fairly high level of sharing of ration pack items was casually observed. Individuals with caloric requirements below the average may have passed uneaten food items to those with higher needs. For this reason, it may not be necessary to provide energy at a level that meets the needs of all individuals within the population. Encouraging food-sharing practices among personnel at mealtime permits the standard to be set close to the population mean requirement, while saving food production and transport costs and reducing waste. Food sharing also helps ensure that individual needs for nutrients other than energy are met, as levels of consumption are, to a certain extent, tied to energy intake.

TABLE 11-2 Type and Duration of Activities of Infantrymen during an Arctic Field Exercise

Study Day	Activity and Average Duration
0	Arrival at hanger
1	Deployment to camp (4), camp setup (6)
2	Skiing (3), ski-during (3), compass training (3)
3	Skiing (3), ski-during (3), compass training (3)
4	Snowmobiling-hunting (5)
5	Snowmobiling-hunting (5)
6	Ski-during (3), snowmobiling (2), ice-fishing (5), hunting (3)
7	Igloo building (8), hunting (3)
8	Snowmobiling (3), return to hanger (4)
9	Public relations exercises (6)
10	Public relations exercises (6)

NOTE: Average duration of each activity in hours is given in parentheses. Ski-during is a troop transport system involving skiers towed behind skidoos. Public relations exercises were held at Iqaluit, Baffin Island, Northwest Territory, Canada.
SOURCE: Jones et al. (1993), used with permission.

Mechanism of Action of Effects of Cold on Metabolism

Johnson and Kark (1947) were the first to speculate on the cause of increased energy requirements in the cold. They suggested that greater energy needs resulted from the hobbling effect of winter terrain, clothing and equipment, as well as the added heat required to maintain the body's thermal equilibrium. Subsequent studies have provided data to support these original suggestions.

Locomotion in snow is energy-intensive due to terrain and friction-related factors. A number of older experiments have characterized the energy cost of specific activities in snow and cold conditions. For instance, the energy costs of snowshoeing and skiing have been reported to be quite significant, though variable, depending on snow conditions and geography (McCarroll et al., 1979).

In addition to the energy cost of activity itself, heavy clothing worn in the cold restricts movement. Indeed the hobbling influence of winter clothing was determined to be a factor contributing to increased energy costs in studies by Gray et al. (1951). They demonstrated that caloric output for a given amount of external work performed at a constant temperature increased about 10 percent between light and heavy clothing, regardless of the environmental temperature. Also, the caloric output for a given amount of external work performed in a given outfit of clothing increased about 4 percent from a working temperature of 90°F (32°C) to one of -15°F (-26°C). These findings suggest that the influence of temperature on energy metabolism involves both hobbling and other factors.

Similarly, and more recently, Teitlebaum and Goldman (1972) demonstrated that the energy cost expended walking while wearing a multilayered arctic clothing system was greater than that expended when subjects carried an equivalent weight as a single-layer outfit plus a belt with added weight. An increase of 16 percent in energy cost was measured in individuals carrying out the same activity while wearing the clothing over that of the belt. This increase was attributed to friction drag between layers of material and interference with movement of body joints because of the bulky clothes. However, the room temperature was 63°F (17°C), which may have produced some overheating in the more heavily dressed subjects.

The second factor that potentially contributes to increased energy requirement in the cold is the need to maintain thermoregulation. It has been established that exposure to cold increases oxygen consumption and metabolic rate (Gray et al., 1951; Timmons et al., 1985). The importance of this second component will depend on such factors as adequacy of thermal insulation of clothing worn to protect against heat loss, as well as environmental temperature, windchill, and duration of cold exposure. It has been suggested that the lack of increased energy requirement observed in some studies is the result of subjects spending long periods indoors (Rodahl, 1954). Thus, when specific logs of activity are not maintained (that is, not only type and duration of activity, but environmental conditions as well), the results of energy requirement studies are of questionable usefulness in determining energy needs under field conditions. This is particularly true for studies based on energy intake data.

OPTIMAL MACRONUTRIENT RATIO IN THE COLD

The second question that must be addressed concerning macronutrient needs in the cold is the pattern (or proportion) of macronutrients required to optimize survival and performance. This question is important because energy sources differ in caloric density. Calories stored as fat provide a higher energy level than the same mass of carbohydrate. If performance is unaltered by the macronutrient ratio, then rations providing a higher percentage of calories as fat would be more compact and lighter.

In addition, association of enhanced thermogenesis with a particular macronutrient may play a role in selecting the optimal dietary blend of nutrients. In this context, it is interesting to examine the diet of indigenous peoples of the North. Hoygaard (1941) reported that primitive Eskimos apparently prefer a diet comprised of almost one-half fat and one-half protein. Eskimos maintain that fat is required to keep them warm on long journeys. Whether this blend of macronutrients is one that possesses thermogenic properties for Eskimos, or whether it is actually the only dietary macronutrient source available during the winter is a provocative question.

Among military personnel, Johnson and Kark (1947) showed that troops consumed a consistent ratio of macronutrients regardless of environmental temperature (Table 11-3). Similarly, Swain et al. (1949) compiled available data to demonstrate that the ratio of protein, fat, and carbohydrate that was consumed voluntarily by troops in the Arctic did not vary significantly from that of troops in other environments (Table 11-4). The proportion of calories

TABLE 11-3 Caloric Consumption and Ratio of Macronutrients Eaten by Representative Groups of Troops in Different Environments

			Percentage of Calories Provided by		
Location, Troops	Environment	Caloric Intake/ Day (kcal)	Protein	Fat	Carbo-hydrate
Canada, mobile force "Musk Ox"	Arctic and subarctic	4,400	11	40	49
U.S.A., ground troops	Temperate	3,800	13	43	44
Colorado Rockies, infantry	Temperate mountain (9,000 ft [2,743 m])	3,900	13	34	53
Pacific Islands, ground troops	Tropics	3,400	13	33	54
Pacific Islands, infantry	Tropics	3,200	12	34	54

SOURCE: Reprinted with permission from R.E. Johnson and R.M. Kark, "Environment and food intake in man," Science 105:378–379. Copyright 1947, American Association for the Advancement of Science.

obtained from each macronutrient was similar in arctic, temperate, and tropical diets. Thus, the tendency of Eskimos to consume high-fat and -protein diets in cold climates was not replicated among military personnel. More recently, King et al. (1993) have shown that troops stationed at Fort Greely, Alaska during winter consumed about 16 percent protein, 37 percent fat, and 48 percent carbohydrate. Also Hoyt et al. (1991) reported that subjects fed field rations consumed an average of 13 percent, 38 percent, and 49 percent of total energy as protein, fat, and carbohydrate, respectively.

TABLE 11-4 Percentage of Macronutrients Eaten by Troops in Various Environments

	Proportion of Macronutrient (%)		
Environment, Location	Protein	Fat	Carbohydrate
Arctic and subarctic areas			
Fort Churchill	13	37	50
Fort Churchill	12	41	47
Fort Churchill	13	42	45
Exercise "Musk Ox"	13	42	45
Temperate areas			
U.S. Army Zone of Interior*	13	43	44
U.S. Army Zone of Interior, mountain troops	14	44	42
Tropical areas			
U.S. Army on Guadalcanal	13	34	53
U.S. Army on Hawaii	13	33	54
U.S. Army on Guam	13	32	55
U.S. Army on Iwo Jima	13	33	54
U.S. Army on Luzon, Philippines	12	34	54

* Zone of Interior, 1941–1943: accumulated data on various phases of messing operations in the training camps of the U.S. Army. The data were obtained over short, unannounced periods of time ranging from 6–10 days in each mess. The results of each post were reported as a 30-d average of these individual surveys, and are considered to provide accurate representative information on average food consumption. 50 posts and 455 messes were surveyed in this manner.

SOURCE: Swain et al., J. Nutrition, 38:63–72, 1949, used with permission.

In summary, there appears to be no tendency on the part of military personnel toward a deliberate shift in the pattern of macronutrients consumed in colder climates. However, consistent with the high-fat diet of the indigenous cultures of the North, there is a suggestion that the macronutrient mixture is modified in the cold. Timmons et al. (1985) showed a decrease in respiratory exchange ratio in individuals exposed to 14°F (-10°C) for 90 minutes, indicating a preferential fat oxidation as much as 41 percent higher than that of controls. In contrast, Vallerand and Jacobs (1989) showed that carbohydrate oxidation was elevated by as much as 588 percent when seven healthy male volunteers, wearing only shorts, were exposed to 50°F (10°C) temperature with a 1 m/s wind.

The reason for the disparity between the results of these studies remains unclear. One possibility that cannot be ruled out is that exercise was a factor in only one of these studies. Finally, Issekutz et al. (1962) showed that a full day of cold exposure resulted in a significant increase in the production of urea, suggesting that protein utilization may become more relevant in prolonged exposure to cold. Continuing efforts should be undertaken to determine further (1) the relative macronutrient requirements to optimize performance and (2) the most acceptable and palatable nutrient ratio. Results of such studies will help to prevent weight loss during highly strenuous cold weather activities.

AUTHORS' CONCLUSIONS AND RECOMMENDATIONS

Although the majority of research in which energy requirement determination is based on measured or reported food intake is consistent with an increased requirement for energy in colder climates, some studies have found no difference compared to more temperate environments. The factors that contribute to this lack of difference include possible underreporting by study subjects and prolonged time spent indoors at warmer temperatures and low activity levels.

To avoid errors that may arise from the underreporting of food intake, energy requirement should be determined by measuring expenditure directly. Several studies that examined expenditure report a range of 45 to 62 kcal per kg body weight per day. Variation in this figure is likely due to both degree of cold and extent of physical activity. Under sedentary conditions in the cold, requirements may range from 3,632 to 4,317 kcal/d or about 46 to 57 kcal per kg body weight per day. In more highly strenuous circumstances in the cold, requirements of 4,200 to around 5,000 kcal/d, or 54 to 62 kcal per kg body weight per day, may be required. The estimate of energy requirement for strenuous circumstances is not out of line with current MRDAs of 4,500 kcal/d or 56 kcal per kg body weight per day for a soldier weighing 80 kg (AR 40-25, 1985). During low-activity situations, particularly in less cold environments, the mean requirement may decrease to almost 900 kcal/d below the current MRDA for cold weather. However, in either circumstance, it is likely that the distribution of requirements will result in the need for some individuals to exceed the MRDA for cold environments.

Sharing of foods between personnel should be encouraged to ensure that the requirements of all individuals are met. Food sharing will also reduce food waste and the labor involved in transporting and preparing foods.

Studies show a weight balance difference between troops in garrison and troops in actual field studies. In garrison, troops reside in a more insulated, low-activity environment, causing no noticeable weight loss. Conversely, troops in field studies are engaged in strenuous activities within the natural arctic environment. This environment causes accelerated weight loss due to increased energy expenditure.

Macronutrient preference does not appear to change with cold climate in settings where subjects freely select their food. In the absence of adequate clothing, carbohydrate oxidation increases substantially during exercise, although increases in fat oxidation have also been reported in response to cold in exercise situations. Further study is required to elucidate the interaction of cold and physical activity on macronutrient utilization. Regardless of which macronutrient is oxidized preferentially in cold conditions, a major objective of field feeding studies should be to minimize body weight loss and, if possible, performance capacity. Thus, given that there is no natural shift in macronutrient intakes in the cold, food acceptability in the field is more important than macronutrient ratio, particularly in high-activity situations. Food should be prepared in as palatable a form as possible to minimize the gap between level of caloric expenditure and that of intake.

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12

Cold Exposure, Appetite, and Energy Balance

Jacques A. LeBlanc[1]

INTRODUCTION

When energy intake is the same as the energy expenditure, body weight remains constant in spite of continuous body energy reserve turnover (Figure 12-1). Appetite, which plays a prominent role in this system, is itself under the influence of many internal and external factors. Situations that increase energy expenditure, such as exercise and exposure to cold, stimulate appetite and cause an enhanced energy intake. There is also some evidence indicating that the climate under which people live may also influence appetite. In a warm environment, energy intake has been shown to be curtailed not only because of reduced physical activity but also because of some influence of climate on appetite (Adolph, 1954). The common belief that appetite and energy intake are stimulated by the cold is based on experimental evidence and anecdotal hearsay. The present review will analyze the components of energy expenditure and intake in cold regions and identify various factors that may influence appetite.

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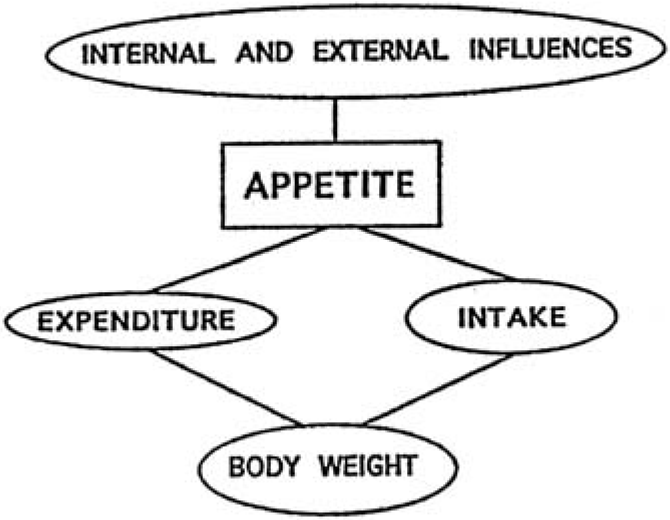

FIGURE 12-1 Schematic representation of interactions between appetite and components of energy balance. SOURCE: J. A. LeBlanc (Unpublished data, Laval University, Quebec City, 1993).

COMPONENTS OF ENERGY EXPENDITURE IN THE COLD

Basal Metabolic Rate

When the total energy expenditure for a typical subject is 2,750 kcal/d, approximately 60 percent of this total energy is due to basal metabolic rate (BMR) (1,500 kcal). Some years ago it was reported that Eskimos had higher BMR than Caucasians. It was suggested that this might be due to an increased thyroid activity induced by cold (Rodahl, 1952a, b). Subsequent work disproved this hypothesis. It was shown that the higher BMR of Eskimos was due to the high protein content of their diet. When Eskimos were made to eat a mixed diet comparable to the one consumed by Caucasian subjects, BMRs were the same for the two groups (Rodahl, 1952a, 1952b, 1955).

Thermogenic Effect of Feeding

The digestion, absorption, and storage of ingested nutrients require energy. The level of expenditure, known as the thermogenic effect of feeding (TEF), is different depending on whether carbohydrates, proteins, or lipids are consumed (Unpublished data, J. A. LeBlanc, Laval University, Quebec City, 1992) (Figure 12-2). For a comparable calorie intake, the TEF is small for fat, intermediary for carbohydrates, and high for proteins. In addition, because of slower absorption, the TEF of proteins may last up to 5 to 6 hours (Jéquier, 1993). For that reason, if a person is to sleep in an unheated tent under arctic winter conditions, the ingestion of proteins at the end of the day may serve—because of their large and long-lasting thermogenic action—as an adjuvant in achieving thermal comfort for part of the night. In contrast, carbohydrates, by supplying energy that is quickly absorbed and readily available for various body activities, would be most useful at the beginning and middle of the day. Fat as a source of utilizable energy would be useful only in situations where there is a calorie deficit. When fed in excess, as part of a mixed diet, fat is not oxidized and is almost entirely stored in fat depots. The belief that large amounts of fat are required in the cold is not substantiated by some recent findings (Flatt et al., 1985; Schutz et al., 1989).

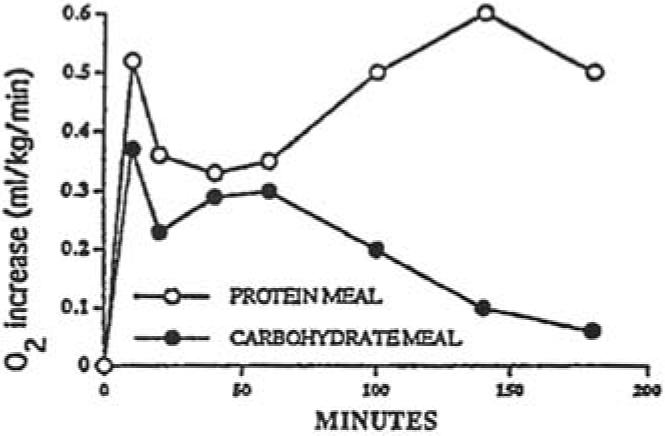

FIGURE 12-2 Thermogenic effect of feeding carbohydrate and protein meals with relation to time. SOURCE: J. A. LeBlanc (Unpublished data, Laval University, Quebec City, 1990).

Thermogenic Effect of Cold

To discuss the importance of the thermogenic effect of cold (TEC) and the thermogenic effect of exercise in the cold, the results of an experiment that was undertaken quite some time ago will be used to introduce the subject (LeBlanc, 1957b). While carrying a packsack and wearing full arctic clothing, a group of soldiers took part in an 18-mi (29-km) march on a road covered with hard snow. They started in the morning as the sun was rising and finished their walk about 2 hours after sunset. During this period, the air temperature remained around -20°C (-4°F), and the wind was low. Heart rate measurements were made throughout the expedition.

Results showed that, in spite of the fact that the rate of walking declined steadily, a gradual elevation of heart rate took place up to mile 13. After that, heart rate fell gradually and reached initial values by the end of the expedition (Figure 12-3). These variations could not be explained by external temperature, which remained constant throughout the day. The curve for solar radiation, however, followed exactly the same pattern as that of heart rate. This suggests that when the sun was out, the subjects became overheated, causing heart rate to go up. Then when the sun disappeared, they cooled down, and heart rates fell.

It was concluded that during this expedition the subjects suffered from heat, not cold, exposure even though the temperature was -20°C (-4°F). With the amount of clothing they were wearing (between 5 and 6 clo[2]) and at the level of activity at which they were functioning (i.e., equivalent to about three times the resting values), subjects would have been relatively comfortable at temperatures as low as -40°C (-40°F).

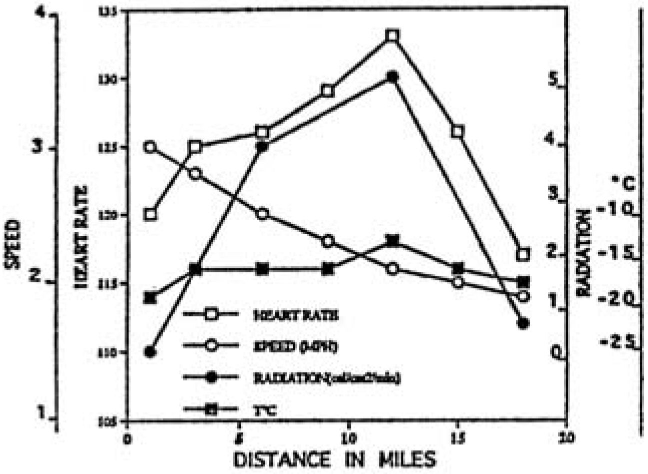

FIGURE 12-3 Heart rate variations in a group of soldiers during an 29-km (18-mi) walk in the Arctic. The outdoor temperature, solar radiation, and speed of movement of the subjects are also given.
SOURCE: LeBlanc (1957b), used with permission.

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[2] The clo is a unit of insulation which corresponds to the clothing required for a resting person to be comfortable in a room at 21°C (70°F) with less than 50 percent relative humidity. It is equivalent to a business suit or one-quarter inch clothing.

It seems then that the TEC is small in the majority of conditions. However, on occasion (i.e., accidentally or when sleep is in an unheated tent) the TEC may become an important and even threatening factor in extreme cold situations. Considering the overall effect of cold, in general the most prevailing hazardous effect of low temperatures is the danger of freezing parts of the face and extremities rather than being victim to insufficient energy production and becoming hypothermic.

Thermogenic Effect of Exercise

Oxygen consumption measurements were made over a period of 24 hours on a group of soldiers during a military exercise in the Canadian Arctic (Welch et al., 1958). For standard tasks and activities comparable to those carried out in a temperate climate, it was found that the total energy expenditure for 1 day was about 3,500 kcal, a value comparable to similar activities in warmer regions. One would expect an excess thermogenic effect on exercise (TEE) in the cold because of the hobbling effect of clothing, which has been shown to cause an increment of about 10 to 15 percent (Teitlebaum and Goldman, 1972). This effect, however, is not very important since for a person walking 15 miles (24.2 km) at an estimated cost of 100 kcal/mile (61.3 kcal/km), the extra energy required would amount to approximately 200 kcal.

Another factor that could affect the TEE is the condition of the terrain. In the Arctic, the absence of trees makes traveling much easier, and since the snow is hard, skis and toboggans can be used. Further south, because of the presence of trees, the snow is soft, and snowshoes have to be used instead of skis, which means greater energy expenditure. Thus, for given activities, the TEE in arctic regions is probably the same if not lower than that in temperate zones.

MEASUREMENTS OF CALORIE INTAKE ON ARCTIC EXPEDITIONS

The caloric content of military arctic rations is based on measurements of food intake during various expeditions. An analysis of the findings is made difficult by the fact that these expeditions were not necessarily planned for research purposes. For that reason the TEE varies a great deal, and it is never measured. The reports simply state whether exercise was light, moderate, or heavy.

Figure 12-4 summarizes the results of some of these expeditions. Rodahl (1958) estimated that Eskimos, when they hunted with dogs and lived in igloos, consumed about 3,000 kcal/d. Considering the weight of these people, which would be about 60 kg, an extrapolated value for a 70-kg man would be about 3,500 kcal.

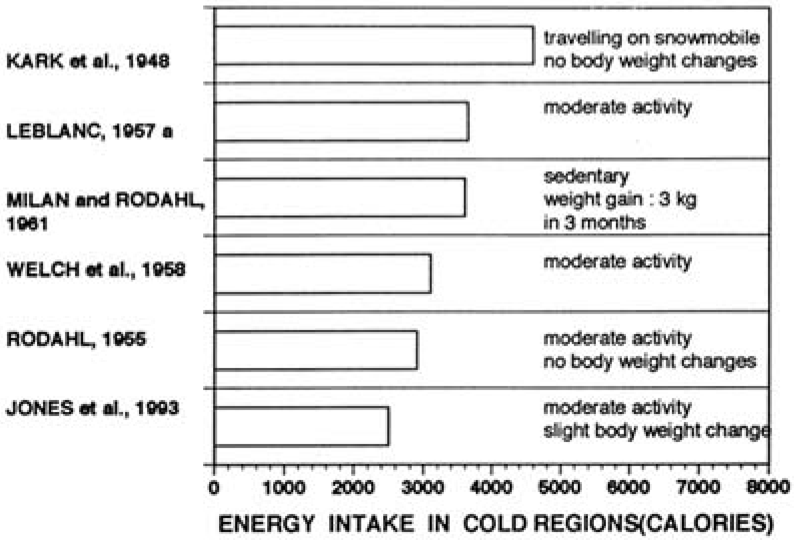

FIGURE 12-4 Energy intake reports in various arctic expeditions. For each study the method used for food consumption measurements and the level of activity are indicated.

Welch et al. (1958), as mentioned above, made accurate measurements of expenditures for moderately active soldiers and arrived at a total energy expenditure of 3,300 kcal.

Milan and Rodahl (1961) measured food intake for long periods in an antarctic expedition and reported an average intake of 3,500 kcal. Because the subjects lived indoors and were sedentary, the intake was excessive and led to an increase of body weight of about 200 g/wk.

Kark et al. (1948) made some estimates of caloric intake in a joint 3-month Canadian and American expedition in the Canadian North. It was a multipurpose exercise that entailed testing equipment and machinery. Food intake was estimated for soldiers traveling most of the time by snowmobile. It was reported that 4,400 kcal/d were consumed. Because there was no body weight change during the expedition, the results suggest that the arctic ration should contain that number of calories. Considering the level of activity of these subjects and the fact that the TEC was negligible, the reported food intake would seem to be quite high. Regarding the method used for arriving at these values, "estimates of food consumption and wastage were made from records of food supplied (21,000 calories a day for 4 men) and from dietary histories taken from the men" (p. 74). In other words, it was left to each man to say how much he ate.

It has been argued in a recent review that this method is not always reliable and may lead to substantial errors (Schoeller et al., 1990). What may have happened is that part of the ration was thrown away, as is commonly done in the field, but it was reported as having been eaten. This suggestion is made because it is estimated, based on the studies already mentioned and considering the low level of physical activity involved in driving vehicles, that the food intake to maintain constant body weight should be about 3,000 kcal or below. This is the expenditure of a 70-kg man engaged in daily activities equivalent to about 1,000 kcal (walking 10 miles or 16 km). The daily expenditure for driving a vehicle is certainly not higher than that. This would mean that two-thirds of the ration was sufficient to maintain an equilibrated energy balance and that the other third was discarded.

A more recent study was described by Jones et al. (1993) in which questionnaires also were used to estimate food intake. Completely opposite results were obtained. During a 10-d arctic expedition, the energy intake of moderately active subjects was reported to be 2,600 kcal/d. The authors concluded that the use of questionnaires to estimate food intake is often unreliable and that it led in this specific study to underestimation of real values.

APPETITE AND BODY WEIGHT GAIN IN ARCTIC EXPEDITIONS

In the six studies mentioned in Figure 12-5, body weight was taken before and after the subjects had stayed in arctic or antarctic regions for periods of 3 to 12 months. An average body weight gain of 1 kg/month was observed in these expeditions. The excess energy intake causing this gain is explained by changes in appetite. The possible factors responsible for an enhanced appetite in cold regions include:

- palatability of food,
- cold temperature,
- season of the year,
- emotional factors (e.g., loneliness), and
- changes in physical activity habits.

Palatability of Food

The palatability of food exerts an important influence on food intake. This is illustrated by a recent report in which the subcutaneous fat layer of young

Eskimos (aged 9 to 19) was shown to be twice as large in 1990 as it was in 1970 (Rode and Shephard, 1992). This difference is explained by the fact that in 1970 these youngsters were fed the traditional Eskimo diet characterized by high protein and fat content and the absence of carbohydrates, whereas in 1990 they ate typical modern western food such as sweets, popcorn, chocolate bars, ice cream, and soft drinks. It is a good example of what a "cafeteria" diet can do to humans. For Caucasian populations that move to the Arctic, it is doubtful that the food becomes more appetizing, especially if it is fed in the form of dehydrated rations.

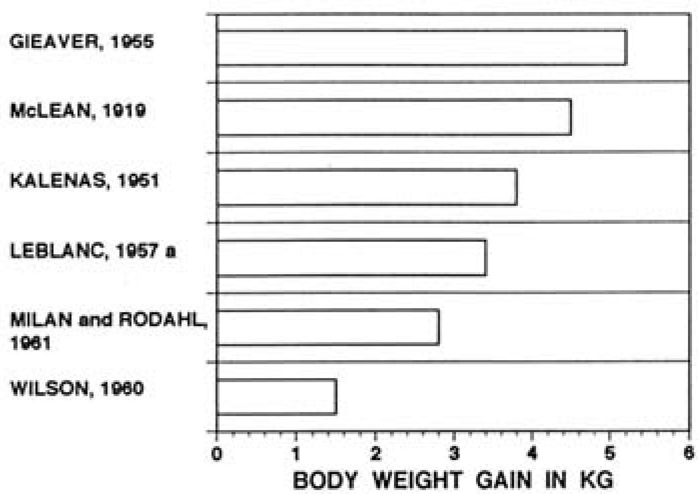

FIGURE 12-5 Body weight gain in various arctic expeditions lasting between 3 and 12 months.

Cold Temperature

Contrary to heat, cold exposure is generally considered as a stimulant of appetite. However, two studies—one by Lewis et al. (1960) in the Arctic and the other by Milan and Rodahl (1961) in the Antarctic—do not seem to substantiate this possibility (Figure 12-6). Both studies have shown large body weight gain between the end of the summer when subjects arrived from warmer climates and the beginning of the winter. However, during the colder months the body weight remained stable, indicating that food intake was not excessive and that appetite was not overly-stimulated. The conclusion from these studies is that cold temperature, in itself, does not have a direct influence on food intake.

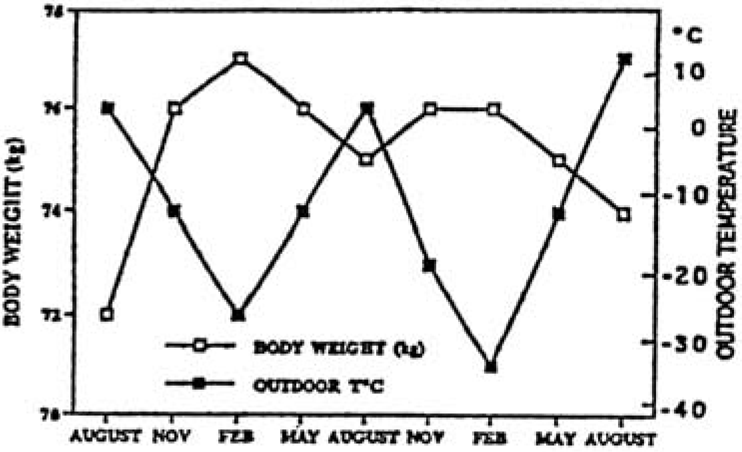

FIGURE 12-6 Body weight and outdoor temperature variations in a 2-yr expedition in North Greenland.
SOURCE: Lewis et al. (1960), used with permission.

Season of the Year

It has been reported that some people during the winter season become depressed and start eating more. This condition, described as the SAD (seasonal affective disorder) syndrome, has been related to the shortening of the days during the winter season (Rosenthal et al., 1985). Some improvement in symptoms has been reported when these persons are exposed to additional daylight. This syndrome is rather rare in a large population, and for that reason it is not likely to explain the increase in body weight commonly observed in large groups of people spending the winter in cold regions as described above.

Emotional Factors

When soldiers are transferred from a southern region to the Arctic to spend the winter, they are suddenly exposed to an unusual environment. Away from friends and family, they are confined to restricted quarters with persons that they do not know. Having few activities besides their work, they may get lonely and bored and may eventually develop a tendency to overeat.

Physical Activity

Changes in physical activity habits may also be related to the excess energy intake reported in cold regions. It is common to observe a rapid weight gain in athletes, or in people engaged in a sustained physical activity program, when they suddenly become sedentary (Marti and Howald, 1990). This happens because the energy intake remains elevated for some time even if the expenditure is reduced. The reciprocal situation is observed when sedentary people engage in regular physical activities. At first a rather accelerated weight loss is often described, which may be due to the fact that energy intake increases immediately to meet the new requirements. In other words it takes time for the appetite to adjust to the changes in energy expenditure. This situation applies to people who move from southern regions at the end of the summer, where they were engaged in various physical activities, to northern regions, where they become more sedentary. Following the same reasoning, when these same people become more active the following summer, they should lose weight and return to their previous level.

The increase in body weight observed in cold regions has been observed in many groups of people. Apparently, it is a normal psychophysiological response to a specific environment. It is comparable to what happens in nature in the fall when wild animals start eating more in order to accumulate body fat reserves as a source of energy and additional insulation for the winter. The mechanism involved for humans, however, may not necessarily be comparable in nature.

AUTHOR'S CONCLUSIONS

The possibility of frostbite and hypothermia are always present in cold regions. For these reasons it is important to be completely familiar with the various parts of the clothing and to pay special attention to the protection of the face and the extremities. On the other hand, perspiration should be avoided whenever possible in a cold environment. The sweat, which accumulates in garments without proper ventilation while exercising, may ice up when the soldier becomes inactive, a process that may significantly reduce the insulating properties of the clothing. In addition, it is also important to have an adequate supply of food as palatable as possible in order to maintain a positive energy balance and good morale.

With proper clothing, the effect of cold, per se, on caloric requirements and appetite does not seem to be very important.

The thermic effect of exercise seems to be somewhat higher in colder regions due to the hobbling effect of clothing. Upon arrival in the Arctic and Antarctic a person's appetite is stimulated, resulting in enhanced caloric intake and body weight gain. The reduction of physical activity, the diminution of daylight, and some emotional factors may explain the stimulation of appetite. Further work is needed, however, to evaluate these possibilities adequately.

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13

Effects of Cold and Altitude on Vitamin and Mineral Requirements

Robert D. Reynolds[1]

INTRODUCTION

The importance of adequate caloric and fluid intake must be rated at least as highly as that of oxygen

(Pugh, 1965, p. 314).

Although Pugh limited his statement about the importance of nutrition at high altitudes to that of energy and fluids, the same concept can be extended to all of the nutrients. However, a superficial perusal of the published literature on the effects of altitude demonstrates that the preponderance of research efforts has been directed to understanding the impact of a limited oxygen supply on human performance. With respect to nutrition, there has been only a modest effort to determine energy intake and to determine the preferred mix of energy derived from carbohydrate, fat, and protein. Unfortunately, a paucity of efforts has been expended to determine the effects of cold and altitude on vitamin and mineral requirements even though these micronutrients are absolutely essential in converting the food consumed into the energy that is

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required to function in these extreme conditions. These micronutrients are no less important than is oxygen. It just takes longer to become deficient in them than it does for oxygen.

In the past, U.S. Army recommendations regarding micronutrient intake for work in cold and high-altitude environments have been limited to three areas of consideration. They have suggested the need for increased requirements for vitamins and minerals to accommodate the caloric requirement of cold and high-altitude operations; a high altitude-induced increase in the requirement for vitamins A, E, and C, specifically; and the need for caution in the use of vitamin and mineral supplements to attempt to prevent cold stress (Thomas et al., 1993a, b; Askew, 1989). However, increased intakes have not been recommended.

Under any environmental condition, it is necessary to measure accurately intake, excretion, and several indices of status to determine nutrient requirements. A complete set of these indices has not been measured for any of the vitamins or minerals for persons living or working in the cold or at high altitudes. Therefore, it is not possible to report here the actual requirements for any of these micronutrients as affected by prolonged exposure to cold or high-altitude environments.

The approach used in this chapter will be to present a short statement on the major role of each vitamin and mineral in human metabolism, followed by a review of reported dietary intakes or status in various populations living or working in cold climates or at moderate to high altitudes. Finally, for each vitamin and mineral, a micronutrient intake goal will be suggested and compared to the current Recommended Dietary Allowance (RDA) (NRC, 1989), the Military Recommended Dietary Allowance (MRDA) (AR 40-25, 1985), and the anticipated intake of each nutrient provided by the Ration, Cold Weather (RCW) as formulated by the U.S. military. Each micronutrient intake goal has been derived by the author from a systematic reading of the relevant published literature and from personal consideration of widely-accepted, general nutrition principles.

Construction of the micronutrient intake goals assumes that the individuals using it are in generally good health and nutrient status prior to beginning the expedition or maneuver. Thus, the aim of the micronutrient intake goals is to keep the individuals healthy rather than to make them healthy. Construction of the micronutrient intake goals should not be constrained by the limitations of the micronutrient availability from foods in the amount normally consumed. Therefore, use of the terms *dietary* or *dietary intake* as they relate to the micronutrient intake goals are not necessarily appropriate.

ESTIMATED ENERGY INTAKES

Many of the nutrients, especially the B vitamins, are involved with the production of energy via numerous steps in the Krebs citric acid cycle. Thus, consideration will be given in the construction of the micronutrient intake goal to the estimated intakes of total food energy by those persons engaged in strenuous work in the cold or at high altitudes.

It has been estimated that in the cold, the average energy consumption by U.S. military soldiers who self-selected foods from the RCW was 2,800 kcal/d, and from the Meal, Ready-to-Eat (four meals) was 3,000 kcal/d (Personal communication, R. W. Hoyt, U.S. Army Research Institute of Environmental Medicine, Natick, Mass., 1994). The current MRDA for energy in cold weather is 4,500 kcal/d (AR 40-25, 1985). Jones and Lee (see Chapter 11 in this volume) estimate that energy requirements (expenditure) for soldiers range between 4,200 and 5,000 kcal/d during periods of physical exertion in the cold. The negative difference between energy intakes and expenditures thereby results in loss of body weight.

During the conduct of Operation Everest II with simulated altitudes up to 8,848 m (29,000 ft), subjects consumed between 2,500 and 3,000 kcal/d, with 45 percent of the energy being provided by carbohydrates (Rose et al., 1987). Estimates of energy expenditure between 4,000 and 5,000 kcal/d have been reported for those engaged in strenuous exertion while at high altitudes (Reynolds et al., 1992). Therefore, for the construction of the micronutrient intake goal, an estimated average energy intake of 4,500 kcal/d will be assumed in order to keep the personnel in energy balance. Any deficit between energy intake and expenditure must result in loss of body tissue.

FAT-SOLUBLE VITAMINS

Vitamin A

Functions

Vitamin A is essential for the visual process, differentiation of epithelial cells, maintenance of the immune system, and integrity of the skin. The normal needs for vitamin A can be met by consumption of either preformed vitamin A or β-carotene, with the latter having a considerably lower toxicity (NRC, 1989).

Intake and Status

Of the fat-soluble vitamins, vitamin A has caused the most problems for polar explorers. Shearman (1978) presented a graphic description of vitamin A toxicity experienced by members of the three-man, 1912–1913 Mawson Australian Antarctic expedition, in which two men died, with only Sir Douglas Mawson surviving. Early in the expedition, Lt. Ninnis and one of the sleds loaded with most of the food fell into a crevasse and disappeared. Over the next 23 days, Xavier Mertz and Mawson were forced to reduce their daily food intake from the normal 34 oz (971 g) to 14 oz (400 g), much of which was dog meat that became available as each dog died (Mawson, 1915). As Mawson reported in his journal, "It was a happy relief when the liver appeared; even if little else could be said for its flavor, it was easily chewed and demolished" (Shearman, 1978 quoting Mawson, 1915, p. 284).

Over a 9-d period, Mertz's health rapidly deteriorated, culminating in his death, with intervening severe bouts of dysentery, fecal incontinence, depression, delirium, peeling skin, and loss of hair—all symptoms characteristic of acute vitamin A toxicity. Shearman (1978) estimated that as little as 100 g of husky dog liver could contain upwards of 1,000,000 international units (IU) (300,000 μg retinol equivalents [RE]) of vitamin A, which was sufficient to cause the toxic symptoms experienced by Mertz.

This was not the only polar expedition that was thwarted by hypervitaminosis A. Today, with knowledge of the potential vitamin A toxicity from consumption of dog, seal, polar bear, or reindeer liver (Shearman, 1978), polar explorers or workers are unlikely to repeat such experiences, but warnings must still be given to those planning to spend long periods of time under such environmental conditions.

Sundaresan and Therriault (1969) studied rats chronically exposed to air temperatures of 5°C (41°F) and observed that the total liver levels of retinol did not differ from rats maintained at 25°C (77°F). Rats kept at 5° or 25°C (41° or 77°F) were injected daily with one of six different levels of retinoic acid. Thirty-day survival was used as the marker for adequacy of retinoic acid. At 5°C (41° F), at least 100 μg retinoic acid daily was necessary for survival and growth, whereas only 5 μg retinoic acid was required daily for survival and growth at 25°C (77°F). From this, they concluded that cold-adapted rats required a 20-fold greater intake of vitamin A than did their room temperature-acclimatized counterparts. Lui and Roels (1980) reported that vitamin A deficiency did not affect energy production by the Krebs cycle, but glycogen synthesis from lactate and glycerol appeared to be slowed down. Thus, restoration of depleted energy stores may be impaired by a severe deficiency of this vitamin.

Draper (1976) reported that Norwegian and Finnish Lapps (a race of formerly nomadic people residing in Northern Scandinavia) consume upwards of 50,000 to 62,000 IU of vitamin A (15,000 to 18,600 μg RE) per day, usually in the form of reindeer liver. Hasunen and Pekkarinen (1976) also reported that Finnish Skolt (a subpopulation of the Lapps) children consumed amounts of vitamin A well in excess (two- to fourfold) of the RDA. Rodahl and Issekutz (1965) reported that Alaskan Eskimos consumed approximately twice as much vitamin A as did U.S. Army or Air Force personnel living under similar conditions (3,750 versus 1,900 μg RE, respectively, or 3.6- and 1.9-fold higher than the RDA, respectively). Thus, indigenous persons living in the higher latitudes of the world continue to demonstrate comparatively high dietary intake of vitamin A.

Compared to the 1989 RDA (NRC, 1989), it was reported that subjects in the 38-d Operation Everest II consumed increased amounts of vitamin A (Rose et al., 1987) as did subjects during an exercise at 3,500 to 4,050 m (11,475 to 13,279 ft) altitude in Bolivia (Edwards et al., 1991). However, Hannon et al. (1976) reported a transient reduction in the consumption of vitamin A by eight women during a sojourn to 4,300 m (14,098 ft) altitude. In addition to a decreased intake, it has been suggested that a malabsorption of fat may occur at high altitudes (Boyer and Blume, 1984; Ward et al., 1989b). This interpretation of the data has been criticized because two of the three subjects were reported to have been fat malabsorbers at sea level altitude prior to the experiment. Thus, it is not known whether impaired intestinal fat absorption occurs at high altitude, and if it does, whether it would be sufficient to affect absorption of the fat-soluble vitamins.

Author's Recommendation

Caution is recommended regarding the consumption of even modest supplements of vitamin A by persons working in cold or high-altitude environments due to the mobilization and utilization of body fat that often occurs under these circumstances and the resultant release of vitamin A stores into the circulation.

It has been reported that 6 months to 2 years is required for a person consuming a vitamin A-deficient diet to become deficient. Thus, there is little justification to recommend intakes of vitamin A above RDA or MRDA levels because most expeditions or maneuvers are of a much shorter duration than the time required to become deficient. Deficiency of the vitamin is initially characterized by a reduction in night vision and dark adaptation, symptoms that are readily noticed by the person involved. Only under such instances of suspected vitamin A deficiency should a supplemental regimen of no more than the current RDA of 1,000 μg RE (NRC, 1989) be considered. Administration of supplemental vitamin A to a person with an adequate vitamin A status does not improve night vision further. Therefore, the suggested micronutrient intake goal for vitamin A is set at the RDA and MRDA level of 1,000 μg RE (Table 13-1). This recommendation is in contrast to the Thomas et al. (1993b)

TABLE 13-1 Suggested Micronutrient Intake Goal for Use in the Cold and at High Altitudes

Nutrient	Micronutrient Intake Goal[*]	RDA[†]	MRDA[‡]	RCW as provided[§]	RCW as consumed[‖]
Fat-soluble vitamins					
Vitamin A (μg RE)	1,000	1,000	1,000	8,022	6,016
Vitamin D (μg)	10	10	—	—	—
Vitamin E (mg α-RE)	400	10	10	21	15.8
Vitamin K (μg)	70–80	70–80	—	—	—
Water-soluble vitamins					
Thiamin (mg)	3	1.5	1.6	5.7	4.3
Niacin (mg)	20	19	21	31	23.2
Riboflavin (mg)	3	1.7	1.9	2.6	1.9
Vitamin B_6 (mg)	2	2	2.2	3.9	2.9
Vitamin B_{12} (mg)	3	2	3	0.8	0.6
Pantothenic acid[#] (mg)	10	4–7	—	—	—
Biotin[#] (μg)	30–100	30–100	—	—	—
Folic acid (μg)	400	200	400	141	106
Vitamin C (mg)	250	60	60	329	247
Minerals					
Calcium (mg)	800–1,200	800–1,200	800–1,200	1,379	1,034
Phosphorus (mg)	800–1,200	800–1,200	800–1,200	2,168	1,626
Magnesium (mg)	400	350	350–400	529	444
Iron (mg)	15–20[**]	10	10–18	19	14
Zinc (mg)	20	15	15	10.8	8.1
Copper[#] (mg)	1.5–3	1.5–3	—	—	—

NOTE: RE, retinol equivalents; α-TE, α-tocopherol equivalents.

[*] As recommended by the author.

[†] Recommended Dietary Allowance for males aged 19–24 and 25–50 (NRC, 1989).

[‡] Military Recommended Dietary Allowance (AR 40-25, 1985).

[§] Micronutrient content of the Ration, Cold Weather (RCW).

[||] Average intake of nutrients contained in the RCW, assuming an average of 75 percent consumption of the contents (see Hoyt and Honig, Chapter 20 in this volume).

[#] Estimated Safe and Adequate Daily Dietary Intake (NRC, 1989).

[**] 15 mg suggested for men, and 20 mg suggested for women.

suggestion that "…the body's need for vitamin A…may increase at altitude" (p. 36).

Whereas β-carotene does not share the toxicity that preformed vitamin A does, there is no RDA or MRDA for this provitamin. Should supplemental amounts of vitamin A be found to be beneficial as a result of future research in this area, thought should be given to supplementing with β-carotene rather than with vitamin A.

Vitamin D

Functions

Vitamin D is important for the absorption and metabolism of calcium and phosphorus. Other roles for this vitamin have recently been elucidated (Suda et al., 1990), but they do not appear to be pertinent to the present discussion.

Intake and Status

Due to the synthesis of previtamin D_3 from 7-dehydrocholesterol during exposure of the skin to ultraviolet irradiation, it is unlikely that a person operating in the cold or at high altitudes would develop a vitamin D deficiency, unless a prolonged expedition occurred during the long polar nights. Even though the sunlight is very oblique at the polar latitudes, the direct solar radiation on the face and any other exposed skin, along with the reflected radiation from the ice and snow, should be adequate to synthesize sufficient vitamin D_3 to meet the nutritional needs of the explorer. High altitudes generally lie at more moderate latitudes with the result of more direct solar radiation. Thus more direct exposure, in addition to increased intensity of the radiation due to the decrease in absorption of ultraviolet rays by the thinner atmosphere, should result in sufficient exposure to ultraviolet irradiation for synthesis of adequate amounts of vitamin D to meet nutritional and functional needs.

Author's Recommendation

The exposure of the skin to ultraviolet radiation, coupled with a possible release of vitamin D stores from mobilization and utilization of fat stores during prolonged and strenuous physical exertion coupled with inadequate energy intake, should provide sufficient vitamin D to meet nutritional needs in both cold and high-altitude environments. In addition to sunlight, the inclusion of vitamin D-supplemented milk powder in the diet should provide sufficient vitamin D to meet nutritional needs. Thus, the suggested micronutrient intake goal for vitamin D is set at the RDA level of 10 µg (Table 13-1).

Vitamin E

Simon-Schnass (see Chapter 21 in this volume) reviews and discusses the literature on vitamin E; therefore, a short comment on another consideration of vitamin E supplementation is included here.

Author's Recommendation

Due to the reduction or prevention of oxidation of fatty acids by vitamin E, it is theoretically possible that supplementation with the vitamin could increase the oxygen supply for such purposes as energy production by the Krebs cycle (Williams, 1989). In addition to the beneficial effects of 400 µg/d vitamin E discussed by Simon-Schnass (see Chapter 21 in this volume), consideration should be given to the powerful epidemiological data recently reported by Stampfer et al. (1993) and Rimm et al. (1993), which demonstrated that consumption of 200 mg or more of vitamin E per day for periods of at least 2 years resulted in a significant reduction in the incidence of heart attacks. Due to the unknown etiology of high-altitude cerebral or pulmonary edema (HACE and HAPE, respectively), consideration should be given to instituting a regimen of elevated vitamin E intakes for substantial periods of time prior to exposure to high altitudes, as well as maintaining this level of intake during exposure to altitude. In view of the extremely low toxicity of vitamin E, this regimen may result in a reduction in either the incidence or severity of HACE and HAPE, both deadly consequences of working at high altitudes. Maintenance of membrane fluidity in a cold environment by supplemental vitamin E also supports such a supplemental regimen for this vitamin (see Simon-Schnass, Chapter 21 in this volume). For these reasons, the suggested micronutrient intake goal for vitamin E is set at 400 mg α-tocopherol equivalents (α-TE) (Table 13-1).

Vitamin K

Functions

Vitamin K functions as a cofactor for several enzymes that modify and activate a number of blood clotting factors (NRC, 1989). Deficiency of the vitamin results in hemorrhages, whereas toxicity from intake of large doses is rare (NRC, 1989). Intestinal microbial synthesis also serves as a source of the vitamin (NRC, 1989).

Status and Intake

There are no known data on either changes in dietary intake or changes in status of this vitamin as a result of exposure to cold or high altitudes.

Author's Recommendation

A long period of time is required to produce deficiency in vitamin K. In addition, the vitamin is synthesized intestinally. Hence, it is suggested that the micronutrient intake goal for vitamin K be set at the RDA level of 70 to 80 μg, which is commensurate with what is found normally in foods.

WATER-SOLUBLE VITAMINS

All of the water-soluble vitamins, with the exception of folic acid and vitamin C, are intimately involved in the oxidation and conversion of food to energy at multiple steps leading up to and in the functioning of the Krebs cycle (see Hunt and Groff, 1990). Thus, an adequate nutritional status with respect to the water-soluble vitamins is essential for the production of sufficient energy for thermogenesis and for physical exertion while in the cold and at high altitudes.

Thiamin

Functions

Thiamin is essential for energy metabolism; it serves as a cofactor in the oxidative decarboxylation of pyruvate to acetylcoenzyme A (acetyl-CoA) immediately prior to its entrance into the Krebs cycle, in the conversion of α-ketoglutarate to succinylcoezyme A (succinyl-CoA) in the Krebs cycle with subsequent oxidation to adenosine triphosphate (ATP), and in the hexose monophosphate shunt. If the thiamin supply is insufficient, the increased demand for acetyl-CoA during physical activity or for thermogenesis may not be met. As a result, more pyruvate will be converted to lactate with subsequent early onset of fatigue (Williams, 1989).

Intake and Status

Draper (1976) reported that inadequate intake of thiamin was one of the primary dietary deficiencies among Norwegian Lapps. Hasunen and Pekkarinen

(1976) reported a similar observation among Finnish Skolt children. Hannon et al. (1976) reported a transient reduction of thiamin intake by women during their sojourn to 4,300 m (14,098 ft). However, there was an increased intake during Operation Everest II (Rose et al., 1987) and during the military exercise in Bolivia (Edwards et al., 1991). It has been suggested that 10 to 14 days are required for consumption of a thiamin-deficient diet to result in the appearance of deficiency symptoms.

Author's Recommendation

Due to thiamin's role in the metabolism of carbohydrate, the RDA for thiamin is based on total anticipated energy intake from carbohydrate and some amino acids (NRC, 1989). There have been many reports of increased intake of carbohydrate, at the expense of fat intake, at high altitudes (Frisancho, 1981; Ward et al., 1989b). Thus, the suggested micronutrient intake goal of this vitamin for those working either in the cold or at high altitudes is set at 3 mg, which is twice the existing RDA of 1.5 mg/d and higher than the MRDA of 1.6 mg/d. The suggested micronutrient intake goal of 3 mg/d is a prudent dose considering the low toxicity (NRC, 1989) of this vitamin.

Niacin

Functions

Niacin as nicotinamide adenine dinucleotide (NAD) functions mainly to produce ATP from glycolysis and from the Krebs cycle. It is also necessary for the conversion of pyruvate to acetyl-CoA, in the hexose monophosphate shunt, and in the synthesis of fatty acids from acetyl-CoA. A deficiency of niacin could impair glycolysis and the Krebs cycle, whereas excessive niacin supplementation may suppress the release of free fatty acids from adipose tissue through decreased lipolysis, resulting in a decreased availability of a major fuel source for utilization during strenuous exercise (Bulow, 1981; Carlson et al., 1963). Thus, if muscle glycogen levels are low, as may occur during prolonged physical exertion in the cold or at altitude, excessive niacin supplements could actually impair physical performance (Williams, 1989).

Intake and Status

An increase in niacin intake was reported among participants in Operation Everest II (Rose et al., 1987) during their simulated exposure to high altitudes and by U.S. Army soldiers during the exercise in Bolivia (Edwards et al., 1991). However, Hannon et al. (1976) reported a reduced intake by women during a sojourn to 4,300 m (14,098 ft) altitude. Niacin status was not determined in any of these studies.

Author's Recommendation

A niacin deficiency severe enough to impair glycolysis is difficult to produce due to the normal formation of niacin from tryptophan, a pathway that produces approximately half as much niacin as that provided by dietary sources alone (NRC, 1989). Thus, due to the inhibition of release of free fatty acids, it appears that an oversupply of the vitamin might be more critical than an undersupply. For this reason, the suggested micronutrient intake goal for niacin is set at 20 mg/d, which is between the RDA and the MRDA (Table 13-1). This amount should be sufficient to prevent a deficiency of the vitamin but not so high as to inhibit release of fatty acids.

Riboflavin

Functions

Riboflavin, as flavin adenine dinucleotide (FAD), is essential for electron transport, which is needed for the conversion of fatty acids to acetyl-CoA and for the conversion of succinate to fumarate in the Krebs cycle (NRC, 1989).

Intake and Status

The U.S. Army reported an increase in the intake of riboflavin by soldiers working at 3,500 to 4,050 m (11,475 to 13,279 ft) in Bolivia (Edwards et al., 1991) and during Operation Everest II (Rose et al., 1987), whereas Hannon et al. (1976) reported a decreased intake of riboflavin by women during a sojourn to 4,300 m (14,098 ft) altitude. The major source of dietary riboflavin is from dairy products, which may be limited during prolonged expeditions and may have been limited during the study reported by Hannon et al. (1976). Strict vegans who consume no meat or dairy products may be at risk for developing a riboflavin deficiency under these environmental conditions (Cooperman and Lopez, 1991). A riboflavin-deficient diet must be consumed for 2 to 6 weeks before deficiency symptoms begin to appear.

Author's Recommendation

Due to the low toxicity, the essentiality for energy production, and the need for increased food intake during prolonged expeditions in the cold or at altitudes, it is suggested that the micronutrient intake goal for riboflavin be set at 2.5 mg/d, which is slightly higher than either the RDA or the MRDA.

Vitamin B_6

Functions

Vitamin B_6 is a required cofactor for glycogen phosphorylase, which converts stored glycogen into glucose, and is essential for the conversion of various amino acids into oxaloacetate as well as the conversion of α-ketoglutarate, succinyl-CoA, and pyruvate into various amino acids (NRC, 1989). Thus, a pronounced deficiency of vitamin B_6 would cause a decrease in the conversion of glycogen into glucose, depleting a major source of fuel (Leklem, 1991). The onset of deficiency may be as short as 2 to 4 weeks.

In addition to its role in glycogen and amino acid metabolism, two of the major forms of vitamin B_6, pyridoxal 5'-phosphate (PLP) and pyridoxal (PL), appear to affect the erythrocyte hemoglobin oxygen binding affinity (Reynolds and Natta, 1985), with PLP reducing the binding affinity and PL increasing the affinity. These effects, observed thus far only in vitro and not yet confirmed in vivo, could have the effect at high altitudes of either lowering the ability of hemoglobin to bind sufficient oxygen in the lungs or of increasing the binding affinity to such an extent that release of the bound oxygen in the peripheral capillary beds is diminished. Either scenario could have serious adverse consequences.

Intake and Status

Deuster et al. (1992) reported that consumption of commercially available dehydrated rations for 31 days provided amounts of vitamin B_6 at or above the RDA, and that physical operations at altitudes of 2,400 to 4,300 m (7,869 to 14,098 ft) did not appear to affect vitamin B_6 status, as determined by concentrations of PLP in serum and erythrocytes. There was an increased intake of vitamin B_6 during Operation Everest II (Rose et al., 1987). However, there was a reduced intake of this vitamin by soldiers during their exercise in Bolivia (Edwards et al., 1991).

Author's Recommendation

There are no known endurance or performance benefits in the cold or at high altitudes from supplementation of otherwise well-nourished individuals with extra doses of vitamin B_6. Due to the unknown effects of supplemental vitamin B_6 on hemoglobin oxygen binding affinity, no increased intakes of vitamin B_6 above RDA or MRDA levels have been included in the suggested micronutrient intake goal (Table 13-1).

Vitamin B_{12}

Functions

Vitamin B_{12} is needed for the conversion of methylmalonyl-CoA into succinyl-CoA, which enters directly into the Krebs cycle. Vitamin B_{12} is also essential for normal cell division.

Intake and Status

An increase was reported in the intake of vitamin B_{12} during Operation Everest II (Rose et al., 1987) and by soldiers working in Bolivia (Edwards et al., 1991). There are no known reports of changes in vitamin B_{12} status among persons living or working in the cold or at high altitude.

Author's Recommendation

Due to the prolonged period of time (5 to 10 years) required to develop a deficiency of vitamin B_{12} (Ellenbogen and Cooper, 1991), it is unlikely that supplementation with this vitamin would be of benefit except for strict vegans who are already at risk for deficiency. Consumption of any fermented food, such as soy sauce or tofu, provides sufficient vitamin B_{12} to meet anticipated needs in the cold or at altitude (Nutritionist IV, 1993). Three μg of vitamin B_{12}, equivalent to the MRDA, has been included in the suggested micronutrient intake goal (Table 13-1) due to the relatively high incidence of vegetarianism among civilian mountain climbers.

Pantothenic Acid

Functions

Pantothenic acid is part of the coenzyme A molecule, which is involved in the oxidation of pyruvate to acetyl-CoA, the conversion of α-ketoglutarate to succinyl-CoA in the Krebs cycle, as well as the metabolism of fatty acids. A deficiency in this vitamin (and thus a deficiency of coenzyme A) may decrease the availability of substrate for the Krebs cycle, thereby shifting energy production to the less-efficient anaerobic glycolysis pathway.

Intake and Status

Nice et al. (1984) reported that supplementation with 1 g pantothenate daily for 2 weeks had no effect on a treadmill run to exhaustion. There are no known reports of either intake or changes in pantothenate status of persons living or working in the cold or at high altitude.

Author's Recommendation

It has been estimated that 4 to 10 days is required for the development of a pantothenic acid deficiency. Due to the low toxicity of this vitamin (NRC, 1989) and due to its essentiality in energy production, 10 mg of pantothenic acid per day is recommended in the suggested micronutrient intake goal (Table 13-1). This is somewhat above the Estimated Safe and Adequate Daily Dietary Intake (ESADDI) (NRC, 1989) level of 4 to 7 mg/d.

Biotin

Functions

Biotin is essential for the conversion of pyruvate into oxaloacetate, the conversion of acetyl-CoA into fatty acids, and the conversion of propionyl-CoA into methylmalonyl-CoA prior to its entrance into the Krebs cycle (NRC, 1989).

Intake and Status

It is difficult to induce deficiency of biotin unless one consumes excessive amounts of raw egg whites, which contain avidin, an irreversible binder of biotin (NRC, 1989). There are no known reports on intake or changes in biotin status of persons living or working in the cold or at high altitude.

Author's Recommendation

Due to the widespread distribution of biotin in foods (Bonjour, 1991) and to the difficulty of inducing a deficiency (NRC, 1989), there is no justification to set the suggested micronutrient intake goal for biotin above the ESADDI of 30 to 100 mg/d (Table 13-1).

Folic Acid

Function

Although not involved in the production of energy, folic acid is essential in the formation of hemoglobin and in methyl transfer involved in cell division (NRC, 1989). It has been estimated that it takes 3 to 4 months of consumption of a folate-deficient diet is required before deficiency symptoms begin to appear. The major dietary source of folic acid is leafy green vegetables (Brody, 1991), which are notoriously scarce on expeditions in the cold or at high altitude.

Intake and Status

Draper (1976) reported that Canadian Eskimos had low serum levels of folate, usually without signs of any hematological problems. This apparent deficiency may be the result of a low consumption of leafy green vegetables by persons living in these geographical areas. Intake of folic acid was reported to be increased during Operation Everest II (Rose et al., 1987) but decreased during the military exercise in Bolivia (Edwards et al., 1991).

Author's Recommendation

Concern exists about the ability of folic acid oversupplementation to mask symptoms of pernicious anemia, particularly in the elderly. Pernicious anemia is caused by decreased absorption or inadequate intake of vitamin B_{12}. It is suggested that the micronutrient intake goal for folic acid be set at 400 μg/d (Table 13-1). This level should provide sufficient folic acid to women of childbearing age to reduce the incidence of neural tube defects in their children (Czeizel, 1993). It is important, however, that this level of folic acid be made available in the foods actually consumed in the cold or at high altitudes due to the lack of fresh leafy green vegetables in the normal diet in these environments.

Vitamin C

Functions

Vitamin C facilitates the intestinal absorption of nonheme iron, is involved in the formation of collagen, and is needed for proper adrenal function (NRC, 1989). A deficiency of the vitamin (intakes of 10 to 20 mg/d) results in scurvy, which is characterized by sore gums, painful joints, and multiple hemorrhages, leading ultimately to an excruciatingly painful death (Friedrich, 1988). Like folic acid, vitamin C is one of the few water-soluble vitamins that is not required for the production of energy. The role of large supplemental doses in enhancing the immune system (Pauling, 1970) is controversial at present.

Intake and Status

Scurvy was prevalent on many of the early polar expeditions. It is possible that as many expeditions failed due to vitamin C deficiency as due to vitamin A toxicity. Only after the discovery by Lind in 1753 of the preventive action of lemons were there opportunities for extended travel to the far northern and southern latitudes for prolonged periods of time without fear of this painful and deadly disease. In 1850, a successful arctic expedition carried lemons. However, other expeditions, such as Sir George Nare's expedition to the North Pole, may have failed due to inclusion of limes rather than lemons as antiscorbutics because limes contain only half the amount of vitamin C of lemons (Nutritionist IV, 1993). It is also likely that the 1913 Scott expedition to Antarctica failed due to the absence of any antiscorbutics (Friedrich, 1988). Thus, vitamin C has a long and colorful linkage with early polar expeditions.

More recently, Draper (1976) reported low dietary intakes of vitamin C by Norwegian Lapps, low plasma levels of vitamin C in the Chukchi people of Siberia, and clinical signs of scurvy in Eskimos in four northern Canadian settlements. Hasunen and Pekkarinen (1976) reported daily dietary intakes of only 17 to 34 mg of vitamin C by Finnish Skolt children. Similarly, Rodahl and Issekutz (1965) reported that adult Alaskan Eskimos consumed only about 28 mg of vitamin C per day. Petrásek (1978) described several Russian studies in which there appeared to be a …considerable vitamin C deficiency in polar explorers on an intake of 100 mg/day…" (p. 509). LeBlanc (1975) reported a low blood level of vitamin C in persons living at Fort Churchill, Manitoba, with the concentration being lower in March than in August. There was an increased intake of vitamin C during Operation Everest II (Rose et al., 1987) and during an exercise in Bolivia (Edwards et al., 1991), but a reduced intake by women during a sojourn to 4,300 m (14,098 ft) (Hannon et al., 1976).

Margaria et al. (1964) administered an acute dose of 250 mg of vitamin C approximately 90 minutes prior to a treadmill run to exhaustion, with no significant beneficial effects of supplementation. Numerous other studies also failed to observe any performance benefit during prolonged exertion from intake of supplemental vitamin C.

LeBlanc (1975) reported that daily supplementation of 407 of the previously mentioned northern Manitoba inhabitants with 1 g of vitamin C during the winter months did not reduce the number of colds per subject or the days of symptoms per subject, but did significantly reduce the number of days they were confined to their houses ($p < 0.001$) when compared to a similar group of 411 control inhabitants who received a placebo. Thérien et al. (1949) showed that supplementation of monkeys with 325 mg of vitamin C per day or humans with 525 mg of vitamin C per day significantly blunted the fall in muscle, rectal, or skin temperatures following exposure to cold air, compared to comparable subjects supplemented with only 25 mg of vitamin C per day. Whereas the actual mean surface or tissue temperature differences were less than 1°C (34°F), this difference may be sufficient in some circumstances to mean the difference between life or death.

With the intake of vitamin C maintained at 91 mg/d, Boutwell et al. (1950) reported a decreased urinary excretion of ascorbic acid when subjects were repeatedly exposed to simulated altitudes of 5,450 m (17,869 ft). They attributed this decrease to an increased utilization of the vitamin because the excretion was also reduced during the intervening periods at low altitudes as well as during the simulated exposures to high altitude.

Mitchell and Edman (1951) reviewed much of the early literature on vitamin C and climatic stress. They reported a decrease in adrenal concentrations of vitamin C in guinea pigs that were exposed to simulated high altitudes.

Recently, Schwartz and Weiss (1994) reported a significant positive correlation between vitamin C intake and forced expiratory volume in 1 second, corrected for body size (FEV_1). Dividing subjects into tertiles based on vitamin C intake from all sources (food plus supplements), persons who were consuming an average of 17 mg of vitamin C per day had an FEV_1 of approximately 2,530 ml, those consuming an average of 66 mg of vitamin C per day had an FEV_1 of approximately 2,550 ml, and those consuming an average of 178 mg of vitamin C per day had an FEV_1 of approximately 2,570 ml (Schwartz and Weiss, 1994). Data were derived from the First National Health and Nutrition Examination Survey, with the total number of subjects being 2,384. Peters et al. (1993) reported that supplementation of ultramarathon runners with 600 mg of vitamin C per day for 3 weeks prior to a race resulted in a significantly lower number of upper respiratory tract infections compared to those taking a placebo. This conclusion, however, has been challenged (Gershoff, 1994; Peters and Noakes 1994). Nevertheless, it is possible that supplemental vitamin C may have protective or beneficial effects on the pulmonary as well as the immunological systems for those engaged in strenuous physical exertion such as occurs when working at high altitudes or in the cold.

Author's Recommendation

Due to the relatively low toxicity of vitamin C, the role of vitamin C in the synthesis of adrenal hormones, its possible role in maintaining core and surface body temperature, its apparent beneficial effects in pulmonary function, and its possible role in maintaining immune function, it is suggested that the micronutrient intake goal be set at 250 mg/d for prolonged expeditions or maneuvers in cold or high-altitude environments (Table 13-1). This recommendation is considerably above the RDA and the MRDA of 60 mg/d. However, this suggested level of intake is commensurate with that already provided in the RCW as reportedly eaten (Table 13-1).

MINERALS

Calcium

Functions

Adequate calcium intake, along with that of vitamin D, is essential for maintenance of bone strength, nerve conduction, muscle contraction, and general inter- and intracellular communication (NRC, 1989).

Intake and Status

Rodahl and Issekutz (1965) reported that Alaskan Eskimos consumed only about one-half to two-thirds the RDA for calcium. Draper (1976) reported a higher than normal rate of bone mineral loss and an increased incidence of osteoporosis among northern Alaskan Eskimos. Mazess and Mather (1976a, b) also observed lower bone mineral content and earlier onset of bone loss among Alaskan and Canadian Eskimos compared to caucasians in the United States. The relatively high consumption of protein, and consequently phosphorus, by these populations may be partially responsible for these findings (NRC, 1989).

Consumption of calcium was increased during Operation Everest II (Rose et al., 1987) but reduced during the women's sojourn to 4,300 m (14,098 ft)

(Hannon et al., 1976). Pugh (1965) reported that two climbers who kept a cursory food journal while climbing from 6,400 to 7,600 m (20,984 to 24,918 ft) altitude on Mount Everest consumed 500 and 750 mg of calcium. Rupp et al. (1982) measured a variety of electrolyte changes in blood and urine of members of a Kanchenjunga expedition. They reported a slight, transient (8 percent) decrease in plasma calcium at higher altitudes, which returned to normal within a few days at altitude.

During the 9-wk On Top Everest '89 nutrition research expedition, the 15 members (10 males, 5 females) maintained full dietary records every day, regardless of their camp location. While some of the records were inadvertently lost, there were a total of 842 dietary records collected (out of a possible 945, for an 89 percent completion rate) and analyzed for intake of energy and various nutrients. The calculated intake of calcium was 910 ± 579 mg/d, with no changes or trends occurring as a result of increasing altitudes.

During this expedition, 24-h urine samples were collected at 28 separate times and analyzed for various compounds. Urinary excretion of calcium and of hydroxyproline, both markers for bone demineralization, were within normal ranges, which suggests that there was no loss of calcium. Also, single and dual photon absorptiometry performed immediately prior to departure from the United States, and at approximately 4 weeks following return to the United States, showed no indication of bone demineralization during exposures to these high altitudes.

Author's Recommendation

Because intakes of calcium have been reported to be near that suggested by the RDA and there have been no indications of an inadequate intake or adverse change in status of calcium during the 9-wk period at high and extreme altitude, there is no basis for recommending the micronutrient intake goal of calcium above the current RDA and MRDA levels of 800 to 1,200 mg/d (Table 13-1).

Phosphorus

Functions

Phosphorus is required for bone formation and integrity, with approximately 85 percent of the total phosphorus in the adult body localized in the bones (NRC, 1989). Phosphorus is involved also in energy metabolism in its role as an enzyme modulator and its essentiality for high-energy bonds in ATP and creatine phosphate.

Intake and Status

Consumption of phosphorus generally parallels that of protein (NRC, 1989). Since elevated intakes of phosphorus increase calcium reabsorption (NRC, 1989) by the kidneys, this largely offsets the adverse effect of high protein intake on calcium reabsorption. Rodahl and Issekutz (1965) reported that Alaskan Eskimos consumed about 1.5- to 2-fold greater amounts of phosphorus than that suggested in the RDA (NRC, 1989). This high intake probably resulted from the relatively high protein intake of these people. Increased intakes were also reported during Operation Everest II (Rose et al., 1987) and during the military exercise in Bolivia (Edwards et al., 1991), but Hannon et al. (1976) reported a transient reduction in phosphorus consumption by women during a sojourn to 4,300 m (14,098 ft).

During the 9-wk On Top Everest '89 expedition, there was a reported intake of 1,249 ± 720 mg of phosphorus per day, with no changes in intake occurring as a function of increasing altitudes. Urinary excretion during this expedition was within normal values.

Jain et al. (1987) reported that phosphate supplementation of persons living at low altitudes resulted, by an unknown mechanism, in a more rapid acclimatization to moderate altitudes as evidenced by increased blood levels of 2,3-dephosphoglycerate, a rightward shift in the oxygen-hemoglobin dissociation curve, and improved performance on cognitive function tests.

Author's Recommendation

Because there has been no indication of abnormally low intake or excessive excretion of phosphorus in the cold or at high altitudes, there is no justification for recommending the micronutrient intake goal for phosphorus above the RDA and MRDA level of 800 to 1,200 mg/d (Table 13-1).

Magnesium

Functions

Magnesium is essential for the production of ATP and for numerous other enzymatic reactions. As stated in the RDA (NRC, 1989), "As the complex Mg-ATP^{2-}, magnesium is essential for all biosynthetic processes, glycolysis, formation of cyclic-AMP, energy-dependent membrane transport, and transmission of the genetic code" (p. 188).

Intake and Status

A decreased intake of magnesium was reported by soldiers working in Bolivia (Edwards et al., 1991). Rupp et al. (1982) reported no changes in plasma concentrations of magnesium when climbers were on Kanchenjunga, but daily urinary output of magnesium decreased approximately 50 percent with no comparable decrease in urinary volume. This output returned to normal following a return to lower altitudes and rest. In general, plasma magnesium concentrations are remarkably constant and are not indicative of magnesium status except under conditions of extreme magnesium deficiency (NRC, 1989).

During the 9-wk On Top Everest '89 expedition, magnesium consumption averaged 236 ± 145 mg/d in the 842 daily diet records, with no significant changes or trends in intake related to increasing altitudes possible. Possible magnesium content of snow-melt used for drinking water was not taken into account in determining total intake.

Author's Recommendation

Due to the essentiality of magnesium in energy production, its low toxicity, and the observed low intake during the On Top Everest '89 expedition, the suggested micronutrient intake goal for magnesium is set at 400 mg/d, which is at the upper range set by the MRDA (Table 13-1).

Iron

Functions

Iron is an essential constituent of hemoglobin and myoglobin as well as several enzymes. As much as 30 percent of the body iron is located in storage forms such as ferritin and hemosiderin (NRC, 1989).

Intake and Status

Numerous studies have documented an increase in erythrocytes (polycythemia) during exposure to altitude, wherein hematocrit values reach upwards of 0.65 to 0.70 (Ward et al., 1989a). At these higher hematocrits, the viscosity of blood becomes an issue of concern, especially in the peripheral tissues, which may have become vasoconstricted due to cold exposure. The causes of this polycythemia are beyond the scope of this chapter (for discussion, see Frisancho, 1981). However, due to the essentiality of iron in hemoglobin for the binding and transport of oxygen by erythrocytes, attention must be given to iron status, especially for those working at high altitudes.

Increased consumption of iron occurred during Operation Everest II (Rose et al., 1987) and by soldiers working in Bolivia (Edwards et al., 1991). Worme et al. (1992) reported consumption of an average 30.8 ± 1.06 mg of iron by a group of men and women working at moderate altitudes (2,400 to 4,300 m or 7,875 to 14,110 ft), with a corresponding increase in serum transferrin during the 31-d expedition. There were no changes in transferrin saturation or serum ferritin, with none of the subjects having a serum ferritin concentration of less than 12 g/liter (although plasma volume was not measured). The lack of decline in serum ferritin indicates that there was an adequate intake of iron and of iron stores to prevent onset of iron deficiency brought on by the altitude-induced polycythemia.

Consumption of iron averaged 15.8 ± 12.4 mg/d during the On Top Everest '89 expedition, with a gradual reduction in intake as altitudes increased. Intakes averaged 16.0, 17.1, 15.8, 7.5, and 11.3 mg/d at base camp and at camps 1, 2, 3, and 4, respectively. All members experienced polycythemia for the duration of the expedition.

Reynafarje and Ramos (1961) reported an increase in intestinal iron absorption during the first several days following exposure to 4,500 m (14,754 ft), reaching a maximum after 1 week and gradually declining over the following month. Conversely, iron absorption decreased in natives from high altitudes when they were brought down to sea level, reaching a minimum at 3 weeks and increasing back to their normal high-altitude absorption by 16 months. Following this adaptation to different altitudes, intestinal absorption of iron was similar for natives living in their own localities at either low or high altitudes.

Beard et al. (1990) reported that nonmalnourished women with diagnosed iron-deficiency anemia were more susceptible to exposure to cold water, resulting in a lower rectal temperature, lower plasma thyroxine and triiodothyronine, and a lower rate of oxygen consumption when compared to women who had an equivalent percentage body fat and were at the same stage of their menstrual cycle, but who were not anemic. Beard et al. (1988) also reported that iron-deficient individuals living in La Paz, Bolivia, at altitudes of 3,600 to 4,100 m (11,803 to 13,443 ft) had a lower maximal workload and a lower voluntary maximal oxygen uptake when compared to controls who had an adequate iron status.

Author's Recommendation

With the increasing number of women of child-bearing age being included in expeditions and military maneuvers, special consideration needs to be given to maintaining the adequacy of iron status. Due to the consistently observed increase in hematocrit as a function of exposure to altitude and to the importance of adequate iron in maintaining core body temperature, it is suggested that the micronutrient intake goal iron be set at 15 mg/d for men and at 20 mg/d for women (Table 13-1) (in comparison, the RCW contains 19 mg of iron). These amounts are low enough to prevent the onset of constipation, which is reported by some persons taking higher amounts of supplemental iron. Due to the high suggested dose of vitamin C, which enhances absorption of nonheme iron, the suggested micronutrient intake goal level of iron should be sufficient to prevent onset of an iron deficiency.

Zinc and Copper

Functions

Both zinc and copper are required as enzyme cofactors, with substantial amounts of zinc stored in bone and muscle tissue (NRC, 1989). Trauma and stresses of various types have been shown to increase the rate of urinary zinc excretion (Moser et al., 1985).

Intake and Status

There was an increased consumption of zinc during Operation Everest II (Rose et al., 1987) but a decreased intake during the military exercise in Bolivia (Edwards et al., 1991). Rupp et al. (1982) reported a 2.3-fold increase in plasma zinc and a significant (12-fold) increase in urinary excretion of zinc during exposure to 8,453 m (27,715 ft) on Kanchenjunga. Both levels remained elevated for the duration of the expedition. It has been shown that muscle breakdown will produce elevated plasma and urine zinc concentrations (Moser et al., 1985). Rupp et al. (1982) were apparently not aware of this phenomenon, however, as they were unable to provide a reasonable explanation for the observed changes in plasma and urine zinc.

In an expedition conducted at moderate altitudes (2,400 to 4,300 m [7,869 to 14,098 ft]), Deuster et al. (1992) reported dietary intakes of zinc and copper of 10.6 mg and 1.0 mg/d, respectively, prior to beginning the expedition. These intakes rose to 16.9 mg and 3.5 mg/d, respectively, during the 31-d expedition, and intakes were 15.5 mg and 1.9 mg/d, respectively, following return to sea level. There were no significant changes in concentrations of plasma or urine zinc, or plasma copper at any of these times.

Consumption of zinc during the On Top Everest '89 expedition averaged 8.4 ± 8.7 mg/d, with no variation in intake related to increasing altitudes. Urinary excretion of zinc averaged between 0.5 and 0.9 mg/d, with the maximum excretion being 3.2 mg (Rose et al., 1987). The highest excretion generally occurred during periods of maximum physical exertion, which suggests that the abnormally elevated excretion was the result of muscle tissue breakdown. Neither intake nor status was determined for copper during this expedition.

Author's Recommendation

Because various stresses increase urinary excretion of zinc, the exertion of living and working in the cold or at high altitudes may be sufficient to warrant intake of zinc above the current RDA and MRDA of 15 mg/d. Thus, the suggested micronutrient intake goal for zinc is set at 20 mg/d (Table 13-1). Due to consistently low intakes and periodic high excretions of zinc during the On Top Everest '89 expedition, it is suggested that the micronutrient intake goal of zinc be provided in the foods actually consumed by soldiers or others working in the cold or at high altitudes. This increased amount of zinc is not high enough to adversely affect copper status (NRC, 1989).

There is no indication that recommended intake of copper needs to be set at levels different than the current ESADDI of 1.5 to 3 mg/d. The high micronutrient intake goal for vitamin C (Table 13-1) is probably not high enough to adversely affect copper status.

Other Trace Minerals

Author's Recommendation

There are no known data on the intake of trace minerals by those working in the cold or at high altitude. Until such data exist, there is no basis to recommend intakes of any of the trace minerals at other than RDA or ESADDI levels.

AUTHOR'S CONCLUSIONS AND RECOMMENDATIONS

Although it is generally agreed that a vitamin deficiency will impair physical performance, Williams (1989) stated that "in general, vitamin supplementation to an athlete on a well-balanced diet has not been shown to improve performance" (p. 163). While this may be true for athletes performing at moderate temperatures and at low altitudes, increased intake of several of the micronutrients may be useful to enhance various aspects of health related to survival for those working for prolonged periods in the cold or at high altitudes.

Persons who live or who engage in prolonged physical exertion for extended periods of time in the cold or at high altitudes appear to have special nutritional needs. Thus, they are justified in consuming levels of specific vitamins and minerals in amounts greater than that set in either the RDA or the MRDA. The micronutrient intake goals (Table 13-1) are recommended to meet these special needs and should be safe for all the nutrients. Performance may not be enhanced by consumption of vitamins and minerals at the micronutrient intake goal level, but various critical bodily functions may be spared stress and chances of survival may be enhanced under these harsh environmental conditions.

The predominantly Western foods now being consumed by expeditions in the cold and at high altitudes as well as the RCW that is consumed during military operations provide the majority of the essential nutrients in adequate amounts (according to the RDA and MRDA). Supplementation with additional vitamins E, C, and pantothenic acid, however, would ensure that these critical nutrients would be provided in amounts that cannot be obtained from the consumption of food alone. Including other vitamins and minerals at or near the RDA and MRDA levels should ensure adequate nutrient status for all metabolic functions. Amounts of each of the nutrients suggested in the micronutrient intake goal in Table 13-1 are recommended as a prudent and safe guide. The recommended amounts are subject to revision as more data are generated.

As with most areas of scientific investigation, substantially more research is needed to establish the effects of cold and altitude on vitamin and mineral requirements. Due to the critical role of vitamins and minerals in energy production, a well-designed human study should be conducted in a location such as the South Pole or Fort Greely, Alaska. During such a study, intake, excretion, and numerous status indices for each of the vitamins and minerals can be measured accurately and correlated with energy intake, expenditure, changes in body composition, and environmental conditions. Duration of this study must be sufficient to allow for changes in nutrient status if any, to occur; that is, a range of 3 to 4 months.

Whereas simulated high altitudes, such as those produced by the excellent studies conducted during Operation Everest II, can be used to investigate the effects of low oxygen pressure on nutrient intakes and changes in status, such hypobaric chamber experiments cannot duplicate the massive expenditures of energy, the prolonged exposure to cold, and the psychological concerns regarding danger and isolation that occur during actual expeditions to high altitudes. For this reason, hypobaric chamber experiments should be viewed as providing supplemental rather than primary information on the effects of high altitudes on vitamin and mineral requirements. There is still a need for well-designed experiments to be conducted at high altitudes to provide the data necessary to determine vitamin and mineral requirements. Even though such research expeditions are logistic nightmares compared to strict mountain climbing expeditions, research expeditions such as the American Medical Research Expedition on Everest (West, 1984) and On Top Everest '89 demonstrate unequivocally that they can be done.

Good nutritional status is mandatory for those facing prolonged periods in the cold or at high altitudes. Survival in such environments depends, in large part, on adequate mental, physical, and nutritional preparation prior to and during exposures to extreme cold or high altitude.

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14

Micronutrient Deficiency States and Thermoregulation in the Cold

John L. Beard[1]

INTRODUCTION

Vitamins and minerals are essential to a myriad of physiologic functions, and a deficiency results in a wide variety of disorders. Among these disorders is the inability of mammals to maintain body temperature adequately in the cold. The purpose of this review is to present current concepts in temperature regulation, with particular emphasis on temperature maintenance in cold environments, and to relate physiologic changes caused by micronutrient deficiency to impaired thermoregulation.

It is well-established in a number of species that limitation of a single micronutrient can result in poor thermoregulatory performance (Lukaski and Smith, in press). Frequently, however, the causal relationship between specific metabolic alterations resulting from that nutrient deficiency and the decreased functional performance of the individual is unknown. Many of the micronutrient deficiency states that will be addressed in this chapter alter nearly all of the processes of heat production and conservation. Of the micronutrients to be

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discussed, only iron deficiency has any significant prevalence in the human population, although selenium deficiency is observed in certain specific regions of China. However, despite the recent evidence showing that peripheral conversion of the thyroid hormone thyroxin (T_4) to tri-iodothysonine (T_3) is performed by a selenium-dependent enzyme, there is no evidence linking selenium deficiency to poor thermoregulation in humans.

Profound and severe exercise, especially of the types undertaken by military personnel in the course of their activities, can also cause a dramatic alteration in plasma concentrations of some of these micronutrients which may lead to acute transitory deficiency states in particular tissues. This notion has not been the experimental paradigm for any of these studies and, therefore, warrants further investigation.

THERMAL BALANCE

The body temperature of an animal is dependent on the balance between processes of heat gain and heat loss. These can be described mathematically by the heat-balance equation:

$$S = M - W - E - C - K - R,$$

where S = net rate of heat storage, M = metabolic heat production, W = mechanical work transferred to the environment, E = evaporative heat transfer, C = convective heat transfer, K = conductive heat transfer, and R = radiant heat exchange.

In an environment that is below thermoneutrality, the sole means of heat gain for homeotherms[2] is metabolic heat production. Heat loss can occur by evaporation, convection, conduction, radiation, and mechanical work. Metabolic heat in mammals comes from the following metabolic sources: basal metabolism, postprandial thermogenesis, diet-induced thermogenesis, shivering thermogenesis, and nonshivering thermogenesis (Gordon, 1993).

Shivering and nonshivering thermogenesis are the main sources of heat production utilized during cold exposure, and both may be affected by micronutrient deficiency states. In the cold, peripheral vasomotor tone is increased via central nervous system control of smooth muscle in arterioles and arteriovenous anastomoses, leading to a decrease in convective and conductive heat loss (Grayson, 1990). There is reason to believe that the failure to control this process is the fundamental reason iron-deficient anemic humans (and animal models) fail to thermoregulate adequately (Beard et al., 1990a, b; Lukaski et al., 1990).

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[2] Any species that maintains a constant body temperature.

Shivering is triggered by a fall in the temperature of the blood, due to body temperature, causing the hypothalamus to stimulate motor neuron activity. Subsequently, increased skeletal muscle tone in antagonistic muscle groups leads to a rhythmic oscillation, probably as a result of feedback from the muscle spindle reflex mechanism (Guyton, 1986). The inability of muscles to conduct this rhythmic muscle contraction may be the result of nutrient deficiency states that lead to a decrease in oxidative metabolism. This may clearly be the case for iron, copper, and zinc deficiency as described further in this chapter, as well as pyridoxine, and thiamin deficiency (Lukaski and Smith, in press) although only the mineral deficiency states have been characterized with regard to thermoregulation.

Nonshivering thermogenesis occurs primarily in brown adipose tissue, a type of fat tissue that produces heat via uncoupling of oxidative phosphorylation in mitochondria (Himms-Hagen, 1981, 1986, 1990). In addition to providing heat for temperature regulation, brown adipose tissue also expends excess energy from overabundant caloric intake, termed *diet-induced thermogenesis* (Rothwell and Stock, 1983, 1986; Stock and Rothwell, 1991). Brown adipose tissue is the main organ for nonshivering thermogenesis in rodents and newborn mammals (Nedergaard et al., 1986), but most adult mammals, including adult humans, have only a small amount of detectable brown adipose tissue (Lean and James, 1986).

The increase in thyroid hormone production and metabolism associated with cold exposure is the probable initiator of heat production in brown adipose tissue (Guyton, 1986). Thyroid hormones, particularly T_3, stimulate a general increase in metabolism by increasing the activity of the enzyme sodium-potassium Adenosine Triphosphatase (Na-K ATPase) (the sodium pump) in the plasma membrane, decreasing the efficiency of oxidative phosphorylation (via changes in the properties of the inner mitochondrial membrane), and possibly increasing calcium ion cycling (Dauncey, 1990; van Hardeveld et al., 1986). T_4, the primary secretory product of the thyroid gland, also plays a pivotal role in thermogenesis. T_4 and its active metabolite, T_3, serve to increase heat production by two independent mechanisms. First, they work in conjunction with the sympathetic nervous system to stimulate heat production in brown adipose tissue. Second, they cause a generalized increase in the metabolic rate of all tissues by stimulating NA-K ATPase-mediated ion transport across the plasma membrane. In response to cold, T_4 production from the thyroid gland increases, often resulting in a rise in plasma T_4 concentration (Fregly, 1989). More notable is a large increase in the level of plasma T_3, a result of increased conversion of T_4 to T_3 by the enzyme thyroxine 5'-deiodinase (Scammell et al., 1988). The synthesis of this enzyme is under the control of both substrate (T_4) availability and sympathetic innervation (Kaplan, 1986).

IRON DEFICIENCY

Several key observations have stimulated interest in the relationship between iron deficiency and thermoregulation. Iron-deficient anemic rats were found to be unable to maintain normal body temperature when exposed to cold (39°F [4°C]) (Beard et al., 1982, 1984; Dillmann et al., 1979, 1980). Accompanying the impairment in thermoregulation were a decrease in the rate of thyroid hormone turnover and an increase in the rate of norepinephrine turnover, as compared to those observed in noniron-depleted cold-exposed (control) rats. Iron-deficient humans are unable to maintain their body temperature during exposure to cool water (82°F [28°C]) (Beard et al., 1990a; Martinez-Torres et al., 1984) or cool air (61°F [16°C]) (Lukaski et al., 1990), compared to subjects with normal iron status and equivalent body composition. Additionally, the iron-deficient subjects had lower thyroid hormone (Beard et al., 1990a) and higher catecholamine responses to cold (Lukaski et al., 1990; Martinez-Torres et al., 1984), similar to the response of iron-deficient rats. After repletion with iron supplements, the previously iron-deficient human subjects showed improved ability to maintain body temperature in the cold. These observations clearly demonstrate the link between iron deficiency and poor thermoregulation.

Anemia vs. Tissue Iron Deficiency

Iron deficiency may exert its effects on thermoregulation through two distinct, yet related, mechanisms, one involving anemia and the other involving tissue iron deficiency. Iron-deficiency anemia results in decreased oxygen transport from the lungs to tissues, and this reduction in oxygen availability inhibits physiological responses to cold, including peripheral vasoconstriction, a heat-conserving process, and increased metabolic rate, a heat-generating process. Hypoxia, created by reducing the oxygen content or the pressure of inspired air, results in hypothermia in rodents (Gautier et al., 1991). The inability to conserve and produce body heat properly accounts for hypoxia-induced hypothermia (Wood, 1991). Lack of oxygen availability for aerobic metabolism causes a decrease in metabolic rate and, subsequently, a decrease in heat production. Hypoxic rats demonstrate decreased shivering and nonshivering thermogenesis (Gautier et al., 1991) and a decrease in body temperature set-point (Gordon and Fogelson, 1991). Impaired neural control of these processes may also account for the effects of hypoxia on thermoregulation (Mayfield et al., 1987).

Tissue iron deficiency, apart from anemia, decreases the ability of muscles to utilize energy for muscular contraction, presumably via a decrease in the activity of mitochondrial iron-containing enzymes required for the oxidative production of ATP (Davies et al., 1984). This decrease in muscular function may impair the ability of iron-deficient animals to produce heat from shivering. The decrease in mitochondrial enzymes that results from iron deficiency may not be a significant factor, however, in limiting the heat production in iron-deficient rats. This is suggested by the observation that iron-deficient rats injected with pharmacological doses of norepinephrine are able to attain metabolic rates that are even higher than those of noniron-deficient control rats given the same dose of norepinephrine (Tobin and Beard, 1990).

Iron-deficient anemic rats rapidly become hypothermic when placed in a cold environment (39°F [4°C]), and correcting their anemia by infusing them with red blood cells restores their thermoregulatory performance (Beard et al., 1984). Likewise, poor cold responses were induced in control rats by transfusion to a lower hematocrit level. Correcting anemia also improved thyroid response to cold. Whereas cold-exposed, anemic, iron-deficient rats did not increase their plasma T_3 and thyroid-stimulating hormone (TSH) levels, correction of the anemia by transfusion resulted in a normal thyroid response to cold exposure (increased plasma T_3 and TSH concentrations). Not all iron-deficiency-induced alterations are reversible by correction of anemia. After an increase in the hematocrit levels of iron-deficient rats, plasma norepinephrine concentrations remained elevated (Dillmann et al., 1979), and the norepinephrine content of heart and brown adipose tissue remained depressed (Beard et al., 1990b) compared to control rats with similar hematocrit values.

Neurohormones

Much of thermoregulation is ultimately controlled by central neural control of blood flow, heat production, and heat loss. Thus, the impact of micronutrient deficiency states on temperature regulation can often be traced to control of neurohormone production (Brigham and Beard, in press).

There is also evidence that iron deficiency may alter neurohormonal control of thermoregulation centers in the central nervous system by way of an effect on dopamine, serotonin, and norepinephrine. The brains of iron-deficient rats were observed to contain excessive quantities of dopamine in the caudate-putamen region, and the number of D_2 receptors in the brain was lowered by iron deficiency (Youdim et al., 1989). Beard and coworkers have recently extended these observations and determined, through the use of in vivo microdialysis, that extracellular dopamine is elevated in awake, freely moving animals who were made iron deficient by dietary means only (Beard et al., 1994). Thus, the down regulation of dopamine receptors by iron deficiency may be the result of a direct effect of iron on receptor biology or may be the result of elevated extracellular-fluid dopamine concentrations. This latter observation is consistent with evidence that dopamine-dependent circadian cycles are reversed in iron-deficient rats (Youdim and Yehuda, 1985), although others have not verified the circadian cycle effect (Hunt et al., 1994). The ability of dopamine to down-regulate its own (D_2) receptors and thus effectively decrease dopaminergic activity suggests a possible mechanism for the iron deficiency-mediated loss of thermoregulation. The decrease in dopaminergic neurotransmission caused by iron deficiency would inhibit the cold-mediated release of thyrotropin-releasing hormone (TRH) from the hypothalamus, as well as the release of TSH from the pituitary, which in turn would attenuate the synthesis and release of thyroid hormone.

Norepinephrine metabolism is clearly altered by iron deficiency. Iron-deficient rats have increased blood and urinary norepinephrine levels compared to control rats (Beard et al., 1984; Dillmann et al., 1979, 1980), and this effect is more pronounced at lower temperatures. Likewise, norepinephrine concentrations in the blood and urine of iron-deficient humans are elevated (Vorhees et al., 1975; Wagner et al., 1979; Webb et al., 1982), and this effect is exacerbated as environmental temperature decreases (Martinez-Torres et al., 1984). Elevated levels of norepinephrine in the blood and urine of iron-deficient rats suggest that sympathetic activity is heightened by iron deficiency (Beard and Tobin, 1987; Beard et al., 1988) and is indicative of a hyperadrenergic state. These alterations are influenced by the severity of iron deficiency (Borel et al., 1991) and reversed by iron repletion, but not by correction of anemia (Beard et al., 1990b; Dillmann et al., 1979). When Smith and coworkers (1992b) administered chlorisondamine, a ganglionic blocker, to iron-deficient rats to interrupt neuronal firing, they observed a rapid increase in the norepinephrine content of iron-deficient hearts to control levels. Coupled with in vitro assessments of tyrosine hydroxylase activity, these results indicate that increased sympathetic firing rate, rather than impaired synthesis, accounts for the decreased norepinephrine content found in the tissues of iron-deficient rats and perhaps the increased concentrations of norepinephrine in the plasma and urine of iron-deficient humans.

Thyroid Hormones

In humans, iron-deficiency anemia is associated with changes in plasma thyroid hormone and norepinephrine concentrations that mirror those seen in iron-deficient rats. In all of the studies cited here (Beard et al., 1990a; Lukaski et al., 1990; Martinez-Torres et al., 1984), iron-deficient anemic subjects had a greater loss of body temperature in the cold than control subjects. In the two studies that matched levels of body fat across treatment groups (an important consideration for studying thermoregulation in humans), oxygen consumption during cold exposure was lower among iron-deficient anemic subjects (Beard et al., 1990a; Lukaski et al., 1990). Plasma T_3 and T_4 concentrations were lower in anemic than control subjects both before and during cold exposure (Beard et al., 1990a), and plasma norepinephrine levels were higher in iron-deficient subjects than in controls after cold exposure (Lukaski et al., 1990;

Martinez-Torres et al., 1984). After iron-deficient subjects were given iron supplements, their ability to maintain normal body temperature in the cold improved, their oxygen consumption in the cold increased, and their plasma thyroid hormone levels partially normalized (Beard et al., 1990a; Lukaski et al., 1990).

In rats, iron deficiency decreases plasma T_3 and T_4 concentrations at room temperature (68°-77°F [20°-25°C]), compared to those of control rats, and the normal increase in the plasma levels of T3 and T4 observed in control rats after cold exposure (39°F [4°C]) is not seen in iron-deficient rats (Beard et al., 1984, 1988; Dillmann et al., 1980; Tang et al., 1988). Additionally, the TSH response to cold in iron-deficient anemic rats was lower than that in control rats but was reversed by exchange transfusion of red blood cells (Beard et al., 1984). Iron repletion of iron-deficient rats normalized the plasma T_3 response to cold within 6 days (Dillmann et al., 1980), a time span that allows for an increase in hematocrit to almost normal (> 80 percent of control) levels (Beard et al., 1990b). Injecting iron-deficient anemic rats with T_3 (10 µg/kg body weight) improved the ability of iron-deficient rats to maintain body temperature at 39°F (4°C) (Beard et al., 1982), but injections of T_4 had no such beneficial effect (Dillmann et al., 1980) because the conversion of T_4 to T_3 by the liver thyroxine 5'-deiodinase is decreased by iron deficiency (Smith et al., 1992a, b; Tobin and Beard, 1990b). This decrease is partially reversed by 7 days of iron repletion (Beard et al., 1990b), and the time course of its increase is paralleled by the rise in plasma T_3 concentration that results. Likewise, T_4 and T_3 production rates, as assessed by plasma kinetics, are decreased by iron deficiency (Brigham, 1995).

In summary, iron deficiency profoundly alters thyroid hormone in animal models and to a lesser extent in humans. The most recent kinetic studies suggest the primary effect is a central nervous system-modulated one; that is, iron deficiency changes the hypothalamic control of thyroid metabolism. The lesser effects in humans likely reflect the lesser severity of anemia than in animal models rather than a species-dependent effect.

COPPER DEFICIENCY

Copper is essential for the functioning of a number of essential oxidation-reduction enzymes, and a deficiency of this mineral is associated with anemia, neural degeneration, cardiac distress, and connective tissue dysfunction (O'Dell, 1990). A deficiency in copper in humans is associated with anemia, presumably due to the role of copper in ceruloplasmin metabolism and hence the incorporation of iron into transferrin or perhaps due to the increased rate of destruction of red cells resulting from a decrease in erythrocyte superoxide dismutase (Milne, 1994; Sandstead, 1995). One of the first documentations of copper deficiency in humans noted the presence of hypothermia along with a myriad of other clinical symptoms, but an underlying explanation was lacking (Menkes et al., 1962). Animal studies showed that a copper-deficient animal has a lowered body temperature along with lowered circulating thyroid hormone levels. This is reminiscent of the observation of poor thyroid function and thermoregulation seen in iron-deficient rats (Hall et al., 1990). These animals are also anemic although the anemia is not as severe as that of rats fed an iron-deficient diet. Thus these studies are confounded with iron-deficiency anemia as well as independent effects that are not easily determined. Some researchers, however, have argued that a copper-dependent cytochrome oxidase deficiency may lead directly to a thermoregulatory defect (Hall et al., 1990).

ZINC DEFICIENCY

In human zinc deficiency there is pronounced growth failure, multiorgan dysfunction, and a generalized systemic effect (Cousins and Hempe, 1990). Because zinc is required for proper functioning of nearly all cells with regard to both energy and protein metabolism, it is not surprising that a zinc deficiency is associated with poor thermoregulation. O'Dell and colleagues (1991) noted that zinc-deficient animals were hypothermic when the nutrient was withheld *in utero* and animals were examined later in life. Other studies in adult rats showed an inability of zinc-depleted rats to thermoregulate with cold air exposure (Topping et al., 1981). There is a clear effect of lowered zinc status on thyroid hormone metabolism in rats (Lukaski and Smith, in press; Lukaski et al., 1992). TRH secretion appears to be decreased in zinc deficiency along with circulating T_3 and T_4. Zinc depletion studies conducted in humans in metabolic wards reported a decrease in circulating total and free T_4 concentrations, similar in magnitude to those observed in iron deficiency (Wada and King, 1986). This study carefully depleted subjects by a dietary restriction of zinc and observed a steady decline in circulating total and free T_4 with lowered zinc status. It is not clear if thyroid kinetics are lowered, although there was a decrease in metabolic rate as thyroid levels were lowered. Results of animal studies further suggest that the decrease in TRH resulting from zinc depletion is due to the deficiency of a zinc-dependent enzyme involved in TRH synthesis (Lukaski et al., 1994).

AUTHOR'S CONCLUSIONS

Although most of this review has focused on the relationship of iron status to thermoregulation, this is not meant to infer that other micronutrients do not have profound effects. It only implies that this micronutrient is the one most thoroughly studied. One of the inherent difficulties in evaluating animal and human research with regard to micronutrient deficiency effects is that the assessment of nutrient status is difficult. Sufficiently sensitive indicators may not be available to allow accurate diagnosis of the size of reserves or even the extent of depletion. It is clear from other chapters in this volume that extreme physical activity can lead to alterations in the fluid and hydration status of individuals, in whom micronutrient status is also being determined. The extreme physical activity may change the status parameters themselves, thus confounding the capacity to evaluate a direct effect of a micronutrient on thermoregulation. When a chronic deficiency state occurs with the minerals copper, zinc, or iron, it is clear that poor thermoregulation will occur. Short-term deficiencies, however, such as those that may be produced by field exercises of only several weeks' duration, will likely not lead to a micronutrient deprivation unless there is preexisting reserve depletion. Nonetheless, certain micronutrients have a profound effect on performance, both physical and cognitive, and every precaution should be taken to minimize the likelihood of a deficiency state.

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15

Drug-Induced Delay of Hypothermia

André L. Vallerand[1]

INTRODUCTION

Humans have always been considered tropical animals because of their high capacity for heat loss and poor resistance to cold (LeBlanc, 1975). It comes as no surprise, therefore, that numerous experiments have attempted to enhance humans' tolerance to cold. Various diets, different exercise regimens, repeated exposures to cold air or cold water, as well as the administration of various hormones and pharmacological agents, have all been used (Vallerand and Jacobs, 1992a; Vallerand et al., 1989). A pharmacological approach with thermogenic agents is certainly an attractive and promising avenue, particularly from a metabolic point of view. In view of the importance and number of animal studies in this field, they will be briefly reviewed first before focusing on human studies.

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ENHANCEMENT OF COLD TOLERANCE IN ANIMALS

During studies of endocrine response of animals to the cold, it was found that the administration of several hormones (for various periods of time) could markedly delay the onset of hypothermia. Such hormones include catecholamines, thyroxine, mixtures of thyroxine and cortisol, and growth hormone (for a review see LeBlanc, 1975; Sellers, 1972). Although these studies were very useful to the understanding of cold-induced thermogenesis—also known as thermoregulatory thermogenesis—it is now apparent that they have little direct application to humans. For instance, the catecholamine-induced improvement in heat production is usually directly related to brown adipose tissue, the long-term use of high doses of thyroxine is not recommended in euthyroid subjects, the long-term use of high cortisol doses increases protein breakdown and is associated with Cushing's syndrome, and finally the long-term use of growth hormone leads to insulin resistance and is associated with acromegaly (for a review, see LeBlanc, 1975; Sellers, 1972). Interestingly, in parallel to the above, a wide variety of pharmacological agents have also been shown to be effective in delaying the onset of hypothermia in animals (Vallerand, 1993).

Dinitrophenol uncouples oxidative phosphorylation, and it is therefore an extremely potent thermogenic agent (Hall et al., 1948). It is rather unfortunate that this uncoupling effect happens to be generalized to virtually all body tissues. The strong thermogenic effect of dinitrophenol is even magnified in the presence of thyroxine (Frommel and Valette, 1950), but again it is difficult to find an application to humans. Other effective compounds in the cold include vitamin C, α-amino acids, strophanthin, chlorpromazine, coramine, and cardiozol (see Vallerand and Jacobs, 1992a). Of much greater interest today are methylxanthines.

Caffeine, the most well-known methylxanthine, is an established and effective thermogenic agent at comfortable ambient temperatures (Acheson et al., 1980; LeBlanc, 1987). In the cold, caffeine has been shown to improve cold tolerance since it significantly reduced the drop in rectal core temperature (T_{re}) in animals (Estler et al., 1978; Gennari, 1940). Another effective xanthine is theophylline. During the last decade, L. C. H. Wang has shown on numerous occasions that the acute administration of theophylline in cold-exposed rats produces significantly warmer T_{re} via its enhancement of thermoregulatory thermogenesis (Wang, 1981; Wang and Anholt, 1982; Wang and Lee, 1990). Other potent agents in the cold include amphetamines, the well-known central nervous system stimulants (Gilman and Goodman, 1970) that, with or without epinephrine, have been shown to markedly increase metabolic heat production (M) and to produce significantly warmer T_{re} in the cold (Pick, 1948). The present animal data could therefore be interpreted as indicating that sympathomimetics and methylxanthines form two classes of pharmacological agents that are likely to be useful for humans exposed to the cold.

ENHANCEMENT OF COLD TOLERANCE IN HUMANS

As early as 1942, it was reported that the ingestion of caffeine in men exposed to a cool ambient temperature reduced the drop in mean skin temperature ($\bar{T}_{sk}$) and thus ensured a warmer $\bar{T}_{sk}$ (Scheurer and Hugo, 1942). Similarly, LeBlanc (1987) found that caffeine ingestion before retiring for the night in a cool environment significantly increased oxygen consumption and provided a warmer $\bar{T}_{sk}$, but without any change in T_{re}. Other studies that have analyzed the effect of caffeine in the cold have confirmed that it has little influence on T_{re}. Contrary to LeBlanc's observations, they have also reported that it tends to exaggerate the drop in $\bar{T}_{sk}$ in cold air (Graham et al., 1991; McNaughton et al., 1990) or that it offers no beneficial effect in cold water, in spite of an important increase in M (Doubt and Hsieh, 1991).

Following up on his animal work (described earlier), Wang and colleagues showed that the drop in T_{re} in cold-exposed individuals can be greatly reduced with the prior administration of theophylline. This was demonstrated in acute cold air studies, with the subjects either at rest or performing intermittent exercise (Wang et al., 1986, 1987, 1989). It was suggested that, as in animals, the effectiveness of theophylline in enhancing human cold tolerance resided in an enhancement of energy substrate mobilization, a factor that was thought to be limiting for cold-induced thermogenesis and consequently cold tolerance (Wang, 1978, 1981; Wang and Anholt, 1982; Wang et al., 1986). Although this theory seems well supported by the animal studies, the corresponding metabolic data in humans are not as convincing, particularly since the marked improvements in the subjects' T_{re}, described above, were not accompanied by any significant increase in M (Wang et al., 1986, 1987, 1989). To clarify the mechanisms by which cold tolerance can be enhanced, Vallerand and coworkers decided to reinvestigate the concept linking energy substrate mobilization, thermoregulatory thermogenesis, and cold tolerance.

Energy Substrate Mobilization and Cold Tolerance

Based on the theory above, which stated that energy substrate mobilization regulates thermoregulatory thermogenesis, a commercially available recreation and sports bar (Cold Buster™) has been recently developed. It is purported to delay markedly the onset of hypothermia in humans as a result of its energy-containing substrates and theobromine content. After proper subject familiarization (i.e., prior exposure to cold and instruments) to ensure a good reproducibility between cold tests (< 5 percent variability) (Vallerand and Jacobs, 1989) and while fasting seminude (jogging shorts only), subjects were exposed to a single-blind protocol.[2] Following the ingestion of either a placebo (artificially-sweetened water disguised as experimental treatment), pure carbohydrates (Canadian Forces Survival Rations), or the above-mentioned sports bar in isocaloric amounts (340 kcal or 1,422 kJ), subjects were exposed for 3 hours on three occasions 1 week apart to cold and wind at 5°C (41°F) and 1 m/s (3.3 ft/s), respectively.

Results showed no differences across all three trials with respect to T_{re}, $\bar{T}_{sk}$, M, and the heat debt (balance of heat production minus all heat losses) (Figure 15-1). Furthermore, whole body carbohydrate oxidation was increased following the ingestion of either the pure carbohydrates or the sports bar (also high in carbohydrates), exactly as expected. For both treatments however, this increase in carbohydrate oxidation took place entirely at the expense of lipid oxidation, which resulted in no change in M (Vallerand et al., 1993). Surprised

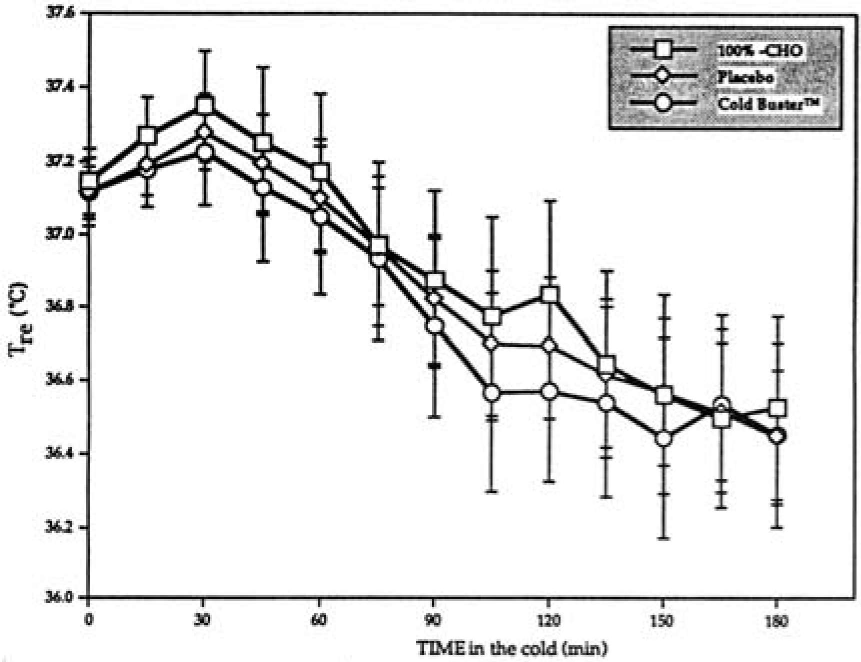

FIGURE 15-1 Influence of Cold Buster™ sports bar, pure carbohydrate (100%-CHO), or placebo on T_{re} profile rectal core temperature during 3-h exposure at rest to 5°C (41°F) and 1 m/s (3.3 ft/s) wind. T_{re} in °C (°F): 36.0°C (96.8°F), 36.2°C (97.1°F), 36.4°C (97.5°F), 36.6°C (97.9°F), 36.8°C (98.2°F), 37.0°C (98.6°F), 37.2° (99°F), 37.4°C (99.3°F), and 37.6°C (99.7°F). Results are mean ± SEM. SOURCE: Adapted from Vallerand et al. (1993).

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[2] Investigators were blind to treatments; subjects were aware of differences in taste.

by the fact that the beneficial effect of the sports bar on cold tolerance noted by Wang et al. (Unpublished data, University of Alberta, Edmonton, Alberta, Canada) could not be reproduced, the investigators immediately retested the theory (and the sports bar) in another study performed in different conditions with different subjects. Identical results were obtained (Figure 15-2).

The first question that arose from the conflicting results between these studies and those of Wang was related to laboratory procedures: Could methodological differences possibly explain the fact that the energy substrate mobilization theory of Wang et al. (1986, 1987, 1989) could not be confirmed? A first possible explanation was that the subjects were at rest in the cold in the sports bar study. With shivering alone, *M* rose to about 2.5 to 3.5 times over resting *M* (Vallerand et al., 1992, 1993). Wang and colleagues have suggested, based on the results of some studies (Wang et al., 1987, 1989), but not all (Wang et al., 1986), that a higher *M*, such as that seen during intermittent exercise, was required to fully exploit the energy-mobilizing effect of ingesting substrates and/or xanthines on thermoregulatory thermogenesis and cold tolerance. Vallerand and coworkers therefore attempted to reproduce such a protocol. However, when *M* was raised in the cold by about 3.4 times and by

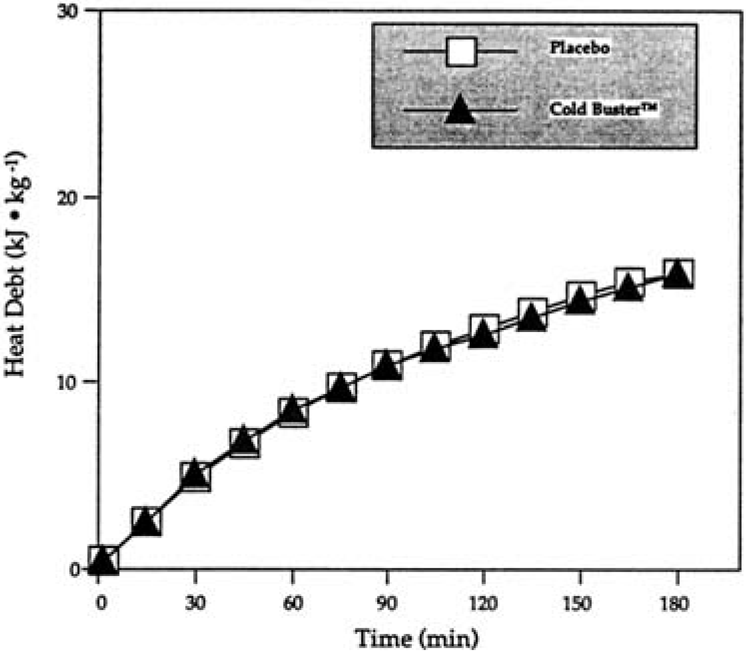

FIGURE 15-2 Heat debt (minute-by-minute balance of heat production minus all heat losses) during 3-h exposure at 10°C (50°F), < 0.4 m/s (1.3 ft/s) wind following the ingestion of Cold Buster™ sports bar or placebo. SOURCE: Adapted from Vallerand et al. (1992).

as much as 6.7 times over resting values at thermal neutrality during an intermittent rest-exercise protocol respectively (similar to Wang et al. [1987, 1989]), the ingestion of a food supplement containing substrates and theobromine had no influence on *M*, T_{re}, $\overline{T}_{sk}$ (not shown), or heat debt (Vallerand and Jacobs, 1993a) (Figures 15-1–15-3). Exactly as in the two previous trials described in Figures 15-1 and 15-2, the food supplement, which was high in carbohydrates, also increased whole body carbohydrate oxidation at the expense of lipid oxidation with no change in *M* (Figure 15-3).

A second possible explanation for the conflicting results may have been that the dose of energy substrates was simply not optimal in the sports bar study to observe a positive influence of substrate mobilization on *M* in this laboratory. However, this explanation is unlikely for two precise reasons. First, previous trials, like those in this laboratory, have mainly used about 300 kcal (1,255 kJ) (Vallerand and Jacobs, 1993a; Vallerand et al., 1992, 1993; Wang et al., 1986, 1987, 1989). Second, this laboratory recently completed a study where subjects ingested as much as 710 kcal (2,970 kJ) in a high-carbohydrate supplement in an effort to maximize substrate mobilization in the cold (Vallerand and Jacobs, 1993b). As above, this treatment had no beneficial effect

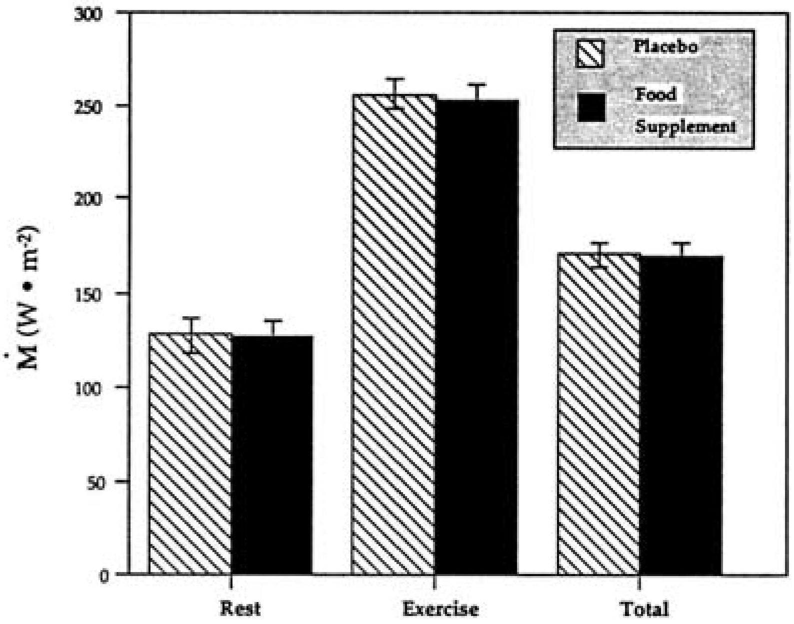

FIGURE 15-3 Average metabolic heat production ($\dot{M}$) in the cold following the ingestion of a food supplement or a placebo while performing intermittent exercise. Data are expressed in watts per square meter of body surface area for the periods of rest, exercise, and timeweighted total. SOURCE: Adapted from Vallerand and Jacobs (1993a).

on any measured thermal physiology parameters, even though carbohydrate mobilization and oxidation were increased at the expense of lipid mobilization and oxidation. Although energy substrate utilization remains crucial and essential to fuel M in the cold (Vallerand and Jacobs, 1992b), data from this laboratory do not support the theory that energy substrate mobilization is limiting for thermoregulatory thermogenesis in humans. It is suggested that other factors are required to enhance heat production, which in turn could reduce the heat debt and thus ameliorate cold resistance. Additional experiments were carried out to explore these factors.

The Effects of β-Adrenergic Agonists and Methylxanthines on Cold Tolerance

Numerous studies have firmly established that β-adrenergic drugs—such as ephedrine—and xanthines—such as caffeine and theophylline—significantly increase resting M in humans who are exposed to comfortable ambient temperatures, either on a short- or long-term basis (Astrup et al., 1985, 1992; Dulloo and Miller, 1986; Dulloo et al., 1990). These studies also demonstrated the efficacy and safety of these antiobesity compounds. Whether mixtures of ephedrine and xanthines can enhance cold thermogenesis and cold tolerance, and by which mechanisms, was examined in two separate studies.

In one study, the ingestion of ephedrine and caffeine (1 mg/kg, 2.5 mg/kg, respectively; double-blind protocol) in the cold significantly increased overall M by 19 percent compared to the same subjects receiving the placebo ($p < 0.05$) (Figure 15-4). This increment in M was fueled almost entirely by a large increase in whole body carbohydrate oxidation ($p < 0.05$), with no change in lipid or protein oxidation and was associated with significantly smaller drops in (and thus warmer) T_{re} and $\overline{T}_{sk}$, a lesser body heat debt, and slightly higher catecholamine levels. In another study of ephedrine and xanthines in the cold, the ingestion of ephedrine, caffeine, and theophylline (44, 60, and 100 mg, respectively) significantly increased M by 17 percent over 3 hours in the cold, in contrast to the placebo condition in the same subjects (Figure 15-5). This was achieved through a significantly greater whole body lipid oxidation and a slightly greater carbohydrate oxidation (Figure 15-5). This enhanced thermoregulatory thermogenesis was directly related to a significantly lower heat debt, slightly warmer T_{re}, and significantly warmer $\overline{T}_{sk}$.

These results clearly demonstrate the beneficial effects of mixtures of ephedrine with one or more xanthines in the cold. The mixtures tested significantly enhanced thermoregulatory thermogenesis, produced warmer body temperatures, and reduced the heat debt (Figure 15-4 and 15-5). When compared to the results of other similar cold studies (Table 15-1), the improvements in several important thermophysiological parameters such as the

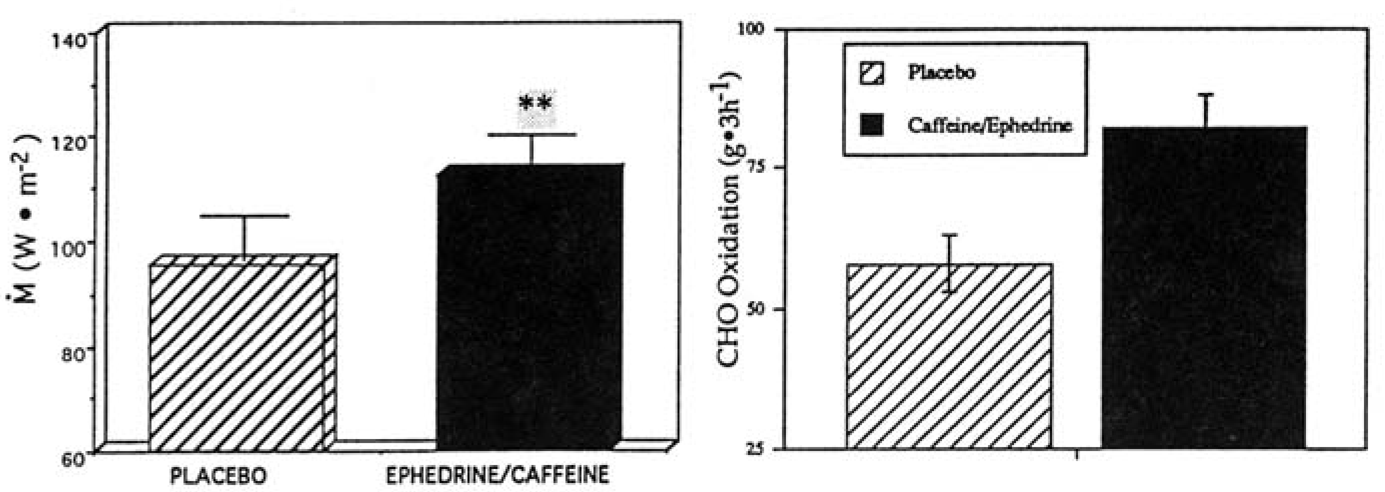

FIGURE 15-4 Influence of ephedrine/caffeine ingestion on average metabolic heat production ($\dot{M}$) and whole body carbohydrate oxidation in cold-exposed subjects. **, $P < 0.01$ vs. placebo. SOURCE: Adapted from Vallerand et al. (1989).

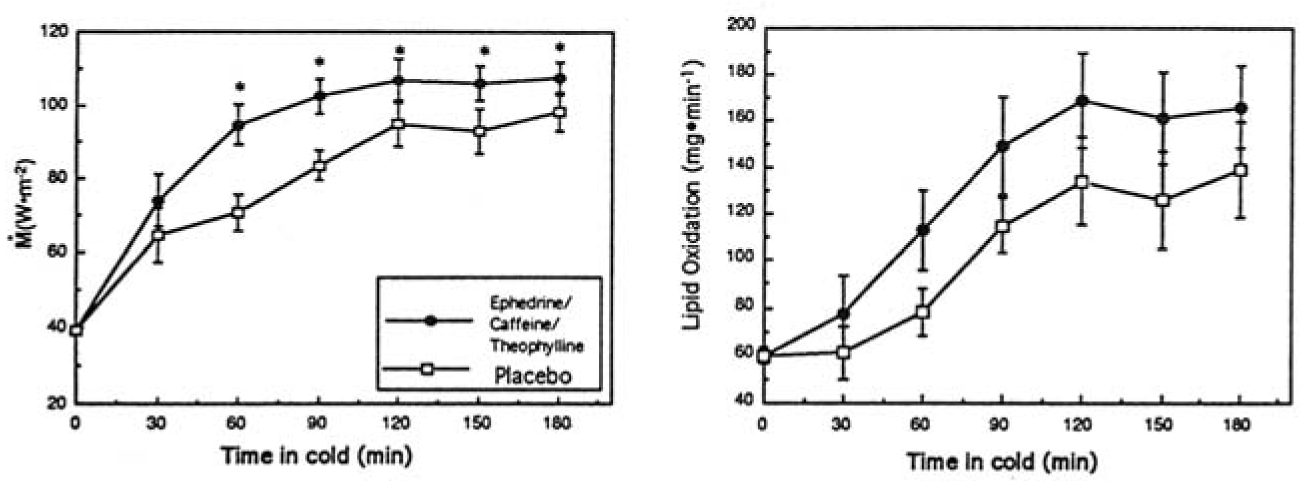

FIGURE 15-5 Influence of ephedrine/caffeine/theophylline ingestion on average metabolic heat production ($\dot{M}$) and whole body lipid oxidation in the cold. **, $P < 0.05$ at least. SOURCE: Adapted from Vallerand (1993).

changes in M, dry heat loss ($R + C$), heat debt (S), as well as ΔT_{re} and $\Delta \bar{T}_{sk}$ appear more favorable with ephedrine and xanthines than with the other treatments. Further, this lab has recently been made aware that a TTCP (the Technical Cooperation Program) Nation (N2) has fielded a mixture of ephedrine/xanthine as a medical countermeasure against performance degradation for survival conditions (Personal communication, I. Jacobs, Defence and Civil Institute of Environmental Medicine, North York, Ontario, Canada, 1996). Table 15-1 also highlights the advantages of a heat balance analysis and the necessity of performing it more often since the heat debt appears as a more robust index of cold resistance than T_{re} alone.

TABLE 15-1 Summary of Important Studies on the Pharmacological Approach to Increase Human Cold Resistance: Comparisons with a Placebo

	M, %	$R + C$, %	S, %	ΔT_{re}, %	$\Delta \bar{T}_{sk}$, %
Ephedrine-Caffeine-Theophylline (Vallerand et al., 1993)	↑17	↑4	↓12	↓24	↓8
Ephedrine-Caffeine (Vallerand et al., 1989)	↑19	↑5	↓14	↓41	↓11
Theophylline-Rest (Wang et al., 1986)	↔	—	—	↓56	—
Theophylline+Substrates-Rest (Wang et al., 1986)	↑3	—	—	↓56	—
Theophylline-Exercise (Wang et al., 1987)	↑3	—	—	↓33	—
Theophylline+Substrates-Exercise (Wang et al., 1986)	↑7	—	—	↓55	—
Cold Buster™ (Vallerand et al., 1993)	↔	↔	↔	↔	↔
Caffeine (LeBlanc, 1987)	↑7	↔	↔	↔	↓7
Caffeine-Rest (McNaugton et al., 1990)	↑16	—	—	↔	↑16
Caffeine-Exercise (Graham et al., 1991)	↔	—	—	↔	↑7
Caffeine-Exercise (Doubt and Hsieh, 1991)	↑16	—	—	↔	↓3

NOTE: M, metabolism; $R + C$, dry heat loss; S, heat debt; ΔT_{re}, change in core temperature, rectal; $\bar{T}_{sk}$, change in mean skin temperature; ↑, increase; ↓, decrease; ↔, no change; —, not available.

The exact mechanism of cellular action of ephedrine and xanthines in the enhancement of thermoregulatory thermogenesis is still uncertain, but an increase in sympathomimetic effect is likely. On the one hand, it is well known that ephedrine is an adrenergic agonist that stimulates both β and α receptors and can increase plasma catecholamine levels (Dulloo et al., 1990; Hoffman and Lefkowitz, 1990). On the other hand, xanthines, such as caffeine and theophylline, act either by inhibition of phosphodiesterase activity, by antagonistic effect at the level of adenosine receptors, or by a translocation of intracellular calcium ions (Dulloo et al., 1990; Rall, 1990). By combining these actions, ephedrine-xanthines compounds could thus increase liver and skeletal muscle glycogenolysis, white adipose tissue lipolysis, and the activation of the sympathetic nervous system (Astrup et al., 1985, 1992; Dulloo and Miller, 1986; Dulloo et al., 1990; Hoffman and Lefkowitz, 1990; Rall, 1990; Vallerand et al., 1989). An increase in either whole body carbohydrate or lipid oxidation would probably be dependent on the actual dosage of ephedrine and xanthines used. However, it is not clear which particular tissue is responsible for the ephedrine and xanthine-induced increase in thermoregulatory thermogenesis. It could well take place in the skeletal muscle, which is a major site of heat production during shivering (see LeBlanc, 1975; Vallerand et al., 1989) and during the ephedrine-induced thermogenesis at comfortable ambient temperature (Astrup et al., 1985). Since ephedrine-xanthines do increase heat production without muscular contractions at comfortable ambient temperatures and since ephedrine-xanthines increase cold thermogenesis without any indication of greater shivering, it is thus possible that ephedrine-xanthines act via mechanisms unrelated to shivering, either at the level of the striated muscle or at the level of the smooth muscle in the vascular bed, as recently suggested (Colquhoun and Clark, 1991). These exciting hypotheses require further study.

AUTHOR'S CONCLUSIONS AND RECOMMENDATIONS

In summary, once the insulation provided by the microclimate and by peripheral vasoconstriction has been maximized, increasing metabolic heat production (M) represents the last line of defence against the cold. This is best illustrated in survival conditions where additional insulation from the environment may not be available. Although several techniques have been used to further enhance M and cold tolerance, a pharmacological approach has attracted a lot of attention. Indeed, recent experiments in cold-exposed humans have shown that the ingestion of a mixture of ephedrine and caffeine enhances M and reduces both the heat debt (body heat deficit) and the drop in T_{re} ($P < 0.05$). The ingestion of a slightly different thermogenic mixture, where theophylline (another methylxanthine) was added to ephedrine and caffeine, produced about the same beneficial effect ($P < 0.05$). Although some authors have reported that theophylline alone reduces the drop in T_{re} (i.e. warmer T_{re}), thus enhancing cold tolerance, these improvements were found difficult to explain in view of the absence of changes in M and mean skin temperature. A theobromine-based (another xanthine) Recreation and Sports bar (Cold Buster™) is purported to greatly reduce the drop in T_{re} and delay the onset of hypothermia. However, these claims could not be confirmed in two different studies performed in this lab. The administration of caffeine (alone) did not alter T_{re} in the cold, despite an increase in M in some studies. In conclusion, it is suggested that ephedrine/xanthine mixtures represent at the moment, a safe and one of the best pharmacological means to enhance thermoregulatory thermogenesis and cold resistance. Future work is required to determine their effectiveness at deeper levels of hypothermia as well as during much longer albeit less severe "survival-like" exposures.

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III

Discussion

RICHARD JANSEN: Dr. Vallerand, could you comment on the mechanism of action of ephedrine and xanthines in their role as stimulants, as well as their metabolic effects? Is the mechanism similar? In other words, is there any rationale for combining these substances as opposed to giving a higher dose of, for example, caffeine? Also, how does the potency of the various xanthines like theophylline and caffeine compare?

ANDRÉ VALLERAND: At the moment, this mixtures of ephedrine/xanthines seem to be favored by many authors in the field of thermogenesis. With respect to the mechanism of action, it appears that the key is the combination of the sympathomimetic effects. For instance, with respect to ephedrine, there is an effect on α- and β-adrenergic receptors. In many cases, an increase in catecholamine levels.

With respect to the xanthines, there is possibly an effect on the inhibition of phosphodiesterase activity, possibly translocation of calcium, and possibly an antagonistic effect on adenosine receptors. It appears to be a combination of these effects that is the key to enhanced thermogenesis, not only from an acute point of view but also in chronic studies. I am also suggesting that they [the subjects] were not able to document a tolerance to this particular drug. So the effect appears to persist over time.

ELDON W. ASKEW: Dr. Vallerand, I was impressed with the success on increasing tolerance you had with the individual pharmaceutical agents. Why didn't you have the same success with the Cold Buster™ bar? Was the dose not high enough? Was it the combination? What is your opinion?

ANDRÉ VALLERAND: This is a good and a tough question at the same time. We have analyzed the Cold Buster™ bar independently. It is a high-carbohydrate sports bar that is loaded with cocoa. We have analyzed the bar, and it appears, like most other cocoa-containing products, to be 2 percent theobromine. Theobromine is another xanthine, probably less potent than caffeine and definitely less potent than caffeine and theophylline.

In this particular application, we were not able to confirm the cold-tolerance enhancement that has been found by the inventor of the bar. We have tried to do so in two different trials, and we have looked at the possibility that perhaps the metabolic rate was not high enough to confirm the theory, but that did not appear to be the case. Then we looked at dose levels. We went to almost 717 kcal (3,000 kJ). Again, we did not observe an enhancement effect.

I do not have a good explanation except that perhaps one needs a bit more punch to enhance thermoregulatory thermogenesis. I would like to return the question maybe to you and also to Dr. LeBlanc.

We were also not sure why we were not able to observe a thermic effect of the food. It is a high-carbohydrate compound. Perhaps the thermic effect of food in those various trials is too small to be detected at those metabolic rates. We do not know.

It is also possible, and this is one area where we would like to focus our research, to switch to survival-like conditions, meaning longer trials and possibly energy-deficient states. Maybe we could see an effect there. At the moment, I do not have a very good answer for you.

ROBERT POZOS: In terms of the sympathomimetic effects you are getting, what do you think are the proposed effects on the neuromuscular system? Because if you are increasing norepinephrine rather than total catecholamines, you might be increasing neuromuscular activity, which might compromise other functions. Have you studied that at all?

ANDRÉ VALLERAND: We have not looked at that. Perhaps we should look deeper into the various mechanisms of action. We tried to stay one step lower or higher, one step, say, above that. We wanted to concentrate more on what would be the best means, either pharmacological and/or dietary, to enhance cold tolerance, and then possibly look at the mechanisms afterward.

HARRIS LIEBERMAN: We have also given sympathomimetic drugs to animals and exposed them to cold stress. We have seen increased activity in what we interpret as positive behavior. I will report on this tomorrow. The drug we used was phenylpropanolamine.

IRA JACOBS: I would like to take Dr. Wang's stance for a minute, because I have worked with him closely in the past. Why does the Cold Buster™ work for him and not for us? He has not published human data with the Cold Buster™ per se. His data, which Dr. Vallerand showed you, were based on theobromine administration.

Most of those studies were on animals, but animals, to my mind, have proven to be very poor models of human body temperature regulation in environmental extremes for a number of reasons.

Dr. Wang would also suggest, perhaps, that the cold stresses that were employed in our experiments were significantly different than his, and that might have an effect. His experiments were done at a range of temperatures, for example, -15°, -10°, and -20°C (5°, 14°, and -4°F).

ANDRÉ VALLERAND: The animal experiments?

IRA JACOBS: No, the human experiments. He titrated his individual temperature exposures for each subject. He wanted to be sure that within 2 or 3 hours, each subject in the placebo situation experienced a 2°C (35.6°F) drop in rectal temperature. Then he used that same temperature for his experimental trial. Dr. Wang would suggest that our cold stress was not significant enough. That is his stance, but we tend to disagree with him for a number of reasons.

I would like to ask a question of Dr. Beard. I thought it was almost oxymoronic to say that there is evidence that highly trained athletes are iron deficient. By their very nature, their performance is high. They are not suffering, or their performance is not.

They are able to perform at extremely high levels, certainly higher than most military personnel would be required to perform. I found that a little confusing, and I began to wonder if perhaps the index used to determine iron status is valid? Does a measure of serum ferritin concentration or the concentration of anything else in serum really reflect the changes in intramuscular levels of substances that are supposed to be under the influence of those serum levels?

JOHN BEARD: I think your first question is a reasonable one. We have a large anecdotal body of information in which people argue that adolescent athletes are at especially high risk for being iron deficient. As an athlete becomes more advanced in terms of national caliber or ranking, the likelihood of iron deficiency goes down quite dramatically, because people are paying more and more attention to the balance between requirements and intake.

So if you look at elite-caliber athletes—people who run in the Boston Marathon or whatever—you are absolutely right. You do not see much iron deficiency. But of the overall population who exercise habitually, not many are of that caliber.

So my comment was that there is a large group of people who exercise a significant amount and who may have a change in iron metabolism because of that exercise. In terms of the elite-caliber athletes, I think more recent data would argue quite the opposite, that one doesn't find iron deficiency anymore. This is because elite-caliber athletes who are on the national teams have trainers and dietitians who are paying attention to such things.

ALLISON YATES: What is the total amount of theobromine in the Cold Buster™ bar?

ANDRÉ VALLERAND: It is 2 g per 100 g.

PARTICIPANT: I think the bar was 38 g.

ALLISON YATES: At this point, has anyone tested theobromine by itself, other than knowing that it is not as active perhaps in humans as theophylline?

ANDRÉ VALLERAND: We have not done similar tests with theobromine by itself. The inventor of the bar, I am sure, has data to match that, but I do not want to speculate or discuss those results here for him.

GAIL BUTTERFIELD: I had some questions for Dr. Beard about the study on young women at Penn State. What was their iron status before you started, and did you keep track of diet?

JOHN BEARD: Yes. We screened over 1,000 people in order to identify about 30 subjects who were matched for body fatness but could be divided into anemic, tissue iron deficient, and iron sufficient categories. Thus, they came into the study iron-deficient or not.

We did nothing to intervene in their dietary patterns other than to provide supplements at the end of the study. The objectives did not include a dietary assessment.

GAIL BUTTERFIELD: So you had this really dramatic improvement in 70 percent of the women, but was that related to where they started?

JOHN BEARD: The supplement was able to correct the anemia in 12 weeks. So as a group, they had hemoglobins between 11 and 12. After 12 weeks of 125 mg of ferrous sulfate, they all were above 12, but their serum ferritin concentrations, to go back to Dr. Jacobs' question, were still low.

So they actually took on the appearance of the tissue-depleted but no longer anemic group. So the model that we still have to work with shows the potential for a functional defect due to tissue iron deficiency that we do not understand. The largest effect is anemia.

GAIL BUTTERFIELD: To say that the exercise had an effect seems to me to be pushing the point.

JOHN BEARD: I was planning to come back to Bob Reynolds' point about additional iron. It is something that we faced in changing the U.S. recommendation for iron for women in pregnancy, a panel I was on last year. Do you work prophylactically, or do you wait for a situation to occur?

My point in raising the iron and exercise issue is that I think there is reasonable evidence now to say that if you are exercising someone hard, there is a good chance their iron status is going to change. It is going to go down, and that has been demonstrated well for women.

A very short study was published in the *American Journal of Clinical Nutrition* a couple of years ago on some Navy SEALs. During 1 week of very hard physical activity and mental stress, their plasma concentrations of iron went down 60 or 70 percent in 2 days. Zinc went down. Selenium went down. I do not remember if copper changed very much. These are labile indicators.

There are no strong data indicating that if you are not anemic but you are tissue iron deficient, there is going to be an effect. But, we may need to act prophylactically and make recommendations accordingly.

Now, back to Dr. Jacobs' question: I do not know if we have a better indicator of iron stores. We have some new indicators that are becoming available. We can now measure the transferrin receptor, which is sloughed off into the plasma pool. Part of the transferrin receptor molecule that sits on the plasma membrane is cut off, and that other fragment now floats around in the plasma pool. There are antibodies now available for measuring that.

It turns out that there is an inverse relationship of iron status to receptor in that individual. The more iron deficient you are, the more receptors you have. You are trying to up-regulate iron movement into tissue. So as somebody becomes iron deficient, you see more and more of these transferrin receptors floating around.

IRA JACOBS: I know of one study where, in fact, cytochrome oxidase activity was measured in skeletal muscle of iron-deficient people. Iron-deficient was defined in clinical terms. He found no impairment of muscle cytochrome oxidase activity.

JOHN BEARD: There are several different approaches that people have used. One has been to take people who naturally became iron-deficient, which is what we did with cold stress. The other uses a paradigm that some people in Seattle actually were the forerunners of, which is to phlebotomize people. Bob

Woodson phlebotomized a group of people and looked at exercise performance after phlebotomy.

Phlebotomy creates a different experimental paradigm, which we do not understand. Biologically, the subjects are different if they are phlebotomized to make them anemic and iron deficient. Somehow the body is reacting differently than if it develops naturally over a longer period of time. We do not understand what the difference is, but I think Celsing's data are at odds with some of the other data about what occurs when there is naturally developing iron deficiency.

ORVILLE LEVANDER: I have two comments, one to Dr. Beard and one to Dr. Reynolds.

John, I sat here for quite a while wringing my hands and wondering whether you were going to say anything about selenium. I am glad that you did.

Do I conclude from your presentation that it is really selenium that is important and not iron in this thermogenesis problem?

JOHN BEARD: Well, Orville, iron is still more important than selenium. I think selenium's proximal site of action is very likely, at the thyroid Type I deiodinase and at glutathione peroxidase (GPX), to have an effect on selenium. If we can understand how selenium moves around and gets put into tissues, then we have some chance of understanding how iron is affecting that process. I think we may see some sort of effect of iron on both GPX and this deiodinase activities by affecting selenium incorporation into tissue.

ORVILLE LEVANDER: Are you aware of the work that John Arthur did on the cold adaptation of rats on selenium-deficient diets and the fact that the iodinase is induced in the selenium-depleted but not in the selenium-deficient animals.

JOHN BEARD: That is right.

ORVILLE LEVANDER: That is very interesting and very pertinent to the discussion today.

Moving on to my old-time friend, Bob Reynolds, the approach that you are advocating to go with this supplement for military personnel, of course, is not without its hazards. If you increase the intake of riboflavin as much as you say, for example, and the squad leaders are instructed to go out and take a look where the men have been urinating to see if they are dehydrated or not, they are going to see all that B_2 on the ground and possibly be misled.

ROBERT REYNOLDS: I don't think that amount of riboflavin is sufficient to color the urine that much. It is a valid point you raise. But, I do not think that is enough to give it an enhanced yellow color. It may be.

ORVILLE LEVANDER: It was meant as a semiserious comment, anyway.

As a follow up, I tried to look for some kind of unifying rationale for the approach that you have taken for the different supplements. You have sort of tailor-made each recommendation for different reasons, ranging from vegetarians in the Armed Forces to lack of fresh vegetables in the diet.

If you take a look, for example, at the different rations and their composition on the sheets that we were provided today, it would appear that many of these supplement levels are already supplied. Thus it may be a nonissue for the military. Even the levels of the ones that you mentioned as being difficult to obtain by dietary means, like vitamin C and magnesium, are pretty well satisfied by the rations as currently formulated. I do not know how they are getting that much vitamin C in there, maybe Tang or something of that sort, but that brings us to vitamin E.

ROBERT REYNOLDS: Can I respond to that? I was very interested in that handout that contained the composition of the rations that came around this morning. That was the reason I raised the question of what percentage of those rations are actually consumed, to see how that actually meshed with what I was talking about.

I agree, and as stated in my presentation, most of these levels can be achieved in the current military rations. If 80 percent of these rations are consumed, that would reduce what I am recommending. But that still does not meet the vitamin E, vitamin C, and magnesium requirements. It comes close.

I also said that as more data are generated—and I consider the handout today as more data—I am willing to change my recommendations on these, and I do not own a vitamin-mineral supplement company.

ORVILLE LEVANDER: Even for magnesium, if 80 percent of rations were consumed, you would still be getting your 350 mg. I do not know why in your expedition those folks were getting only half the RDAs.

ROBERT REYNOLDS: It is a very good question. I don't know, either. Virtually all of our food items were commercially available.

ORVILLE LEVANDER: The vitamin E question is a difficult one to tackle. It is based, I guess, on one study, or perhaps two studies. We have also heard recommendations in some areas to decrease iron intakes on the basis of one study linking high iron intake to cardiovascular disease.

I think that until we have more data, it might be premature to go to the supplement levels that you are recommending. If this group did that, it would find itself pretty far away from the mainstream of nutrition thought.

ROBERT NESHEIM: One of the things the committee has to do is to take a look at all of the available information and decide where the information leads. That is why your papers are published as presented; they are not peer reviewed. They are your opinions, which our committee takes as part of the information. The other part we take from other resources and ultimately end up with recommendations that we are willing to make to the Surgeon General about ration composition.

ROBERT REYNOLDS: I would like to make one quick response to Orville about the vitamin E level. Until September of this past year, I did not take any supplements. I now take 400 mg of vitamin E per day based on the Harvard studies that looked at the several hundred thousand man-years. It has turned me from a scoffer into a believer. So perhaps the mainstream will follow.

ORVILLE LEVANDER: Well, Dan Steinberg, whose work led to the hypothesis of antioxidants and atherosclerosis, testified at a recent Food and Drug Administration hearing here in Washington that he is still advocating holding the vitamin E recommendation.

ROBERT REYNOLDS: Right. There has been much more use documented for the safety of vitamin E than for any drug that has ever been prescribed. I do not adhere to his position. That is why we have these differences.

WILLIAM BEISEL: I want to comment on the iron question. We have to think of any acute changes in iron and zinc as possible cytokine-mediated sequestrations. So acute data, that is data gathered during infections, after trauma, or after severe stress and exercise should not be included in our thinking about long-term iron needs.

JOHN BEARD: The only exception to that may be that some of these proteins—deiodinase protein may be one of them—turn over relatively rapidly. The half-life of the protein is only 18 hours. If you have acute muscle trauma due to a forced march in which you have IL-2 being released as a normal response to that, and you have iron being sequestered; it is likely this deprivation of iron in the plasma pool leads to a decrease in deiodinase activity. This results in a decline in circulating T_3 concentrations.

WILLIAM BEISEL: Certainly a decrease in the production of hemoglobin or red cells is possible.

JOËL GRINKER: This is a question for either John Beard or Robert Reynolds. Can you partition out the effects of either altitude or strenuous exercise from long-term chronic exposure to cold for some of your recommendations, particularly the iron?

ROBERT REYNOLDS: In coming up with this hypothetical recommended vitamin-mineral supplement, I tried to do that. It is very difficult for the simple reason that when you have extreme altitude, you also simultaneously have very cold temperatures. The resulting energy expenditure can be quite high. For example, we saw during the On Top Everest '89 expedition that one man was burning on average approximately 9,000 kcal/d for a 3-wk period. This was measured by doubly labeled water. Thus at high altitude, you have the altitude, the cold, and the exercise. I find it almost impossible to separate them out.

JOËL GRINKER: I was thinking about the cold without necessarily the altitude.

ROBERT NESHEIM: We will be talking about altitude tomorrow, and then we have a panel discussion later in the afternoon to try to integrate some of the data we have discussed on cold and altitude. I think we can probably hold that particular discussion until then.

PETER JONES: Dr. Reynolds, based on your rationale, are you saying then that the MRDAs should be elevated in terms of your suggested supplements?

ROBERT REYNOLDS: I really would have to spend more time thinking about what the different T Rations and the Rations, Cold Weather provide, how much is actually consumed, and the massive interaction of the B vitamins in controlling energy production.

PETER JONES: The reason I am bringing it up is because an RDA, I think, is defined as the level of a specific nutrient consumed which, based on the best available information, meet the needs of the majority of individuals.

When you talked about folate, I remember you mentioned that it is a problem in northern climes. If we go by the strict definition of the RDAs or the MRDAs, which are based on the same rationale, we are looking at recommended intakes. The issue of availability may be something quite distinct.

So in terms of supplements, it may well be that troops in the cold or at high altitude require supplementation. However, whether we should change the RDAs or MRDAs may be a separate issue that is based more on requirement, as you point out, for some nutrients, perhaps increased energy levels. Because they are not getting enough of the nutrient does not necessarily mean we should increase the MRDAs.

ROBERT REYNOLDS: I agree, and this is something I need to spend some more time thinking about. What should be changed? Maybe my goal should be to say what I think is a reasonable goal for each of these nutrients and then see how the MRDA or the RDA meets that goal.

JOHN BEARD: These are open questions to any of the people who have presented data here today. It is a scientific issue that gnaws at me a little bit. What do we know about biologic variance within our subjects—not between but within our subjects—and in terms of a research design question, how many subjects do you need to show a significant difference in the treatment group? This is a question about basic biology. I have not heard it mentioned at all, other than the mention this morning of rhythms and the timing of events.

First question: If Dr. Jacobs repeats the same exact study in the same exact subject, will he get the same exact number out of that subject? Probably not. How much variability exists?

Second question: How much of that variability has to do with genetic diversity among population groups? Let me give you an example. We know in the iron field that our indices for anemia for blacks are different than they are for whites. It is very clear now, and it is a huge controversy, because nobody wanted to admit that there is a genetically different circulating hemoglobin concentration in blacks and whites that defines anemia differently in the two groups. We will likely have at some time in the near future a different requirement for public health officials to define anemia in a black population versus a white population.

My main question is, do we know of similar sorts of differences for these biologic outcome variables related to temperature regulation?

ANDREW YOUNG: I want to respond to the within-subject variability question. In my lab, we have done cold acclimation studies in which I have required subjects to be immersed in cold water, 5 d/wk for 5 consecutive weeks. So we have a lot of opportunities to watch each subject each day respond to the cold.

In a just-completed training study we have the same subjects over an 8-wk period perform 5 d/wk of cold-water immersions. We have a lot of experience with repeated cold exposure. I have not done a systematic data analysis, but it is my impression that a given subject repeats his or her characteristic responses, to the point where you can predict that certain people show a rise in temperature within the first 10 minutes of cold exposure due to their intense shivering; they will always increase their metabolic rate very rapidly. Someone else will take 30 or 40 minutes. You can characterize it and bet on it.

Therefore I think that given individuals are very reliable in terms of their metabolic response and their change in core temperature. Over the long term, say a year, then we see changes for a given individual. There are big differences among individuals, so big that it makes doing research on human physiology difficult, as we said earlier.

JOHN BEARD: So you would say coefficients of variations of 5 or 7 percent?

ANDREW YOUNG: It depends on the parameter. I think that body temperatures are probably tighter than that, but if we were to look at norepinephrine response to cold, we would see coefficients of variation greater than that. So it depends on the parameter. But I think body temperature response and at least the spirometry-measured changes in metabolic rate are fairly reliable, probably 5 percent or less.

ORVILLE LEVANDER: I have a couple of comments. First, I do not have any answer to the variability question, but I think it might be of interest to this group that there will be a conference at the Human Nutrition Research Center here in Washington. I think it is February 22 and 23, and one of the themes will be diversity of human nutritional requirements. Perhaps some of these topics will be discussed there.

I want to react to something that Peter Jones said. I thought I heard him use the term "requirements" for these numbers. These are not requirements. These are allowances, and allowances are requirements plus safety factors, so that things like bioavailability and other matters are theoretically all taken into account to come up with this final number. I think you have to keep that in mind.

The other comment I would make is that, if the decision were to make some sort of recommendation such as this, particularly for vitamin C, magnesium, and vitamin E, we would have to change the name. We could not call it MRDA any longer, because it is a dietary allowance, and there is no way you can meet these levels of nutrients with a diet.

ROBERT REYNOLDS: That is a very good point that Orville makes. It is not dietary any longer.

JOËL GRINKER: I have a question about the nature of the supplements. Does it matter, for example, the kind of fat or carbohydrate that is being supplemented, or is everybody using relatively the same kinds of basic supplements? We know that even in temperate situations it is going to make a difference in terms of long-term metabolism. How much difference does that add to the experimental paradigms, if any? I do not know. Maybe Dr. Jones or somebody can comment.

ROBERT NESHEIM: Joël, some people could not hear your question. Could you please repeat it?

JOËL GRINKER: My question was whether or not the nature of the fat, for example, Eskimo blubber, makes a difference in supplementation. Has that been explored in any detail in terms of improvement of performance issues?

PETER JONES: I think the answer is yes. Polyunsaturated fats and fish oil have been shown by a number of groups, including our own recently in the *Journal of Nutrition*, to tend to up-regulate energy metabolism.

JACQUES LeBLANC: I have a comment on the practical remark that was made this morning by COL Schumacher of the Marine Corps regarding meal frequency. He suggested that instead of feeding the soldier three large meals a day, they might be fed snacks, because this is what they want anyway.

I did an experiment recently where we fed one large meal to subjects, and on another occasion, we fed the same number of calories in five or six small meals. We found that when they ate more frequently, they were more thermogenic, and they were using their fat. Measuring the respiratory quotient indicated that the extra energy they were producing came from the fat.

We made insulin measurements at the same time. When you take a large meal, whether it is carbohydrate or protein, the insulin goes up a great deal, whereas with a small meal, there is an almost insignificant increase in insulin. Because insulin blocks lipid utilization, we conclude that possibly by eating more frequently, the ability to use fat reserves is increased.

I wonder whether anyone has done experiments on meal frequency.

ROBERT NESHEIM: There have been. Bob, you have done some work on meal frequency.

ROBERT REYNOLDS: No, we have not done that, but I think that frequent meals are now highly recommended in weight-loss clinics as a means of utilizing stored fat. Eating smaller, more uniform, more frequent meals results in a more rapid utilization of fat. It is not just the colder altitude.

ANDRÉ VALLERAND: Was this research done in humans or in dogs?

JACQUES LeBLANC: It was done in humans.

ANDRÉ VALLERAND: Okay. What percentage difference are we talking about in comparing the large meal and many small meals?

JACQUES LeBLANC: Feeding the large meal, the increase was about 15 percent over a period of time, whereas with the many small meals, it was about 25 percent. That makes a significant difference.

JOHN VANDERVEEN: Several times today we have heard information about adaptation being a very significant factor, certainly for persons at high altitudes and perhaps under cold stress. I would like to know if researchers involved in these areas would make different recommendations for acute situations like you saw in the airplane crash versus a more long-term operation where there would be some preparation involved prior to the initiation of the activities.

ANDREW YOUNG: I think the point there is the one Ira Jacobs raised. You have your emergency survival situations and then all the other situations. Cold acclimatization or cold acclimation or cold habituation—whatever process we are measuring—can be seen by physiologists, measured in the lab, and written about. But the reality is that in terms of gross temperature, gross defense of body heat stores and nutritional requirements, cold acclimation or acclimatization probably has no effect on the nutrient requirements, be they the macro energy requirement or the micro.

These factors are physiologically curious and it is interesting for scientists to study Ama diving women and the people who repeatedly immerse themselves in cold water for weeks at a time. We are not sure what to make of cold acclimatization physiologically, but I do not think that cold acclimatization has an effect on the nutritional requirements.

The other question concerned the difference between the emergency or survival situation and operational environments. I think that the situations are greatly different.

JOHN BEARD: I am not sure you can say that, because as Bob Reynolds pointed out before, we do not have the data. I mean, you talk about requirements. You are making static measurements in concentration or appearance of urine. These are kinetic and dynamic processes.

ANDREW YOUNG: Well, we do have measurements on metabolic heat production.

JOHN BEARD: No, I am talking about nutrients, micronutrients, more specifically. You cannot tell me that we have any information whatsoever about ascorbate metabolism in cold or even at high altitude.

ANDREW YOUNG: My point is that acclimation or acclimatization is not going to make much difference in your requirements. Cold may or may not, but humans just do not exhibit that large a spectrum of physiological change with chronic or repeated cold exposure. It is not the same as adaptations to chronic heat stress or exposure to high altitudes. We do not have the same capacity to adjust ourselves to cold exposure as we do with chronic heat exposure.

IRA JACOBS: I agree entirely with what Andy just said. Furthermore, we do have evidence that troops are operationally effective and have been for a long time in the cold and seem to be able to cope with it without a problem nutritionally. We do not have any medical evidence or reports that the cold, per se, is causing health risks other than peripheral cold injury.

JOHN BEARD: Do we have any information that ascorbate turnover or utilization has changed? Do we have any information that selenium has changed?

IRA JACOBS: I do not know.

ANDREW YOUNG: What are the medical symptoms of changes in utilization of ascorbate or selenium? I would turn it around.

JOHN BEARD: No, it is a different question. One is that you may have intakes that are 5, 8, 10 times the requirement for these micronutrients, and you can double or triple the utilization rate, and you are not going to see anything because you are still well above some sort of balance point. That is not the same thing as saying that there is not an effect.

IRA JACOBS: From an operational point—the colonel should be standing up and saying this—so what?

ELDON W. ASKEW: The old literature with regard to ascorbate was based largely on animal studies. It got people excited, and they found resistance to cold injury in animals with high levels of ascorbate. But it never seemed to go past that point. It never made the transition to humans, as far as I know.

RICHARD JANSEN: Well, we know there are many vegetarians out there. Number one, they are not consuming any heme iron at all, and their intake of nonheme iron is not great. Now, of course, they may consume a larger amount of nonheme iron, but when you compare their performance, they perform very well. I mean, a lot of athletes are consuming very little heme iron. I find it very puzzling then to see an aerobic dance causing an iron deficiency by your definition.

JOHN BEARD: No, I am saying it is causing an iron depletion. The amount of storage iron that is there is going down. They are not adapting. It may be because they are in a study. These are free-living subjects who are participating in a study. It is not the same thing as somebody who is not in a study and has several other options available. The body does not care where iron comes from once it gets in there. It does not care if it is from meat or from a supplement or from wherever.

RICHARD JANSEN: But the absorption of heme iron is so much more.

JOHN BEARD: Absolutely.

RICHARD JANSEN: Okay, so you are talking about these subjects. I mean, you are saying it is not a deficiency, but in fact you are suggesting that it is a deficiency.

JOHN BEARD: I am saying that you need to be cautious.

RICHARD JANSEN: I am saying that real-world experience does not seem to track with that in terms of vegetarians performing over many years and consuming diets that are lower than the RDA in iron.

DAVID SCHNAKENBERG: Dr. Ira Jacobs, in looking at a food bar that might enhance survival, for instance in that downed aircraft, I have a question. Most of those supplements have been carbohydrate to date. Has someone tried using a primarily protein supplement? I think the data indicate that you get a greater thermic heat rise from consuming 100 g of protein than you would from 100 g of carbohydrate. Is that a possibility for exploration?

Of course fluid intake becomes a concern with higher a protein bar, but if the issue is overnight survival perhaps the heat is more important. Maintaining the heat is more important than the fluids.

ANDRÉ VALLERAND: I would like to answer that question. I believe the thermogenic effect of food (TEF) for protein ingestion is about 25 percent of the energy intake. So it is the highest of the three macronutrients with respect to the TEF.

As far as I'm aware, little data exist that bears directly on this issue. If others have additional data, please provide it, but I seem to recall there are only a few studies in the 1950s where they have tried protein supplements during the night. I think they were able to show slight improvement in core temperatures or mean skin temperature, but I could be wrong.

ELDON W. ASKEW: Mitchell and coworkers[1], in their work from the late 1940s at the University of Illinois with thermoregulation and nutrients, were interested in the same thing. They were aware of the potential of protein to increase thermoregulation because of its high specific dynamic action, but they could not find this effect when they conducted long-term dietary studies with human subjects. They found that, given the same caloric dose, carbohydrate

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[1] H.H. Mitchell, N. Glickman, E.G. Lambert, R.W. Keeton, and M.K. Fahnestock. 1946. The tolerance of man to cold as affected by dietary modification: Carbohydrate versus fat and the effect of the frequency of meals. Am. J. Physiol. 146:85–96.

maintained a higher core temperature during cold exposure than did fat or protein. Protein was the worst, and no one has really been able to explain that.

PATRICK DUNNE: As a biochemist who likes to know about mechanisms, I would like to stimulate a little discussion. We are really interested at Natick in different forms of carbohydrates, such as those that stimulate insulin release and those that do not.

So looking at the mechanisms of nonshivering thermogenesis, are there unifying themes? There seem to be some that work on carbohydrates and the futile cycles. I do not know how viable that is in human beings, because animal enzymes that participate in the futile cycles are induced in response to cold. Human beings seem not to do that. Therefore, some of your animal models are out because different levels of enzymes are induced.

Then we can go to fats and look at mitochondria. Something we are not hearing enough about is where the thyroxine loop is coming in. I think there might be a role for the right kind of fat-based supplement. Looking at uncouplers of oxidative phosphorylation and at your chocolate bar, if you have ever overdosed on chocolate you do get a hot flush. I think there may be something to these things, but you have to really look at them at a mechanistic level and sort them out. I hope the committee can help guide us.

ANDRÉ VALLERAND: I will try to answer that to the best of my capability. With respect to futile cycling in humans in the cold, we are in the process of studying that right now with stable isotopes. We hope to be able to report something to the committee in the future.

With respect to different carbohydrates in the cold, there really has not been much done. Perhaps more should be performed on this particular point of view.

With respect to uncouplers of oxidative phosphorylation, I think that would be the next Nobel Prize. If one could localize uncouplers in a particular tissue, you could solve obesity problems and survival in the cold overnight with a hypermetabolic approach.

MURRAY HAMLET: Although I was not impressed over the years with the quality of the Soviet doctrine and their science, they have for a long time used vitamin supplements—fairly high vitamin supplements—in cold exposure. Whether there are data in the former Soviet Union on vitamins that might be useful is up for grabs. There may be a mechanism in the future to get that data; for example, paying them to do literature searches on various subjects. This might be something for this committee to pursue.

They use megadose vitamins in Antarctica, in Vladivostok, and their other stations daily. They have long used them for their oil-drilling rigs in Siberia. So they are proponents of heavy vitamin supplementation, and even more for cold weather exposure. But again, I do not know the scientific basis.

ROBERT REYNOLDS: Yes, what is the basis for it?

MURRAY HAMLET: No idea.

ANDRÉ VALLERAND: I have a question for Dr. Young. I enjoyed your presentation this morning. One of the slides that you showed described thermal modifying factors. It summarized the effect of age, fitness, hydration, diet, and acclimation. I must have been out for a few seconds. I missed your comments with respect to the effects of diet on cold tolerance. Could you summarize?

ANDREW YOUNG: No, I did not say anything about diet. The only things I have done in our lab with cold were the studies that I reported, in which we manipulated the carbohydrate content. You have heard something about that from both Ira and myself.

DAVID SCHNAKENBERG: Along that line is the observation that a lot of our soldiers who go to the field and who are eating our rations do not obtain enough calories to meet their energy demands. They do begin to lose weight.

In that situation where they are perhaps doing heavy work, they might be at a 1,500 to 2,000 kcal/d deficit relative to expenditure. Does the literature give us any clue as to the point at which they might be at greater risk of a cold injury if they are exposed? For example, does it require 5 days of total starvation before you have a loss of body fat insulation that would contribute to an increased risk of injury? Or is there some intermediate point at which insufficient calories to meet energy expenditures might increase the risk of suffering a cold injury or becoming hypothermic?

ROBERT NESHEIM: That is an interesting question. As I recall, some of the data we were looking at in ration consumption showed there was an increase in the consumption of rations in cold weather, but it still did not meet their energy expenditure. It was around 1,000 or 1,200 kcal/d less intake than what estimated expenditure was. That is about what we tend to see in more moderate temperatures. Even though they ate more, they still did not meet their energy requirements.

PETER JONES: Studies that were conducted in noncold situations—actually, it was with the Irish hunger strikers some years ago—showed that they did not actually start to show ill effects until they had nearly exhausted their fat reserves and reached a critical mass in terms of lean body fat-free mass. Once you reach the end of your fat reserves and begin to deplete your lean mass reserves, it is at that point that you become much more susceptible to disease.

The hunger strikers, I think, were able to go between 30 and 60 days.

DAVID SCHNAKENBERG: I know about disease. I was wondering about reduced capability to thermoregulate in the cold.

JOHN VANDERVEEN: I think the prisoners of war returning from Vietnam had a terrible time when it got down to the near-freezing temperatures in some of those camps, despite the fact that they had what we would consider reasonable blanket capability. They shivered all night long.

New recruits coming in to the country at the same time were able to maintain body temperature, and were comfortable, but those who were down to 4 to 5 percent body fat just were not capable of thermoregulation.

Quite a bit of documentation was collected on that.

DAVID SCHNAKENBERG: In fact, in some of the earlier Ranger studies, they were forcing a 2,000 or 2,500 kcal/d deficit on people and were expecting them to do field maneuvers in the mountains in the cold weather. Were they at any greater risk of cold injury within that 8-wk scenario?

ANDREW YOUNG: If you remember the slide that I showed that plotted the thermal conductance or the insulation as a function of subcutaneous fat thickness, I believe that about a 5-mm change in subcutaneous fat thickness would be a very physiologically significant reduction in insulation.

I do not know what would be required dietarily to produce a 5-mm reduction in subcutaneous fat over the entire body. Maybe somebody else could comment on that. But at approximately 5-mm and beyond, there is a much greater risk of hypothermia.

JAMES DeLANY: But on that same slide you had the Eskimos, and they were the leanest.

ANDREW YOUNG: That is absolutely correct. That slide was drawn for another purpose, which was to show that the Eskimos were not particularly protected. In the particular database we were looking at, the differences in thermal conductance between the Eskimos and the Caucasians or the Inuits and the Caucasians was simply due to the fact that the population of Inuit was leaner.

But once we plotted the data on the same graph, we found they had the same slope. In other words, fat is fat. It does not really matter whose fat it is.

JAMES DeLANY: No. The Eskimos are the native people. They do not freeze.

ANDREW YOUNG: Well, they also do not get exposed to the cold, because they traditionally wear excellent clothing.

JAMES DeLANY: Better than our soldiers?

ANDREW YOUNG: I would say probably equivalent, or certainly it protected them more.

MURRAY HAMLET: The clothing? Functional Eskimo clothing has significantly higher insulation values than any…

ANDREW YOUNG: Their hands also sleep in warm shelters. The Eskimos are probably not particularly adapted. They are a very poor example of natural cold acclimatization.

ANDRÉ VALLERAND: What about local adaptation with respect to the Eskimos? What about, for instance, the hands, face, and feet?

ANDREW YOUNG: The hands are different.

ANDRÉ VALLERAND: Their hands look like really thick leather. I think you have done some work, Dr. LeBlanc, with respect to this?

JACQUES LeBLANC: I would agree that, systemically, they are not exposed to cold any more than anyone else.

ANDRÉ VALLERAND: Yes.

MURRAY HAMLET: Their hands will acclimatize. Their cold-induced vasodilatory responses (CIVDs), will be more frequent and heightened, as you have shown many times. That is a trainable response, but essentially, they are not exposed.

ROBERT NESHEIM: One of the things this committee was interested in doing when reviewing two of the Ranger studies was looking beyond mean data. We would like at some point to see some more definitive analysis done on the outliers with regard to body weight, because some of these people lost a large amount of body weight. It would be interesting to see what problems they experienced in terms of illness or injury, more than what was observed for the mean or the ones who maintained higher body weight. I think a comparison of the outliers would be a useful thing to do sometime.

ROBERT SCHOENE: It is interesting to look at regional geographic differences. The Sherpas who we measured 12 years ago or so had 4 percent body fat, and they tolerated cold very well.

JOHN VANDERVEEN: I forgot to mention that most of the returned prisoners of war were very low in thiamin, so that also created a problem with regulation.

KARL FRIEDL: There is more to it than just the body fat layer. The Rangers certainly feel more cold sensitive. At different phases of the study, they are naked, and one area of the room has a bit of air conditioning. We actually felt warm, and they were all shivering and felt cold. So they were definitely more susceptible to cold. The question is whether this is due to their fat insulation or if there is something else going on here, like the drop in thiamin, which was 50 percent of normal. Remember that Dr. John Kinney was particularly interested in the cold sensitivity question. That is something that still has to be followed up.

ELSWORTH BUSKIRK: One of factors here is the persistent vasoconstriction that goes on in all the chronic cold exposures. In World War II we had the trenchfoot phenomenon. We had it in Korea, and then in the chamber studies at Natick with just exposure to cold air. Where there is persistent vasoconstriction, you get chronic injury. Of course, with frostbite and the other things associated with actual freezing, that is a different situation.

Those people who were very thin were more susceptible to chronic vasoconstriction than were those who had a larger body burden of fat. But the differences were not all that great. They were subtle, and it took something like 8 or 9 days to get to that stage where there was a cold injury.

MICHAEL SAWKA: I have a question to follow Dave Schnakenberg's question to either André or Ira. We have talked about the different nutritional modifiers of thermoregulation as well as whole body heat balance. Might there be a nutritional impact on cold-induced vasodilation that can alter susceptibility to cold injury? Has this been studied apart from whole-body balance? Is there any reason to believe that there might be dissociations between whole-body thermal balance and specific effects on limbs or fingers, making people more susceptible?

IRA JACOBS: From what I have read and from our own database, I believe there is no relationship between CIVD response—in other words, peripheral response to cold—and whole-body metabolic response to cold. Someone who may have more of a prophylactic effect peripherally because of what might be called a good CIVD response is not necessarily someone who is going to be more resistant to decreases in body temperature in reaction to a given cold stress, everything else being equal. There does not seem to be any relationship at all.

In terms of whether or not there have been studies of nutritional supplements, I think that some of the older studies—military studies that were done here and in Canada and some of the proceedings that COL Askew alluded to at the beginning—did include CIVD tests as a peripheral indicator for responses. There were nutritional manipulations, but I do not remember the data.

ROBERT REYNOLDS: High doses of niacin in the range of 1 g will create tremendous vasodilation, which is commonly used to bring cholesterol down. That is one nutritional example.

IV

THE HIGH-TERRESTRIAL ENVIRONMENT

PART IV BEGINS BY EXPLORING THE PHYSIOLOGICAL and mental responses that uniquely characterize high altitudes. Chapter 16 details the physiological and pathological effects of high-altitude exposure. An initial weight loss accompanies the ascent to altitude because of increased water losses and decreased energy intake relative to expenditure. Altitude-related illnesses, such as acute mountain sickness and high-altitude cerebral edema, may cause further complications because they affect nutrition. Chapter 17 reviews the effects of lowered oxygen transport on physical performance as well as cardiac, hematologic, and nervous system responses at high altitudes. In Chapter 18, fluid metabolism at high altitudes is discussed. The literature presents conflicting data due to the differences in methodology and the presence of variables such as the effects of altitude-related sickness. Water retention contributes to the development of these illnesses, and exercise stimulates the accumulation of body water and electrolytes.

At high altitudes, diuresis, decline in appetite, and increase in basal energy needs contribute to weight loss. Chapter 19 finds that adequate energy intake can eliminate this problem, as well as decrease the diuresis that results from acute altitude exposure. Carbohydrate is the metabolic fuel that ensures adequate energy intake. Total energy requirements at high altitude are discussed in Chapter 20. The type and duration of physical activity, preexisting energy stores, and environmental conditions determine these energy needs. Because the energy requirements for work at high altitudes are higher and appetite tends to decline, energy intakes are often inadequate to meet these increases.

Chapter 21 presents evidence suggesting that there is increased oxidative stress at high altitudes, which impairs blood flow and physical performance. Inadequate levels of antioxidants may impair metabolic functions at altitude, and some studies show that vitamin E is beneficial.

16

The Physiology of High-Altitude Exposure

Allen Cymerman[1]

INTRODUCTION

The problems inherent in traversing, fighting, and surviving at altitude are as true today as they were almost 2,000 years ago. This is evident by the quotation from Tookim, a Chinese official addressing the Generalissmo Wang Fung in 35 B.C. after crossing the Greater and Lesser Headache mountains near the Korakorams: "…men's bodies become feverish, they lose colour, and are attacked with headache and vomiting: even the asses and cattle being all in like condition" (Ward et al., 1989, p. 26).

Despite the technological advances made in protecting humans from exposure to environmental extremes such as heat and cold, the problems at altitude are as true today as they were in Tookim's time. It must be remembered

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[1] Allen Cymerman, Altitude Physiology and Medicine Division, Environmental Physiology and Medicine Directorate, U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760-5007

that the only effective means for protection from the effects of hypoxia are the body's own adaptive physiological responses.

There are a host of factors found in the mountain environment that can affect a soldier's well-being. All of the factors shown in Figure 16-1 are important when troops are rapidly deployed to a high-terrestrial environment. Some are operational and can be controlled by trained soldiers; others are unavoidable. Many of the factors are interrelated and are often found in the presence of each other. Although many of these factors have been described and studied individually, they may not be independent of each other and probably act additively or synergistically.

FACTORS IN A MOUNTAIN ENVIRONMENT

Cold and Heat

Average ambient temperatures are reduced 2°C (3.6°F) for every 300-m (984-ft) rise in elevation. This means there is usually about an 8°C (14.4°F) difference between Colorado Springs, Colorado, at 1,829 m (6,000 ft) and the summit of Pikes Peak at 4,300 m (14,110 ft), a temperature and altitude change that is well within the limits of exposure that can be handled by the U.S. soldier of today. At any given hour, the "physiologic" temperature could drop 20°C (36° F) with changes in solar load and wind. In a relatively short time, a soldier could easily go from a sweating situation with several layers of

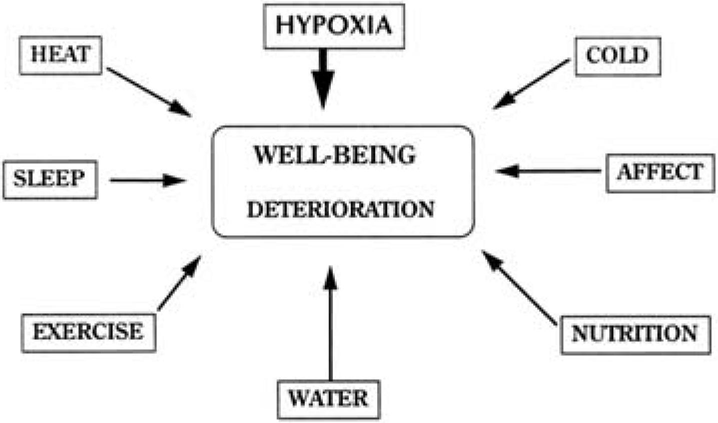

FIGURE 16-1 Interaction of various factors impinging on the well-being of individuals at high terrestrial elevations.

clothing to one in which there could be a freezing injury. Thus, a soldier could experience heat stress while overdressed and exercising in the sun and a short time later expose a hand to extreme wind chill because of a lost glove. This chapter does not review potential additive or synergistic effects of other environmental factors such as temperature but focuses on the effects of acute and long-term hypoxia per se on soldier well-being.

Affect

Studies of acute exposures to altitudes as low as 3,000 m (9,843 ft) show alterations in subjects' cognitive, motor, and affective modalities. After an initial period of euphoria, continued exposure to moderate and high altitudes may produce measurable degradations in personality and cognitive abilities. These degradations can be sufficiently severe to be classified as paranoia, obsessive-compulsive behavior, depression, and hostility. Although changes to this degree are rare, some changes in personality traits are noticed in most individuals (Nelson, 1982; Shukitt and Banderet, 1988; Tune, 1964).

Water

Water lost to the environment is characterized as both sensible and insensible. Sensible water losses include that lost through urination (1,500 ml/d), feces (100 to 200 ml/d), and perspiration (100 ml/d). Sensible perspiration can be as high as 2 liter/h or more depending on body temperature, exercise level and duration, and body weight. Insensible water loss is defined as losses due to vaporization through both the lungs and skin and can average about 700 to 1,000 ml/d (Noakes, 1993; Rhoades and Tanner, 1995).

Expired air is normally saturated with water at body temperature (47 mm Hg at 37°C [99°F]) regardless of the ventilatory rate and the altitude. Because relative humidity is generally lower and ventilatory rates higher with increasing altitude, the amount of insensible water loss can be large enough to cause dehydration and weight loss. Estimates of insensible water loss at high altitudes have been derived from sea-level measurements since no direct measurements have been made. Milledge (1992) estimates a water loss of about 1 liter/d for a ventilation rate of 40 liter/min in dry air at -15°C (5°F). The calculation is based on an equation developed by Ferrus et al. (1984) and assumes that expired air temperature is below normal body temperature and not fully saturated. This is comparable to the value of 750 ml/d predicted by Buskirk and Mendez (1967). Pugh (1964) estimated that to maintain a urine output of 1.5 liter/d, ingestion of 3 to 4 liters of fluid was required in men climbing for 7 hours. His direct measurements of water loss for the lungs during exercise were about 2.9 g/100 liter of air (body temperature pressure saturated or BTPS[2]).

Another factor to consider with the increases in ventilation associated with altitude is increased respiratory heat loss. Given the same ventilatory rate at sea level and 4,572 m (15,000 ft) (i.e., a lower workload at altitude) and no decrease in expired air temperature, it is estimated that at the same ventilatory rate of 100 liter/min, the respiratory heat loss would be 1.6 times greater (Gonzalez et al., 1985).

It is generally believed that an altitude-induced diuresis normally occurs during the initial phases of altitude acclimatization when acute mountain sickness, high-altitude pulmonary edema, and high-altitude cerebral edema are not present. When significant symptomology of altitude illness is present, there is evidence of fluid retention and weight gain (Bärtsch et al., 1991; Hackett et al., 1981, 1982; Singh et al., 1969).

Exercise

Exercise is an inescapable consequence of traveling to high mountainous areas. The two factors associated with exercise that relate to weight loss are the increased water loss caused by high ventilatory rates and the increased energy output. The influence of exercise and energy expenditure on nutrition is covered by Schoene and by Hoyt and Honig (see Chapters 17 and 20 in this volume).

Sleep

The quality and quantity of sleep at altitude are important contributory factors that determine whether individuals acclimatize well or slowly deteriorate. Disturbances in sleep are related to the terrestrial elevation and the length of exposure. Many studies at very high and extreme altitudes confirm that sleep arousals of up to 30 to 40 per night can occur. These arousals are probably caused by increased episodes of periodic breathing. There is also a concurrent 50 percent reduction in total sleep time and a fivefold reduction in the REM (rapid eye movement) sleep stage. Less-disturbed sleep is observed at lower altitudes, but the phenomena may still last for weeks. Individuals commonly report "being awake half the night," "not being able to sleep," and having "frequent disturbing dreams." Problems of sleeping can contribute to mood changes during the day, loss of appetite, and daytime somnolence

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[2] BTPS is one of the sets of standard conditions under which pulmonary gas volume can be defined; the volume that is actually exhaled.

(Anholm et al., 1992; Goldenberg et al., 1992; Normand et al., 1990; Sutton et al., 1979; Weil, 1985; White et al., 1987).

STUDY LOCATION

Before considering the requirements for nutrition in a high mountain environment, it is extremely important to remember that current knowledge of the effects of altitude exposure is provided by studies conducted over a wide range of locations and conditions. Data have been collected on climbing expeditions to extreme altitudes, on military field exercises, in mountain laboratories, during trekking excursions, and under simulated conditions in hypobaric chambers. Volunteers for these studies have ranged from average college students, Army soldiers, and Special Forces Mountain Teams to experienced mountain climbers. Many high-altitude researchers simply chose not to conduct nutritional studies in the field because of the difficulty of establishing appropriate controls, heterogeneity of populations, increased study time, and expense. The resultant confounding experimental circumstances can lead to potential complications in interpretation of results, especially where diet, nutrition, and energy balance are concerned.

Factors affecting studies conducted in various locations are shown in Table 16-1. Given the same "physiological" altitude, the stresses placed on the individual can vary greatly depending on the study location. Obviously, the more variables (e.g., temperature, humidity, food, exercise) are controlled and the more simulated the condition, the closer one is to studying the physiology of pure hypoxia.

BIOPHYSICS OF THE ATMOSPHERE

The earth is surrounded by an envelope of compressible gases comprised essentially of 20.95 percent oxygen and 78.08 percent nitrogen. This relationship remains constant up to an elevation of approximately 90 km. Because of the compressibility of gases, the pressure at sea level exerted by these gases is 14.7 lbs/in^2 (760 mm Hg), and it decreases proportionately with ascent. Figure 16-2 displays several significant elevations relative to the summit of Mount Everest and illustrates the curvilinear relationship between barometric pressure and terrestrial elevation.

Assuming that cold is not a contributing factor, the problems of high-altitude exposure can be initially attributed to the reduction in the partial pressure of oxygen in the ambient atmosphere and the body's subsequent responses. The relative concentration of oxygen in the atmosphere remains constant at 20.95 percent up to approximately 110,000 m (360,892 ft), but because air is compressible, the pressure it exerts is highest at sea level and is

TABLE 16-1 Advantages and Disadvantages of Different Hypoxic Environments

Mountain	Mountain Laboratory	Hypobaric Chamber
Real-life situational stresses	Stable and controlled food and water supply	Sophisticated measurement and study design
Novel food; possible food contamination	Protection from inclemency; stable temperature	Stresses of confinement, noise, etc.
Availability of potable water	Sleep disturbances	Sleep disturbances
Adverse weather; low ambient temperature	Infinite exposure time	Controlled environmental conditions for temperature, pressure, and humidity
Psychological effects; sleep disturbances	Constant altitude	Controlled nutrition and exercise
Equipment and clothing problems	Controlled exercise	
Abrupt, constant changes in elevation		
Frequent bouts of demanding exercise or long periods of inactivity		

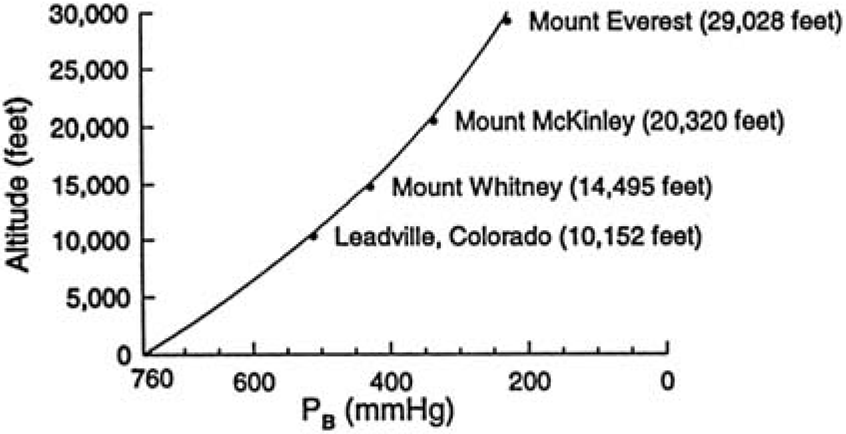

FIGURE 16-2 Relationship between altitude and barometric pressure (P_B), with significant high-altitude locations in North America relative to Mount Everest highlighted (3,094; 4,418; 6,194; and 8,848 m [10,152; 14,495; 20,320; 29,028 ft]).

proportionately reduced with altitude. In a field situation, actual barometric pressure at any given elevation is also dependent on the latitude, whereas chamber studies usually utilize a standardized chart based on the ICAO (International Civil Aviation Organization) Standard Atmosphere (Anonymous, 1954).

The ICAO standard is used universally to equate atmospheric pressure and elevation in chambers and aircraft. However, in actual field situations, discrepancies in the ICAO pressure-elevation relationship occur because of temperature (season), latitude, and weather influences. These discrepancies become larger with increasing elevation.

The percent oxygen in levels of the atmosphere remains essentially the same as at sea level regardless of the elevation and latitude. The reduction in barometric pressure, however, does cause a concomitant, obligatory decrease in the *partial pressure* of oxygen (Po_2), which is defined as the specific fractional composition of the mixed gas expressed as a pressure. For example, at sea level, the barometric pressure (P_B) is 760 mm Hg, and Po_2 is about 160 mm Hg (760 mm Hg × 0.21). At 5,500 m (18,045 ft, $P_B = 380$ mm Hg), the Po_2 is only 80 mm Hg (380 × 0.21). In the pulmonary alveoli, this reduction becomes significant because of the almost constant partial pressures of both water vapor (47 mm Hg at 37°C [99°F]) and carbon dioxide (CO_2) (40 mm Hg with normal ventilation).

The decrease of ambient Po_2 is the direct cause of many medical problems at altitudes above 2,438 m (8,000 ft). This decrease causes several interrelated physiologic responses that function to improve oxygen delivery to the tissues. Depending on the conditions of exposure and the characteristics of the individual, these responses can also be maladaptive, causing illnesses and dysfunction that could compromise performance and well-being (Cymerman and Rock, 1994).

ACUTE PHYSIOLOGICAL RESPONSES

The first consequence of a significant reduction in *ambient* Po_2 is a decreased *arterial* Po_2 that stimulates peripheral and central chemoreceptors. This stimulation occurs when the inspired Po_2 is lowered to approximately 122 mm Hg or 1,524 m (5,000 ft) elevation. The sensitivity of peripheral chemoreceptors to hypoxemia (decreased blood oxygenation) is characteristic of an individual and is probably genetically determined. However, it can be modified by external factors such as respiratory depressants (alcohol, soporifics) and stimulants (caffeine, cocoa), but not physical fitness.

Chemoreceptor stimulation causes an increase in ventilation. This increase does not entirely compensate for the decrease in the inspired Po_2. As a result, there is a sustained decrease in hemoglobin saturation and arterial Po_2 that is proportional to the altitude. Hyperventilation results in a reduction in arterial CO_2 (respiratory alkalosis) that limits the increase in ventilation.

Within several days, the kidneys compensate for the respiratory alkalosis by increasing excretion of bicarbonate. Resting ventilation continues to rise slowly, reaching a maximum in about 1 week. With continued ascent, the process is repeated to a smaller degree with further increases in ventilation. Increased ventilation is the principal characteristic of acclimatization (the adaptation to altitude exposure) and is the primary mechanism responsible for improving the oxygen availability at the cellular level.

Figure 16-3 illustrates the relative changes in ventilation, end-tidal CO_2 partial pressure, and blood oxygen saturation over the course of 20 days at the summit of Pikes Peak (4,300 m [14,110 ft]). Resting minute ventilation of approximately 5 to 7 liter/min at sea level can increase to almost 15 liter/min at this elevation. The increase observed in blood oxygen saturation is not entirely independent of ventilatory acclimatization. Some of the increase can be attributed to changes in lung parenchyma, circulation, erythrocytes, and metabolism (Bender et al., 1989).

Figure 16-4 shows that the initial increase in cardiac output is caused principally by the increase in heart rate with little or no change in stroke volume.

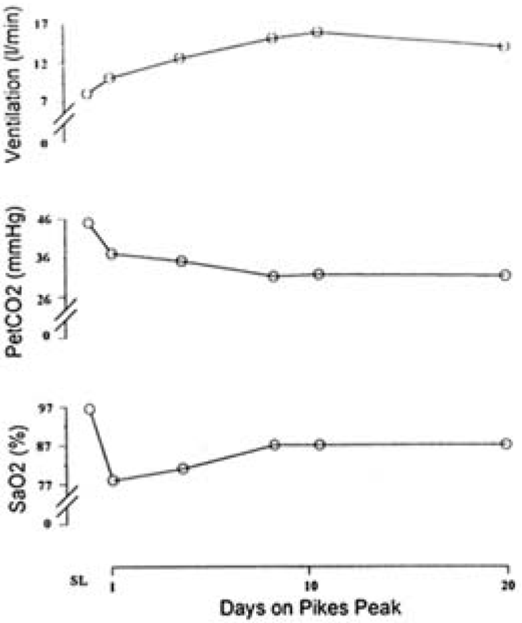

FIGURE 16-3 Resting respiratory responses during acclimatization to 4,300 m (14,110 ft) altitude. SaO^2, arterial oxygen saturation; $PetCO^2$, end tidal partial pressure of carbon dioxide. SOURCE: Adapted from Bender et al. (1989).

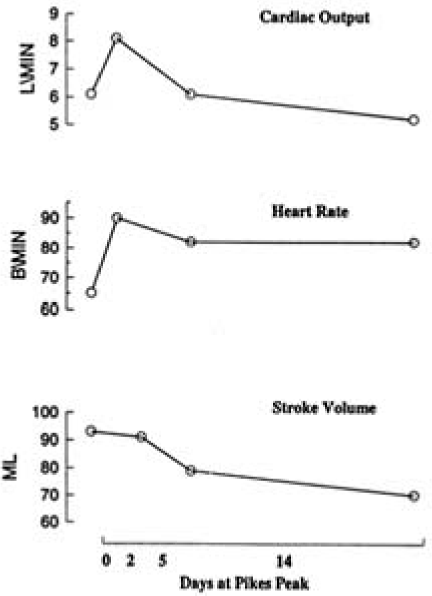

FIGURE 16-4 Relationship between cardiac output, heart rate, and stroke volume during 14 days of acclimatization to 4,300 m (14,110 ft). ML, milliliters; B/MIN, beats per minute; L/MIN, liters per minute. SOURCE: Adapted from Hannon and Vogel (1977).

With continued exposure, stroke volume falls as a result of the reduced plasma volume and decreased venous return. After 1 week of exposure, cardiac outputs are essentially normal or only slightly reduced (Hannon and Vogel, 1977).

Stimulation of the sympathetic nervous system, principally secretion of norepinephrine, as a response to altitude exposure has been confirmed in many studies (Brooks et al., 1991a; Cruz et al., 1976; Cunningham et al., 1965; Hoon et al., 1976; Kotchen et al., 1973; Mazzeo et al., 1991; Moncloa et al., 1965; Reeves et al., 1992a; Young et al., 1989). The typical response of an increase in norepinephrine without a corresponding increase in epinephrine is depicted in Figure 16-5. This increase is probably responsible for many of the cardiovascular and metabolic changes seen with acclimatization, such as augmentation of metabolic rate, lactate accumulation during exercise, and increased heart rate. Norepinephrine increases may also be correlated with alterations in myocardial contractility, atrial natriuretic factor, angiotensin, and aldosterone (Reeves et al., 1992b).

Exact indices of acclimatization are difficult to determine and are altitude- and time dependent. Some of the physiological variables used to delineate successful acclimatization include the plateauing of the rise in ventilation, the compensated respiratory alkalosis, the increased real hematocrit, the restoration of normal blood flow distribution, and altered metabolic pathways.

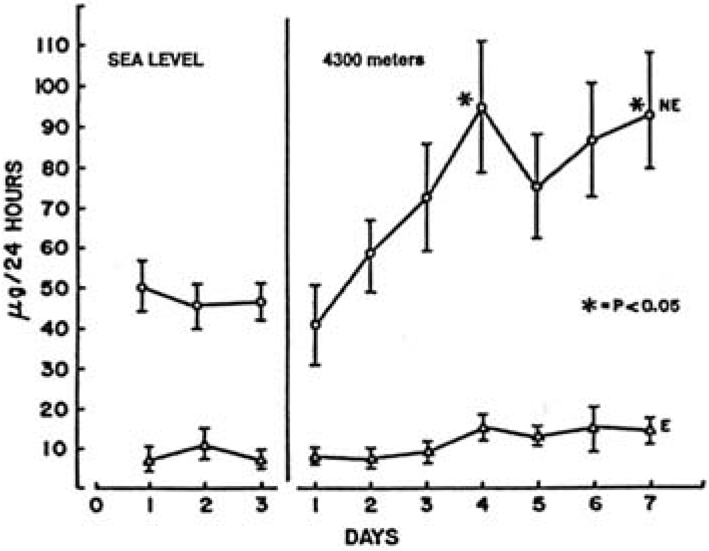

FIGURE 16-5 Differential response of urinary norepinephrine (NE) and epinephrine (E) during 7 days of exposure to 4,300 m (14,110 ft). SOURCE: Adapted from Burse et al. (1987).

The degree of adaptability of the human organism to very high terrestrial elevations is best exemplified by the natives of the Andes mountains. From present-day observations and historical records of South American Indians, there is evidence that oxygen concentrations as low as 10.5 percent (equivalent to 5,500 m or 18,045 ft) can be tolerated to do heavy physical work as long as the natives sleep at a lower altitude. High-altitude natives can apparently maintain a routine of working in mines at 5,500 m (18,045 ft) and sleeping at lower elevations for extended periods of time without marked deterioration.

For sojourners to high altitudes without any acclimatization, this level of exposure would result in marked deterioration and illness. The ability for newcomers to acclimatize adequately to a moderate altitude is dependent on the rate of ascent and the time allowed for acclimatization. Figure 16-6 illustrates the relative time, magnitude, and direction of changes at the respiratory, circulatory, and cellular levels with respect to their relationship to general health and performance at 4,267 to 4,572 m (14,000 to 15,000 ft).

Several illnesses can occur with ascent to altitude. Of these, only two are of real concern for the purposes of this book. A brief discussion of these illnesses is warranted because they affect nutrition. These illnesses are termed *acute mountain sickness* (AMS) and *high-altitude cerebral edema* (HACE).

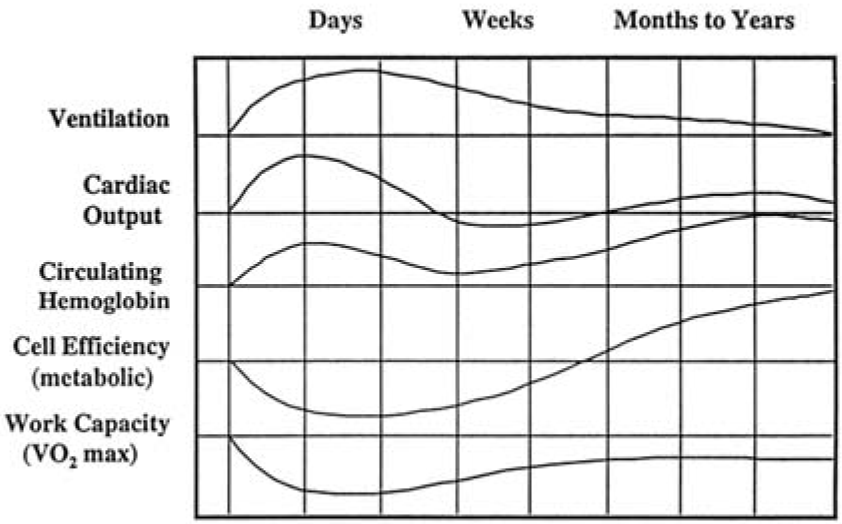

FIGURE 16-6 Approximate size, direction, and temporal changes that occur during acclimatization to 4,267 to 4,572 m (14,000 to 15,000 ft). SOURCE: Adapted from Houston (1982).

AMS is the most common manifestation of the altitude illnesses. It is associated with rapid exposure of the unacclimatized individual to altitudes above 3,048 m (10,000 ft). Symptoms usually start after several hours of exposure. The illness is self-limiting, remitting over the course of 3 to 7 days, depending on staging (temporary residence at an intermediate altitude) and any changes in elevation.

Prominent manifestations of the disorder are listed in Table 16-2. Sleep disorders characterized by periodic breathing are not uncommon. A factor not

TABLE 16-2 Symptoms of Acute Mountain Sickness (AMS) and High-Altitude Cerebral Edema (HACE)

AMS	HACE
Headache	Severe headache
Nausea	Nausea
Vomiting	Vomiting
Weakness	Extreme lassitude
Lassitude	Truncal ataxia
General malaise	Altered mental status
Decreased coordination	Ataxic gait
Dizziness	Generalized neurologic abnormalities
Oliguria	

related to AMS per se, but one that probably affects food consumption, is gas expansion in the gastrointestinal tract. The problem obviously persists with continued ascent due to the continued reduction in barometric pressure.

HACE is thought to be a progressive form of AMS with similar symptoms as shown in Table 16-2, albeit on a more severe scale. The incidence of HACE is extremely low but requires immediate attention and medical treatment. From a nutritional standpoint, it should not be a concern for troops at high terrestrial elevations.

WEIGHT LOSS AT ALTITUDE

Altitude exposure usually leads to significant weight losses in nonacclimatized individuals. Table 16-3 summarizes the weight losses of subjects from several selected studies conducted on high-altitude expeditions, in high-altitude field laboratories, and in hypobaric chambers. This weight loss has been attributed to the novelty of the environment, the effects of altitude-related illnesses, and to the factors shown in Figure 16-7. These factors may or may not be related to altitude-induced illness. Weight loss appears to occur in those whose travel commences at sea level and stabilizes with acclimatization. It does not occur to any appreciable extent in high-altitude natives.

The degree of weight loss is apparently dependent on the altitude and the duration of stay at high altitudes. The direct relationship between the severity of hypoxia and body weight loss has not been demonstrated decisively for humans, but has been demonstrated in animals (Schnakenberg et al., 1971). With acclimatization, weight loss may not be observed unless the altitude is extreme, that is, above 5,000 m (16,404 ft). In fact, Pugh (1962) observed an increase in body weight in one subject on the 1960–1961 Silver Hut Expedition when that subject had a respite of 20 days at 4,500 m (14,764 ft) after descent from 5,800 m (19,029 ft). Even in mountain laboratories at moderate altitudes where diet was controlled, there may not be evidence of an obligatory loss of weight (Butterfield et al., 1992; Kayser et al., 1993).

All of the factors shown in Figure 16-7 can contribute to an overall loss in body weight in deployed soldiers who may not have the benefit of time for acclimatization that is afforded to mountain trekkers and climbers.

Diuresis and Hypodipsia

Hypoxia-induced diuresis and subliminal thirst (hypodipsia) are usual occurrences in healthy subjects acutely exposed to altitudes similar to the summit of Pikes Peak (4,300 m [14,110 ft]). With individuals having symptoms of AMS, fluid retention that is independent of fluid intake has been observed. These individuals are characterized by a gain in weight. Bärtch et

TABLE 16-3 Reductions in Body Weights from Selected Expeditions, Field Laboratories, and Hypobaric Chamber Studies

Study	Site	Elevation (m [ft])	Sample Size	Durations (days)	Δ Weight (kg)	Loss (%)
Surks et al., 1966	Pikes Peak	4,300 (14,110)	5	8	-2.4	3.4
Siri et al., 1969	Mount Everest	5,400-7,000 (17,717-22,966)	10	63	-10.4	12.9
Grover et al., 1976	Chamber	4,300	4 5[*,‡]	5 5	-3.4 +2.0	- -
Boyer and Blume, 1984	Mount Everest	5,400	8 8	32 47	-1.2 -6.5	1.6 8.8
Rose et al., 1988	Chamber	8,848[†] (29,030)	6	40	-7.4	8.9
Boutellier et al., 1990	Mount Lhotse	8,398 (27,550)	6	58	-1.5	2.2
Bärtsch et al., 1991	Capanna Margherita	4,559 (14,960)	15[‡]	5	-2.25	-
Edwards et al., 1991	Potici, Bolivia	3,500 (11,483)	20	16	-3.0	4.0
Butterfield et al., 1992	Pikes Peak	4,300	7	21[§]	-2.0	-
Kayser et al., 1993	Italian Research Lab, Nepal	5,050 (16,568)	8	7 14 28	-0.3 -2.7 -2.6	0.4 3.5 3.4

[*] Subjects received supplemental CO_2 to prevent respiratory alkalosis.

[†] Simulated ascent of Mount Everest; inspired Po_2 to 43 torr

[‡] Subjects who had a weight gain became ill.

[§] No evidence of weight loss with adjusted energy intake after 7 days.

al. (1988) found reduced diuresis associated with severe AMS, as have several other investigators (Hackett and Rennie, 1979; Hackett et al., 1976, 1981; Singh et al., 1969). Headache, the most prominent symptom of AMS, can be sufficiently severe to have a negative impact on food intake. It is estimated that food intakes are decreased by as much as 25 to 50 percent during the first 3 days of acute exposures to 4,300 m (14,110 ft), the period when illness symptoms are at their peak (Consolazio et al., 1966; Janoski et al., 1969; Surks et al., 1966).

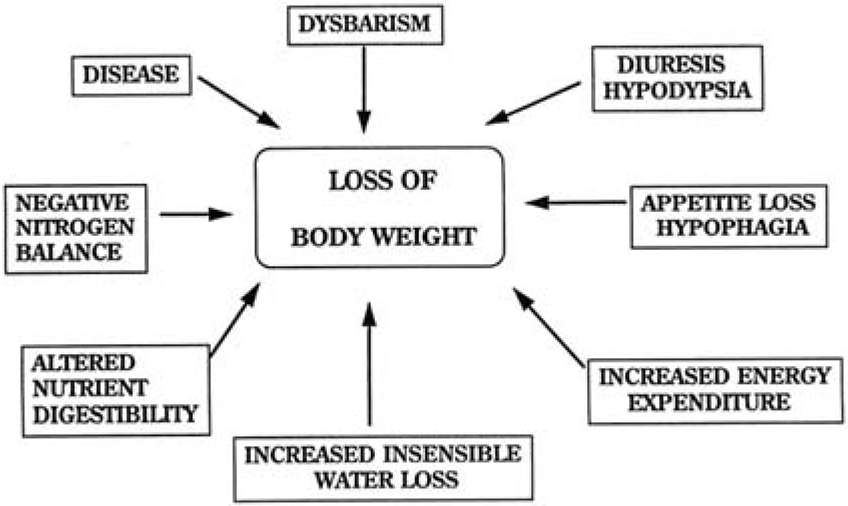

FIGURE 16-7 Factors affecting weight loss at altitude that do not involve altitude-specific illnesses.

Dysbarism

Dysbarism is a symptom complex resulting from exposure to decreased or changing barometric pressure unaffected by hypoxia. Although decreased energy intake per se can be associated with gastrointestinal upset, gas expansion above 3,353 m (11,000 ft) intensifies the degree of distress. The expansion of intraluminal gas, which can be caused by both gas expansion and a high-fiber mountain diet, may be very disconcerting and even painful (Hultgren, 1983). If diet and constantly changing altitudes are continued for any length of time, there can be adverse effects on food consumption.

Anorexia

In addition to a possible direct effect on brain centers controlling appetite, changes in menu inherent in military mountain field studies usually result in reduced dietary nutrient intake. Although palatability of food may have been a factor with early dietary studies, a caloric deficit secondary to appetite suppression (anorexia) may still occur when the best possible food is available.

Edwards et al. (1994) studied nutritional intakes and the effects of carbohydrate supplementation of 67 soldiers performing moderate amounts of physical work at altitudes of 3,200 to 3,500 m (10,499 to 11,483 ft) for 13 days. They concluded that despite the availability of ample, well-cooked food, soldiers with high rates of energy expenditure failed to maintain their body weights and lost approximately 1.7 kg. The effect of solid carbohydrate supplementation was not significant. Even when the diet may not be as palatable as in the Edwards study, Butterfield et al. (1992) showed that in seven young men exposed to 4,300 m (14,110 ft) for 21 days and given a supplemented Ensure diet$^{\copyright}$, weight loss appeared to be halted after the energy intake was purposefully increased to compensate for measured increases in basal metabolic rate during the second week of exposure.

In a short review of nutrition and altitude exposure, Kayser et al. (1992) also concluded that with maintenance of adequate intake, body weight losses attributable to water, fat loss, and muscle wasting could be avoided. The implication from the latter two studies is that there is no dysfunction of nutrient absorption at altitudes up to 5,000 m (16,404 ft); rather, energy intakes are voluntarily reduced for some unexplained reason. The result is that with continued residence at a constant, moderate altitude such as 4,300 m (14,110 ft) and no illness symptomatology, there may be progressive loss of body weight in a military population performing tasks requiring a high level of exertion.

When military operations require "living off the land," the problems associated with ingestion of indigenous foods are common and well known. Often the basic principles of sanitary food preparation are dismissed when time is limited and basic supplies are in short supply or rationed. Proper sterilization of water is also often neglected when the supply is thought to be clean because of remoteness. This type of negligence usually results in a wide range of gastrointestinal problems such as parasitic infection, anorexia, and diarrhea.

Imbalance Between Energy Intake and Expenditure

The discordance in energy intake and expenditure is evident in military field situations irrespective of the terrestrial elevation. It is not unusual for daily energy expenditures to be on the order of 4,000 to 6,000 kcal, with contributions of approximately 1,200 to 2,800 kcal/d from body energy stores.

This expenditure could produce energy deficits as high as 31 percent (Moore et al., 1992). In two different studies of soldiers on field training exercises at moderate terrestrial elevations (2,200 to 3,100 m [7,218 to 10,171 ft]), Hoyt et al. (1991, 1994) using the doubly labeled isotope method found mean total energy expenditures of 4,919 kcal/d for 11 days and 4,558 kcal/d for 5 days. This level of energy expenditure resulted in body weight losses of 2.5 and 1.3 kg, respectively. It appears that body weight losses, especially at altitude, are inevitable in field studies involving high levels of strenuous exertion, regardless of the availability of food. A more definitive discussion of energy expenditure is provided by Hoyt and Honig (see Chapter 20 in this volume).

Loss of Body Water

Losses in sensible and insensible body water due to working in a high, dry environment can have serious consequences on the ability to function and survive. Insensible water losses are discussed in the section on water. Losses via both avenues, however, will occur at altitude under conditions that are high-hot and high-cold and that result in voluntary dehydration—the difference between water intake and water losses. Especially when exertion is involved, voluntary dehydration will be a universal phenomenon at altitude. The condition occurs soon after exposure and probably lasts for an indefinite period of time. The loss of total body water combined with fluid shifts within the extravascular compartment can interfere with the standard measurements of energy expenditure and body composition (Fulco et al., 1985). Relative hypodypsia—decreased water intake—can be as much as one-half of the fluid loss with active periods in a hot, dry environment (Adolph et al., 1947). It is anticipated that it could be higher under high-altitude conditions.

Nutrient Digestibility

Some studies have suggested a malabsorption of nutrients from the gastrointestinal tract at altitude. Most of these studies have involved mountaineering expeditions and altitudes in excess of 5,000 m (16,404 ft). For example, Pugh (1962) found visual evidence of steatorrhea (excess fat in the stools) at 4,570 m (14,993 ft), and Boyer and Blume (1984) found increased fecal fat content at 5,400 m (17,718 ft). However, the consensus of findings is that fat digestibility is normal up to altitudes of 5,000 m (16,404 ft). The same conclusion has been drawn for carbohydrate absorption and protein (Chesner et al., 1987; Imray et al., 1991; Kayser, 1992; Kayser et al. 1992; Rai et al., 1975; Sridharan et al., 1982). Both Butterfield et al. (1992) and Kayser et al. (1993) conclude that there is no dysfunction of absorption but rather a dysfunction of intake and that loss of weight can be avoided by matching energy input to expenditure.

When analyzing the results of nutrition studies at altitude, it may be difficult to compare and interpret the conclusions. Boyer and Blume (1984) noted that weight loss on expeditions may be due to the fact that climbers will "bulk up" before expeditions in anticipation of increased energy expenditure and that different genetic and cultural factors may be operative. Sherpas, members of the Tibetan people living on the high southern slopes of the Himalayas, do not undergo the same body composition changes as do Caucasians above 5,400 m (17,718 ft). Statistical problems are also encountered when subject numbers are so low that including or excluding one aberrant subject is sufficient to place the significance of changes in doubt.

In conclusion, at moderate altitudes there appears to be no problem in the digestion and absorption of nutrients from the gastrointestinal tract. Palatability, however, may be altered. Most climbers prefer a high-carbohydrate, low-fat diet, with fatty foods actually becoming distasteful.

Studies bearing on the composition of a "mountain" diet indicate that rations used at sea level would be adequate at moderate altitudes. It is generally believed that high-carbohydrate diets may be beneficial at high altitudes with regard to both amelioration of high-altitude illness symptoms and physical performance (Dramise et al., 1975; Hansen et al., 1972; Strange et al., 1990). In fact, a greater reliance on glucose as an energy source has been demonstrated in several studies of acute and long-term altitude exposure (Brooks et al., 1991b; Dramise et al., 1975; Johnson et al., 1974).

Protein Metabolism

With even a minimal loss of weight at high altitudes, there will be a loss of lean body mass. However, care should be used when interpreting results based on skinfold measurements alone. Skinfold measurements may not be accurate in a high-altitude environment. Skinfold measurements used in equations for estimating fat mass and fat-free mass tend to underestimate the former and overestimate the latter (Fulco et al., 1992).

When intake of food is limited for whatever reason, the body does not appear to use fat stores preferentially over carbohydrate and protein. In the best of diets aimed at reducing fat stores, there is still a 25 percent loss of lean body mass. Of the weight loss observed with long-term exposure, a sizable fraction is due to the reduction in muscle size. Feretti et al. (1990) and Rose et al. (1988) found decreases of up to 14 percent in vastus lateralis cross section. Although detraining (inability to maintain sea-level workloads and exercise durations) of elite climbers may be a possibility to explain the reduced muscle mass, there are indications that smaller fiber sizes may be beneficial in that capillary density is increased and diffusion distances are decreased.

Interestingly, when endurance training is performed in the presence of hypoxia, there is an increase in capillarity and muscle fiber size (Hoppeler and Desplanches, 1992).

There is still evidence that protein metabolism may be altered with moderate hypoxia, at least acutely. Rennie et al. (1988) found significant effects on leucine metabolism in the forearm, and Surks (1966) demonstrated a significant increase in albumin degradation during the first 3 days at 4,300 m (14,110 ft).

AUTHOR'S CONCLUSIONS AND RECOMMENDATIONS

The following conclusions are made regarding the physiology of high-altitude exposure:

- Initial weight loss with altitude exposure may be unavoidable due to increased water losses and decreased energy intake relative to expenditure.
- Weight loss is due to an initial loss of water followed by loss of fat and muscle.
- Increasing food intake can prevent loss of body weight, with energy intake matching expenditure as much as possible.
- There is no problem of nutrient digestibility at moderate altitudes.
- Sea-level rations are well tolerated for several weeks at moderate altitudes.
- A high-carbohydrate, low-fat diet, with a possible liquid carbohydrate supplement, may be the preferred altitude ration.
- Confounding effects of altitude-related illness, uncontrolled physical exertion, and differences in ultimate altitudes complicate interpretations between studies.

Recommendations for future research include controlled studies designed to answer the following questions:

- Can altitude-induced weight losses be reduced? Can weight losses be reduced, stopped, or reversed at any point in the exposure by dietary manipulation? Is the weight loss detrimental?
- Would additional carbohydrates in the diet, especially in liquid form, be efficacious in ameliorating illness and improving physical performance?
- Are the combined effects of altitude and cold or hot conditions additive? How much more energy is required under these conditions to perform a standard amount of physical work? How much more insensible and sensible water is lost?
- Is muscle function altered as a result of loss of muscle mass?

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17

Physical Performance at High Altitudes

Robert B. Schoene[1]

INTRODUCTION

Upon ascent to high altitudes, work capacity decreases (Cymerman et al., 1989; Pugh et al., 1964; Sutton et al., 1988; West et al., 1983) (Figure 17-1). After acclimatization at moderate altitudes (3,000 m [9,843 ft]), much of the loss in exercise performance is regained (Buskirk et al., 1967); whereas, at higher altitudes (3,000 to 8,000 m [9,843 to 26,247 ft]), no matter how long the acclimatization period, full recovery of aerobic function is never achieved (Cymerman et al., 1989; Pugh, 1964; Sutton et al., 1988; West et al., 1983). In fact, at extreme altitudes, deterioration occurs that may be complicated by psychological and cognitive impairment (Hornbein et al., 1989). Even at moderate altitudes, factors that impair exercise may be confounded by concomitant maladaptation or altitude illness (see Anand and Chandrashekhar, Chapter 18 in this volume).

The purpose of this chapter is to review the adaptations that optimize the transport of oxygen from the air to the cell in an environment where the barometric

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pressure is lower and thus the availability of oxygen is less. Additionally, limits to these adaptations will be discussed, and suggestions for areas of further research will be proposed.

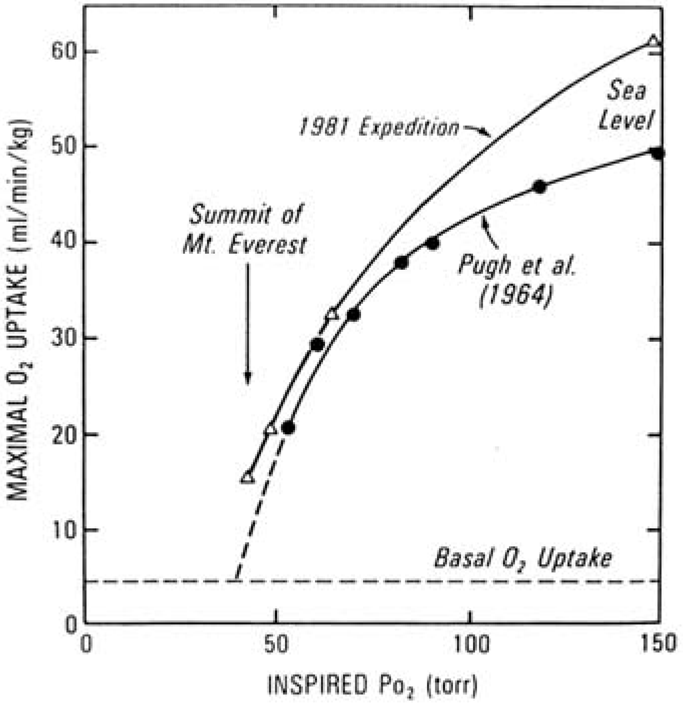

FIGURE 17-1 Data taken from two expeditions to high altitudes showing the decrease in maximal oxygen consumption that occurs with a decrease in inspired partial pressure of oxygen as one ascends to high altitudes. SOURCE: West et al. (1983), used with permission.

ADAPTATIONS AND LIMITS

Ventilation

Minute ventilation (the quantity of air inspired in 1 minute) increases on ascent to high altitudes (Boycott and Haldane, 1908; Dempsey and Forster, 1982; Houston and Riley, 1947; Rahn and Otis, 1949). This response is mediated by stimulation of the carotid body by the low partial pressure of oxygen in the blood (Lahiri et al., 1981; Vizek et al., 1987; Weil, 1986) and is measured by the increase in ventilation, the hypoxic ventilatory response (HVR) (Weil et al., 1970). For instance, at 6,100 m (20,013 ft), ventilation for a given metabolic rate is almost four times that at sea level (Sutton et al., 1988; West et al., 1983) (Figure 17-2). Extraordinary degrees of hyperventilation have been measured on the summit of Mount Everest, which demonstrates the very high levels of ventilation that can be achieved (West et al., 1983) (Figure 17-3). There is inherent individual variation in this response (Weil et al., 1970), but people who adapt normally at moderate and higher altitudes experience an ongoing augmentation of breathing for 10 to 14 days such that oxygenation of the blood continues to improve with acclimatization (Weil, 1986).

A wealth of data shows that individuals with blunted ventilatory responses are predisposed to altitude illnesses (Hackett and Rennie, 1979; Hackett et al., 1981, 1982, 1988). Almost everyone, however, if they allow enough time for adaptation, will experience an adequate degree of ventilatory augmentation such that altitude illnesses are not experienced. At extreme altitudes, a brisk HVR and subsequent ventilatory response at rest and during exercise convey an advantage in physical performance (Schoene et al., 1984). Although HVR, which is a marker for the overall ventilatory response, can be measured, it is not necessary to screen individuals for tolerance to high altitudes.

Three limitations are inherent in the ventilatory response at high altitude: (1) constraints in lung mechanics, (2) degree of an individual's chemosensitivity and subsequent ventilation, and (3) dyspnea. The first probably is not a

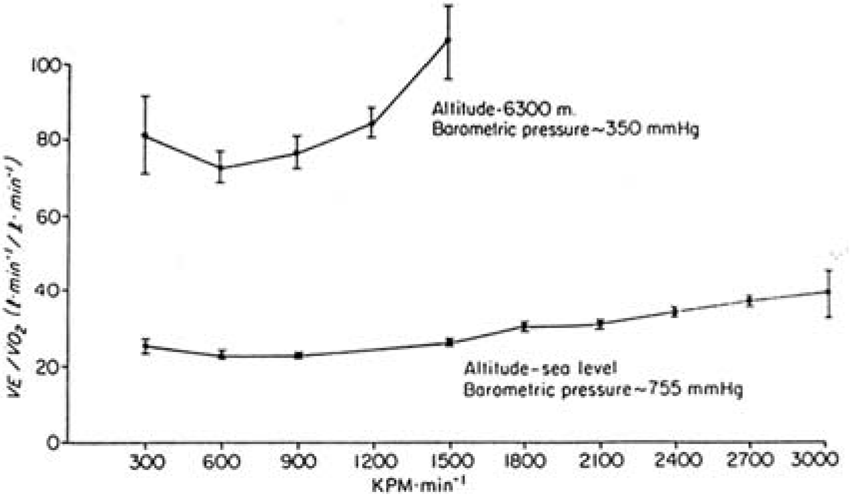

FIGURE 17-2 Ventilatory equivalents (VE/ $\dot{V}_{o2}$) for oxygen consumption during exercise in the same individuals at sea level (bottom line) and 6,300 m (20,669 ft) after 6 weeks of acclimatization. KPM, kilopound meters. SOURCE: Schoene, et al. (1984), used with permission.

major factor (Coates et al., 1979); the second has been discussed in the previous paragraph; and the third has not been studied.

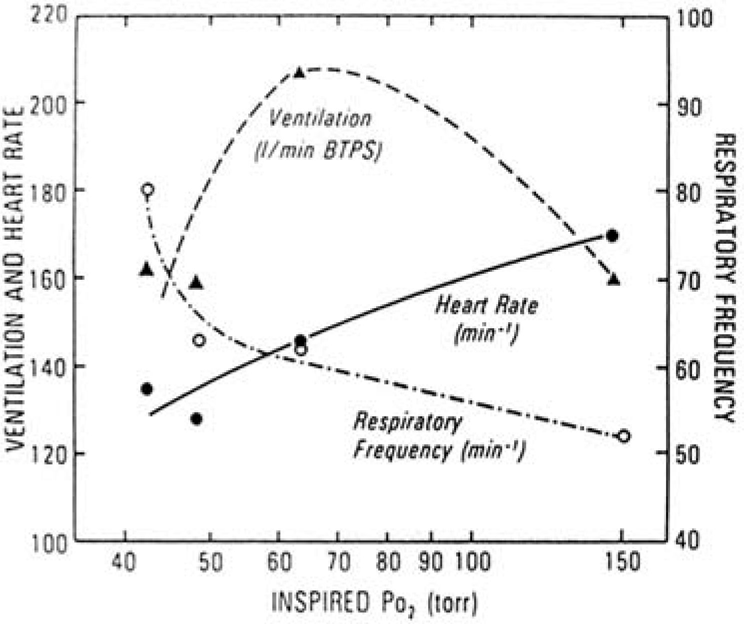

FIGURE 17-3 Respiratory frequency, heart rate, and ventilation as a function of the partial pressure of inspired oxygen. Minute ventilation during maximal exercise increases as the partial pressure of inspired oxygen decreases until an extreme altitude is reached such that a very low work rate and subsequent decrease in ventilatory demand are achieved. Additionally, maximal heart rate decreases in acclimatized individuals. BTPS, Body Temperature Pressure Saturated. SOURCE: West et al. (1983), used with permission.

Gas Exchange

At sea level, transfer of oxygen from the air to the blood takes place with little or no restriction because perfusion to the lung is well matched to ventilation, and the driving pressure for oxygen from air to blood is high, thus allowing adequate time for equilibration of oxygen from the air to the blood. At high altitude, however, a diffusion limitation exists at the air-blood interface such that the alveolar-arterial oxygen difference is accentuated and is further exaggerated with exercise (Gale et al., 1985; Wagner et al., 1986, 1987; West et al., 1962) (Figure 17-4).

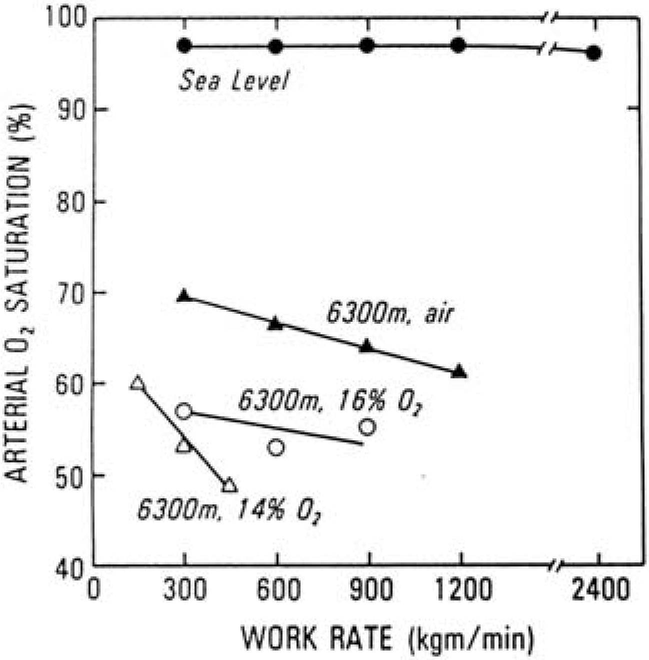

FIGURE 17-4 Arterial oxygen saturation (%) during exercise at sea level and 6,300 m (20,669 ft) with simulated higher altitudes (8,000 and 8,800 m [26,247 and 28,871 ft]). A diffusion limitation for oxygen exists at high and not low altitudes and is accentuated with each increase in altitude.
SOURCE: West et al. (1983), used with permission.

A growing body of research has helped to elucidate why this diffusion limitation exists. Not only is there less oxygen available in the ambient air, but there is also smaller gradient in oxygen at the alveolar-capillary barrier than occurs at low altitudes. The higher one goes, the greater is the drop (Wagner et al., 1987; West et al., 1983). The hypoxic pulmonary vasoconstrictive response (HPVR) results in improved matching of blood flow to ventilation. Nevertheless, the diffusion limitation persists because of (1) a lower driving pressure for oxygen from air to blood, (2) the decreased transit that results from a higher cardiac output (especially with exercise), and (3) the fact that the acquisition of oxygen by hemoglobin takes place on the steep part of the oxygen-hemoglobin dissociation curve (Gale et al., 1985; Wagner et al., 1986, 1987; West et al., 1983).

Cardiac Response

Cardiac output increases upon acute ascent to high altitudes but then decreases to a level that is comparable to sea-level values for any given metabolic rate (Astrand et al., 1958; Hartley et al., 1967; Klausen, 1966; Pugh, 1964). Myocardial function is well preserved, even at extreme altitudes and in spite of high pulmonary vascular resistance from HPVR and exercise (Groves et al., 1987; Reeves et al., 1987). Upon first ascent, the heart rate at set workloads is higher than at sea level. With adaptation, these heart rates return toward sea level values. Maximum heart rates at very high altitudes, with acclimatization, however, are lower than sea level maximum values (Reeves et al., 1987; West et al., 1983) (Figure 17-3). After much speculation, most physiologists agree that the lower maximum rate is not secondary to hypoxic depression (maximum heart rate) or primary myocardial dysfunction but is merely an appropriate response to the metabolic rate, which is limited by other factors (Reeves et al., 1987). The heart, therefore, appears to function well in the high-altitude environment.

Hematologic Response

Oxygen delivery to the tissues is improved by the hematologic response at high altitudes. This response occurs in two ways: (1) erythropoiesis, which results in greater carrying capacity of the blood to transport oxygen to the tissues (Abbrecht et al., 1972; Erslev, 1953; Faura et al., 1969); and (2) at very high altitudes, a profound respiratory alkalosis contributes to a leftward shift in the oxygen-hemoglobin dissociation curve which optimizes loading of oxygen to the blood at the lung but probably does not impair unloading at the tissues where other factors may facilitate unloading (Winslow et al., 1984). The erythropoietic response is mediated by a rapid increase in erythropoietin but is not manifest by a higher blood hemoglobin for at least 7 to 14 days.

Limitations to this response lie in either an impairment to erythropoiesis from nutritional deficiencies or in an overresponse, resulting in polycythemia, higher blood viscosity, a decrease in perfusion, and subsequent lower oxygen delivery to the peripheral tissues (Aggio et al., 1972; Humphrey et al., 1979; Messmer, 1975; Winslow et al., 1987). The polycythemia may be accentuated by the diuresis that occurs at high altitudes and the tendency of individuals not to take enough fluid, especially with prolonged sojourns. Thus, excessive hyperviscosity may be minimized by ensuring adequate fluid ingestion.

Peripheral Tissues

Utilization of oxygen at the tissue level requires an adequate availability of oxygen to the cells and mitochondria and sufficient substrate for oxidative metabolism. Appropriate responses, therefore, entail: (1) improving blood flow by increasing capillary density, (2) maintaining adequate fuel, and (3) increasing mitochondrial density. What actually happens is not very clear.

Substrate availability (availability of free fatty acids and glycogen) remains good, even at extreme altitudes (Green et al., 1989). An apparent increase in capillary and mitochondrial density with prolonged stay at high altitudes may in fact be merely a reflection of muscle cell atrophy, such that morphometric measurements of capillary and mitochondrial densities may be misleading (Banchero, 1982; Green et al., 1989).

Other limitations may be imposed by diffusion limitation of oxygen from the blood to the tissues. Data at very high simulated altitudes in a hypobaric chamber in Operation Everest II suggest that the low driving pressure for oxygen in the periphery imposes a predictable limitation that is greater the higher one goes (Wagner et al., 1987). This finding is controversial because it is not clear what the minimal level of oxygen is that will allow diffusion of oxygen from hemoglobin, across the cell membrane into the cytoplasm, and into the mitochondria (Hochachka et al., 1983). Some researchers feel there is adequate oxygen available for this process even in extreme hypoxemia, and recent data using nuclear magnetic resonance (NMR) spectroscopy show that in acute hypoxia in the exercising human forearm, phosphocreatine regeneration is not impaired (Conley et al., 1994). More work is necessary to elucidate this critical issue.

Nervous System

The data about oxygen delivery from the air to the tissues do not explain fully why exercise is decreased at high altitudes, so one must turn to the central and peripheral nervous system to look further. It is conceivable that hypoxia may suppress the brain, and the subsequent neural output to the peripheral nervous system and/or hypoxia itself may actually inhibit neuromuscular transmission of impulses. Some data exist that help in part to elucidate this question.

Exposure to extreme altitudes results in at least transient neuropsychometric dysfunction (Hornbein et al., 1989; Regard et al., 1989). Climbers on Mount Everest, as well as subjects on a simulated ascent to Mount Everest in a hypobaric chamber (Operation Everest II), experienced word aphasia (difficulty in speaking) and apraxia (difficulty in manual dexterity), as well as neurological impairment in tasks such as memory recall and rapid finger tapping. In the climbing group, the finger-tapping function remained decreased a year later while the other tests had returned to normal. The subjects from the chamber experiment were not studied again. Interestingly, there was a correlation between the subjects' HVRs and neuropsychometric dysfunction, such that those who had higher HVRs, subsequent higher oxygen saturations at rest, less profound desaturation with exercise, and better physical performance at altitude had more impairment (Hornbein et al., 1989). The authors speculated that those subjects who had greater hyperventilation and therefore hypocapnia (the fall in carbon dioxide levels that results from hyperventilation) also had more cerebral vasoconstriction and lower oxygen delivery to the brain. This phenomenon may also occur during sleep since more periodic breathing and oxygen desaturation has been documented in those with higher HVRs (Lahiri et al., 1983; White et al., 1987).

Other studies have investigated some of the same variables in climbers with repeated exposure to extreme altitudes (Clark et al., 1983; Jason et al., 1989; Regard et al., 1989). Some of the same impairments are present, but they do not correlate with length of time spent above 8,000 m (26,247 ft), and the retrospective nature of the studies make interpretation of the data tenuous. Impairment in memory was documented in Himalayan climbers (Cavaletti, 1987; Regard et al., 1989), but other investigators have not duplicated these findings (Clark et al., 1983; Jason et al., 1989). Interpretation of these studies must be tempered with the thought that severe environmental hypoxia may be necessary to induce these changes and that there may be individual variability in susceptibility to hypoxia.

Neuromuscular function results from messages from the central nervous system to the peripheral nervous system. In the peripheral nervous system, successful contraction requires transmission of the signal from central sources along the lower motor neuron across the neuromuscular junction. Using both electrically stimulated and voluntary muscle contractions of the ankle flexors, investigators from Operation Everest II, the simulated ascent of Mount Everest, found evidence of central fatigue (evidence of decreased neurologic signals from the central nervous system) as well as decreased transmission along the nerve fiber but preservation of function at the neuromuscular junction (Garner et al., 1990).

More recent data, collected before and after a 1-month residence at less-extreme altitudes (5,000 m [16,404 ft]), showed preservation of peripheral nervous system function but modest inhibition in parameters of central nervous system output (Kayser et al., 1994). The authors thought that these data could explain the decrease in exercise performance and the lower lactate accumulations that have been documented repeatedly at high altitudes. The investigation of nervous system function is still a fertile area and may hold the essential information for the understanding of physical performance at high altitudes.

THE FUTURE

A great deal of work has been done in order to understand the decrease in performance at high altitudes. A better understanding of the transport of oxygen from the hypoxic environment to the cell has emerged, but there are several glaring omissions in this puzzle, which provide areas for future work.

First, most of the exercise studies have been performed with maximum-exercise protocols. There are good reasons for this approach: a wealth of research over many years at all altitudes, reproducibility, and ease of administration. Although the information gathered from these studies is invaluable, humans at high altitudes perform for hours, days, or months at submaximal levels, which involves a complex interaction of oxygen transport, adequate nutrition, and cerebral and psychologic function. Studies to elucidate the relationship among these factors are obviously more difficult to perform and interpret, but attention must be focused in these areas.

Second, the last topic discussed, that of central and peripheral nervous system integrity, still holds a number of mysteries that need unraveling.

Third, the delivery of oxygen from the blood to the cell and mitochondria is not fully understood, and the proposed mechanism is controversial at best. Further work is necessary in this area as well.

The most important step, however, is the interpretation and integration of these data with the goal of practical application. Fortunately, most investigators in the field are aware of this need, and important advances have been made to facilitate the sojourner's journey to high mountain regions of the world in a healthy and safe manner.

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18

Fluid Metabolism at High Altitudes

Inder S. Anand[1] *and Y. Chandrashekhar*

INTRODUCTION

Ascent to high altitude is invariably associated with changes in fluid and electrolyte composition in humans and animals. Although these changes are detectable even in those who do not exhibit any of the ill effects of high altitudes, the most florid alterations occur in those who develop high altitude-related illness (Anand et al., 1990; Bärtsch et al., 1991a; Hackett et al., 1981; Hecht et al., 1959; Levine et al., 1989). There is also evidence that subjects who develop acute mountain sickness at high altitudes may be identified prior to the onset of symptoms by distinct changes in fluid balance and in hormones regulating salt and water metabolism (Bärtsch et al., 1991a; Singh et al., 1969). One of the seminal observations in this field was made in Indian soldiers serving at high altitudes (Singh et al., 1969). They found that soldiers predisposed to develop high-altitude pulmonary edema had a reduction in urine output before they developed respiratory symptoms. This finding led to an intense study of fluid metabolism at high altitudes.

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A number of high altitude-related syndromes are associated with abnormal salt and water retention. The first such syndrome was described in cattle grazing at high altitudes. This condition, called brisket disease because of fluid retention in the brisket area, is characterized by severe congestive heart failure due to pulmonary arterial hypertension (Hecht et al., 1959). Some degree of peripheral edema is often seen in temporary visitors to high altitudes. Hackett et al. (1981) noted that fluid retention is common to all forms of acute mountain sickness and postulated a spectrum of derangements in fluid metabolism in these conditions. Fluid retention also occurs in two high altitude-related syndromes recently described by these authors: Infants born at low altitude in mainland China and taken to reside at high altitudes in Tibet develop a fatal condition called subacute infantile mountain sickness (Sui et al., 1988). This condition is characterized by severe hypoxic pulmonary hypertension leading to congestive heart failure. The second condition, adult subacute mountain sickness, occurs in adults exposed to extreme altitude and presents with severe salt and water retention without significant pulmonary hypertension (Anand et al., 1990). Therefore, changes in fluid metabolism at high altitudes appear to have important pathogenetic implications and merit detailed study.

PROBLEMS WITH AVAILABLE DATA

One of the major difficulties in making a meaningful interpretation of fluid metabolism at high altitudes is the lack of reliable data. Because experiments at high altitudes are difficult to organize, various approaches have been used to predict the response at high altitudes. These include acute and chronic experiments in hypobaric hypoxic chambers and use of low fraction of inspired oxygen (FIO_2) gas mixtures at sea level. Studies during ascent (trekking, flight, etc.) have been made at different altitudes and after varying periods of time at high altitudes. Therefore, the lack of any uniformity in the degree or type of hypoxia makes the comparison of these studies very difficult. Moreover, serial measurements of body fluid compartments on the same subjects have seldom been made despite the fact that changes in fluid metabolism appear to depend on the duration of stay at high altitudes (Hannon and Rogers, 1975; Jain et al., 1980, 1981). Furthermore, some of the older studies were carried out with inadequate methodology, which makes interpretation of data difficult. Thus it is not uncommon to find the same group of investigators reporting different conclusions in successive studies because of methodological differences.

Confounding Variables

Exercise and increased physical activity soon after ascent to high altitudes can significantly alter fluid and hormonal responses (Milledge, 1992). While acute exposure to high altitudes may be associated with dehydration, increased physical activity soon after ascent to high altitudes causes significant salt and water retention (Withey et al., 1983). Therefore, studies that did not control for physical activity may have tested the effects of exercise plus hypoxia, rather than hypoxia alone. Likewise, it is unclear which studies in the literature excluded subjects who might have had early features of acute mountain sickness (AMS). Like exercise, AMS has been shown to have totally different effects on salt and water metabolism as compared to hypoxia alone (Milledge, 1992). Finally there is evidence that fluid responses at high altitudes may be species dependent (Ashack et al., 1985). Thus much of the data in the literature is confusing, controversial, and inconclusive. This chapter identifies some of the major studies on this subject and tries to present a consensus view of the effects of high altitudes on fluid metabolism.

FACTORS INFLUENCING RESPONSES AT HIGH ALTITUDES

A number of factors influence fluid metabolism at high altitudes. The most important ones are the degree of hypoxia, cold, hypobaria, and physical activity. Most workers feel that hypobaria by itself has little effect on fluid metabolism (Epstein and Saruta, 1972; Heyes et al., 1982). The effect of cold is discussed elsewhere (see Freund and Sawka, Chapter 9 in this volume) and will not be considered here. However, details of the interaction between cold and hypoxia remain to be determined.

FLUID METABOLISM AT HIGH ALTITUDES

Fluid metabolism at high altitudes has been studied in several ways. A frequent approach has been the use of simple intake-output data. Some studies have inferred changes in body fluid from the change in weight and energy balance. The best data, however, come from studies of body fluid compartments using isotope dilution techniques. Table 18-1 summarizes the findings of major published studies where body fluid compartments were measured at high altitudes. Most of these studies only report the effects of acute exposure, that is, changes occurring during the first 2 to 3 weeks at high altitudes (Frayser et al., 1975; Hannon et al., 1969; Hoyt et al., 1992; Jain et al., 1980, 1981; Krzywicki et al., 1971; Singh et al., 1990; Surks et al., 1966). Very few studies followed the effect of prolonged stay at high altitudes (Anand et al., 1993; Hoyt et al., 1991; Phillips et al., 1969; Singh et al., 1990). Human studies

TABLE 18-1 Some Major Studies Detailing Alterations in Body Fluid Compartments During Ascent or Stay at High Altitudes

Authors	Study Details	Comments
Acute and subacute responses at moderate altitudes (< 4,500 m [14,764 ft])		
Surks et al., 1966	Five males, 19–23 yr, studied at SL and on days 4 and 8 at 4,267 m (14,000 ft). Ascent was rapid. Used ISA, Evan's Blue, D_2O.	Body weight and PV decreased. TBW data unreliable. Fat accounted for most of weight loss.
Hannon et al., 1969	Nine males, 20–24 yr, studied at SL and on days 3, 7, and 14 at 4,300 m (14,110 ft). Ascent was rapid. TBW: BD, 4-AA, and D_2O.	TBW increased at 2 weeks, PV and ECV reduced, redistribution from ECV to ICV. D_2O data unreliable. Weight loss primarily due to loss of fat.
Kryzwicki et al., 1971	Two groups of six males studied at SL, day 6 at 4,300 m, and SL again. Ascent was rapid. TBW: D_2O. ECV: thiocynate.	TBW and ICV reduced, ECV increase insignificant. Hypohydration even with good intake.
Frayser et al., 1975	Eight males, 14–37 yr, studied at SL, on day 5 at 2,926 m (9,600 ft), and on days 5 and 10 at 5,334 m (17,500 ft). Ascent was rapid with halt at 2,926 m (9,600 ft) for nonacetazolamide group. TBW: 4-AA. ECV: thiocynate, PV: Evan's Blue.	All compartments uniformly reduced.
Jain et al., 1980	Eighteen male soldiers, lowlanders, mean age 27 yr. Studied at SL and on days 3 and 12 at 3,500 m (11,483 ft). No exercise at high altitudes. TBW: $3H_2O$. ECV: sulphate. PV: ISA.	All compartments reduced including ECV. 80% weight loss explained by water loss.

Authors	Study Details	Comments
Jain et al., 1981	Twenty male high-altitude residents studied on days 3 and 21 after descent to SL and again at 3,500 m (11,483 ft) on days 3 and 12. No exercise at altitude. Eighteen male soldiers, lowlanders, studied at SL and on days 3 and 12 at 3,500 m (11,483 ft). Ascent was rapid.	SL residents behaved as in Jain et al. (1980). Highlanders seemed to retain more water on re-ascent.
Singh et al., 1990	Ten male soldiers, age 22–27 yr, studied at SL and on days 3 and 12 at 3,500 m (11,483 ft). Six-months data on some. No exercise at altitude. TBW: $3H_2O$. ECV: sulphate. PV: ISA.	All compartments reduced at 3 and 12 days but TBW and ECV as percent body weight slightly increased at 6 months.
Hoyt et al., 1992	Nine males, 23–33 yr, studied at SL and on day 10 at 4,300 m (14,110 ft). TBW: $H_2{}^{18}O$. ECV: Br.	TBW, ICV, and PV reduced at altitude. ECV unchanged.
<u>Extreme altitudes and/or chronic responses</u>		
Phillips et al., 1969	Sheep at 6,200 m (20,341 ft). Studied on days 10 and 32. TBW: $3H_2O$. ECV: Cl. PV: ISA.	TBW reduced, PV unchanged. (ECV increased but data unreliable due to technical problems.)
Hoyt et al., 1992	Goats at 5,500 m (18,045 ft) for 16 days. TBW: $3H_2O$. ECV: Inulin. PV: ICG.	TBW and PV reduced at altitude. ECV increased unlike humans.
Anand et al., 1993	Ten males, mean age 25 yr, 6 month-stay at over 6,000 m (19,685 ft). Exercise allowed except on day of study.	All compartments markedly increased. RBF decreased, $TBNa_E$ increased.

NOTE: SL, sea level; ISA, iodinated serum albumin; D_2O, deuterium oxide method; PV, plasma volume; TBW, total body water; BD, body density method; 4-AA, aminoantipyrine method; ECV, extracellular volume; ICV, intracellular volume; $3H_2O$, tritiated water; Br, Bromide; Cl, chloride space; ICG, indocyanine green; RBF, renal blood flow; $TBNa_E$, total body exchangeable sodium.

were made mainly at moderate altitudes of 3,500 to 4,500 m (11,483 to 14,764 ft). Only one study investigated extreme altitudes (over 6,000 m [19,685 ft]) (Anand et al., 1993), and one reported the effect of descent from high altitudes (Jain et al., 1981).

Moderate Altitudes

Probably the most comprehensive human data on body fluid compartments at high altitudes come from studies on Indian soldiers (Jain et al., 1980, 1981; Singh et al., 1986, 1988, 1990). These investigators had the unique advantage of a captive population that they could study at sea level and then again, under strict conditions of complete rest, for a period of up to 12 days after being flown to 3,500 m (11,483 ft). The soldiers lost about 3 percent of body weight during the first 3 days, with a further decrease in weight of about 1 percent during the next 10 days. Total body water (TBW) decreased by about 3.5 percent during the first 3 days but showed no further significant decrease until day 12. Extracellular volume (ECV) fell by a much smaller amount. The most significant change was seen in the plasma volume (PV), which was reduced by about 8 percent on day 3 with a further decrease over the next 10 days. When these changes in body fluid compartment are expressed as percent of body weight, no change in the calculated TBW is noted (Figure 18-1), suggesting that the decrease in TBW is in proportion to the decrease in weight.

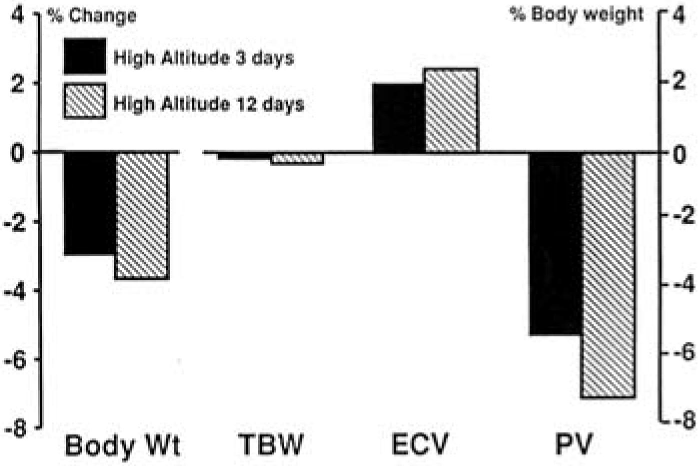

FIGURE 18-1 Changes in body fluid compartments expressed as percent body weight in soldiers taken to 3,500 m (11,483 ft). TBW, total body water; ECV, extracellular volume; PV, plasma volume. SOURCE: Adapted from Jain et al. (1980).

The ECV increases but not significantly, and PV remains reduced even when expressed in this manner. The problem with interpreting such data is that it is not known exactly what happens to body composition as subjects lose weight at high altitudes. If weight loss is entirely due to loss of fat, then the TBW should remain unchanged but show an increase when expressed as a percent body weight. The finding of normal TBW as percent body weight would, therefore, suggest hypohydration. However, if weight loss was only due to loss of muscle mass, then TBW should fall roughly in proportion to body weight. Unfortunately, body composition data on humans at high altitudes are confusing and not reliable (Consolazio et al., 1968; Rose et al., 1988; Surks et al., 1966; Westerterp et al., 1992). Data from Operation Everest II showed that only one-third of the decrease in body weight at simulated altitude was attributable to loss of fat and the remaining two-thirds to loss in fat-free mass (Rose et al., 1988).

Analysis of the carcasses of animals taken to high altitudes is more reliable for assessing changes in body composition (Chinn and Hannon, 1969; Christensen et al., 1975; Hannon and Rogers, 1975; Schnakenberg et al., 1971). Figure 18-2, drawn from data of Hannon and Rogers (1975), shows body composition of mice in Denver (1,600 m [5,249 ft]) and after being kept at a simulated altitude of 4,300 m (14,110 ft) for 3 and 7 days. Carcass analysis showed that mice lost weight during the first 3 days at high altitudes but not thereafter. After 3 and 7 days at high altitudes, TBW as a percent of

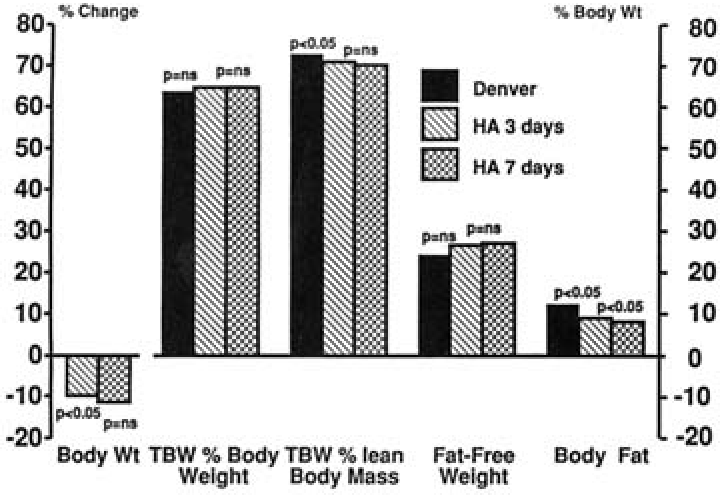

FIGURE 18-2 Carcass data of mice in Denver (1,600 m [5,249 ft]) and after being kept at a simulated altitude of 4,300 m (14,110 ft) for 3 and 7 days. For body weight, *p* compared to baseline at Denver. ns, not significant; HA, simulated altitude of 4,300 m (14,110 ft); TBW, total body water. SOURCE: Adapted from Hannon and Rogers (1975).

body weight did not change from the Denver value but fell significantly when expressed as a percent of lean body mass. Fat-free mass remained unchanged, but the animals lost fat throughout the stay at high altitudes. These findings, therefore, confirm that although most of the weight loss at high altitudes was due to loss of body fat, the animals also lost body water, became dehydrated, and remained so throughout the 7-d experiment.

In an earlier experiment, the same group (Chinn and Hannon, 1969) found that rats kept at similar altitudes for a longer period of time (26 days) did not show any decrease in TBW even when it was expressed as a percent of lean body mass (Figure 18-3). Weight loss was due to loss of body fat with no change in fat-free mass. Unfortunately, serial measurements were not made on these rats. Therefore, it is not clear whether these animals had initial dehydration from which they had recovered.

In a careful study of goats kept at a higher simulated altitudes (5,500 m [18,045 ft]) for 16 days, Hoyt et al. (1991) found that weight loss was accompanied by a loss of TBW, suggesting dehydration (Figure 18-4). They also found a shift of body fluids so that the ECV increased at the expense of the intracellular volume. This result is in sharp contrast to the findings of other authors (Hannon et al., 1969; Jain et al., 1980, 1981; Singh et al., 1990). Hoyt and coworkers (1991) also found that PV decreased, but the blood volume (BV) did not change because the hematocrit increased.

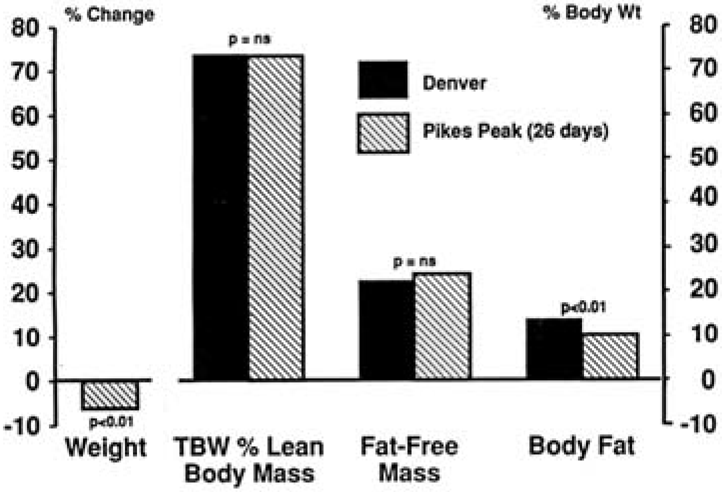

FIGURE 18-3 Carcass data of rats in Denver (1,600 m [5,249 ft]) and after being kept at Pikes Peak (4,300 m [14,110 ft]) for 26 days. ns, not significant; TBW, total body water. SOURCE: Adapted from Chinn and Hannon (1969).

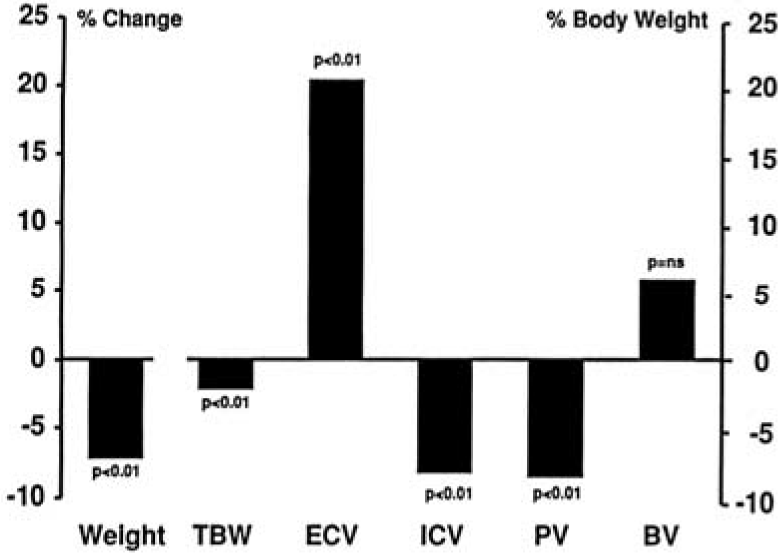

FIGURE 18-4 Changes in body fluid compartments in goats kept at 5,500 m (18,045 ft) for 16 days. ns, not significant; TBW, total body water; ECV, extracellular volume; ICV, intracellular volume; PV, plasma volume; BV, blood volume. SOURCE: Adapted from Hoyt et al. (1991).

Phillips et al. (1969) carried out one of the few studies that tested the effect of prolonged stay at simulated extreme altitudes. They found that sheep kept at 6,200 m (20,341 ft) for up to 32 days had an initial weight loss that later stabilized (Figure 18-5). At 10 days, sheep were hypohydrated with a significant decrease in TBW, but by 32 days, the animals had regained all the lost water. PV, unlike results in most other studies, did not change and BV increased. Therefore, the initial response of the body even at extreme altitudes is hypohydration lasting a few days. Thereafter the body fluids normalize. Whether further stay at that altitude would have caused fluid retention was not tested.

Singh et al. (1990) studied body fluid compartments of soldiers who had stayed at high altitudes (3,500 m [11,483 ft]) for 6 months and compared the findings with those seen in normal subjects at sea level. They found that despite the fact that the weight of these subjects continued to remain low, their TBW and ECV as a percent of body weight were greater than normal. Although this study was not made on the same subjects at sea level and high altitudes, the findings suggest that with chronic exposure to moderate altitudes, subjects are no longer hypohydrated, instead tend to retain fluid, and might eventually become hyperhydrated. However, plasma volume still remains markedly reduced.

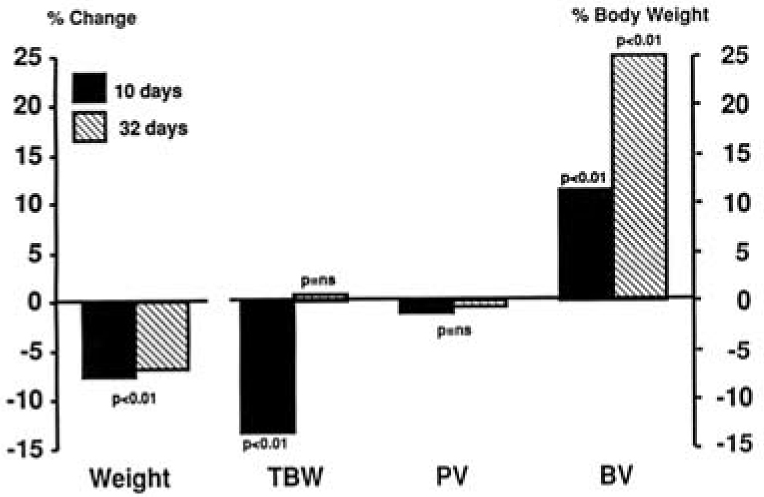

FIGURE 18-5 Changes in body fluid compartments in sheep kept at simulated extreme altitude (6,200 m [20,341 ft]) for 32 days. ns, not significant; TBW, total body water; PV, plasma volume; BV, blood volume. SOURCE: Adapted from Phillips et al. (1969).

Extreme Altitudes

Although it is generally believed that humans are incapable of surviving at extreme altitudes for prolonged periods of time (Pugh, 1962; West, 1984), the recent experience of warfare at altitudes above 6,000 m (19,865 ft) on the Indian subcontinent has belied that impression (Anand and Chandrashekhar, 1992; Anand et al., 1990). Prolonged stay at that altitude causes subacute mountain sickness in some subjects (Anand et al., 1990). This syndrome is characterized by severe edema, ascites, and even generalized anasarca resembling severe congestive heart failure. The pathogenesis of this condition remains unknown, but hypoxic pulmonary hypertension causing congestive heart failure is unlikely to explain the syndrome. This laboratory measured body fluid compartments in a group of asymptomatic soldiers who had been at an altitude of over 6,000 m (19,865 ft) for at least 10 weeks (Anand and Chandrashekhar, 1992). TBW in these soldiers was increased by about 20 percent above normal, PV was 30 percent above normal, hematocrit was 40 percent above normal, and calculated BV was nearly 80 percent above normal (Figure 18-6). These data suggest that although humans can survive at extreme altitudes for prolonged periods of time, many develop fluid retention, and a small subset of them develop subacute mountain sickness. Even those who remain well and asymptomatic tend to retain significant amounts of salt and water.

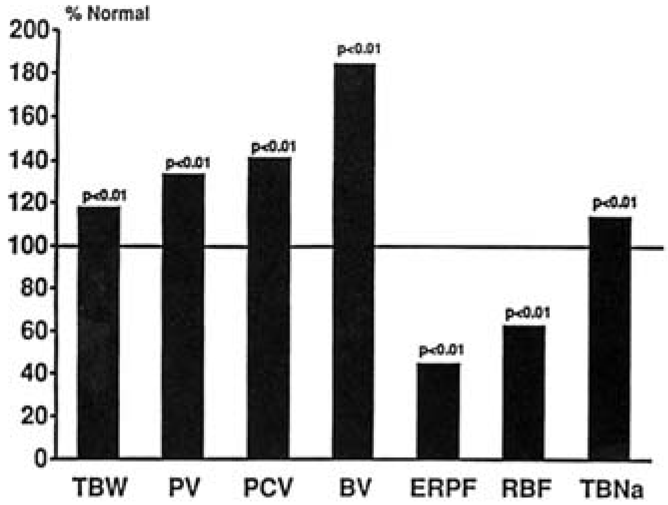

FIGURE 18-6 Body fluid compartments in normal subjects living at extreme altitudes (> 6,000 m) for a prolonged period (> 10 weeks). TBW, total body water; PV, plasma volume; PCV, packed cell volume; BV, blood volume; ERPF, effective renal plasma flow; RBF, renal blood flow; TBNa, total body sodium. SOURCE: Adapted from Anand et al. (1993).

Effect of Exercise

Milledge and his coworkers (Withey et al., 1983) have shown that physical activity soon after ascent to high altitudes has a dramatically opposite effect on fluid metabolism than does ascent alone. Instead of developing hypohydration, subjects retain sodium and water when ascent to high altitudes is combined with hill walking. In contrast to subjects who do not exercise at high altitudes, plasma volume in these subjects increases during the exercise period, causing a fall in hematocrit.

To summarize, acute exposure of humans and animals to moderate altitudes, in the absence of exercise, leads to weight loss and hypohydration. TBW and PV are reduced, and there may be a shift of body fluids between the intra- and extracellular compartments. These changes tend to return towards normal within weeks. Prolonged exposure to high altitudes lasting months may cause fluid retention with an increase in TBW, but the body weight and PV continue to remain low. Physical activity soon after ascent to high altitudes leads to fluid retention. Acute effects of extreme altitudes are not known, but prolonged stay at extreme altitudes may lead to severe salt and water retention.

DETERMINANTS OF FLUID METABOLISM

The major determinants of fluid metabolism at high altitudes include fluid intake and urine output, alterations in neurohormones, and renal function.

Intake-Output Data

Intake-output data at high altitudes are often too crude and unreliable to assess fluid balance accurately. Nevertheless, such data do provide useful information that helps in the understanding of fluid metabolism at high altitudes. A number of studies have shown that intake is reduced at high altitudes whenever fluids are allowed ad libitum but is normal when intake is strictly enforced (Claybaugh and Wade, 1987). Decrease in appetite and thirst, lack of available water, and physical exertion probably all contribute to reduced intake. However, the chief mechanism appears to be a decrease in the sensation of thirst (Jones et al., 1981a, b). Reduced fluid intake can account for approximately 2 to 3 liters of negative fluid balance during the initial few days at high altitudes. The exact mechanism of reduced thirst is also unclear. Changes in antidiuretic hormone (ADH) cannot fully explain it, since thirst is reduced even in patients with diabetes insipidus (a condition characterized by the inability to produce or respond to ADH) (Jones et al., 1981a, b). Similarly, changes in circulating atrial natriuretic peptide (ANP) and angiotensin II do not seem to play a major role in the reduced sensation of thirst (Jones et al., 1981b). Changes in the central release of these hormones may be important, but this has never been proven. The sensation of thirst returns to normal over a period of a few days despite continued stay at high altitudes.

Changes in urine output are also common at high altitudes, but the data are controversial. This laboratory reviewed 57 studies where urine output was measured at high altitudes. The data suggest that there is usually a transient diuresis at high altitudes lasting, on an average, 3 to 4 days. Diuresis is common at moderate altitudes, in subjects who do not exercise soon after transfer to high altitudes, in subjects who do not develop AMS, and in subjects for whom fluid intake is strictly enforced. Diuresis is also seen in acute experiments at sea level when subjects breathe hypoxic gas mixtures (Ashack et al., 1985). In contrast, anti-diuresis commonly accompanies severe hypoxia, at extreme altitudes, in subjects who exercise soon after arriving at high altitudes, and in those who are prone to and later develop AMS.

Other factors that might lead to dehydration at high altitudes include an increase in insensible loss because of low humidity and hyperventilation. The magnitude of this effect is not clear. Malabsorption of various nutrients has also been described at high altitudes (Chinn and Hannon, 1969), but the effect of this phenomenon on fluid metabolism has never been evaluated.

Hormones and High Altitudes

Hormones are important in the control of fluid metabolism both in normal and abnormal conditions. Neurohormonal changes precede the development of salt and water retention. A number of hormones are important in this process (Anand et al., 1989; Packer, 1988), the important ones being renin, aldosterone, catecholamines, ANP, and ADH. Cortisol, prolactin, and growth hormone can also contribute indirectly to salt and water metabolism. A number of studies have investigated the role of these hormones under different conditions of hypoxia, with and without exercise (see Table 18-2).

Renin-Angiotensin-Aldosterone Axis

Aldosterone. At least 20 studies in the literature investigated the effect of hypoxia or high altitudes on aldosterone. High altitudes or hypoxia at rest caused a decrease in aldosterone level in 15 studies (Bouissou et al., 1989; Colice and Ramirez, 1985, 1986; Heyes et al., 1982; Hogan et al., 1973; Maher et al., 1975; Maresh et al., 1985; Milledge et al., 1983; Olsen et al., 1992; Raff et al., 1986; Ramirez et al., 1992; Shigeoka et al., 1985; Slater et al., 1969a, b; Sutton et al., 1977), an increase in 5 studies (Anand et al., 1993; Bärtsch et al., 1991a, b; Frayser et al., 1975; Okazaki et al., 1984), and had no effect in another 3 studies (Ashack et al., 1985; Bärtsch et al., 1991b; Frayser et al., 1975). Most studies also showed that hypoxia attenuated the normal increase in aldosterone seen with exercise at sea level (Maher et al., 1975; Milledge et al., 1983; Olsen et al., 1992; Shigeoka et al., 1985). Thus, although hypoxia acutely reduces aldosterone, it is not clear whether this reduction in aldosterone has a role in the acute diuresis seen at high altitudes. The effect of hypoxia on aldosterone is, however, different in subjects who are prone to develop AMS. Bärtsch et al. (1991a) studied a group of subjects who had never developed AMS and another group who had AMS on at least one occasion and were therefore prone to develop symptoms on re-exposure to high altitudes. At rest both groups showed a similar reduction in aldosterone at high altitudes (Figure 18-7). During exercise at high altitudes, subjects who later developed AMS showed a significantly greater increase in aldosterone, which suggests that aldosterone may be involved in the pathogenesis of this condition.

Renin Activity. A wide variety of changes in plasma renin activity (PRA) has been described at high altitudes. There are at least 16 studies in the literature where PRA was measured during hypobaric hypoxia (Ashack et al., 1985; Bouissou et al., 1989; Colice and Ramirez, 1985; Heyes et al., 1982; Hogan et al., 1973; Keynes et al., 1982; Maher et al., 1975; Milledge et al., 1983; Okazaki et al., 1984; Olsen et al., 1992; Raff et al., 1986; Shigeoka et

TABLE 18-2 Human Studies Detailing Hormonal Alterations During Hypoxia or Ascent or Stay at High Altitudes

Authors	Study Details	Comments
Acute hypoxia		
Heyes et al., 1982	Eleven males, 18–40 yr, tested with hypoxia, with and without hypobaria.	ALDO reduced, prolactin rose. AVP increased only with hypotension. Hypobaria not important except for prolactin.
Okazaki et al., 1984	Eighteen males, two females, 23–48 yr, studied at 6,000 m (19,685 ft) for 3 hours in chamber.	No change at 4,000 m (13,123 ft). At 5,000 m (16,404 ft), PV fell, ALDO and ACTH rose. At 6,000 m, ALDO, PRA, and cortisol increased.
Aschak et al., 1985	Ten males, 18–24 yr, usual diet. 10.5 and 12 percent FIO_2. PO_2 35–46 mm Hg. Water loading and replacement of urine volume.	No change in ALDO, AVP, PRA, NE, bradykinin. No change in urine volume, urine sodium. AVP increased only when subjects had nausea.
Colice and Ramirez, 1985	Group 1: hypoxia (SAT 90 percent) for 1 hour. Group 2: hypoxia (SAT 90 percent) for 1 hour, (SAT 80 percent) for 1 hour. Studied twice with normal and low-salt diet.	ALDO reduced; PRA and ACE unchanged. No further increase in second hour PRA-ALDO uncoupled. No change in hemodynamics. ALDO reduction significant only when both groups pooled. Diet sodium important in degree of response.
Maresh et al., 1985	Seven low-altitude and seven high-altitude natives (1,830–2,200 m [6,004–7,218 ft]). Tested in hypobaric chamber (447 mm Hg) for 2 days.	ALDO reduced; cortisol increased. High-altitude natives have similar but damped responses. ERPF and heart rate increased.
Hypoxia-high altitude studies; no exercise		
Frayser et al., 1975	Nine subjects studied at SL, day 5 at 3,048 m (10,000 ft), days 3 and 7 at 5,334 m (17,500 ft). Eight subjects at SL, day 5 at 2,926 m (9,600 ft), days 5 and 10 at 5,334 m (17,500 ft). Four subjects got acetazolamide before ascent to 5,334 m (17,500 ft).	At 2,744–3,049 m (9,000–10,000 ft), ALDO, PRA unchanged, cortisol rose. At 5,335 m (17,500 ft), PRA and cortisol rose. Normal by day 5.
Olsen et al., 1992	Eight males, 27–42 yr, studied at SL and after 48 hours at 4,350 m (14,272 ft). Measurements at rest and exercise. One-half liter water load.	Increase in NE, fall in ALDO and PRA. Epi and ANP unchanged.

Authors	Study Details	Comments
Ramirez et al., 1992	Four males and three females. Mean age 43 yr, studied with hypoxia with and without hypobaria. Hypoxia Po_2 55–59 mm, SAT 90 percent. High-altitude 3,000 m (9,843 ft), day 3–4 sodium load excretion also tested.	ALDO and ADH fell while NE rose. More sodium load clearance with hypoxia.
Hypoxia-high altitude studies; effect of exercise		
Milledge et al., 1983	Six males on fixed diet studied at SL and 3,100 m (10,171 ft). Exercise: 7-h hill walking per day for 5 days.	PRA and ALDO increased, peak on day 2. ALDO rise similar to SL, PRA 4 times more. Uncoupling of PRA-ALDO at altitude.
Shigeoka et al., 1985	Six males, four females, 15–34 yr. Treadmill exercise on room air or hypoxia (17 percent O_2 or 1,300 m [4,265 ft]).	Effect on PRA independent of hypoxia. ALDO less during hypoxic exercise. Effect of hypoxia carried over to normoxic exercise. PRA-ALDO uncoupling.
Bouissou et al., 1989	Six males and six females. Bike exercise at SL and day 3 at 4,350 m (14,272 ft). Effect of beta blockade also tested.	ALDO and PRA reduced (rest and exercise) at altitude. Mild rise in ANP, catecholamines lower with exercise at altitude. Pindolol did not significantly influence ALDO or PRA.
Bärtsch et al., 1991a	Seventeen males, age 25–61 yr, previous experience at altitude. Ascent to 4,559 m (14,957 ft) over 22 hours. Stay 3 days.	Subjects predisposed to AMS showed more rise in ALDO and ADH during exercise. Can be used to predict risk of AMS.
Olsen et al., 1992	Eight males, 27–42 yr, studied at SL and after 48 hours at 4,350 m (14,272 ft). Measurements at rest and exercise. One-half liter water load.	Exercise at altitude increased NE more than at SL. Epi and ANP responses similar at both altitude and at SL.
Extreme altitude studies		
Anand et al., 1993	Ten males, mean age 25 yr, 6 month-stay at over 6,000 m (19,685 ft). Fully active except on day of study.	Increase in NE, ALDO, cortisol. No change in Epi, ANP, and PRA.

NOTE: ALDO, aldosterone; AVP, arginine vasopressin; PV, plasma volume; ACTH, adrenocorticotropic hormone; PRA, plasma renin activity; FIO_2, fraction of inspired oxygen; Po_2, partial pressure of oxygen; NE, norepinephrine; SAT, oxygen saturation; ACE, angiotensin-converting enzyme; ERPF, effective renal plasma flow; SL, sea level; Epi, epinephrine; ANP, atrial natriuretic peptide; ADH, antidiuretic hormone; AMS, acute mountain sickness.

al., 1985; Slater et al., 1969a, b; Sutton et al., 1977; Tuffley et al., 1970). At rest, hypoxia decreased PRA in 7 studies (Bouissou et al., 1989; Hogan et al., 1973; Keynes et al., 1982; Milledge et al., 1983; Olsen et al., 1992; Slater et al., 1969a; Sutton et al., 1977), increased it in 3 studies (Frayser et al., 1975; Okazaki et al., 1984; Tuffley et al., 1970), and had no effect in 6 studies (Ashack et al., 1985; Bouissou et al., 1989; Colice and Ramirez, 1985; Heyes et al., 1982; Raff et al., 1986; Tuffley et al., 1970). In contrast, hypoxia caused an attenuation of the increase in PRA normally seen with exercise at sea level.

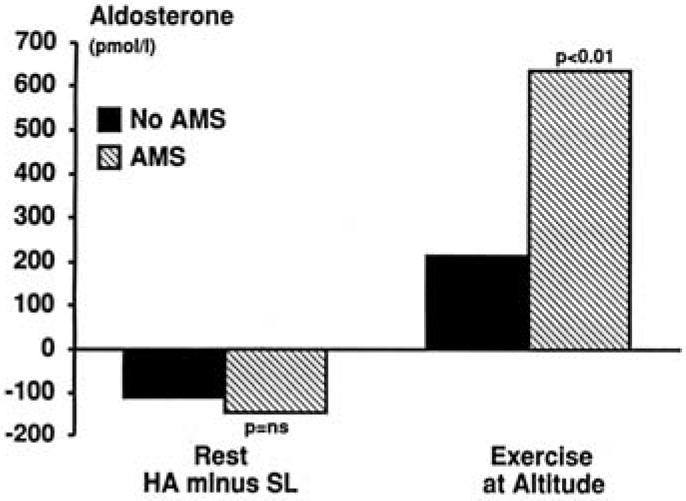

FIGURE 18-7 Effect of exercise at high altitudes (HA) on aldosterone level in subjects susceptible to acute mountain sickness (AMS) compared with nonsusceptible subjects. Ns, not significant. SOURCE: Adapted from Bärtsch et al. (1991a).

The overall effect of hypoxia on PRA, therefore, remains unclear. The more important effect of hypoxia appears to be on the renin-angiotensin-aldosterone axis. Normally this axis is tightly coupled in humans and animals. One consistent feature of exposure to high altitudes is the uncoupling of this tight renin-aldosterone relationship, both at rest and during exercise. For any increase in PRA, the increase in aldosterone is markedly reduced during hypoxia (Bouissou et al., 1989; Colice and Ramirez, 1985, 1986; Milledge et al., 1983; Purshottam et al., 1978; Shigeoka et al., 1985; Slater et al., 1969a, b; Sutton et al., 1977). Milledge et al. (1983) showed a brisk and marked increase in aldosterone during exercise at sea level as compared to a blunted response at high altitudes while the PRA rose normally. The cause of this uncoupling is not understood. Adrenal glands are normal or hypertrophied at high altitudes (Gosney, 1985) and respond normally to angiotensin II and adrenocorticotropic hormone (ACTH) infusion (Colice and Ramirez, 1986).

Angiotensin-converting enzyme activity in cultured endothelial cells and in peripheral blood was shown to be reduced during hypoxia (Stalcup et al., 1985), and this was considered to be the cause of reduced aldosterone at high altitudes. There is now some doubt about this finding (Milledge and Catley, 1987). Plasma potassium may be important in regulating aldosterone secretion (Curran-Everett et al., 1988). However, the role of potassium in modulating the acute effects of hypobaric hypoxia are unclear.

Antidiuretic Hormone. Antidiuretic hormone (ADH) is a stress hormone that increases thirst and reduces free water clearance. Both osmolality and volume status modulate its level. Changes in ADH response would be an attractive explanation for the alterations in fluid metabolism seen at high altitudes. Thirteen studies were examined where the effect of hypoxia on ADH was investigated (Ashack et al., 1985; Bärtsch et al., 1991a; Brahmachari et al., 1973; Claybaugh et al., 1982, 1987b; Forsling and Milledge, 1977; Hackett et al., 1978; Harber et al., 1981; Heyes et al., 1982; Okazaki et al., 1984; Porchet et al., 1984; Ramirez et al., 1992; Subramanian et al., 1975). The results are controversial, and there is both evidence for an increase in ADH with hypoxia (Hackett et al., 1978; Singh et al., 1974), no change (Ashack et al., 1985; Forsling and Milledge, 1977; Heyes et al., 1982; Porchet et al., 1984), or a decrease (Brahmachari et al., 1973; Porchet et al., 1984; Subramanian et al., 1975). Part of the explanation for this disagreement may lie in the variety of methods used in these studies and the differences in the nature and degree of hypoxia used (Subramanian et al., 1975). Mild hypoxia causes a reduction in ADH and may be important in the diuresis seen in the early stages of high-altitude ascent (Brahmachari et al., 1973; Porchet et al., 1984). Although ADH is important in mediating thirst, reduced thirst at high altitudes cannot be explained by a change in ADH since a similar response is seen in diabetes insipidus (Jones et al., 1981a, b). Severe hypoxia, extreme altitudes, exercise, and any form of stress, including nausea and vomiting, increase ADH (Ashack et al., 1985; Heyes et al., 1982). ADH is increased in AMS, and subjects prone to develop this condition show an exaggerated increase in ADH during exercise at high altitudes (Figure 18-8).

Atrial Natriuretic Peptide. Atrial natriuretic peptide (ANP) has a number of important physiological effects that can potentially counteract the effects of various salt-retaining hormones. It is natriuretic and diuretic, inhibits aldosterone secretion, and reduces thirst. Despite these interesting effects, the role of ANP at high altitudes appears minimal. More than 10 studies report the effects of hypoxia on ANP (Anand et al., 1993; Bartsch et al., 1986; Bärtsch et al., 1991a, b; Bouissou et al., 1989; du Souich et al., 1987; Hackett et al., 1978; McKenzie et al., 1986; Milledge et al., 1989; Olsen et al., 1992, 1993; Ramirez et al., 1992; Singh et al., 1974). Most of these studies found no change or a mild increase in ANP with hypoxia (Bouissou et al., 1989; Olsen et al., 1992; Ramirez et al., 1992). Even in studies where ANP levels were high, no significant protective role against salt and water retention was seen (du Souich et al., 1987). The reason for this is unclear. Although there is evidence that ANP receptor down regulation may occur in conditions with prolonged elevation of circulating ANP, like congestive heart failure, such evidence is lacking in subjects at high altitudes. Like ADH, ANP is high in AMS and in subjects prone to develop this condition even before the onset of symptoms (Figure 18-9).

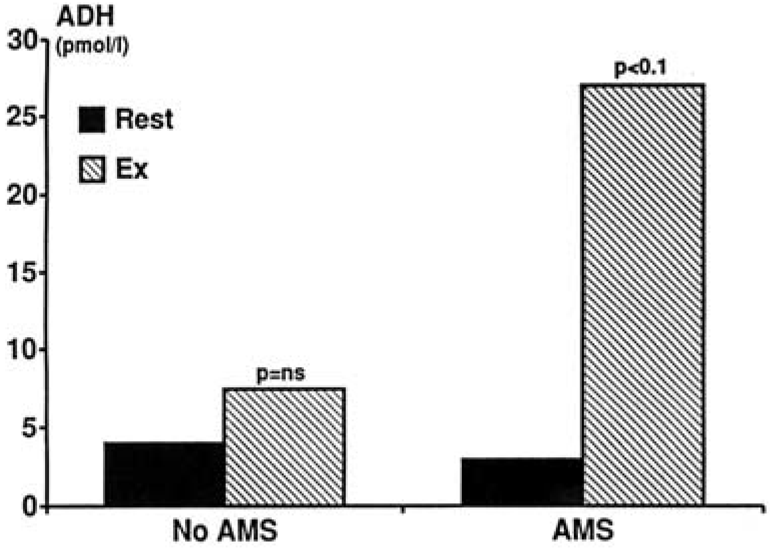

FIGURE 18-8 Effect of exercise at high altitudes on antidiuretic hormone (ADH) level in subjects susceptible to acute mountain sickness (AMS) compared with nonsusceptible subjects. ADH is significantly increased by exercise in AMS-susceptible individuals. ns, not significant. SOURCE: Adapted from Bärtsch et al. (1991a).

Catecholamines. Catecholamines help to retain salt and water by modulating renal blood flow (RBF) (Anand et al., 1989; McMurray et al., 1988; Olsen et al., 1993; Packer, 1988). Nearly all studies that measured catecholamines at high altitudes demonstrated an increase in norepinephrine both at rest and during exercise (Anand et al., 1989, 1993; Maher et al., 1975; Olsen et al., 1992, 1993; Ramirez et al., 1992).

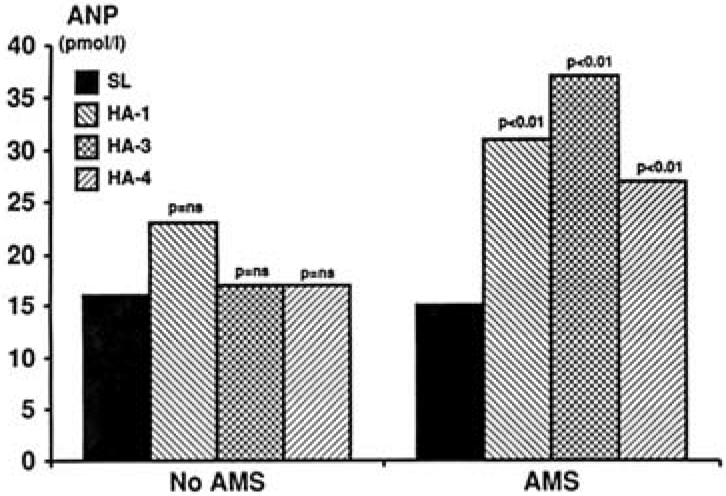

FIGURE 18-9 Effect of exercise at high altitudes on atrial natriuretic peptide (ANP) level in subjects susceptible to acute mountain sickness (AMS) compared with nonsusceptible subjects. ns, not significant; SL, sea level; HA, high altitudes.
SOURCE: Adapted from Bärtsch et al. (1991a).

Renal Function

RBF is an important determinant of salt and water metabolism. Unfortunately, renal functions have not been adequately studied at high altitudes. Eighteen studies were reviewed that reported renal responses to hypoxia or high altitudes (Anand et al., 1993; Ashack et al., 1985; Axelrod and Pitts, 1952; Berger et al., 1949; Castenfors, 1967; Freund et al., 1991; Guiol et al., 1986; Heyes et al., 1982; Maher et al., 1975; McDonald and Kelley, 1948; Monge et al., 1969; Olsen et al., 1993; Ou et al., 1984; Pauli et al., 1968; Rennie et al., 1972; Selkurt, 1953; Subramanian et al., 1975; Ullmann, 1961). As with most high-altitude studies, variation in methodology and experimental design has caused considerable confusion. It appears, however, that moderate acute hypoxia at sea level increases RBF. In contrast, most studies at high altitudes have shown a reduction in effective renal plasma flow (ERPF) with minimal change in glomerular filtration rate (GFR), which suggests a greater efferent than afferent arteriolar vasoconstriction (Olsen et al., 1993). Chronic severe hypoxia, or hypobaria by itself, reduces RBF. ERPF is low even in high-altitude natives, but the RBF is normal because of an increase in hematocrit (Ou et al., 1984). The cause of the decrease in RBF following ascent to high altitudes is unclear, but it is probably due to increased circulating catecholamines and blood viscosity at high altitudes.

EXTREME ALTITUDES

Earlier in this chapter it was shown that prolonged stay at extreme altitudes can lead to considerable salt and water retention in otherwise normal subjects (Figure 18-6). Measurement of renal function in these subjects showed that the ERPF was significantly reduced to around 45 percent normal (Anand et al., 1993). And despite the marked increase in hematocrit, the calculated RBF was still only 60 percent of normal. Total body exchangeable sodium had increased by about 15 percent above normal (Figure 18-6). There was significant increase in norepinephrine, aldosterone, and cortisol (Figure 18-10). Therefore, prolonged stay at extreme altitudes can lead to severe salt and water retention probably because of a reduction in renal blood flow due to high circulating catecholamines. High levels of aldosterone could also contribute to sodium and thereby water retention. These may be the mechanisms responsible for adult subacute mountain sickness reported at extreme altitudes (Anand et al., 1990, 1993).

AUTHORS' CONCLUSIONS AND RECOMMENDATIONS

An extensive review of the literature on fluid metabolism at high altitudes shows that the data are confusing, controversial, and inconclusive. Inadequate

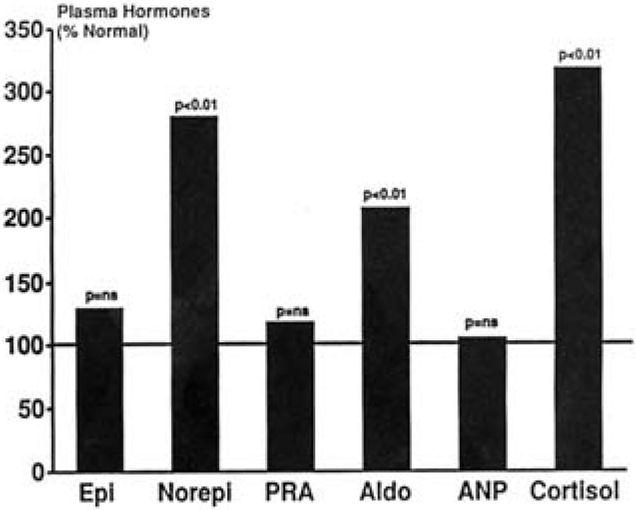

FIGURE 18-10 Neurohormones and renal function in normal subjects living at extreme altitudes (> 6,000 m [19,865 ft]) for a prolonged period (> 10 weeks). ns, not significant; Epi, epinephrine; Norepi, norepinephrine; PRA, plasma renin activity; Aldo, aldosterone; ANP, atrial natriuretic peptide. SOURCE: Adapted from Anand et al. (1993).

methodology, lack of serial measurements on the same subjects, and the presence of confounding variables—like the use of exercise and the presence or absence of AMS in subjects under investigation—are some of the reasons for the dissimilarities in the findings. Moreover, there are virtually no data at extreme altitudes and after prolonged exposure to moderate altitudes. Nevertheless, it appears that acute exposure to moderate altitudes causes transient hypohydration, which is due to increased diuresis and an acute reduction in fluid intake because of decrease in thirst. The meager data available on the effects of chronic hypoxia in sheep and humans suggest that modest fluid retention may occur. Prolonged stay at extreme altitudes may cause severe salt and water retention in otherwise normal subjects. The role of hormones in normal fluid metabolism at high altitudes is unclear, but a number of hormones appear to play a role in the retention of salt and water in pathologic states like acute and subacute mountain sickness. RBF is probably reduced at high altitudes and more so at higher altitudes. Finally, exercise and increased physical activity at high altitudes favor the mechanisms that retain salt and water.

It is recommended that the acute and long-term effects of moderate and extreme altitudes on body fluid compartment and its determinants (neurohormones and renal function) need to be investigated using the same group of subjects and more sophisticated technology. The role of confounding variables like physical activity needs to be better defined. Subjects at high altitudes are almost always involved in some form of physical activity, which at times is fairly strenuous, especially for those engaged in military activity. Only by making serial measurements on the subjects would it be possible to confirm the impression that a prolonged stay may lead to some degree of fluid retention at moderate altitudes and to severe salt and water accumulation at extreme altitudes. Finally, the interaction between cold and altitude also needs to be determined. Such studies would be helpful in identifying subjects prone to high altitude-related illness and in establishing guidelines about the "safe" length of time humans can spend at various altitudes.

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19

Maintenance of Body Weight at Altitude: In Search of 500 kcal/day

Gail E. Butterfield[1]

INTRODUCTION

Weight loss while visiting at elevations not normally inhabited by the sojourner (at altitude) has been considered by some as inevitable (Boyer and Blume, 1984; West et al., 1983). However, acceptance of the inevitability of this weight loss may lead to a decrease in muscle mass (Rose et al., 1988), a decrease in performance capacity (Sridharan et al., 1987), and in the military arena, failure of a military campaign. Thus, the determination of the truth of the dogma of inevitability of weight loss at altitude and the understanding of its causes and consequences becomes important to the success of any endeavor at high elevations.

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ENERGY BALANCE AT ALTITUDE

The Scenario of Weight Loss at Altitude

Weight loss at altitude is accompanied by anorexia (Boyer and Blume, 1984; Consolazio et al., 1968, 1972; Guilland and Klepping, 1985; Hannon et al., 1976; Kryzywicki et al., 1971; Pugh, 1962; Rose et al., 1988; Westerterp et al., 1992; Whitten and Janoski, 1969) and often diuresis (Boyer and Blume, 1984; Guilland and Klepping, 1985; Koller et al., 1991; Krzywicki et al., 1971), both thought to begin with acute exposure. The weight loss occurs continuously throughout exposure in most studies (Rose et al., 1988); the diuresis may be a transient response (Boyer and Blume, 1984). Where monitored, nitrogen balance (a measure of the maintenance of lean body mass) has usually been negative (Guilland and Klepping, 1985; Hannon et al., 1976), which suggests a breakdown of lean tissue. Basal metabolic rate (BMR) is elevated over sea-level values initially but falls toward sea level over time (Hannon and Sudman, 1973; Stock et al., 1978). Studies on fuel utilization at altitude show glycogen sparing (preferential use of a fuel other than glycogen) and increased circulating glycerol and triglycerides with exercise after acclimatization (Young et al., 1982). These data have been interpreted to mean that the metabolic fuel chosen for maintenance of energy needs at rest and during exercise changes from carbohydrate to fat with acclimatization (Young et al., 1982).

The Scenario with Starvation: Consequences of Negative Energy Balance

This picture of weight loss during acute exposure to altitude sounds suspiciously similar to the series of events accompanying weight loss due to starvation. *Starvation* may be defined as a state where energy intake does not match energy need or as a state of negative energy balance. Ancel Keys in his seminal work on starvation in male conscientious objectors (Keys et al., 1950) described the sequelae of events in response to diminished energy intake, which included negative nitrogen balance accompanied by a decline in lean body and fat mass and by a concurrent decrease in BMR. Keys and coworkers (1950) also noted a decrease in overall activity level, which was thought to represent a mechanism to conserve existing energy stores. Further work on starvation by other investigators has shown a shift in energy metabolism toward mobilization and utilization of fat and ketone bodies under circumstances of negative energy balance (Saudek and Felig, 1976). The ultimate adaptation to inadequate energy intake was the failure of appetite (Keys et al., 1950).

That these two states, exposure to high altitudes and starvation, share such a similar description of symptoms bears investigation (Brouns, 1992). Is the sequence of events that accompanies acute exposure to altitude a result of negative energy balance similar to starvation (Consolazio et al., 1972), and thus preventable (Butterfield, 1990), or is it in some part a response to the hypoxia, and even perhaps an important adaptive mechanism for acute acclimatization, as has been suggested by some (Hackett et al., 1981). The remainder of this review will attempt to answer this question.

Negative energy balance may be the consequence of changes on either the intake or the expenditure side of the energy balance equation, or it may be the algebraic sum of both. Testing the hypothesis of the inevitability of weight loss requires matching both sides of this equation as closely as possible and evaluating the physiological changes seen. Few studies have attempted to balance this equation (Consolazio et al., 1972), and those that have (Milledge et al., 1983; Withey et al., 1983) are directed primarily toward the question of fluid homeostasis and have not presented data on food intake, weight change, or components of body composition other than fluid.

Anorexia at Altitude: The Intake Side of Energy Balance

Anorexia is defined as *loss of appetite*. As there is no direct measure of appetite, the question of anorexia at altitude has been approached primarily by monitoring food intake. Figure 19-1 represents a compilation of data from studies in which food consumption was essentially ad libitum, and reliable information is available on both sea-level (assumed to represent sea-level need) and high-altitude intakes. As can be seen, energy intakes under the two conditions are closely correlated, and altitude energy intake appears to be about 180 kcal/d lower than sea-level intake in these studies. Note that neither altitude nor activity level was considered in making this figure. The high intakes were reported in studies involving training at sea level and at altitude, whereas the lower intakes represent experiments done using more sedentary individuals. The lowest values are derived from a study in women (Hannon et al., 1976). Energy values for studies conducted at altitudes as low as 3,500 m (11,483 ft) (Sridharan et al., 1987) fall on the same line as the mean intakes for subjects studied at the barometric equivalent of the top of Mount Everest (Rose et al., 1988).

Attempts to Correct Anorexia

Attempts to prevent or correct this anorexia have been frustrating. Before 1968 Consolazio and colleagues (1968) attempted an enforced feeding study with U.S. Army recruits using standard Army rations, but the diet was so unpalatable that energy intakes dropped to less than 2,000 kcal/d in these individuals training at altitude. Whitten and Janoski (1969) provided a liquid formula (33 percent fat), which was so unpalatable that mean energy intake for 9 days at altitude was only about 750 kcal/d, whereas sea-level intake had been about 2,700 kcal/d, presumably on the same diet. Rate of weight loss in the study of Whitten and Janoski (1969) approached 0.5 kg/d. Data from these experiments were not used to generate the regression line in Figure 19-1 because of the abnormal qualities of the diets.

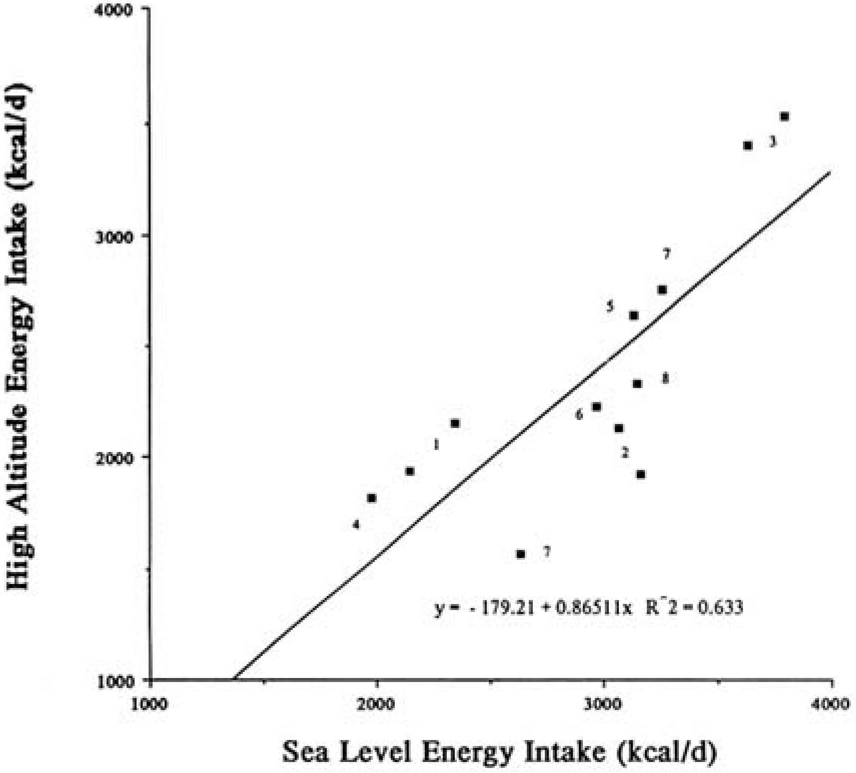

FIGURE 19–1 Relationship between seal-level energy intake (kcal/d) and high-altitude energy intake (kcal/d) compiled from studies involving ad libitum food intake and providing accurate measures of both parameters. Numbers next to boxes indicate reference used: 1, Consolazio et al. (1968); 2, Krzywicki et al. (1969); 3, Consolazio et al. (1972); 4, Hannon et al. (1976); 5, Sridharan et al. (1982); 6, Boyer and Blume (1984); 7, Guilland and Klepping (1985); 8, Rose et al. (1988).

A second attempt at providing adequate food intake by Consolazio in 1968 (Consolazio et al., 1972) was more successful. High-altitude energy intakes accomplished with strong encouragement (but still ad libitum), and a food and formula diet, a diet composed of foods and special liquid supplement, were only about 200 kcal/d less than the intake at sea level. In this short-term study (6 days at altitude), nitrogen balance was positive, possibly due to the training regimen imposed on the recruits. Positive nitrogen balance under circumstances of negative energy balance has been demonstrated by Todd et al. (1984) at sea level in individuals initiating a moderate exercise program. Weight maintenance was not accomplished in the Consolazio experiment, and the rate of weight loss after the first 2 days was similar to that seen in other studies where energy intake was not enforced (146 to 188 g/d; see Table 19-1).

Other studies have attempted to maintain food intake by providing extremely palatable food. Rose and colleagues (1988) allowed subjects in the simulated ascent of Mount Everest (Operation Everest II) to request desired foods, but food intake declined with time, and weight loss continued throughout the ascent (Figure 19-2). Most other attempts at providing very palatable food have been equally futile (Kayser et al., 1992), although Hannon et al. (1976) found that food consumption at altitude returned to sea-level intakes within 7 days in women given standardized frozen dinners. These authors suggested, as a consequence of these and other data, that women may adapt better to altitude than do their male counterparts.

More recent attempts by Butterfield and associates (1992) to feed moderately active male subjects sufficient energy as a formula and food diet (individually designed to meet energy need as determined from sea-level energy requirement and changes in BMR at altitude) were successful in curtailing weight loss after the initial week at 4,300 m (14,110 ft) in four of seven subjects. Weight loss in the other three was slowed to a rate of less than 50 g/d, a rate much lower than that found in the ad-libitum feeding studies (see Table 19-1). Subjects in this experiment were highly motivated and involved, and food intake was strictly enforced. Additionally, the investigators joined the subjects in their enforced dietary regimen, and thus increased the motivation and compliance of the subjects. In a second study by the same team, enforcing food intake to meet individual needs from day 1 at altitude was successful in halting weight loss completely in a similar group of sedentary men (Roberts et al., in press b).

In active individuals performing at altitude, however, energy needs are higher than those of sedentary sojourners, making attainment of adequate energy intake more difficult. Studies using doubly labeled water suggest that the total energy requirement at altitude is 2.2 to 2.3 times (Westerterp et al., 1992) the sea-level basal requirement (total energy requirement in working individuals at sea level for similar lifestyles would be 1.8 to 2.0 times basal energy requirement [Butterfield et al., 1992; Schutz et al., 1981]). Worme and coworkers (1991) were able to encourage an expeditionary team to increase energy intake above sea-level need using a special high-carbohydrate military ration (mean energy intake at altitude was about 3,600 kcal/d whereas sea-level intake was 2,600 kcal/d). However, dissatisfaction with the rations and gastrointestinal

TABLE 19-1 Rate and Composition of Weight Loss at Altitude

Reference	Altitude (m [ft])	Time at Altitude (days)	Total Weight Loss (kg)	Rate of Weight Loss (g/d)	Composition of Weight Loss	
					(kg lean)	(kg fat)
Consolazio et al., 1968	4,300 (14,100)	28	2.66[*]	95		
Whitten and Janoski, 1969	4,300	9	4.27	474		
Krzywicki et al., 1969	4,300	12	3.54[†]	295	2.24	1.29
			3.96	330	2.51	1.46
Consolazio et al., 1972	4,300	6	0.88	147		
			1.13	188		
Hannon et al., 1976[‡]	4,300	7	1.00	143		
Boyer and Blume, 1984	<5,400 (< 17,717)	23	1.90	83	0.56	1.34
	> 5,400 (> 17,717)	26	4.00	154	2.80	1.20
Guilland and Klepping, 1985	4,800–6,000 (15,748–19,685)	20	3.95	198		
Bradwell et al., 1986	4,846 (15,900)	16	4.50	281		
Rose et al., 1988	up to 8,846 (29,025)	38	7.40	196	5.05	2.51
Worme et al., 1991	2,400–4.300 (7,874–14,110)	31	1.90	61	0.90	2.80
Westerterp et al., 1992	7,000 (22,966)	10	2.20	220	0.80	1.40
Butterfield et al., 1992	4,300	21	2.20	104		

[*] In this study, speed of ascent was different in two groups.

[†] In this study, diets differing in carbohydrate content were fed.

[‡] Study on women.

distress thought to be brought on by the diet limited food intake, and the troops were unable to meet energy needs as estimated from changes in body composition (mean energy deficit calculated from change in lean and fat tissue was 850 kcal/d, making total mean energy need for the time at altitude 4,450 kcal/d). The energy intake achieved, however, was sufficient to maintain performance parameters and lean body mass in these training troops, which suggests that the training had a protective effect on protein utilization as has been shown previously at sea level (Todd et al., 1984).

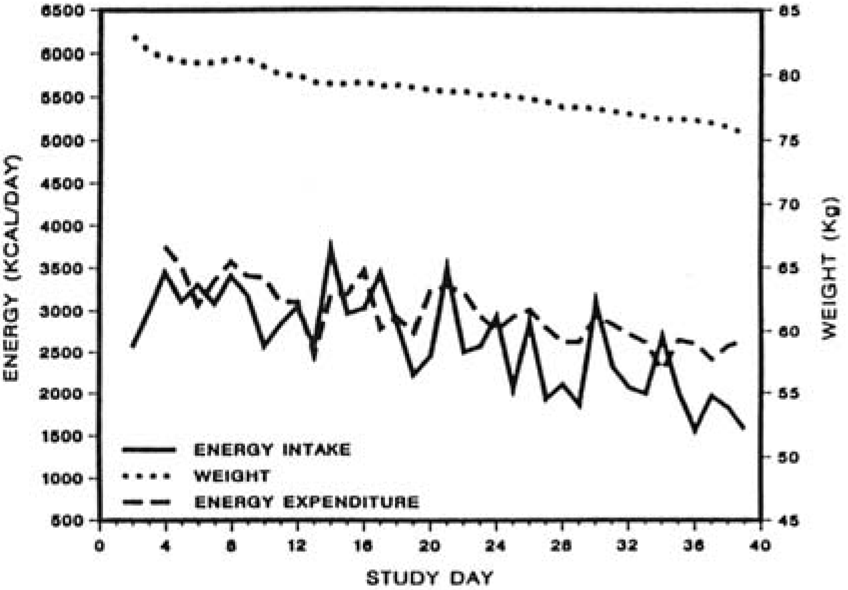

FIGURE 19-2 Changes in mean energy intake and expenditure in relation to body weight during progressive decompression to the barometric equivalent of Mount Everest. SOURCE: Rose et al. (1988), used with permission.

Indian investigators have been particularly successful at accomplishing weight maintenance or even weight gain at altitude. Sridharan and colleagues (1987) accomplished weight maintenance and improved work capacity (as measured by exercise tolerance in a Harvard step test [test of endurance by stepping up repeatedly on a 10-inch step]) in road construction workers at altitude (2,750 m [9,022 ft]) by enforcing intake of food slathered in oil (energy intake increased from 3,100 kcal/d to 3,750 kcal/d with the inclusion of additional fat in the foods). Rai and coworkers (1975) actually accomplished weight gain in a group of soldiers working at 3,500 to 4,700 m (11,483 to 15,420 ft) for 4 months when they were fed their usual diet of 3,700 to

3,900 kcal/d with an additional fat intake of 45 to 324 g (400 to 2,900 kcal/d) as butter or hydrogenated oil.

Thus, anorexia appears to be an immediate consequence of altitude exposure. The continuation of anorexia over time may be a consequence of continued negative energy balance, as is seen with starvation.

A Shift in Appetite

Anecdotal reports of climbers suggest that appetite switches from a preference for fat to carbohydrate after several days at altitude (Gill and Pugh, 1964). Carbohydrate represents the most oxygen-efficient fuel (Brooks and Fahey, 1984), and some investigations have shown that carbohydrate has a protective effect against clinical symptomology associated with hypoxia, ameliorating acute symptoms of mountain sickness (Consolazio et al., 1969), and positively affecting arterial oxygen concentration (Hansen et al., 1972) and pulmonary function (Dramise et al., 1975). In studies where composition of diet has been considered, if a voluntary switch in composition has occurred between sea level and altitude, it has most frequently been to maintain or increase absolute (Boyer and Blume, 1984; Worme et al., 1991) or relative (Guilland and Klepping, 1985) carbohydrate intake at the expense of fat and protein. A major exception to this observation are the results of the simulated ascent of Mount Everest (Operation Everest II), where subjects decreased the proportion of their diminishing food intake provided by carbohydrate (Rose et al., 1988). However, shifts in composition of diet may be dependent, at least in part, on the foods served (Hannon et al., 1976; Worme et al., 1991). In studies where food composition has been manipulated to enforce decreased carbohydrate intake at altitude, exercise performance has been adversely affected (Bigard et al., 1993).

Increased Energy Need: The Output Side of Energy Balance

Basal Energy Needs

Several reports in the literature suggest that BMR (the energy required to maintain body functions in the most minimal state) increases at altitude (Butterfield et al., 1992; Gill and Pugh, 1964; Hannon and Sudman, 1973; Stock et al., 1978), especially during the first week. The early work in this area is confounded by a lack of standardized methodology for determining BMR: some studies collected data on resting metabolic rate (measured after arising and moving around), others on true BMR (measured before arising), and still others measuring one parameter at sea level and another at altitude. In studies where valid measurements were made across several weeks, the elevation in energy expenditure in the resting state declined to near sea level by 2 to 3 weeks of exposure (Hannon and Sudman, 1973; Stock et al., 1978). The literature on measurement of BMR at altitude has been reviewed elsewhere (Butterfield, 1990). The cause for the return toward sea-level values in BMR after the first few days at altitude is thought to be associated, at least in part, with a loss of metabolically active tissue consequent to energy imbalance and weight loss (Butterfield, 1990), as in the circumstances of starvation. This change in metabolic energy need has not been monitored or addressed in most studies attempting to match food intake to energy requirement at altitude.

In fact, energy needs and energy intake may interact. In contrast to previous reports where energy intake was reduced compared to sea level, Butterfield and coworkers (1992) found that when energy intakes were maintained at or above sea-level values throughout 3 weeks of exposure to altitude, BMR rose initially, then fell slightly, but remained elevated above sea-level values by 17 percent (see Figure 19-3). The level at which basal energy needs stabilized in this study (221 ml of oxygen per kg per hour) is similar to that found by other investigators in individuals living chronically at high altitudes (247 ml of oxygen per kg per hour in miners living at 4,900 m [16,076 ft] for greater than 4 months [Picon-Reategui, 1961]; 232 ml of oxygen per kg per hour in climbers at 5,800 m [19,029 ft] for several weeks

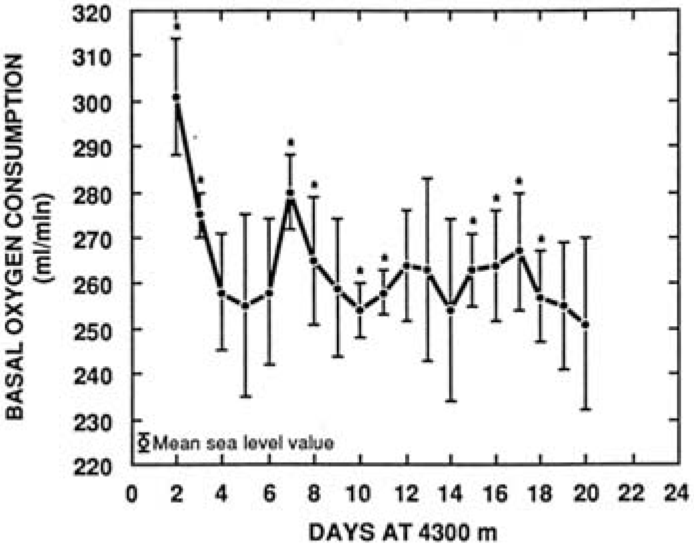

FIGURE 19-3 Basal oxygen consumption at sea level and at 4,300 m 14,110 ft). Values are means ± SE for seven subjects. *, Significant difference from sea level ($P < 0.025$).
SOURCE: Butterfield et al. (1992), used with permission.

[Gill and Pugh, 1964]). Interestingly, Butterfield and coworkers (Roberts et al., in press b), in a study subsequent to that mentioned above, matched energy intake with energy need (including increased basal needs) from day 1 of a 3-wk exposure to 4,300 m (14,110 ft) and found that BMR rose upon acute exposure to altitude, but did not spike on the first days at altitude. BMR rose to and remained elevated at about 17 percent above sea level for the duration of the study. Thus, adequate feeding may in fact, increase overall energy needs at altitude by maintaining increased basal needs. These needs must be addressed in designing food programs for high-altitude residents.

Decreased Absorption

If absorption of nutrients were hampered at altitude, increased intake would be required to cover this increased need. However, malabsorption at altitude is primarily reported anecdotally. Pugh (1962) reported "greasy stools" at altitude in the subjects on the Himalayan Medical and Mountaineering Expedition. Boyer and Blume (1984), in an attempt to evaluate the possibility of fat malabsorption at 6,300 m (20,669 ft), studied fecal fat in three individuals, all of whom appeared to have symptoms of malabsorption even at sea level (mean sea-level net fat absorption was 79 percent, when normal net fat absorption would be expected to be about 95 to 96 percent). In several reports carefully evaluating the issue, no evidence of malabsorption of fat at altitudes from 3,500 m (11,483 ft) (Sridharan et al., 1982) to 4,700 m (15,420 ft) (Rai et al., 1975) could be found using fecal fat as a measure, nor was fat absorption affected at 5,500 m (18,045 ft) (Imray et al., 1992) as monitored by ^{13}C-palmitate absorption. Attempts to show malabsorption of protein at 3,500 m (11,483 ft) (Sridharan et al., 1982), 4,300 m (14,110 ft) (Butterfield et al., 1992), or 5,000 m (16,404 ft) (Kayser et al., 1992) have proven futile, as has the quest to identify alterations in the absorption of carbohydrate (Butterfield et al., 1992) or total energy (Butterfield et al., 1992; Kayser et al., 1992; Sridharan et al., 1982) below 5,000 m (16,404 ft). Few studies of absorption have been conducted above that altitude. Thus, while it has been contended that energy requirements at altitude are elevated due to decreased availability of nutrients through the gastrointestinal tract, the available data confirm that this is not of concern at the altitudes at which military maneuvers will occur.

Energy Expended in Activities

Energy expended in activities could be affected by altitude in two ways. High altitudes could increase the energy required to do any activity, or they could change overall energy requirement by affecting the amount of activity performed. Regarding the latter possibility, most studies at altitude have involved recruits in training or mountaineers performing strenuous exercise and thus involve situations where the energy requirement for activity is increased over sea-level requirement by the protocol. There are few reports in the literature of activity patterns in moderately active individuals subjected to altitude. Butterfield and colleagues (1992) found a significant decrease in the energy expended at strenuous activities during discretionary time by their sedentary subjects at altitude as compared to sea level, which was possibly an adaptive mechanism to offset the increase in basal energy needs. Such a mechanism acting in other studies may have resulted in a diminished negative energy balance and a moderation of weight loss, giving a false impression of the overall effect of altitude on changes in body weight or total energy need.

The question of energy efficiency at altitude has been more thoroughly investigated. Early work suggesting an increased energy requirement for work at fixed power outputs at altitude (Billings et al., 1971) was done using subjects walking on a treadmill, with and without added weights, a situation where metabolic response is known to be dependent on mass and mechanical efficiency (Brooks and Fahey, 1984). This theoretical increase in need was successfully ruled out by West and associates (1983), who showed that the linear relationship known to exist at sea level between oxygen uptake and power output had the same slope and *y* intercept at altitudes as high as 6,300 m (20,669 ft). This question has been reviewed recently elsewhere (Butterfield, 1990), with the conclusion that energy expended in activities of comparable intensity is constant throughout the range of altitudes where humans may be expected to work, and that this aspect of the energy balance equation does not increase energy needs at altitude.

WEIGHT LOSS AT ALTITUDE

Thus, as a consequence of decreased energy intake and increased basal energy needs, most individuals acutely exposed to high altitudes experience a significant negative energy balance and subsequent weight loss. In the discussion above, the daily energy deficit between sea-level and high-altitude intakes was estimated to be approximately 180 kcal/d. Basal energy need, however, has been shown by Butterfield and colleagues (1992) to be elevated by about 17 percent (about 300 kcal/d) in individuals who consume adequate energy when acutely exposed to altitude, giving a total potential energy deficit of about 480 kcal/d in individuals allowed to eat ad libitum at altitude. Such an energy deficit would be sufficient at sea level to cause a weight loss of about 0.5 kg of fat tissue per week (or about 70 g/d). As will be seen below, the actual rate of weight loss in most studies is somewhat higher than this amount, which suggests that there may be additional elements to be considered in the issue of weight loss at high altitudes.

Magnitude of Weight Loss

The magnitude of weight loss at altitude appears to depend to some extent on the duration of the stay, the conditions of the ascent, and the final altitude attained. Table 19-1 depicts data from studies that have provided adequate data to assess rate of weight loss. Although rates of weight loss range from 85 to 474 g/d, this table shows that the average rate of weight loss in ad libitum studies is about 200 g/d, or about 1.4 kg/wk, about three times greater than would be predicted from the potential negative energy balance estimated above. This weight could have an energy equivalent of as much as 1,800 kcal/d if it were assumed to be all fat, or as low as 200 kcal/d if it were assumed to be lean tissue, 73 percent of which is assumed to be water.

Composition of Weight Loss

The composition of the tissue lost at altitude is controversial, and results obtained depend on the methodologies used to determine body composition. Because most body composition measures are indirect, assumptions are made as to the density and electrolyte composition of the tissues being measured. These assumptions are essentially negated by shifts in fluid from one compartment to another, which may change the concentration of solutes in the tissue in an unknown way. Such fluid shifts are well documented at altitude (Krzywicki et al., 1971; Withey et al., 1983). In addition, acute exposure to altitude results in a diuresis of varying magnitude (Boyer and Blume, 1984; Guilland and Klepping, 1985; Koller et al., 1991; Krzywicki et al., 1971), which may increase weight loss and complicate the determination of composition of that weight loss. Diuresis is not found in all studies, however (Consolazio et al., 1968; Hannon et al., 1976), and may be related to exercise level (Withey et al., 1983), diet (Krzywicki et al., 1971), degree of acclimatization (Koller et al., 1991), or gender of the subjects (Hannon et al., 1976). Unfortunately, measurement of body composition at altitude by routine field methods (skinfold measurement [Fulco et al., 1985]; electrical impedance [Fulco et al., 1992]) has been found to be unsatisfactory. The composition of weight loss at altitude has been reviewed recently elsewhere (Butterfield, 1990; Kayser, 1992).

The issue of concern in the discussion of weight maintenance at altitude, however, is which of these compositional changes are a consequence of exposure to hypoxia, and thus unavoidable, and which are associated with inadequate energy intake. Discussion below will concern itself with direct measures of changes in composition, that is, with measures of lean body mass (nitrogen balance) and water loss.

Lean Tissue

The few studies in which nitrogen balance has been measured show that the decline in body weight with exposure to altitude is accompanied by an increase in urinary nitrogen (and a decrease in the balance between nitrogen intake and total nitrogen output as urine and feces, or nitrogen balance). These results suggest a degradation of lean tissue (Consolazio et al., 1968; Guilland and Klepping, 1985), reflective of the energy deficit incurred.

The work of Butterfield and colleagues (1992) suggests that this decline in nitrogen balance can be avoided if sufficient energy is provided in the diet. Figure 19-4 shows nitrogen balance at various times during their experiment. Subjects were in nitrogen balance during the sea-level control phase, which suggests that the energy intake provided during this time met energy needs (Calloway, 1975). During the first week at altitude, when energy intake was equivalent to that at sea level (and thus slightly lower than need, not having been adjusted for increased BMR), nitrogen balance was negative and weight loss occurred. When energy intake was increased to cover the increased needs imposed by elevated BMR, nitrogen balance became positive and remained

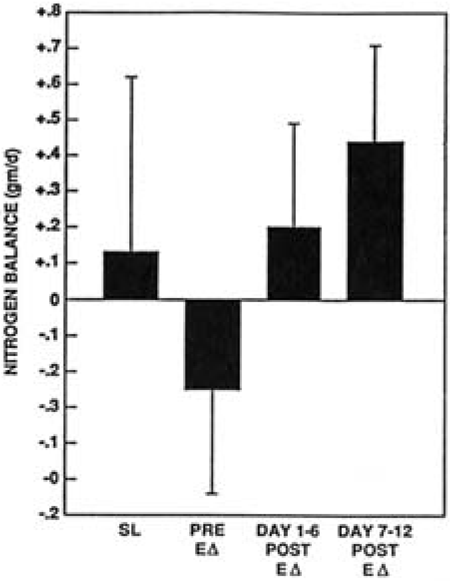

FIGURE 19-4 Mean nitrogen balance for 3 days at sea level (SL), 6 days at altitude before increase in energy intake (PRE EΔ), 6 days immediately after increase in energy intake (days 1–6 POST EΔ), and last 5 days of collections (days 7–12 POST EΔ). Values are means ± SE for six subjects. Increase in nitrogen balance from before to after energy intake increase statistically significant ($P < 0.05$) by repeated-measures analysis of variance.
SOURCE: Butterfield et al. (1992), used with permission.

positive throughout the remainder of the 3-wk stay, while weight loss slowed in all and ceased completely in four of the seven subjects. A subsequent study by the same group suggests that both nitrogen balance and body weight can be maintained throughout a sojourn of 3 weeks at 4,300 m (14,110 ft) if aggressive attempts are made to cover increased energy needs by increased energy intake (Roberts et al., in press b).

As previously noted, studies at altitude where the training regimen is strenuous have been able to accomplish the maintenance of lean tissue (as measured by nitrogen balance [Consolazio et al., 1972] or densitometry [Worme et al., 1991]) in the presence of a moderate negative energy balance (about 200 kcal/d). These results suggest a protective effect of exercise on protein utilization at high altitudes, as has been previously shown at sea level (Todd et al., 1984).

Water

Net loss of body water at high altitudes may occur as a result of increased insensible losses to the dry environment (Ferrus et al., 1984) or consequent to diuresis (Krzywicki et al., 1971). The latter is considered to be a mechanism of adaptation to altitude and appears to be controlled, at least in part, by hormones affecting kidney function and thirst (Milledge et al., 1983). However, diuresis is also a common consequence of rapid weight loss (Fisler and Drenick, 1987), and the magnitude of diuresis found in most studies during the initial days of exposure to hypoxic conditions may be the sum of the consequences of altitude and of weight loss due to negative energy balance.

The magnitude of respiratory fluid losses to the environment is determined by the partial pressure of water in the surrounding air and the frequency of respiration (Ferrus et al., 1984). Respiratory losses at altitude have been estimated to be about 600 ml/d (Westerterp et al., 1992) and may be compensated for by increases in metabolic water production accompanying increased exercise (Kayser, 1992). Insensible sweat losses, representing losses from the body surface, are somewhat more difficult to measure, but may be substantial (Consolazio et al., 1968). Water balance studies have suggested that total insensible losses (sweat and respiratory losses combined) are at least 1,900 ml/d (Butterfield et al., 1992; Consolazio et al., 1968) at 4,300 m (14,110 ft).

Thus, water requirement at altitude may be very high, and diuresis with acute exposure may determine the overall state of hydration even after diuresis ceases. The magnitude of diuresis with acute exposure (and the overall negative water balance) was estimated by Consolazio and coworkers (1968) to be about 200 ml/d in individuals inadequately fed or in those purported to be "adequately" fed (Krzywicki et al., 1971).

However, work by Butterfield and associates (Roberts et al., in press a, b) suggests a greater difference between the urinary losses of individuals inadequately and truly adequately fed. Figure 19-5 depicts urine volumes from two studies conducted at 4,300 m (14,110 ft) in which fluid and food consumption requirements were similarly enforced and environmental conditions were comparable. In the first study, energy intake was adjusted for increased needs after the first 7 days of altitude exposure, and weight loss occurred over the first week. In the second study, energy intake was adjusted from day 1 of exposure, and weight loss was prevented in 9 of 11 subjects studied. As can be seen from Figure 19-5, fluid losses in urine were significantly decreased under the circumstances of adequate energy intake, which suggests that at least some of the diuresis reported in the past may be a consequence of weight loss and may not be necessary under circumstances of hypoxia. The diuresis that did occur during the second study, however, was not accompanied by weight loss in most of the subjects studied.

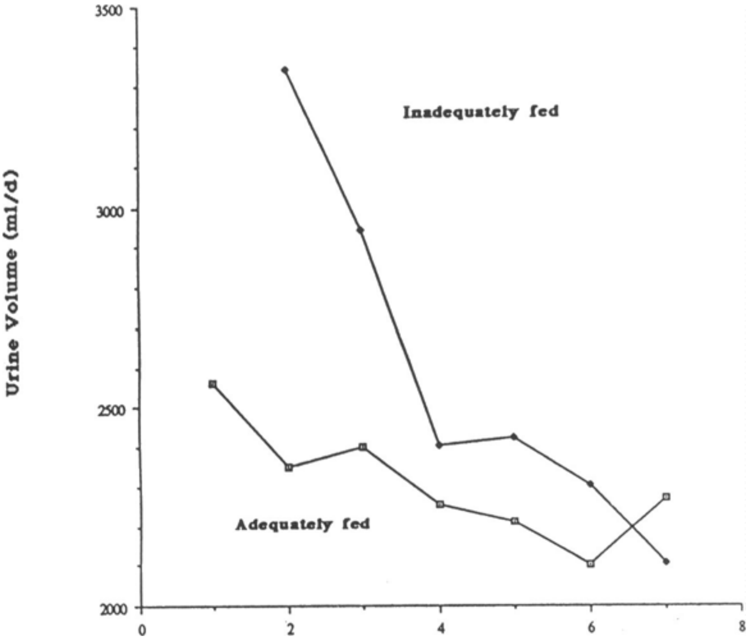

FIGURE 19-5 Total daily urine volume produced by men acutely exposed to 4,300 m (14,110 ft). Inadequately fed group (n = 7) were required to drink 4 liters fluid from food and water each day and consumed sea-level energy intake as food and formula for first 7 days at altitude. Adequately fed group (n = 11) had same fluid requirements, but energy intake was matched to energy need from the first day at altitude. Diet composition was the same in both groups.

FUEL USE AT HIGH ALTITUDES

The individual forced to consume energy sufficient to cover energy needs at altitude appears to respond differently to altitude than does the inadequately fed individual. Basal energy needs remain elevated in the adequately fed individuals, diuresis is minimized, and body weight and composition are maintained. These observations suggest that acceptance of the dogma of the inevitability of weight loss at altitude may have led to a misinterpretation of the consequences of altitude exposure on other physiological parameters as well.

For example, it is commonly accepted that the primary source of energy for exercise changes from carbohydrate to fat with acclimatization (Young et al., 1982). This dogma is based on inferential measures of (1) glycogen stores in muscle that are maintained after exercise at altitude, and (2) circulating levels of glycerol, free fatty acids, and triglycerides that are increased with exercise after acclimatization to high altitudes. However, the same metabolic picture accrues in the circumstances of starvation (Saudek and Felig, 1976). Thus, in a circumstance where most of the individuals previously studied were in negative energy balance, it is not unexpected that they would be utilizing body stores of fat as a predominant energy source.

However, Brooks and colleagues (1991) found that in men fed sufficient energy to cover need, the primary source of energy at rest and during exercise appeared to be carbohydrate, specifically glucose (see Figure 19-6), after 3 weeks of acclimatization to 4,300 m (14,110 ft). Teleologically, this choice of fuel is more economical in an oxygen-poor environment, as more energy is derived per liter of oxygen from carbohydrate than from any other metabolic fuel source. Using substrates labeled with stable isotopes to evaluate fuel utilization, both acutely and after 3 weeks of exposure to altitude, these investigators have further shown that in fact fatty acid consumption at rest and during exercise decreases markedly with acclimatization in men fed sufficient energy to cover need and that glucose is indeed the "fuel of choice" under these circumstances (Roberts et al., in press a, b).

Thus, the acceptance of the inevitability of weight loss at altitude may have several significant outcomes. First, the physiological response to hypoxia may be confused with the physiological response to negative energy balance, giving an incorrect picture as to the metabolic consequences of high-altitude exposure. This consequence is primarily a scientific one and may be acceptable. But more important to the individuals who must live and work at high altitudes, the acceptance of weight loss as a consequence of hypoxia creates the possibility of acceptance of decreases in lean tissue mass, with accompanying decreases in strength. Such a scenario may result in diminished performance in a survival situation and could result in injury or death to the high-altitude sojourner. This consequence is not acceptable. A shift in the dogma followed by education of the high-altitude sojourner as to the causes and consequences of weight loss at altitude, as well as provision of palatable rations and enforced food intake, may allow for a better matching of energy intake and energy requirement and may well be the difference between life and death for these individuals.

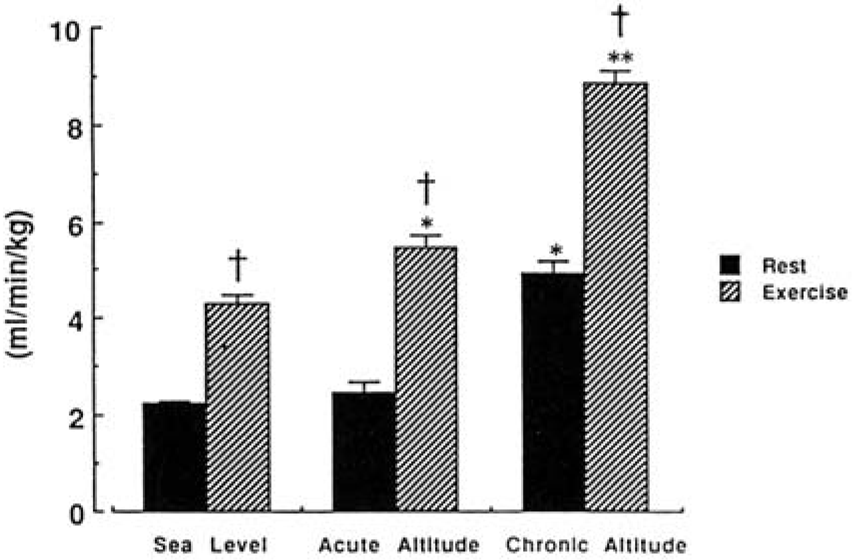

FIGURE 19-6 Effects of altitude, acclimatization, and exercise on arterial blood glucose MCR (ml/min/kg) (MCR = R_d/[glucose]; means ± SE of six or seven subjects at each point). *, Different from sea level; **, different from sea level and acute altitude; t, different from rest; MCR, metabolic clearance rate; R_d, rate of disappearance. SOURCE: Brooks et al. (1991), used with permission.

AUTHOR'S CONCLUSIONS AND RECOMMENDATIONS

Causes for Weight Loss at Altitude

A variety of causes for weight loss at altitude have been previously delineated (Butterfield, 1990). They generally include anorexia, increased energy need due to increased maintenance requirements or malabsorption of energy components in the diet, fluid losses due to diuresis and insensible losses, and detraining.

Altitude appears to depress appetite by about 200 kcal/d in most studies, but this anorexia can be successfully overcome and weight loss prevented by education, strong encouragement, and the provision of palatable and easily consumed (formula) foods.

Energy requirements are elevated at altitude. Basal energy requirements are elevated by at least 17 percent and remain so, especially in adequately fed individuals, resulting in an increased energy requirement for the sedentary individual of 200 to 300 kcal/d. However, there is no convincing evidence for malabsorption of fat, carbohydrate, or protein as a consequence of altitude exposures of less than 5,500 m (18,045 ft). Even above this altitude, the evidence for malabsorption is equivocal. Thus, energy requirement is not further increased as a consequence of malabsorption. Inclusion of the increased basal needs in the calculation of energy requirements at altitude is mandatory for overcoming weight loss.

Fluid losses at altitude may approach 2 to 4 liter/d, with insensible losses amounting to about 2 liters and urine accounting for the rest. Diuresis in response to acute exposure may be minimized by feeding, but a degree of diuresis appears to be necessary as a positive adaptive mechanism. This diuresis may be accomplished without measurable weight loss.

Detraining will only be an issue in those studies where exercise is not part of the protocol. Allowed to use discretionary time as desired, individuals exposed to hypoxia may decrease strenuous activities as a means of conserving energy stores. Energy required to perform standard activities does not vary with the altitude at which the exercise is performed, and consequently, this mechanism does not alter energy requirement.

Under circumstances of adequate energy intake, physiological parameters measured at altitude, such as metabolic fuel source, will more adequately reflect the true response to hypoxia uncomplicated by negative energy balance.

Weight loss at altitude is preventable and is unacceptable.

Author's Recommendations

To minimize weight loss with altitude exposure, the following recommendations are made:

- Energy requirement at altitude for moderately active individuals is 2.2 to 2.3 times sea-level basal requirements (which can be successfully computed from Harris-Benedict equations [Harris and Benedict, 1919]); further adjustments must be made for other strenuous activities performed, such as marching or climbing. Successful consumption of this energy intake may require strong incentives; frequent encouragement; and special high-calorie, nutrient-dense, palatable products. Education about the causes and consequences of weight loss at altitude may be especially important for ensuring compliance. Compliance with this recommendation should essentially eliminate weight loss at altitude.

- The composition of diet should be as follows:

  a. Protein intake of 0.8 g/kg for sedentary individuals; 1.2 to 1.5 g/kg for those performing strenuous endurance activities (Meredith et al., 1989) (result is about 12 to 15 percent of total energy intake).
  b. Carbohydrate intake should supply around 60 percent of total energy intake to cover increased need for carbohydrate in the adequately fed individual. This carbohydrate should be consumed as complex forms to minimize gastrointestinal distress.
  c. Fat intake could be as low as 25 to 28 percent, and such levels of intake may decrease some of the intestinal distress that may accompany large intakes of simple carbohydrate (Worme et al., 1991).

- Develop a drinkable, high-carbohydrate, moderate protein and fat supplement containing about 500 kcal; inclusion of such a product in the rations of sojourners at altitude will help to remedy the consequences of increased need and decreased appetite.
- Determine amount of diuresis that is necessary for optimal adaptation to altitude. Provide fluid sufficient to cover high insensible losses and diuresis (4 liter/d).
- Determine the possible positive effects of feeding on the development of symptoms of acute mountain sickness. Evaluate the effect of meal composition on these symptoms.

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20

Energy and Macronutrient Requirements for Work at High Altitudes

Reed W. Hoyt[1] *and Arnold Honig*

INTRODUCTION

During military operations in the mountains foot soldiers are challenged with rugged terrain and long, physically demanding days. Hypoxia, cold temperatures, and restricted food and water availability can impose additional stresses. Developing operational field rations that meet nutritional demands under these conditions requires accurate estimates of soldier energy requirements. Energy requirements determine the total caloric contribution required from food and body energy stores. The specific fuel combusted to meet energy requirements depends primarily on the intensity and duration of work performed, macronutrient availability from rations and body energy stores, and environmental conditions (Ahlborg and Felig, 1982; Felig and Wahren, 1975; Stein et al., 1989; Young and Young, 1988).

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It is increasingly evident that soldiers participating in field training exercises, particularly those in mountainous terrain, consistently have high rates of energy expenditure and limited dietary energy intakes (Hoyt et al., 1991, 1994a) (Table 20-1). Why are soldiers characteristically in negative energy balance? The following discussion will attempt to address this question and others posed by the Committee on Military Nutrition Research.

ENERGY BALANCE

Exercise Energy Expenditure

Duration of Activity

High rates of energy expenditure can be attributed in part to the large portion of the day that soldiers spend in physical activity. For example, monitoring of ambulatory activity showed that soldiers were active around 17.3 ± 0.2 h/d (mean ± SD) (*n* = 20) over the course of 11 days during a physically demanding winter military training course (Hoyt et al., 1991). Similarly, Special Operations Forces soldiers were active about 16 ± 2 h/d during a 6-d military field training exercise at 2,500 to 3,100 m (8,202 to 10,171 ft) elevation on Mount Rainier (elevation = 4,392 m [14,410 ft], Mount Rainier National Park, Wash.) (Hoyt et al., 1994a).

TABLE 20-1 Ration Consumption and Estimated Energy Expenditure of Soldiers in the Field

Test duration	3 to 34 days
Energy expenditure	3,490 ± 640 kcal/d (range: 2,000 to 4,700 kcal/d)
Food energy intake	2,410 ± 400 kcal/d (range: 1,780 to 2,880 kcal/d)
Carbohydrate intake	280 ± 70 g/d (range: 190 to 385 g/d)

NOTE: These data are from 11 recent field studies of 781 soldiers. Values are means ± SD of study averages for each ration tested. Meal, Ready-to-Eat versions III (*n* = 61), VI (*n* = 342), VII (*n* = 129), and VIII (*n* = 148); Ration, Lightweight (*n* = 253); and Ration, Cold Weather (*n* = 48) were tested. About two-thirds of the available food energy was consumed.
SOURCE: Compiled from Jones et al. (1990).

Work Intensity

Average daily multiples of basal metabolic rate (BMR) have been used to classify occupational work levels as light (1.55 × BMR), medium (1.78 × BMR), or heavy (2.10 × BMR) (FAO/WHO/UNU, 1985). Recent studies using the doubly labeled water method to measure total daily energy expenditure have found that the work level of soldiers commonly exceeds 2.10 × BMR. In a winter military training course, work levels averaged 4.03 ± 0.22 × BMR (7,131 ± 225 kcal/d) over the first 4 days when the soldiers were particularly active, with an overall average of 2.8 ± 0.2 × BMR (4,919 ± 190 kcal/d) for the entire 11-d study (Hoyt et al., 1991). Similarly, an average of 2.5 × BMR was expended over 7 days by soldiers training for jungle warfare (Forbes-Ewan et al., 1989), while the work level of Special Operations Forces soldiers on Mount Rainier was 3.2 ± 0.2 × BMR (4,558 ± 566 kcal/d) (Hoyt et al., 1994a).

By comparison, the work level of trained amateur cyclists studied over a 3.5-d period that included 2 days of heavy activity (two 4-to 5-hour bouts of exercise to exhaustion per day) averaged 2.6 × sleeping metabolic rate (Westerterp et al., 1988). Examples of extreme work rates (4.2 to 5.3 × BMR) have been reported for cyclists in the Tour de France (Westerterp et al., 1986) and in trained athletes in the laboratory (Stein et al., 1987). The predicted maximum rate of daily energy expenditure of ultra-long-distance runners is about 7.6 × BMR or 14,000 kcal/d (Davies and Thompson, 1979)

What is the Effect of Altitude Exposure on $\dot{V}o_{2\,max}$ and Physical Endurance?

The cardiorespiratory responses to exercise at moderate altitudes are well documented (Fulco and Cymerman, 1988; Grover et al., 1986; Young and Young, 1988). Although variable among individuals, an approximate 10 percent decrease in maximal oxygen uptake ($\dot{V}_{o2}$ max) occurs for every 1,000 m (3,280 ft) increase in elevation above 2,000 m (6,562 ft). The $\dot{V}_{o2}$ at any given submaximal power output, however, remains unchanged from sea level to altitude. Consequently, exercise at altitude at a given power output requires a greater percentage of $\dot{V}_{o2}$ max, that is, a higher relative exercise intensity.

Acclimatization to moderate altitudes dramatically increases endurance exercise capacity (time to exhaustion during sustained exercise at a constant exercise intensity) (Horstman et al., 1980; Maher et al., 1974), but it has little or no effect on $\dot{V}_{o2}$ max (Boutellier et al., 1990; Horstman et al., 1980; Young et al., 1982). Compared to sea level, cycle ergometer endurance time at 75 percent of $\dot{V}_{o2}$ max increased 61 percent after 12 days at 4,300 m (14,110 ft) (Maher et al., 1974), while time to exhaustion with treadmill running at 85 percent of $\dot{V}_{o2}$ max increased 41 percent after 16 days at 4,300 m (14,110 ft)

(Horstman et al., 1980). The increase in endurance capacity with acclimatization to altitude appears to be related to improved oxygen delivery.

Resting Energy Expenditure

Does Altitude Exposure Increase Basal Energy Requirements?

Short-term measurements of gas exchange during several field studies suggest that acute hypoxia increases BMR and possibly even the energetic costs of exercise. The work of Schneider et al. (1924) suggested that oxygen consumption tended to increase after 3.5 to 8 hours of exposure to 400 mm Hg (about 4,900 m [16,076 ft]). Leulier (1954) found that 19 of 29 subjects exhibited increased BMR at an elevation of about 3,000 m (9,843 ft). Increased BMR was evident in 10 men and 2 women studied at sea level and during a 12-d sojourn at 1,850 m (6,070 ft) (Terzioglu and Aykut, 1954). Grover (1963) reported a small (5 percent) but significant increase in BMR in two women and four men with the transition from 1,580 m to 4,300 m (5,184 to 14,110 ft). Gill and Pugh (1964) found that six of eight expedition members showed a 10 percent increase above BMR values predicted for sea level. In a study by Surks et al. (1967), mean oxygen consumption in five young males increased significantly on the first day at altitude, remained significantly elevated on day 4, and then decreased progressively towards control values by day 8. Nair et al. (1971) reported that BMR increased significantly after 7 days at 3,353 m (11,000 ft), then returned to sea level values by day 14. This result is generally consistent with the findings of Meda (1955), who reported that no difference in metabolic rate was evident in seven adults (three males and four females) tested at sea level and after 7 to 17 days at 3,000 m (9,843 ft). In Hannon and Sudman's (1973) study of eight young women, exposure to an elevation of 4,300 m (14,110 ft) increased basal oxygen consumption, with the maximum increment at 36 hours. In a study of five males who were taken from 1,600 to 4,300 m (5,249 to 14,100 ft) (Huang et al., 1984), resting metabolic rate increased 16 percent on day 1 and remained elevated through the end of the experiment on day 5. In a recent study by Butterfield and coworkers (1992), BMR increased 27 percent on day 2, decreasing to +17 percent by day 10, in seven men taken to 4,300 m (14,110 ft) elevation. After 1 week at 3,650 m (11,975 ft) elevation, fasting resting metabolic rate and exercise metabolic rate in six volunteers, four males and two females, had increased significantly over sea-level values (Stock et al., 1978). Significant increases in oxygen uptake during standardized treadmill exercise were noted in a study of 27 young men after 4 to 9 days at 4,300 m (14,110 ft) (Johnson et al., 1971).

Although these field studies suggest that BMR increases with acute hypoxia, no consensus exists as to the magnitude of the effect. This conclusion is, in part, due to the very short duration of the gas exchange measurements used to estimate BMR, the unavoidable lack of control in field studies, and the broad range of reported increases in BMR.

The effects of menstrual cycle on energy expenditure may contribute to variation in the effects of hypoxia on BMR. Significant (6 to 15 percent) increases in energy expenditure during pre- to postovulation are reported (Bisdee et al., 1989; Webb, 1986). Additionally, in a study of 10 women, a relatively large intrasubject coefficient of variation in resting energy expenditure was attributed in part to the effect of the menstrual cycle on energy expenditure (De Boer et al., 1987).

Energy Intake

Field Ration Consumption at Sea Level

Soldiers normally, perhaps innately, do not consume enough food to meet the energy demands of strenuous field training exercises, regardless of the type of field ration they are consuming (Table 20-1). Voluntary consumption of currently available field rations rarely exceeds 3,000 kcal/d, with food wastage averaging about a third of the total calories available. The only instance in which physically active soldiers have maintained energy balance while in the field was when they were provided hot A Rations at regularly scheduled meal times (Rose and Carlson, 1986).

Inadequate food intake in the field has been ascribed to poor ration palatability, menu boredom, inability to work on a full stomach, lack of water, decreased appetite due to increased exercise, lack of specific meal periods and time to prepare meals, anxiety due to field conditions, and intentional dieting (Popper et al., 1989; Rose and Carlson, 1986). In animals, it is thought that anorexia (reduced food intake even when food is readily available) may improve survival and competitive success during important activities such as defense against predators, seeking shelter from bad weather, migrating, and courtship (King and Murphy, 1985; Mrosovsky and Sherry, 1980). The universality of the voluntary anorexia seen in soldiers during field exercises suggests that a similar innate process may be occurring. Although it is difficult to quantify the adaptive value of anorexia to soldiers operating in a field environment, it is possible that anorexia helps soldiers adapt to demanding situations. A decrease in food intake may benefit soldiers by limiting postmeal impairments in the ability to maintain attention and react quickly (Smith and Miles, 1986). A decrease in the need to carry, prepare, and eat rations would decrease the energetic cost of load carriage and increase the amount of time and resources available for more important military tasks.

Does Altitude Exposure Influence Appetite?

Under resting conditions in rats, acute exposure to moderate and well-tolerated, high-altitude hypoxia inhibits not only food and salt appetite but also thirst, probably by independent but still not fully understood mechanisms (Behm et al., 1984, 1989; Fregly et al., 1976; Schnakenberg et al., 1971, 1973). Food and water intake are inhibited only in the first 1 to 4 days of well-tolerated hypoxia, whereas salt intake can be inhibited for a longer time. This picture might be modified by physical exercise and during extreme or badly tolerated hypoxia where the general aversion to food, water, and salt intake may simply reflect altitude illness rather than an adaptive physiologic mechanism. The reduced appetite and thirst with acute exposure to moderate, well-tolerated altitudes appears to support physiologic hypohydration and adaptation to acute hypoxia (Hoyt and Honig, 1996). The primary adaptive value of anorexia in the first days at high altitudes may be to reduce dietary salt intake, with the reduction in caloric intake as a secondary effect.

Is There Any Significant Effect of the Type of Ration on the Total Calories Consumed or the Percentage of Calories as Carbohydrate?

No effect of ration type on total caloric consumption was evident in a study of 28 Marines during a strenuous, 11-d cold-weather field exercise at 2,200 to 2,550 m (7,218 to 8,366 ft) elevation (Hoyt et al., 1991; Morgan et al., 1988) (Table 20-1). Energy expenditure, measured by the doubly labeled water method, was 4,919 ± 190 kcal/d (mean ± SD, $n = 23$). Three different ration types were issued: the standard Meal, Ready-to-Eat (MRE: 5,192 kcal/d, 644 g carbohydrate); the Ration, Cold Weather (RCW: 4,470 kcal/d, 661 g carbohydrate); and the Ration, Lightweight (RLW: 4,219 kcal/d, 400 g carbohydrate). Mean daily caloric intakes (MRE: 3,217 ± 285 kcal/d, $n = 8$; RCW: 2,892 ± 326 kcal/d, $n = 10$; RLW: 3,205 ± 433 kcal/d, $n = 10$) and the amount of carbohydrate consumed (MRE: 367 ± 34 g/d; RCW: 410 ± 47 g/d; RLW: 345 ± 47 g/d) did not differ significantly among the three ration groups. The percent contribution of carbohydrates to total calories consumed ranged from 43 go 57 percent (MRE: 46 percent; RCW: 57 percent; RLW: 43 percent). Neglecting modest body carbohydrate reserves, the percent contribution of dietary carbohydrate to total energy expenditure was only 28 to 33 percent. Significant differences in carbohydrate consumption between the MREs, RLWs, and the higher-carbohydrate RCW ration may have been evident if a larger group of volunteers had been studied. In any case, the RCW ration barely met the recommended minimum carbohydrate consumption of 400 g/d (IOM, 1992). A carbohydrate supplement is probably needed to meet the carbohydrate demands of physically active soldiers.

What is the Ideal Macronutrient Composition for a High-Altitude Diet?

Under resting conditions during the first 1 to 3 days at well-tolerated altitudes, subjects should eat a diet poor in salt and rich in carbohydrates. Drinking water should be freely consumed to foster physiologic natriuresis. Advantages of a carbohydrate-rich diet include oxidative end products, carbon dioxide and water, which have little impact on renal function, and an energy yield per liter of oxygen higher than that of fat (Lusk, 1928). After the initial period of adaptation to hypoxia, subjects should resume eating a normal, sea-level diet. Thus pure water, salt-free fluid, tea, or coffee should be readily available and consumption encouraged or even required.

Sources of Metabolic Fuel

Body Fat and Carbohydrate Reserves

Although soldiers normally do not consume enough food to meet energy demands in the field, they generally have substantial body fat available to meet the deficit. For example, a typical young male soldier weighing 74 kg has approximately 13.5 kg of body fat (Fitzgerald et al., 1986). This is equivalent to about 81,000 kcal, assuming that body fat energy density is 7,700 kcal/kg and that a minimum of 4 percent body fat or about 3 kg of fat is needed for normal physiological function (Friedl et al., 1994). This fat energy reserve, which constitutes approximately 98 percent of the body's energy reserve (Sahlin, 1986), is enough energy to meet a 2,000 kcal energy deficit per day for over a month.

In contrast to the large fat energy reserves, body carbohydrate reserves constitute only around 2 percent of the body's energy reserves and are readily depleted in the absence of adequate dietary carbohydrate intake (Sahlin, 1986). If the total daily energy expenditure of a soldier during a mountain operation is 4,000 kcal/d with an average respiratory exchange ratio of 0.85, a carbohydrate combustion of about 500 g/d would be expected. However, carbohydrate intake in the field is typically around 300 g/d (Table 20-1) (Hoyt et al., 1991, 1994a), far short of the minimum 400 g per soldier per day needed for a reasonable rate of glycogen resynthesis (IOM, 1992). When carbohydrate reserves are depleted there is a switch to a fat-predominant fuel metabolism characterized by decreased physical performance (Costill, 1988; Phinney et al., 1983) and loss of lean body mass (Askew et al., 1987b). Easily consumed carbohydrate beverages (Askew et al., 1987a) or high-carbohydrate supplements (Edwards et al., 1989) are needed to boost carbohydrate intake to the recommended minimum of 400 g per soldier per day (IOM, 1992).

Does Altitude Exposure Alter Metabolic Fuel Sources for Work at High Altitudes?

The high rates of energy expenditure and large energy deficits during field training exercises at altitude (Hoyt et al., 1991, 1994a) can result in an acute shift from a carbohydrate- to a fat-predominant fuel metabolism (Felig and Wahren, 1975; Stein et al., 1989). Body fat reserves meet fat energy needs, but carbohydrate deficits shift fuel metabolism from carbohydrate to fat. The time course of this transition depends on the subject's $\dot{V}_{o2}$ max, physical activity, and diet (Ahlborg and Felig, 1982; Felig and Wahren, 1975; Stein et al., 1989). Exercise- or diet-induced transitions to a fat-predominant metabolism are usually associated with muscle glycogen depletion and a reduction in maximum sustainable exercise intensity (Hultman, 1967; Phinney et al., 1980). In contrast, exercise after altitude acclimatization is associated with greater endurance exercise capacity, less muscle glycogen utilization (Young et al., 1982), and less muscle lactate accumulation (Green et al., 1989) than exercise of the same relative intensity at sea level.

Can Specific Fuel Requirements Be Quantified?

The specific macronutrient requirements of physically active soldiers cannot be quantified without detailed and accurate information on the intensity and duration of work performed. Little information of this kind is currently available. However, recent findings suggest new approaches to this problem.

First, a new ambulatory monitor has been developed and validated that accurately estimates the metabolic cost of human locomotion from total body weight and the time during each stride that a single foot contacts the ground (Hoyt et al., 1994b; Kram and Taylor, 1990; Taylor, 1985). This approach is based on the fact that the rate of metabolic energy expenditure during walking or running is primarily determined by the cost of supporting body weight and the rate at which this force is generated (Kram and Taylor, 1990). Thus, the rate of force generation can be estimated as total body weight divided by the time during each stride that a single foot was in contact with the ground (Hoyt et al., 1994b; Kram and Taylor, 1990).

A second, related finding is that soldiers performing similar tasks in mountainous terrain have energy expenditures proportional to their total weight (Hoyt et al., 1994a). Differences in fat-free mass and total weight among the subjects explained 89 and 95 percent of the variance in total daily energy expenditure. This variance is consistent with previous studies showing a correlation between total daily energy expenditure and fat-free mass or total weight in subjects with similar activity patterns (Cunningham, 1991; Schoeller and Van Santen, 1982).

These and other findings suggest that energy expenditure patterns of soldiers during field exercises can be accurately estimated from a soldier's total weight, foot contact time, and the nature of the terrain (footing, grade) (Hoyt et al., 1994b; Pandolf et al., 1977). Field studies are planned to test whether macronutrient requirements of physically active soldiers can be quantified using this approach.

AUTHORS' CONCLUSIONS AND RECOMMENDATIONS

Soldiers participating in field training exercises, particularly those in mountainous terrain, are characteristically in negative energy balance. This energy deficit is attributable to the large portion of the day spent in physical activity, heavy work loads, increased basal energy requirements at altitude, and limited consumption of field rations. Food and salt intake also appear to be inhibited by the physiologic processes associated with adaptation to altitude. Although substantial body fat reserves are available to meet the fat energy deficit, carbohydrate intake falls short of the minimum 400 g per soldier per day recommended by the Committee on Military Nutrition Research (IOM, 1992).

The following recommendations are made:

- Formally incorporate easily consumed liquid and/or solid carbohydrate supplements into the military ration system.
- Investigate whether restricting sodium intake while promoting carbohydrate and water consumption facilitates adaptation to acute hypoxia.
- Test whether macronutrient requirements in the field can be accurately estimated from a soldier's total weight, speed of locomotion, and nature of the terrain.

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21

Oxidative Stress at High Altitudes and Effects of Vitamin E

I. Simon-Schnass[1]

INTRODUCTION

In the course of evolution, life found a way to use the high-energy potential of reducing oxygen to water within the mitochondrial respiratory chain. At the same time, however, it was not possible to prevent the formation of other reduced forms of oxygen with toxic properties (Reznick et al., 1993). Therefore, the life and development of cells within an oxygen-containing environment would not be possible without a defense system against these prooxidants. This defense system comprises enzymes as well as low-molecular weight compounds that are categorized as antioxidants (Halliwell et al., 1987).

Aerobic life is characterized by a steady state between prooxidants and antioxidants. To maintain this homeostasis a continuous regeneration of the antioxidative capacity is necessary. If this capacity is insufficient, there is an accumulation of oxidative damage. A shift to the prooxidative state is called *oxidative stress* (Sies, 1993). The antioxidative "strategy" of aerobic cells is targeted at inhibiting or blocking potentially toxic oxygen species or their

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derivatives at the various levels of formation, or blocking their reaction with biomolecules (Elstner, 1990). There is growing evidence that oxidative injury mediated by free radicals is an important factor in various pathologies, including adverse metabolic reactions at high altitudes. Table 21-1 summarizes the many intra- and extracellular sources of free radicals. The mitochondrial electron transport chain as an important source of free radicals is described in more detail below.

PHYSICAL EXERCISE AS A CAUSE OF OXIDATIVE STRESS

Each physical movement is associated with the turnover of substrates including oxygen and thus with energy consumption. From a simplified point of view, blood circulation is no more than an aid to substrate delivery and removal.

Circulation increases during dynamic activity; otherwise, the increased consumption of substrates and the removal of end products would not be possible. However, muscular contraction also leads to vascular compression, which in turn causes a regional and short-term reduction in circulation with limited hypoxia. This effect particularly applies to persons participating in sports activities with concentrated power development. However, when performing

TABLE 21-1 Sources of Oxidative Stress

1) Autoxidation	2) Enzymatic Reactions
Redox cycling	Cytochrome P-450
Quinones	Hemoglobin
Redox dyes	Xanthine oxidase
Melanin	Peroxidases
Iron complexes	Aldehyde oxidases
3) Cellular Sources	4) Environment
Mitochondrial and microsomal electron transport chains	UV radiation
Leukocytes	Ultrasound
Macrophages	γ rays, X rays
	Toxic chemicals, including drugs
	Metal ions

SOURCE: Adapted from Elstner (1990).

sports with an emphasis on overall endurance rather than on individual muscles, the transport capacities of the blood and oxygen exchange into the cell become the limiting factors. In both cases, transient oxygen deficiency can occur, despite the high oxygen turnover (Berg et al., 1987).

Classical sports physiology has concerned itself intensively with the phenomena of availability, turnover, and regeneration of substrates for obtaining energy. In addition, the effects on the structured components of the cell are of essential relevance, a fact that has as yet hardly been acknowledged. It is no coincidence that compartmentalization of the cell is a major feature of higher organisms. The cell membrane contains important switching points for transport processes as well as for reactive processes. Indeed this is the basis of cell function. Membranes participate in some form in the vast majority of metabolic processes. The main objective, even in the case of intense physical performance, is always to maintain the integrity of the membrane structures or at least to ensure that changes are reversible (Berg et al., 1987).

The major cause of membrane damage is the formation of free radicals that can arise from various processes during metabolism. In the aerobic energy supply, most of the adenosine triphosphate (ATP) is formed during *endoxidation*, when electrons of a substrate (e.g., pyruvate or succinate) are transformed via a so-called redox chain to oxygen. The end product formed is water (reduction of the oxygen to water), where:

$$O_2 + 4H^+ + 4e^- \text{ ---> } \quad 2\,H_2O \qquad \text{(water).}$$

It is known that free radicals can arise in the case of incomplete oxygen reduction. If less than four electrons are made available, the following activated oxygen forms are created:

$$\begin{array}{llll}
O_2 + 1e^- & \text{--->} & O_2^{\overline{\cdot}} & \text{(superoxide radical)} \\
O_2 + 2e^- + 2H^+ & \text{--->} & H_2O_2 & \text{(hydrogen peroxide)} \\
O_2 + 3e^- + 3H^+ & \text{--->} & H_2O_2 + OH\cdot & \text{(hydroxyl radical)}
\end{array}$$

In the resting state, 250 to 300 ml of oxygen per minute are usually taken up. Under physical exertion, oxygen uptake can increase to 4,700 ml/min, or even more, depending on training conditions. Around 3 to 10 percent of the metabolized oxygen is not completely reduced to water but to these different radicals (Demopoulos et al., 1986). The increased formation of oxygen radicals is also termed *oxidative stress* (Demopoulos et al., 1986).

Other metabolic processes also lead to the generation of free radicals. Physically strenuous activity induces certain inflammatory-like reactions that are associated with the increased formation of radicals (e.g., leukocyte activation with phagocytosis, leukotriene synthesis). In addition, radicals from outside are taken up into the body, for example, from air pollution, ultraviolet radiation, and cigarette smoke. These sources can also be of great relevance because the damaging reactive mechanisms of these radicals do not differ greatly from the reactions mentioned above (Packer, 1984).

One characteristic of free radicals is their high, at times extremely high, reactive capability. Activated oxygen species react very readily with other substances and thus form other radicals. Particular mention should be given to reactions with lipids. A generalized scheme of lipid peroxidation is given in Figure 21-1.

Free radicals also react with proteins, particularly those that contain functional sulfhydryl (SH) groups, which leads to inactivation and the formation of carbonyls. Destructive chain reactions, which will be mentioned later, can be set off that may lead to functional impairments ranging up to complete destruction of the cell (Packer, 1984).

In the case of extreme physical activity (the term *extreme* should always be considered in a relative manner and defined on an individual basis), the following factors can lead to an increased discharge of free radicals. Oxygen turnover can be increased up to 20 times that of resting consumption. Accordingly, the incomplete reduction of oxygen to water and the associated formation of free radicals can also increase. Hypoxic cells are particularly susceptible to oxidative stress, a phenomenon commonly referred to as the oxygen

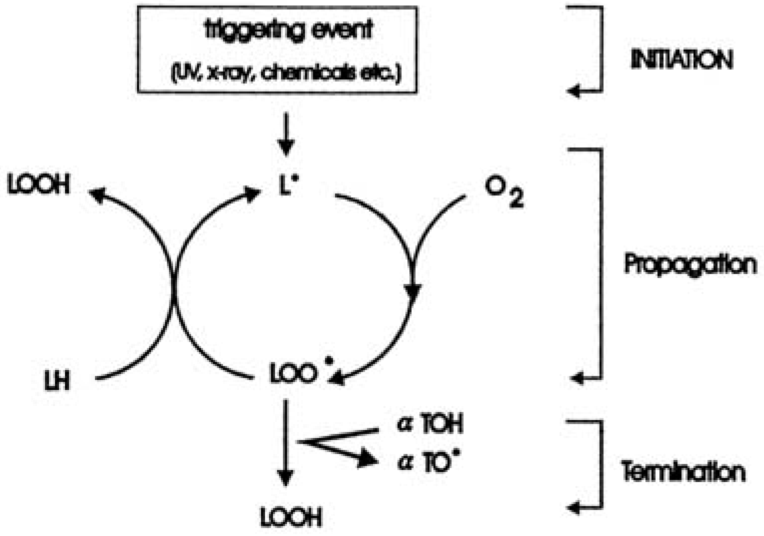

FIGURE 21-1 Scheme for lipid peroxidation chain reactions initiated by free radicals. LH, lipid molecule; L·, lipid radical; LOO·, lipid peroxyl radical; LOOH, lipid hydroperoxyl radical; α-TOH, alpha-tocopherol; α-TO·, alpha-tocopherol radical. SOURCE: Adapted from Sies (1993).

paradox (Demopoulos et al., 1986). If there is not enough oxygen available to accept electrons, they will be transferred to other low-molecular-weight molecules, which in turn induce radical chain reactions (Demopoulos et al., 1986). When the pH drops (metabolic acidosis during extreme physical exertion), superoxide anion ($O_2^{\cdot -}$) can be converted into the highly toxic peroxyl (OOH·) radical. $O_2^{\cdot -}$ is derived from the respiratory chain, whereas the required hydrogen is supplied by the lactic acid that is formed. At physiological pH, only around 1 percent of the superoxide is converted to a peroxyl radical. However, the percentage increases with increasing acidosis (Demopoulos et al., 1986; Simon-Schnass, 1993).

THE DEFENSE SYSTEM

As mentioned above, the antioxidative strategy of aerobic cells is targeted at inhibiting or blocking potentially toxic oxygen species or their derivatives at the various levels of formation or blocking their reaction with biomolecules (Elstner, 1990). The most important components of this defense system against oxidative stress are:

Vitamins and other antioxidants

- vitamin E,
- vitamin C,
- β-carotene,
- flavonoids,
- ubiquinones, and
- glutathione.

Enzymes

- catalases,
- superoxide dismutases
- peroxidases, and
- transferases.

Typical *detoxification enzymes* are superoxide dismutase, the catalases, and various peroxidases. If the organism is confronted with radicals, as is the case in physical activity, these enzymes are reactively synthesized to an elevated degree (Simon-Schnass, 1993). Clearly, a certain time lag between the occurrence of the noxae (radicals) and the higher enzymatic level as a protective measure cannot be avoided. If the stimulus for the increased enzyme formation ceases, the enzyme drops back to its original level (Simon-Schnass, 1993). This effect suggests that enzymatic protection against oxidation can only be effectively boosted by regularly taking part in sports. From this point of view, athletes who train irregularly and/or at varying degrees of intensity are relatively insufficiently protected against oxidative stress by enzymes (Simon-Schnass, 1993).

However, the defense system comprises various antioxidants in addition to the antioxidative enzymes. Many substances that function as antioxidants in vitro also occur physiologically (in vivo). Until now, practical relevance has only been found for vitamins E and C, β-carotene, and other carotenoids, as well as glutathione, some flavonoids, the ubiquinones, and, in certain cases, uric acid, taurine, the amino acids cysteine and histidine, and several xenobiotics (Elstner, 1990).

Vitamin E is a lipophilic radical inhibitor. Correspondingly, its action is mainly limited to the region of the lipophilic membrane. Because it is stored there in the immediate vicinity of the substances in danger of oxidation, vitamin E can very effectively circumvent the peroxidation of fatty acids, as well as the oxidation of cholesterol and proteins. This is of great importance for membrane integrity. Even during vitamin E deficiency, no other antioxidant has yet been shown to serve as a substitute to break the radical chain reaction in the lipophilic area of the cell (Elstner, 1990). This means that vitamin E cannot be replaced by any other substances at its functional site. In addition to the inhibition of lipid peroxidation in the lipophilic centers of biological membranes, vitamin E also appears to play a role in the repair of oxidized amino acids, which otherwise may contribute to the formation of lipofuscin (cross-linking of protein and other high-molecular fragments). In this way, vitamin E could also be attributed a special role in the repair of damaged amino acids in the integral membrane proteins (Elstner, 1990).

Vitamin C is known as an excellent water-soluble antioxidant with a strong reducing potential. It is capable of scavenging a wide variety of different oxidants. For example, it has been shown to scavenge effectively superoxide anions, hydrogen peroxide, the hydroxyl (OH·) radical, aqueous peroxyl radicals, as well as singlet oxygen (Stocker and Frei, 1991). As an antioxidant, vitamin C undergoes a two-electron oxidation to dehydroascorbic acid with the intermediate formation of a relatively unreactive ascorbyl radical (Bielski and Richter, 1975). Dehydroascorbic acid is unstable and hydrolyses readily to diketogulonic acid. However, it also can be reduced back to ascorbic acid by glutathione in erythrocytes and other blood cells (Hughes and Maton, 1968).

As a water-soluble substance, vitamin C is predominantly found in plasma and the aqueous phase of the cell. In particular, vitamin C deactivates the extracellular oxidants generated by activated neutrophils (Halliwell et al., 1987) but also quenches radicals diffused to the extracellular space. Moreover, vitamin C interacts with the membrane-bound vitamin E by reducing the tocopheryl radical back to tocopherol (Packer et al., 1979).

In addition to vitamin E, β-carotene, which is also lipid soluble, has been shown to be an effective chain-breaking antioxidant (Sies, 1993). The peroxyl-trapping activity of β-carotene and possibly other carotenoids is dependent on the partial pressure of oxygen (pO_2). It is less effective in the presence of air, but becomes a good peroxyl radical trap at the low pO_2 that prevails in biological tissues (Burton and Ingold, 1984). At very low pO_2 (4 torr), it inhibited lipid peroxidation even better than vitamin E (Vile and Winterbourn, 1988).

The antioxidative strategy of aerobic cells is aimed at reducing or blocking the potentially toxic effects of activated oxygen species that are generated by various metabolic processes and which may cause oxidative stress. The question now is whether oxidative stress occurs to a greater extent during a prolonged stay at high altitudes. In the following discussion, several possible sources of free-radical generation are discussed.

EVIDENCE FOR INCREASED OXIDATIVE STRESS AT HIGH ALTITUDES

With respect to life, the main characteristics of high altitude are the decreased availability of oxygen, with its influence on metabolism and thereby on physical and mental performance, as well as increased ultraviolet radiation, wide temperature differences, sometimes increased psychological stress, dehydration, and insufficient nutrient intake.

High-Altitude Hypoxia

Aerobic energy supply is necessary for all higher life forms. In accordance, an inadequate oxygen supply leads to unnoticed metabolic impairments that may ultimately create a direct life threat. A drop in arterial oxygen pressure below a nominal level may be due to a number of factors, including a decrease in inhaled oxygen because of the low partial pressure that occurs at high altitudes.

Acute exposure to high altitudes results in a decreased amount of oxygen available to the body and thus to a decreased arterial blood oxygen saturation. This leads to a reduction in maximal aerobic power of approximately 1 percent for every 100 m (328 ft) above 1,500 m (4,921 ft) (Buskirk, 1966). However, because the body has compensation mechanisms to counteract the resulting hypoxia, acclimatization is possible. This effect includes an increase in hematocrit and hemoglobin to improve the transport capacity for oxygen (compensatory polycythemia) and a shift in oxygen binding to hemoglobin, as well as an increase in capillary density, mitochondria, and tissue myoglobin (Eckhardt et al., 1989; Hannon et al., 1969). Moreover, muscle glycogen is saved, and mobilization and metabolism of free fatty acids are improved as shown by a decrease in blood lactate and ammonia during submaximal exercise (Young et al., 1982, 1987). These changes are remarkably similar to those induced by endurance training and are aimed at reducing the oxygen demand of the body.

Direct Studies on Oxidative Stress at High Altitudes

The exhalation of pentane can be considered a result of lipid peroxidation (Kappus, 1985). In animal as well as in human studies it was related to vitamin E status (Bland, 1986; Dillard et al., 1978; Schwarz, 1962). Various conditions, such as an increased energy turnover and/or hypoxia, favor lipid peroxidation (Demopoulos et al., 1984; Dillard et al., 1978). Vitamin E is one of the most effective membrane-bound radical scavengers. In animals, exercise-induced lipid peroxidation was prevented by vitamin E administration (Dillard et al., 1977; Packer, 1984).

To test if there is indeed an increased oxidative stress leading to increased lipid peroxidation at high altitudes, the amount of exhaled pentane was determined by gas chromatography (Simon-Schnass and Pabst, 1988). Twelve mountaineers were supplemented with 400 mg of vitamin E per day (test group) or a placebo (control group) during an expedition to K2 (8,611 m [28,250 ft]). Baseline tests were done in Scardu, Pakistan. Supplementation began upon departure from Scardu to base camp, which was established at 5,100 m (16,732 ft) 2 weeks after departure from Scardu. Pentane was measured twice—the baseline value at Scardu and a second value after a 2-wk stay at base camp. The results are shown in Figure 21-2.

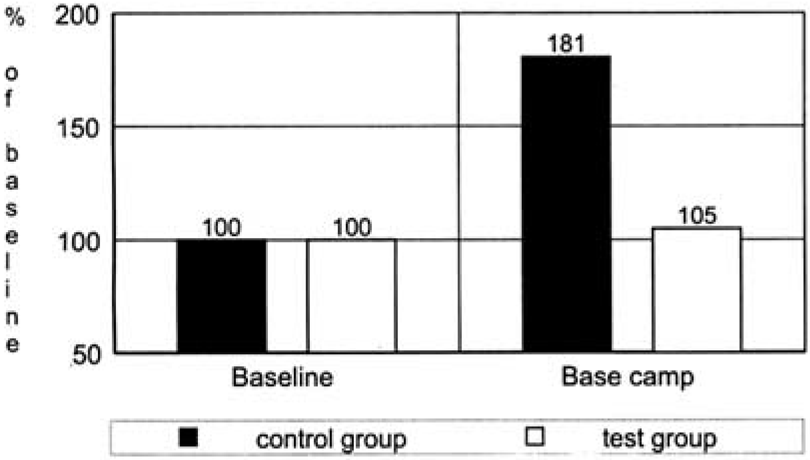

FIGURE 21-2 Pentane exhalation (percent of baseline) of 12 mountaineers during an expedition to K2 with (test group) or without (control group) a supplementation with 400 mg of vitamin E per day. SOURCE: Adapted from Simon-Schnass and Pabst (1988).

There was no significant difference between the initial pentane exhalation of the two groups, but after 4 weeks of supplementation and 2 weeks at high altitudes, the exhaled pentane increased significantly ($p < 0.01$) in the control group. In the treatment group, there was no noticeable change. It can be concluded from this study that high-altitude climbing incurs a considerable risk of metabolically induced cell damage. This risk can be counteracted by supplementation with antioxidants.

As mentioned above, membranes are most susceptible to oxidative stress because of their high amount of polyunsaturated fatty acids. Erythrocytes are able to change their shape due to their membrane fluidity, among other factors. The loss of this fluidity can be influenced by factors such as acidosis, hyperthermia, and immobilization (stasis), due to, for example, aggregation, membrane defects, and cell aging (Thews and Vaupel, 1982). Because the important underlying phenomenon is considered to be an oxidative change of membrane lipids and proteins, it is suggested that these changes may be triggered by free radicals (Kappus, 1985). The filterability of the red blood cells is considered a measurement of their flexibility (Schmidt-Schönbein et al., 1973). This parameter was tested during two other expeditions at high altitudes.

During the first study, 13 mountaineers were supplemented with either 400 mg of vitamin E per day (test group) or a placebo (control group) during an expedition to Annapurna (8,091 m [26,545 ft]) (Simon-Schnass and Korniszewski, 1990). Baseline tests were done in Kathmandu, Nepal. Supplementation began upon departure from Kathmandu to base camp, which was established at 4,300 m (14,108 ft) 2 weeks after departure from Kathmandu. The destination of the second expedition was the Solo Khumbu area near Mount Everest. The members were scientists who stayed for several weeks at an altitude of 5,000 m (16,404 ft) for research reasons. Ten of them took part in the study described later. Baseline tests were done after arrival at this altitude. Supplementation began immediately after the baseline tests.

For standardization reasons, erythrocyte filterability is expressed as the ratio of the turbidity of an unfiltered to a filtered sample. These data are given in Figure 21-3.

It was shown that red blood cell filterability deteriorates at high altitudes. The fact that no change in erythrocyte filterability was detected in the test group indicates that protection from oxidation was adequate there. The significant drop in filterability in the control group ($p < 0.05$), however, permits the conclusion that the oxidative stress led to depletion of vitamin E and/or other antioxidative substances.

To prove that the reason for this depletion was indeed the effect of an increased free radical production, the test was repeated during the above described expedition to Solo Khumbu (Simon-Schnass, 1994). Ten scientists were supplemented with either 400 mg of vitamin E per day (test group) or a placebo (control group). The tests were conducted in a permanently established laboratory at an altitude of 5,000 m (16,393 ft). The results are shown in Figure 21-3. Unfortunately, only data from 1 and 3 weeks after arrival at the laboratory were available because the laboratory heads would not be convinced to agree to the determination of low-altitude values as well. In this case, the first term at altitude is the baseline value. Although the values are higher in general, the trend is very similar to the first experiment. The difference between the two groups after 2 weeks at altitude is again significant ($p < 0.05$).

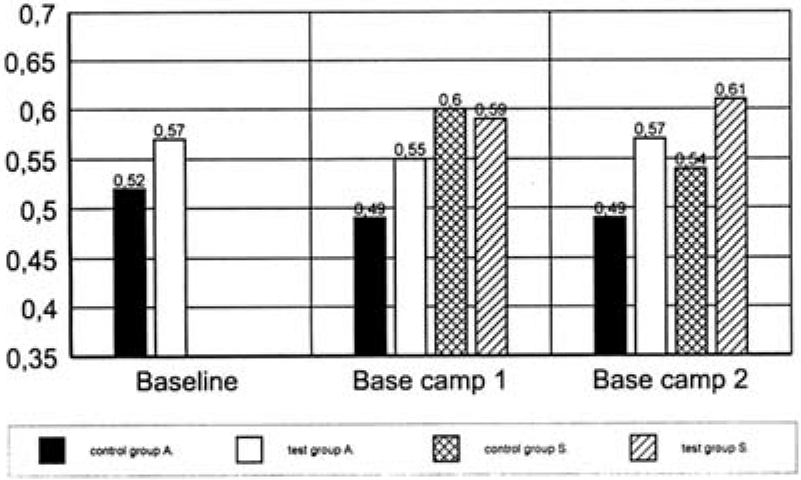

FIGURE 21-3 Filterability of red blood cells (without dimension) from subjects of two different expeditions to high altitudes. In both studies the subjects were divided into a test group and a placebo group. The test group was supplemented with 400 mg of vitamin E per day, whereas the control group received a placebo. In one study (Annapurna), there is a baseline value from a blood sample taken before the start of the expedition and two more with 2-wk difference. In the other study (Solo Khumbu), a baseline value at low altitude could not be achieved; so, there are only two samples at high altitude, one taken shortly after arrival and the other 2 weeks later. SOURCE: Annapurna, adapted from Simon-Schnass and Korniszewski (1991); Solo Khumbu, adapted from Simon-Schnass (1995).

In addition during the second experiment (study at the Solo Khumbu area), the susceptibility of the erythrocytes of the same blood sample to peroxidation was tested by measuring the amount of thiobarbituric acid reactive substances (TBARS), which were determined at the Rowett Research Institute in Aberdeen, Scotland by a method established in this laboratory. In contrast to the slight decrease in TBARS formation in the test group, there was a tremendous increase in the control group. This result clearly documents increased oxidative stress at high altitudes. As shown later, the average daily intake of vitamin E of this group was 16.8 mg. Obviously this amount was inadequate to meet the demand at high altitudes. The data are given in Figure 21-4.

There was also a negative correlation between the filterability of the erythrocytes and the amount of TBARS measured during this test ($r = -0.9190$ for the test group and $r = -0.8218$ for the control group). This result indicates that membranes that are more susceptible to oxidative stress in vitro (as determined by increased TBARS) are also more susceptible in vivo (as measured by decreased filterability) (Simon-Schnass, 1994). Given the results of the pentane measurement, these results show that there is increased oxidative stress at high altitudes and that supplementation with vitamin E, an antioxidant, can counteract its negative consequences.

Increased Ultraviolet Radiation with Increasing Altitude

The skin is exposed to radiation of a wavelength between about 300 and 3,000 nm, including infrared, visible light, and ultraviolet (UV) radiation (made up of UV-A and UV-B wavelengths). The proportion between the different kinds of radiation is not constant but is influenced by the sun's position (depending on locus, season, and time of day), altitude, ozone content of the stratosphere, and extent of air pollution (Kindl and Raab, 1993). Radiation intensity is proportional to the angle at which the sunlight has to

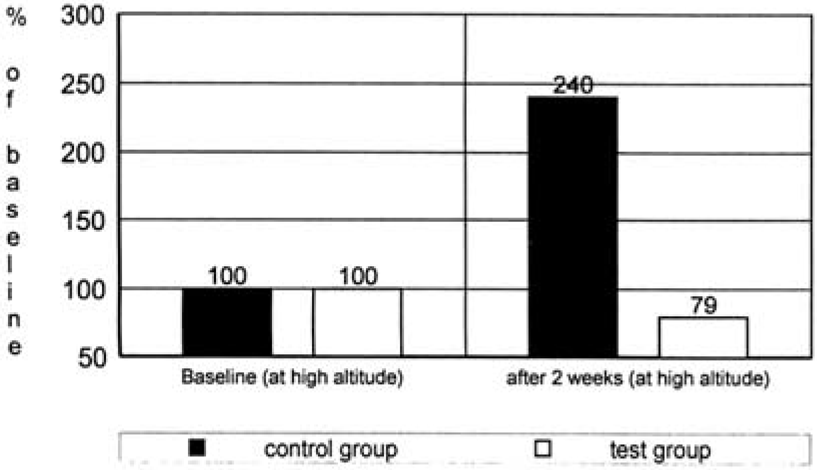

FIGURE 21-4 Thiobarbituric acid reactive substances (nm/g Hb) generated by erythrocytes of 10 subjects after arrival at high altitudes and after 2 weeks shown as percent of baseline. After taking the baseline samples, the test group was supplemented with 400 mg of vitamin E per day, whereas the control group received a placebo. SOURCE: Adapted from Simon-Schnass (1995).

pass before it reaches the ground. The shorter the wavelength, the higher the losses (Kindl and Raab, 1993). Therefore UV-B radiation is much more susceptible to scattering than UV-A radiation and visible light. This is also the reason why UV-B radiation increases dramatically in clean air and high altitudes. As shown in Table 21-2, for every 1,000 m (3,281 ft) of altitude, the UV-B intensity increases by 15 to 20 percent, whereas the UV-A intensity increases to a much lower degree (Kindl and Raab, 1993).

The basis for a photochemical reaction in the skin is the interaction between a light quantum and biological material, which means that an electron is lifted to a higher orbit. In the case of a stable electron condition, the energy is absorbed. However, there is a characteristic borderline, the so-called ionization potential. If the absorbed energy is higher than the binding energy of the electron, the electron is detached (ionized). Visible light and UV radiation have a quantum energy of 40 to 150 kcal/mol. This amount is within the order of the intramolecular binding energy, which is the reason why singlet and triplet forms as well as free radicals can be produced (Kindl and Raab, 1993). The increased UV-B radiation at high altitudes may thus be an important reason for increased oxidative stress at high altitudes.

Irradiation of the skin with UV-A and UV-B radiation can induce the formation of lipid peroxidation products. In human skin, surface lipids are peroxidized by UV-A radiation, whereas UV-B causes a remarkable decline in unsaturation of fatty acids (Fuchs and Packer, 1991). This increased lipid peroxidation could be proved by the elevated levels of TBARS in chronically sun-exposed human skin (Niwa et al., 1987). Lipid peroxides are cytotoxic and have a proinflammatory potency. Both are thought to play a role in skin inflammation induced by UV-B radiation (Ohsawa et al., 1984).

Various cellular compounds, such as carotenoids, vitamin E, vitamin C, and sulfhydryls, are effective radical scavengers. Especially carotenoids may play a role in protection against UV-radiation damage. Carotenoids have been

TABLE 21-2 Increase of Ultraviolet Radiation, UV-B and UV-A, with Increasing Altitude

Altitude Difference (m [ft])	UV-B Increase (%)	UV-A Increase (%)
1,000 (3,281)	20	17
2,000 (6,562)	35	27
3,000 (9,843)	50	34
5,000 (16,404)	70	44

SOURCE: Adapted from Kindl and Raab (1993).

shown to inhibit UV-B-induced epidermal damage and tumor formation (Mathews-Roth, 1985). Vitamin E is increased in chronically sun-exposed skin, perhaps as an adaptive reaction of the body (De Simone et al., 1987). However, the vitamin E level is decreased immediately after UV-B irradiation of mouse skin (Fuchs et al., 1989). The total amount of vitamin C does not change with sun exposure to mouse skin, but there is no information about the ratio between ascorbic and dehydroascorbic acid (Fuch et al., 1989).

Oral β-carotene administration significantly increased the minimal erythema dose of solar radiation in humans (Mathews-Roth et al., 1972). This result may be caused by the photoprotective mechanism of β-carotene, a potent singlet oxygen scavenger at low partial pressure of oxygen (Mathews-Roth et al., 1972). A similar effect of vitamin E is likely (Shindo et al., 1993).

Because UV radiation increases tremendously at high altitudes (see Table 21-2), prophylactic supplementation for people who want to go to the mountains is highly recommended. Until now, no specific investigations have examined this topic.

Indirect Studies on Oxidative Stress at High Altitudes

Physical Exercise

One of the very few studies on the influence of an antioxidant (vitamin E) on physical performance at varying altitudes is that of Nagawa et al. (1968). The authors concluded that vitamin E might have an enhancing effect on endurance due to its ability to increase activity of respiratory enzymes in mitochondria of muscle cells and thereby improve the utilization of oxygen in muscle during activity, especially at high altitudes.

This hypothesis is supported by the results of a later study on the effect of vitamin E on physical performance at high altitudes (expedition to K2, described earlier) (Simon-Schnass and Pabst, 1988). As an objective parameter of performance, the anaerobic threshold of subjects was determined before departure and three times at base camp separated by intervals of 2 weeks. *Anaerobic threshold* is generally defined as the work load that leads to a lactic acid blood level of 4 mmol/liter. Accumulation of lactic acid in plasma was caused by performing graded exercise until exhaustion on a bicycle with 3-min load steps starting at 50 watts and with increments of 50 watts. Given the baseline performance at the anaerobic threshold as 100 percent, performance during the other three time periods is expressed in percent of baseline. These data are shown in Figure 21-5.

There was no significant difference between the baseline values of the two groups. During the experiment, the anaerobic threshold of the treatment group increased, while in the control group it initially increased to a smaller degree and then decreased compared to the initial value. The difference between the changes of the anaerobic threshold of the treatment group and the control group became significant ($p < 0.01$) after 4 weeks, as shown in the third and fourth panels from the left in Figure 21-5.

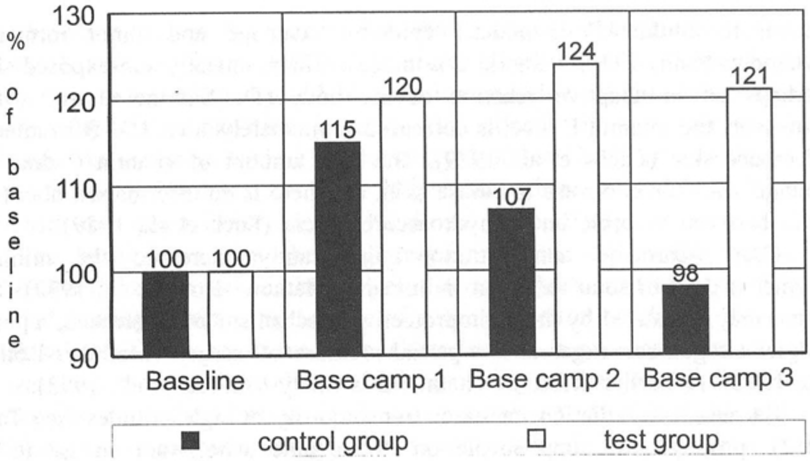

FIGURE 21-5 The anaerobic threshold given in watts as percent of mountaineers at baseline, after arrival in base camp 2 weeks later, and after 2- and 4-wk stay at base camp. Subjects were divided into a test group and a placebo group. The test group was supplemented with 400 mg of vitamin E per day, whereas the control group received a placebo. SOURCE: Adapted from Simon-Schnass and Pabst (1988).

Little research has been performed on the effect of altitude on anaerobic threshold. Results of the placebo group in the above described study, however, confirm the previous observation that a prolonged stay at high altitudes leads to reduced physical performance, reflected in a decreased anaerobic threshold.

By its stabilizing effect on various components of the respiratory chain, vitamin E contributes to aerobic energy production (Cormier, 1977; Schwarz, 1962, 1972). A local vitamin E deficiency leads to disturbances of electron transport and thus to reduced cell respiration (Carabello, 1974; Carabello et al., 1971; Fedelesova et al., 1971). This effect is especially apparent when the available oxygen is also limited, which occurs due to high demand, poor local supply, or low partial pressure of oxygen. It can be expected that the impairment of metabolism is especially pronounced under conditions of increased physical load at high altitudes. Investigations have shown that a prolonged stay at extreme altitudes leads to a loss of activity of succinate and lactate dehydrogenase (Cerretelli and di Prampero, 1985). The activity of both enzymes in skeletal muscle is also decreased by vitamin E deficiency (Bertolotty et al., 1965; Chen and Lin, 1980; Tureen and Simons, 1968). This decrease can be explained by the enzymes' content of labile SH groups, which have to be protected by the antioxidant.

The possible involvement of labile SH groups suggests that free radical reactions must be taken into consideration. Only very few studies have shown an increased risk of free radical production during exercise at high altitudes. Three of them are described in more detail here.

As shown, increased free radical production not only influences physical performance by damaging energy metabolism but also has a negative influence on membranes. This effect was demonstrated by the experiments on red blood cells and is of central importance especially at high altitudes.

Blood Flow

At high altitudes the body attempts to boost the blood's oxygen transport capacity by increasing erythropoiesis, resulting in a compensatory polycythemia. This effect has significant influence on capillary blood supply, which is mainly determined by cardiac output, vascular resistance, and the rheological properties of the blood or its constituents.

The special rheological properties of blood arise from its two-phase composition of plasma and blood cells. The viscosity of the blood depends largely on the packed cell volume, plasma viscosity, the deformability of the erythrocytes, and their tendency to aggregate (Ernst et al., 1985).

The viscosity of blood varies as a function of flow conditions. The very same blood can at one time be highly fluid and rapidly flowing and at another highly viscous with sluggish flow. In in vitro measurements, an elevated hematocrit level is discernible immediately, whereas the situation in vivo is much more complex. Because of the special two-phase composition of blood, under normal conditions a high hematocrit does not necessarily cause changes in flow characteristics in the terminal vessels because the local hematocrit in the capillaries is much lower (with a high flow rate) than in the larger blood vessels (Schmidt-Schönbein, 1982). There are limits even to this mechanism, however. Thus, it is assumed that at hematocrit levels of greater than 50 to 55 percent, the oxygen transport capacity falls again, not only at high altitudes but also in pulmonary diseases (Oelz, 1984; Winslow, 1984). Hematocrit levels of 60 percent or more are not a rare finding in high-altitude climbers. In the event of a general or localized reduction in flow velocity, however, the capillary hematocrit level approaches the venous hematocrit, and aggregation occurs. In this case, the hematocrit becomes highly important.

In the case of a high hematocrit, one of the major factors determining if local oxygen supply is improved or decreased is the flexibility of the erythrocytes, which is highly dependent on membrane integrity. As discussed above, hypoxia leads to oxidative stress. There is increased formation of free radicals, which triggers lipid peroxidation. As a result, membrane fluidity (measured by erythrocyte filterability) deteriorates. Because vitamin E is directly incorporated into the membranes, it should counteract such processes there.

In addition to blood viscosity, the elasticity and integrity of the vascular wall play an important role in capillary blood supply. Here too, oxidative changes are discussed as a pathogenetic factor (Kappus, 1985). The release of tissue hormones, such as histamine, kinins, and prostaglandins, also plays an important part in the damage of the vascular wall (Schmidt-Schönbein and Neuman, 1985). Endothelial lesions may lead to disturbances in microcirculation. These disturbances may be compounded by activation of the coagulation system, with resultant consumption coagulopathy (see Stedman's Pocket Medical Dictionary, 1987, p. 149). This result can lead to the formation of microthrombi and, consequently, increased reactive fibrinolysis, which in turn results in an increased tendency to hemorrhages (Hiller and Reiss, 1988).

The aforementioned disturbances are frequently found during a prolonged stay at high altitudes. Here, the pathological changes are mainly in the area of the pulmonary and cerebral capillaries, but changes also occur in the retina and the mucosa (Volger, 1984).

Both the radical-binding properties of vitamin E and its involvement in the metabolism of eicosanoids (which may be related to each other) indicate that this vitamin has an effect on the phenomena described above (Chow, 1979; Leibovitz and Siegel, 1980; Simon-Schnass and Koeppe, 1983).

In the aforementioned study (expedition to Annapurna), the influence of supplementation of 400 mg of vitamin E per day on several of these rheological parameters was tested. The parameters included whole blood and plasma viscosity, white blood cells, platelets, antithrombin III, and protein C (Simon-Schnass and Korniszewski, 1990). In this chapter, only the data on white blood cells and two antiaggregational substances are discussed.

The viscosity of blood is mainly determined by the amount of blood cells, their flexibility, and the plasma viscosity. Results from this author's studies (Simon-Schnass, 1994) and the experience of mountaineers (Oelz, 1982) show that an adequate fluid intake not only maintains the hematocrit in a physiologically acceptable range, but it can also prevent hemoconcentration and a related increase in plasma viscosity. Because there was no correlation between hematocrit and plasma viscosity, it can be assumed that the volunteers in the study did not experience any appreciable dehydration. The increase in whole blood viscosity was therefore mostly the result of the increase of blood cells and their membrane rigidity.

Because of their rigidity and spherical shape, leukocytes cannot pass through the terminal vessel as easily as erythrocytes. Even under physiological conditions there may be a reduction in flow velocity or even temporary stasis in the passage of leukocytes through the capillaries (Asano et al., 1973). If the perfusion pressure falls, pronounced disturbances of microcirculation occur, mainly due to the white blood cells. Thus, there may also be, for example, occlusion of the arterioles and venules due to adhesions to the vascular walls

(Bagge et al., 1986; Lipowsky et al., 1980). After stimulation (e.g., by activation of complement, endotoxins, immune complexes, or leukotriene B_4), there is a particularly substantial rise in the tendency of the leukocytes and, in particular, the granulocytes, to aggregate. This aggregation in turn leads not only to a further increased risk of occlusion, but also to increased release of intracellular proteases (Harlan et al., 1981). As shown in Figure 21-6 a marked increase in white blood cells was shown in the control group, whereas no change occurred in the supplemented group.

On the basis of data in the literature, an increased granulocyte stimulation can be assumed to occur in such a situation. The proteases then released can split not only the endothelial cells and the proteins bound to the endothelial cells, but also proteins free in the plasma (Benjamini and Leskowitz, 1988; Weis and Regiani, 1984). This assumption could explain the significant drop in protein C observed in the control group ($p < 0.05$) as well as the drop in antithrombin III, which did not reach the borderline level for significance ($p < 0.052$). The data are shown in Figure 21-7.

Another possible cause of disturbances in microcirculation seems to be a modulation of endothelial cell function in hemostasis. On the one hand, endotoxins (the presence of which was indicated by the rise of leukocytes) can

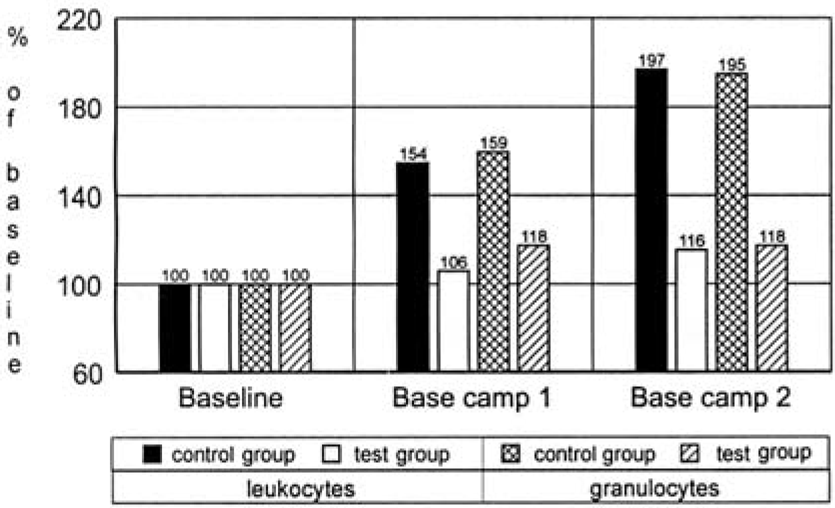

FIGURE 21-6 Leukocyte and granulocyte counts (× 10^9/Liter) of 13 mountaineers during an expedition to Annapurna. Subjects in the test group were supplemented with 400 mg of vitamin E per day, whereas the control group received a placebo.
SOURCE: Adapted from Simon-Schnass and Korniszewski (1991).

reduce the concentration of available thrombomodulin so that there is only reduced protein C activation (Moore et al., 1987). Blockade of the binding sites could then result in increased protein C clearance. On the other hand, increased formation of the inflammation mediator interleukin-1 may cause similar reactions (Nawroth et al., 1986). Many of these reactions produce or are influenced by free radicals. Supplementation with antioxidants seems to stabilize both leukocytes and the endothelial cells and to protect against splitting of proteins.

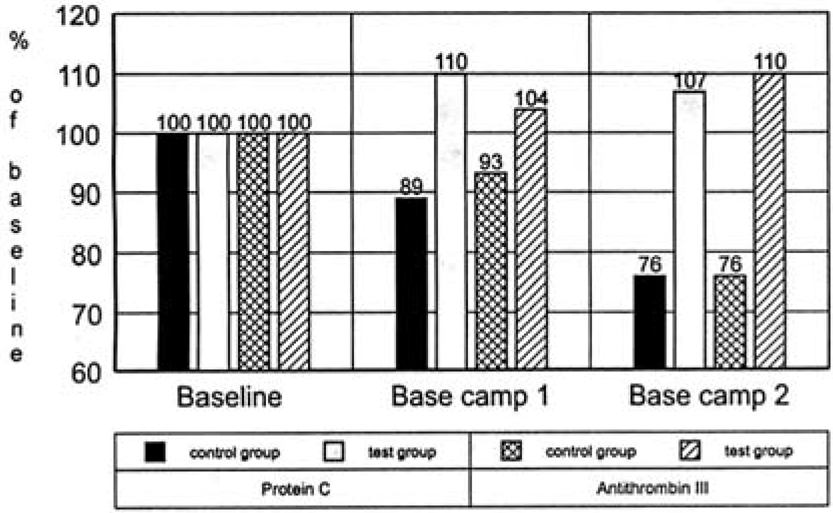

FIGURE 21-7 Activity of protein C and of antithrombin III (percent of activity compared to standard provided by the manufacturer) of 13 mountaineers during an expedition to Annapurna. Subjects in the test group were supplemented with 400 mg of vitamin E per day, whereas the control group received a placebo.
SOURCE: Adapted from Simon-Schnass and Korniszewski (1991).

All the mentioned changes in the various tested parameters point clearly to impaired blood rheology at high altitudes. In this context it should be borne in mind that mountain sickness is often attributed to general microcirculation disturbances (Olez, 1984), which explains the tendency to frostbite, retinal hemorrhage, and cerebral and pulmonary edema. Because supplementation with 400 mg of vitamin E per day was able to prevent some of these changes (Simon-Schnass and Korniszewski, 1990) and vitamin E is known to be an effective radical scavenger, free radical-related reactions are most likely. Unfortunately there are still many more questions than answers in this field of research.

Wide Temperature Differences at High Altitudes

Wide temperature differences are typical at high altitudes. There are not only considerable temperature differences between day and night but also temperature differences related to the presence of sunshine or especially wind. For example, at an altitude of more than 4,000 m [13,123 ft], it is not unusual for the afternoon temperature in the sun to be about 30°C (86°F) or more and after sunset for the temperature to drop within 15 minutes to below 0°C (32°F). Although there have been no known investigations of changes in metabolism caused by these rapid changes in air temperature, one can speculate about such a relationship.

Until now no data have been collected concerning the increased production of free radicals in hot environments. However, it has been suggested that work in hot environments could create a hypoxic condition in muscle due to the redistribution of blood from the muscle to the skin (Young, 1990). Although no studies have examined the amount of lipid peroxidation in hot environments, it is possible that the combination of hypoxia, dehydration, and other changes such as heat stress could exacerbate oxidative stress in the muscle. If this hypothesis can be confirmed, the use of antioxidants should be recommended (Clarkson, 1993).

Hypothermia may also be an important reason for damage to the blood vessels and may induce a deterioration in the rheological properties of blood. The degree of deterioration varies, but it is clearly temperature dependent. Schmidt-Schönbein and Neumann (1985) gave an excellent overview. Under hypothermic conditions, erythrocytes tend to aggregate more easily, and the aggregates are more resistant to hydrodynamic dispersion. This result is consistent with the observation that together with a membrane stiffening, the deformation of aggregated red blood cells in stasis is made worse in (Schmidt-Schönbein and Neumann, 1985). From the start it has been impossible to decide if the stiffening of the membranes is only a temperature phenomenon or the result of an increased lipid peroxidation. In any case, after stasis occurs, tissue hypoxia is most likely, and thus oxidative stress increases.

Until now, blood rheology has been understood to be dependent on many factors. Clearly some minor changes in variables may result in big effects. The prophylactic use of antioxidants at high altitudes or in the cold may be one of these variables. Certainly they will not prevent frostbite in all conditions, but it seems worthwhile to do more research on the possibility that influencing the metabolism in a way that makes blood cells and vessel intima more resistant to factors that initially disturb blood rheology may prevent harmful events in some cases.

It is well known that temperature influences hormonal status. Noradrenalin, for example, plays an important role in nonshivering thermogenesis. It was shown that incubation of mitochondria with noradrenalin caused a significant increase in hydrogen peroxide production and, thus, of oxidative stress. The same author was able to demonstrate this same effect in animals exposed to cold temperatures (Swaroop et al., 1983).

Dehydration

Fluid demand increases at high altitudes depending on temperature and humidity of the air. Working in hot or even warm surroundings causes more or less intensive perspiring. As mentioned earlier, even at high altitudes temperatures can rise considerably. Working to a more or less intensive degree is obligatory when staying in the mountains. Thus, fluid loss through perspiration is common. Undoubtedly these losses of water as well as of electrolytes must be replaced, and in this case, an electrolyte drink is useful.

With increasing altitude, fluid losses from the lungs as a consequence of breathing the increasingly dry air tend to dominate over perspiration. There is evidence that this fluid loss can increase to 6 or more liters per day at extremely high altitudes (Olez, 1984). Because the melting of 1 liter of water from snow takes about 1 hour under these conditions, it is not surprising that high-altitude climbers generally do not meet their fluid demand and return to base camp more or less dehydrated (Personal communications with experienced climbers during the various expeditions, 1986, 1988, 1990). In this case, the fluid deficit can be compensated for by water only, but in practice it is usually by tea (Personal communications with experienced climbers during the various expeditions, 1986, 1988, 1990).

Because dehydration is one of the important risk factors for frostbite, it is necessary to test for a proper fluid balance before starting to climb. This balance can be easily measured by checking hematocrit or urine osmolarity regularly.

No known studies have examined whether dehydration is involved in increased free radical production. Clarkson (1993) mentions dehydration as a possible risk factor. Because dehydration is such a big problem at high altitudes, studies on this question are highly desirable.

CONSEQUENCES OF OXIDATIVE STRESS WITH RESPECT TO NUTRITIONAL RECOMMENDATIONS

Nutrient deficiency may be a problem at low altitudes, but it most certainly is one at high altitudes. In Table 21-3, some data are shown that were produced by calculating nutrient intake during two different expeditions. The food supply of the first (K2, 1986) was determined carefully by a nutrition professional, taking the limited food items available during an expedition into consideration. The second expedition was a scientific project in the Solo Khumbu for which the food supply was organized by experienced mountaineers. In the first case, data were obtained by weighing the food consumed by the group over the entire period and then calculating the average intake by dividing this amount per person and day at the base camp. In the second case, nutrient intake was calculated from 7-d food records. Because there was not much chance for varying the meals individually during the time period, the data can be considered representative for the entire expedition (Simon-Schnass, 1994). Data shown in Table 21-3 are limited to the intake of water and some vitamins and minerals.

TABLE 21-3 Average Daily Intake of Selected Nutrients from Food during Three Different Expeditions to High Altitudes, Given as Percentage of the Recommended Dietary Allowance

Nutrient	K2, 1986	Solo Khumbu, 1990	Kangchenjunga, 1992
Vitamin E	159	140	203
Vitamin C	85	183	76
Vitamin B_2	105	50	165
Zinc	44	25	45
Selenium	103	43	129

SOURCE: Adapted from Simon-Schnass (1995).

From Table 21-3 it can be seen that nutrient intake may be lower than recommended intakes, and thus, an increase risk of deficiency may easily occur during high-altitude climbing. There can be no trend identified, which nutrients are the most critical ones. That depends completely on the knowledge and financial resources of the organizing team and whether fresh food items are available at base camp. Because price and weight of food as well as loss of appetite often are limiting factors, such concerns are not surprising.

No known investigations have looked at nutrient intake during trekking and altitude training of athletes. Because increased oxidative stress at high altitudes can be presumed, especially the antioxidative nutrients such as β-carotene, vitamin E, vitamin C, selenium, and zinc should be taken into consideration. The relatively high intake of vitamin C during the second expedition (Table 21-3) was due to a regular supply of fresh potatoes, cabbage, and apples. Such supplies depend largely on area and season and cannot be relied upon. In general, the food supply is limited, especially with respect to fresh food. Therefore, supplementation is advisable.

SUMMARY

Considerable evidence suggests that there is increased oxidative stress at high altitudes. The most important causes of free radical formation are the respiratory chain itself, hypoxia, and increased ultraviolet radiation. Whether high and/or low temperatures and dehydration lead to an increased formation of free radicals is not clear at the present time. Certainly there are other causes for increased oxidative stress, such as disease and/or intake of medication. However, these should be discussed separately.

Several studies indicate that oxidative stress impairs physical performance as well as blood flow. Both are of particular importance for people at high altitudes.

A nutritional survey (Simon-Schnass, 1995) showed that inadequate nutrient intake, especially of antioxidants, may not always meet the increased demand at high altitudes. Inadequate levels of antioxidants clearly impair metabolic functions at high altitudes, and the recommendations for people living at lower altitudes are insufficient for this special situation. Because the food supply is limited during a prolonged stay at high altitudes (e.g., during a trekking tour or an expedition), supplementation with antioxidants is advisable. The only known studies (Simon-Schnass, 1994; Simon-Schnass and Korniszewski, 1990; Simon-Schnass and Pabst, 1988) available have shown a beneficial influence of vitamin E on physical performance, blood flow, and some parameters, indicating an increased oxidative stress at high altitudes. However, the synergistic functions of other antioxidants, such as β-carotene and vitamin C (Halliwell et al., 1987), justify the recommendation of a supplementation.

Not all of the aforementioned factors influence all groups of people to the same degree. However, in general their importance and occurrence increases with altitude. A great deal of research still needs to be done in this field.

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IV

Discussion

JOHN BEARD: I wanted to ask Gail Butterfield a question about the changes in energy requirements at altitude. Reed Hoyt mentioned some changes in mechanical efficiency that perhaps figure into that equation. Would either or both of you want to discuss whether or not all of the change in energy requirements is accounted for by change in BMR?

GAIL BUTTERFIELD: In the studies we did, it probably is. We increased their energy intake only by the equivalent of the increase in basal metabolic rate. Our studies were in sedentary individuals. They did some routine bicycling to maintain their training level so that they remained essentially as untrained as they were at sea level. By simply addressing the increase in BMR, we were able to maintain body weight.

REED HOYT: Clearly, soldiers can have high rates of exercise energy expenditure at altitude due to the high cost of traversing mountainous terrain. This high cost is not unexpected given the steep grades and poor footing that characterize mountainous terrain, as well as the heavy loads soldiers often carry. Further research is needed to understand the more subtle effects of hypoxia on exercise efficiency and BMR. Clearly, one needs to acknowledge how much physical work soldiers do and explore ways to get food into them in spite of anorexia and other problems.

ROBERT SCHOENE: I heard twice this morning—once from Reed Hoyt and maybe from Al Cymerman—that this initial fluid depletion—diuresis—that occurs at high altitude had some effects on optimizing oxygen consumption at the cellular level. I had not heard that before, and I need to have it explained a little bit more. Reed, do you want to address that?

REED HOYT: The observation at high altitude is that there are improvements in endurance performance that are not explained. In our experience, there is a transition to more fat metabolism. Our suggestion is that changes in the conductance of oxygen down to the cell level may be responsible for these observed changes.

It is not associated with an increase in $\dot{V}_{o2}$ max, because clearly, the number of capillaries and the number of mitochondria are not increasing. In our minds, it is a change in the geometry that facilitates the conduction of oxygen. The change in geometry accompanies diuresis. Clearly, those places where there are no transport pigments between the red cell and the target cell are particularly high resistance points in the conduction of oxygen. So I think that the resistance at those junctures is changing with the changes in fluid distribution. You are familiar with the pathological aspects of anti-diuresis, fluid retention, and altitude illnesses, too, and that is the other side of the coin.

INDER ANAND: One question and a comment. The comment is that the studies that suggest an increase in efficiency came from work on the Quechua Indians.

REED HOYT: Right, you are referring to Hochachka's work.

INDER ANAND: Yes, and those studies were done on subjects whose fluid status was not assessed. So I do not think we can make a deduction from this data regarding efficiency and fluid status.

REED HOYT: Right. The connection with body water is not clear from most studies. It is Hochachka's view, however, that oxygen transport is more tightly coupled. That is, skeletal muscle ATP demand and ATP supply are more tightly linked. Closer coupling means that increases in work rate are accompanied by smaller than expected changes in cell phosphorylation potential, phosphocreatine, and pH, and consequently less stimulation of glycolysis and less lactate accumulation[1]. Clearly, that means a more effective oxygen delivery system, much as one would see in an endurance-trained individual. You see improved oxygen delivery and an increased reliance on fat oxidation. But I agree with you, we need to explore further.

INDER ANAND: My question is to you or to Gail. I want to know whether studies from Operation Everest II can account for all the weight loss simply on the basis of less food intake and more energy expenditure. My interest is that Operation Everest II showed that expenditure went down, as you indicated in your slide, and the intake went down as well. Therefore, when you take the two into account, you cannot account for the 7 1/2-kg loss of weight. You can only account for about a kilogram and a half loss of weight.

GAIL BUTTERFIELD: They do not account for the increase in basal metabolic rate; Operation Everest II (OE II) just looked at activity patterns. So there is approximately 250 kcal/d in their estimate of energy expenditure that is not accounted for.

INDER ANAND: So you believe that you can account for all the weight loss by increases in expenditure and intake?

GAIL BUTTERFIELD: I think you can. As I showed in one of the last slides, there is some diuresis even in the fed individual, but it amounts to less than a half a kilogram effective weight loss over a long period of time.

ALLEN CYMERMAN: I am in the position of having supported three studies now that showed three different findings on fat metabolism. I would like to know, does altitude acclimatization occur to the point where glycogen stores are spared as Andy originally showed?

GAIL BUTTERFIELD: The 1988 study that we did found no change in glycogen stores. We did not measure fat in that study. In 1991 when we studied fat, we showed that fat utilization was down at rest and during exercise. I do not know what the glycogen data are, but I would assume that the conditions were essentially the same, that glycogen was spared. The question that Reed asked me, and I do not have the answer, is what are they burning then? Clearly, glucose utilization goes up.

ROBERT SCHOENE: But Reed shows just the opposite. It is a different situation.

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[1] G.O. Matheson, P.S. Allen, D.C. Ellinger, C.C. Hanstock, D. Georghiu, D.C. McKenzie, C. Stanley, W.S. Parkhouse, and P.W. Hochachka. 1991. Skeletal muscle metabolism and work capacity: A ^{31}P-NMR study of Andean natives and lowlanders. J. Appl. Physiol. 70(5):1963–1976.

GAIL BUTTERFIELD: Yes, you have a fed- versus a fasted situation.

IRA JACOBS: I have a comment related to Dr. Cymerman's question. I think you are confusing apples and oranges here. In some of our studies, we are looking at utilization at the same absolute work load, and in some we are looking at the same relative work load. Those are two entirely different conditions. Let us assume, as you said, that the same amount of oxygen is required to perform the same amount of work at high altitude. But the ceiling that each individual has is reduced. Nobody will debate that, at high altitude. I have not seen any data showing that with acclimatization $\dot{V}_{o2}$ max does come back to normal. This is different from what we heard from Robert Schoene, when he suggested that oxidative enzyme adaptations also cannot be restored to normal. They can be trained somewhat, but they are never restored.

Although the 100 percent ceiling is reduced, you have to do the same absolute work load from a military perspective. You have to take apart an artillery piece, or you have to move 100 m (328 ft) or 200 m (656 ft) or 1 km up a hill. To perform that same amount of work at high altitude is going to cost more carbohydrates, because carbohydrate oxidation is solely a function of relative exercise intensity, everything else being equal. So carbohydrate requirements have to be greater for the same absolute work load. I would be interested in knowing if there is debate about that.

ROBERT REYNOLDS: I might mention what we saw with respect to carbohydrate and fat intake on the Everest 1989 expedition. We saw, like everybody else, a decrease in total caloric intake, yet the ratio of energy consumed from fat was maintained at 30 percent, regardless of whether they were at base camp or camps one, two, three, or four, which goes up to 8,000 m (26,230 ft). So before we give fat a bad name in consumption, consider the calls on the radio from camp four to send up more of those sausages and more of the cheese. Now, these were acclimatized individuals, as much as you can be at 8,000 m (26,230 ft). But there was a 30 percent intake of energy from fat, and that did not change as a function of altitude.

ROBERT NESHEIM: I am not surprised at that, because there has to be a certain amount of caloric density in the diet, or they will not get enough food. I am surprised it was not more than 30 percent fat.

ELDON W. ASKEW: I have a comment with regard to what Dr. Anand brought up about Operation Everest II. We had the same question when we reviewed the data. Madeleine Rose and I both arrived at about the time OE II was getting going, and we did not really have any input into the design of it. If we could have, I think we would have called for some 24-h urine collections and fecal collections to rule out that there was any malabsorption. Those were our questions: what happened to the nitrogen balance, and what happened to the efficiency of the absorption? But I agree, there is a little bit of noncorrespondence here.

A. J. DINMORE: I have a question about malabsorption at high altitude. You say that at 4,000 m (13,333 ft.) you did not show any decrement. But at extreme altitude, we actually measured mediated uptake of glucose analogs, and we showed there was a roughly 50 to 60 percent reduction from sea level at 5,000 m (16,393 ft) and above. We have published these results in abstract form, and we have papers coming out shortly.

DAVID SCHNAKENBERG: I was quite interested in Dr. Butterfield's results. I believe that with a primarily liquid diet, she was able to maintain energy balance. It is interesting that Frank Consolazio's studies showed benefits to reducing high-altitude symptoms when he used a liquid diet. Eldon Askew did a study on a mountain in Hawaii where he gave a liquid supplement, and he was able to reduce symptoms and enhance running endurance time at high altitude. Al Cymerman said earlier that although you must lose weight you must lose fluids because that is an adaptive response to prevent symptoms. If you do not reduce your intake and lose water, you are going to have a high incidence of altitude symptomatology. What happened with your subjects?

GAIL BUTTERFIELD: In the two studies we did, we had one young man who was taken down from the mountain the first night due to severe headache. He was brought back up the next day, and he did fine. About half of the subjects in each experiment experienced slight headaches. Some of them had to take Tylenol to alleviate those symptoms. This is only anecdotal, but the frequent comment to me in the morning was "Hurry up and get that food on the table. I want to eat because it makes me feel better."

DAVID SCHNAKENBERG: Did you give out Al Cymerman's symptoms questionnaire?

GAIL BUTTERFIELD: Yes.

ALLEN CYMERMAN: We did, but I do not remember the results.

GAIL BUTTERFIELD: I never saw the results, so I do not know.

DAVID SCHNAKENBERG: It might provide useful data to compare with the same instruments used time and time again at high altitude, even though you did not have a control group.

GAIL BUTTERFIELD: We did have a control group at sea level.

ALLEN CYMERMAN: To answer your question, when weight was controlled, these subjects, from what I remember, were not overly sick from acute mountain sickness.

DAVID SCHNAKENBERG: So you do not think that feeding them adequately made them more sick?

ALLEN CYMERMAN: No. There was no vomiting. There was nothing that I saw along those lines. Anecdotally, the time that I saw the worst acute mountain sickness was at Pike's Peak. They had gone to Denny's the night before and had overindulged on buttermilk pancakes and milk with the works. The next morning, every one of them was vomiting.

DAVID SCHNAKENBERG: One more quick comment on two studies, Reed Hoyt's and Gail Butterfield's, as to whether the subjects stayed with carbohydrate metabolism or were shifting to lipid metabolism. In Reed's study, they were in caloric insufficiency, and in Gail's they were calorically adequate. I think much of the confusing literature about whether high altitude shifts people to lipid metabolism is debated on energy balance.

I will go back to my first study on altitude. I pair-fed rats and took half to a high-altitude while half were kept in Denver. The purpose of the experiment was to answer the question of whether the weight loss and change in body composition in rats at high altitude is due to the altitude or to an altitude-induced reduction in appetite. Both sets of rats experienced the same weight loss and change in body composition.

ELDON W. ASKEW: I want to clarify one thing that Dr. Schnakenberg said, which relates to what Dr. Schoene said regarding carbohydrate diets and acute mountain sickness. We did a study on Mauna Kea, and we reported it in a technical report. We got a significant increase in physical performance at high altitude, both running time and endurance time in subjects consuming a carbohydrate supplement.[2] It was not a large increase—about 12 percent—but it was significant. However, we did not observe a similar decrease in symptoms of acute mountain sickness that Frank Consolazio reported[3] in response to carbohydrate. The regimen he used was that subjects exercised

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[2] E.W. Askew, J.R. Claybaugh, G.M. Hashiro, W.S. Stokes, A. Sato, and S.A. Cucinell. 1987. Mauna Kea III: Metabolic effects of dietary carbohydrate supplementation during exercise at 4100 m altitude. Technical Report No. T12-87. Natick, Mass.: U.S. Army Research Institute of Environmental Medicine.

[3] C.F. Consolazio, L.O. Matoush, H.L. Johnson, H.J. Krzywicki, T.A. Daws, and G.J. Isaac. 1969. Effects of high-carbohydrate diets on performance and clinical symptomatology after rapid ascent to high altitude. Fed. Proc. 28:937–943.

very intensely and for a very short period of time, and basically they were sedentary the rest of the time. Maybe they had more time to reflect on their symptomatology; I do not know. But we did not see a big change. The high carbohydrate diet is what I am talking about.

MARY MAYS: It is also true that these Marines and Special Forces troops pride themselves on having attained a 5 percent fat-free mass. Gail, you characterized your subjects as "couch potatoes" on several occasions. It is true in other studies that expedition people bulk up before they go. They try to put on some insulation, as well as do some carbohydrate loading. Does that account for any of this?

GAIL BUTTERFIELD: I characterized my gentlemen as "couch potatoes," but their body fat was between 10 and 12 percent, so they were not bulked up.

EDWARD HIRSCH: Pursuing the question that Dave asked of Gail and Reed, it struck me during Gail's presentation that her subjects were professional Pike's Peak subjects. Were they?

GAIL BUTTERFIELD: No, they were students from Stanford, world travellers. There was one from Australia, another from Israel; they were adventurers of some sort.

EDWARD HIRSCH: This relates to the question of which comes first: low intake or sickness? This morning Allen Cymerman told us about how sick people become at high-altitude. You do not have to study food intake to know that sick people do not eat. Neither one of you reported it as acute mountain sickness.

GAIL BUTTERFIELD: As I said, in both studies there was only one fellow who had a severe-enough headache that we took him down the hill. He was the only one who had previously been to high altitude. He spent a lot of time in Tibet, and he knew that he got mountain sick. We took him on the expedition anyway; I do not know why. The rest of them had not been exposed to high altitude.

ALLISON YATES: Gail, could you talk about when your subjects were at sea level? How long did you feed them and how long did it take for you to determine their energy requirements? How long did they stay at that kcal level and protein intake before you took them up there?

GAIL BUTTERFIELD: Good question. The baseline period was a 2-wk feeding period. Because we were doing nitrogen balance studies, we put them on the diet for a week before we brought them into the metabolic unit. During that week, we adjusted energy intake to try to maintain body weight. We had a fair amount of experience at guessing at energy requirements to start with, so we were pretty good at determining their energy requirement during that first week, and their body weight was fairly constant.

During the second week, when they were in the unit for the entire time and we measured body weights in the morning, their body weights were constant. By the time those 2 weeks were over, we were pretty sure what their energy requirement was. Then there was a 3-wk period between the end of baseline and the time they went on the diet again. They were on the diet for 1 week before they went on the mountain. Thus they were in the same shape when we did the acute measurements as they were when we did the sea-level measurements.

ALLISON YATES: Regarding your baseline measurements at sea level where there was some fat utilization, were you pretty sure at that point that they were getting adequate intake?

GAIL BUTTERFIELD: Yes. They were in nitrogen balance during that time.

ALLISON YATES: What did you use to increase their caloric intake; what food component?

GAIL BUTTERFIELD: Carbohydrate and fat. We kept the protein constant because we were doing nitrogen balance, and we did not want to interfere with that. So we increased their carbohydrate, primarily in the form of the fluid electrolyte drink that they consumed, and we increased their fat with cookies that were approximately 85 percent fat. They did not like those much.

JOHN BEARD: I would like to return to the carbohydrate question again and perhaps add an additional glitch to it. Perhaps the driving force for this increased carbohydrate utilization might be that the individuals are experiencing another aspect of hypoxic drive. George Brooks and Peter Dallman have shown it, and we have shown it a number of times. Peter Farrell and I have published a couple of papers that show that iron-deficient anemic animals in which we used hyper-insulinemic euglycemic clamps, had increased glucose utilization, and an increased sensitivity to insulin. If in fact the underlying biology here is another aspect of hypoxic drive, then perhaps these acute high-altitude exposures are one of the influences.

GAIL BUTTERFIELD: That has been remarked upon as well.

DAVID SCHNAKENBERG: I would like to ask a question on the use of enhanced levels of antioxidants in the diet. Being a soldier exposes a person to lots of different types of what I think to be oxidative stress. Imagine yourself operating in a combat vehicle in which there is the smoke and the exhaust, as well as the gasses that may come from the repeated firing of weapons. You might also be operating next to a microwave-emitting system. You may be even firing a shoulder-fire weapon with a blast-over pressure phenomenon.

Do we need to give some serious consideration to examining these data and whether we should consider pumping up the antioxidant nutrients in our combat rations over and above what might be needed for the person who works in a laboratory in Beltsville all day long?

ROBERT NESHEIM: Maybe Orville will respond to that.

ORVILLE LEVANDER: Vitamin E is a remarkable substance. It protects against a lot of different things. Our own work has shown that it protects against lead toxicity, and ethyl mercury poisoning. People have shown that it protects against ozone, sulfur oxides, nitrogen oxides, carbon tetrachloride; you name it, vitamin E just seems to have a very good effect.

What impressed me, however, is the high biological specific activity of this substance, and how little is needed to offer protection in a variety of animal experiments. It is very easy to demonstrate effects between deficient and normal levels of vitamin E. It is not quite so easy to go from normal to, shall we say, super normal or super nutritional levels. I take your comments at face value, that going from 20 to 400 is not a dose-response curve. I think that under the condition of so many stresses on one individual, it may be necessary to have more than the usual RDA. I find it hard to accept that you need 400 units.

I. SIMON-SCHNASS: I did not intend to imply that you need 400 units. What I am trying to say is that 20 units is not enough, and 400 units is enough. We don't know the minimum amount of vitamin E necessary to prevent the adverse changes observed in the placebo group.

ORVILLE LEVANDER: I understand that, but I just want to make it clear to this group.

I was curious about your methodology. I wondered what technique you used to measure the red cell filtration, for example, in your subjects.

I. SIMON-SCHNASS: It was a simple filtration via a micropore filter with a 5-nm force and without any pressure.

ORVILLE LEVANDER: These were done on site?

I. SIMON-SCHNASS: On site, yes.

ORVILLE LEVANDER: That is a pretty tricky technique. We have some experience with that ourselves, and it is vulnerable to a lot of influences.

I. SIMON-SCHNASS: It is difficult to compare results from different studies, that is true, because it depends a lot on the handling of the samples by different persons. But I did all filtrations myself in both studies using the same techniques, so that error is minimized. It is hard to compare with other studies, that is true, but not these two studies with each other.

ORVILLE LEVANDER: It is a remarkable accomplishment to do that kind of study under those conditions. I congratulate you for that.

IRWIN TAUB: I want to pursue this point about the vitamin E as an antioxidant. Your results are very interesting because they parallel those from radiation chemistry and even from lipid oxidation in food. Whereas you correctly indicate the key to vitamin E effectiveness is the interaction with the lipid peroxyl radical, what then becomes important is that the amount of vitamin E is limiting. It can be consumed by that and other processes. So in radiation chemistry and in lipid oxidation, we enhance the effectiveness of the vitamin E. Actually we regenerate it by having ascorbyl palmitate in the system, and that becomes a sacrificial lamb and regenerates the vitamin E.

Could you consider in any future studies making sure that the combination of vitamin E and perhaps ascorbyl palmitate, if that can survive digestion, would be equally if not more effective, so that you would not even have to go to the 400 mg. I wonder if that would be objectionable to use in food. We do use it in food, but I mean pumping it up.

I. SIMON-SCHNASS: I agree with you that vitamin C enhances the effectiveness of vitamin E to handle oxidative stress. That is why in the first two expeditions (Solo Khumbu and Annapurna) the subjects were supplemented with a multivitamin which contained one RDA equivalent of vitamin C and the other vitamins. This was done in order to prevent a reduced regeneration of vitamin E because of not enough vitamin C present. So I think that the effect I found is really and effect of vitamin E alone.

This was different in the expedition to Solo Khumbu. This was a purely scientific expedition during which a variety of tests were done on the same subjects. This included some psychological tests, and the psychologists refused to permit supplementation of the subjects. I do not agree with them that supplementation might have interfered with the results of their psychological tests, but rather a deficiency might interfere with their results. And the diet at that time was deficient in some vitamins and minerals.

K. K. SRIVASTAVA: I would like to make a comment on the nature of oxidant injury in high mountains. When you are moving up, the partial pressure of oxygen is coming down, and therefore there is very little chance of oxidative radicals going up. On the other hand, when you come down from the high altitude and then you get a resurging oxygen intake, it is very well known that at that time free radical injury is very common. Therefore, for the people who stay a long time in high mountains and keep on sequencing from lower altitudes to higher altitudes or vice versa, and also for the people who leave and then go back to the high mountains, the incidence of oxidant injury is much more common.

Therefore, perhaps because these mountaineers kept moving from lower to higher elevations, there might have been a total oxidant injury, and their requirement of vitamin E or other antioxidants might become much greater. I would like you to consider this point. For military operations, this becomes important because soldiers stay in the mountains for a longer period of time. They keep on sequencing during patrols and other operations from lower to higher altitudes. They go on leave or training, and then they return to the high mountains. In those cases, the oxidant injury is much more important than in the case of mountaineers.

I. SIMON-SCHNASS: That is true, but with oxygen metabolism it is very complicated. You have this oxygen paradox. That is, if you have hypoxia, you have increased oxidative stress. That means if there is not enough oxygen to produce enough reducing equivalents, then the oxygen cannot be reduced completely to water. This results in all these reactive oxygen species.

On the other hand, if you have hyperbaric oxygen, you have this classical oxygen toxicity. So oxygen is a very dangerous friend. You need it in any case, but it must be handled very carefully. That is why there are the antioxidants.

K. K. SRIVASTAVA: No, that shows that there is a need for the measurement of the free oxide radicals or hydroxy radicals in the environment of high mountains or in the hypoxia. These data are not yet available, to the best of my knowledge.

PATRICK DUNNE: I have a follow-up question to that. A couple of biochemical issues came to mind. This sounds very much like a reperfusion injury. When I used to teach metabolism, the question was, what is basal metabolic rate? A lot of it is pumping ions, and I wonder if anyone has looked at some of the ATPases, especially in light of what we are learning in reperfusion injury, and calcium ATPases. As far as cellular-level research in this area, it might be worth pursuing.

I have another mechanistic question. One way of shifting the oxygen-binding curve, which has not been discussed but birds do it and some people do it, is with organic phosphates. I wonder if any of this adaptation is being looked at, as far as shifting of the binding curve with 2,3-diphosphoglycerate

(2,3-DPG) or some of the other things? As we shift into different carbohydrate metabolism, we might shift some of these binding curves as well.

ROBERT SCHOENE: From the clinical perspective, we are talking about oxygen radicals and injury among mostly young, healthy people. When I hear people in my department talk about oxygen radical injury, they are really talking about long-term endothelial damage that may predispose people to thrombi and atherosclerosis and so forth.

I believe in vitamin E, but are we really talking about injury that is significant clinically or in terms of performance in young, healthy troops, for instance?

MURRAY HAMLET: I would suggest that much of what we have been discussing is endothelial cell dysfunction—the inability to manage fluids across membranes—not only in injury, but in cold injuries. Endothelial cells are probably the target organs. So it might be a subclinical injury to endothelial cell function.

K. K. SRIVASTAVA: It is functional damage, not real pathological damage. If you are typically going to the mountains, it might aggravate the situation. What remains a functional deterioration might become a permanent deterioration. That is an open question.

ALLEN CYMERMAN: I would like to respond to Pat Dunne's question about 2,3-DPG. That work was done about 20 or 30 years ago. They thought that the phosphate would shift the curve, and everybody would be very happy at high altitude. It turns out that it is a give and take, what you get on the delivery side, you lose on the pick-up side. People who, for example, climbed Mount Everest were extremely alkalotic. The importance of 2,3-DPG, as far as altitude acclimatization is concerned, has waned through the years, and no one thinks that it is the body's true response to oxygen. It shifts the curve to the right and unloads oxygen in the periphery.

K. K. SRIVASTAVA: This is true, but it depends on the altitude. If you are at moderate or low altitudes, the 2,3-DPG mechanism will deliver the goods. But if you are at a higher altitude, beyond 5,000 or 5,500 m (16,393 or 18,033 ft), then this 2,3-DPG mechanism does not work well. However, the concentration is increased.

ALLEN CYMERMAN: There is no question that the concentration is increased, but the respiratory alkalosis shifts the curve the other way.

K. K. SRIVASTAVA: That is right, but at higher altitudes.

ALLEN CYMERMAN: We could argue that. Lenfant said 4,000 m (13,115 ft), but it is borderline at 4,000 m. Above 5,000 m (16,393 ft), yes, there is no question.

ORVILLE LEVANDER: I would like to comment on the question about clinical aspects and whether we are talking about chronic or acute situations. We have used two infectious models to study vitamin E deficiency and requirements. One is a Coxsackie virus, which is implicated in Keshan disease in China. It is a cardiotoxic virus. We can increase the cardiotoxicity of the virus remarkably by giving it to a vitamin E-deficient animal. These are all animal model systems.

The other model is mouse malaria. In that case, the vitamin E deficiency protects against the malaria, because the parasite is more susceptible to the oxidative stress in the host. So you can choose your disease and get your results.

V

PERFORMANCE IN COLD AND IN HIGH-ALTITUDE ENVIRONMENTS

PART V FOCUSES ON THE MENTAL aspects of performance in the cold and at high altitudes. Chapter 21 describes the adverse changes in mood, behavior, and cognitive performance that accompany exposure to high altitudes. Initial impairments in many critical behavioral functions such as memory, reasoning, and vigilance affect both judgment and rate of performance. These behavioral decrements may be attributable to neurochemical changes.

Exposure to hypobaric hypoxia and to extreme cold at high altitudes can cause deficits in mental performance, as noted in Chapter 22. The causal relationship between changes in brain catecholaminergic neurons and the stress that accompanies them is important in understanding the mechanisms that cause the decline in mental function in adverse environments. The use of catecholaminergic agonists like tyrosine and other food constituents such as caffeine may provide a common approach to treating the adverse effects of cold exposure and stress.

22

The Effect of Altitude on Cognitive Performance and Mood States

Barbara Shukitt-Hale[1] and Harris R. Lieberman

INTRODUCTION

High-altitude environments can be debilitating to unacclimatized individuals exposed to elevations above 3,000 m (9,843 ft) for periods ranging from several hours to days. Moderate hypoxia induces substantial alterations in physiological and psychological parameters within a few hours (Bahrke and Shukitt-Hale, 1993). Immediately upon ascent to high altitude, there is decreased blood oxygenation, which reduces the oxygen supply throughout the periphery and in the brain. With time the body compensates, at least in part, for the lack of oxygen with a variety of physiological responses and adjustments. In aggregate, this is termed *acclimatization*.

Adverse changes in mood states, as well as impairment in mental performance, occur during altitude exposure (Bahrke and Shukitt-Hale, 1993). Although numerous reports have been published concerning the physiological

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alterations that occur under conditions of hypoxia, there have been few investigations of the mood and behavioral changes associated with altitude. This chapter discusses both field and laboratory studies conducted to assess changes in these parameters.

MOOD STATES

Observed behaviors and personal anecdotes suggest that the initial mood experienced at altitude is euphoria, followed by depression. With time, individuals may also become quarrelsome, irritable, anxious, and apathetic (Van Liere and Stickney, 1963). Unfortunately, although disturbances in emotional control have been noticed at altitude for decades, there are few quantitative studies assessing mood changes at altitude.

Shukitt and Banderet (1988) conducted one of the first systematic studies of mood changes at altitude. Self-rated moods were evaluated in 35 subjects using the Clyde Mood Scale. The Clyde Mood Scale (Clyde, 1963) consists of 48 adjectives rated on a 4-point scale: "not at all," "a little," "quite a bit," and "extremely." These adjectives cluster into six mood factors: friendly, aggressive, clear thinking, sleepy, unhappy, and dizzy. Baseline values were determined at 200 m (656 ft); moods were then assessed for 2 days at 1,600 m (5,250 ft) in one group, or for 4 days at 4,300 m (14,110 ft, at the top of Pikes Peak) with a second group.

At 4,300 m (14,110 ft), moods differed from baseline (200 m [656 ft]) on the day of arrival (day 0) and differed even more after 1 day (Figure 22-1). Subjects became less friendly, less clear thinking, and dizzier. They also became sleepier and happier, while aggressiveness stayed the same (Figure 22-2). Only sleepiness changed at 1,600 m (5,250 ft), with the subjects becoming sleepier at this altitude compared to sea level. However, by day 2 after ascent to 4,300 m (14,110 ft), all changes had returned to baseline levels. Therefore, at 4,300 m (14,110 ft), the altered moods differed from baseline on the day of arrival (1 to 4 hours), differed even more after 1 day (18 to 28 hours), and returned to baseline by day 2 (42 to 52 hours). Mood states are thus adversely affected by both duration and level of altitude, and changes in mood states at altitude have a distinct and measurable time course.

In another study, Shukitt-Hale et al. (1990) evaluated mood states during a climb of Mount Sanford, Alaska to determine the extent to which mood was dependent not only on the altitude and rate of climb, but also on the length of stay and effort expended to reach the desired altitude. Self-rated moods were determined with the Profile of Mood States (POMS). This questionnaire (McNair et al., 1971) is a 65-adjective questionnaire, with the adjectives rated on a 5-point scale. It measures six mood factors: tension, depression, anger, vigor, fatigue, and confusion. Seven male volunteers from the U.S. Army were

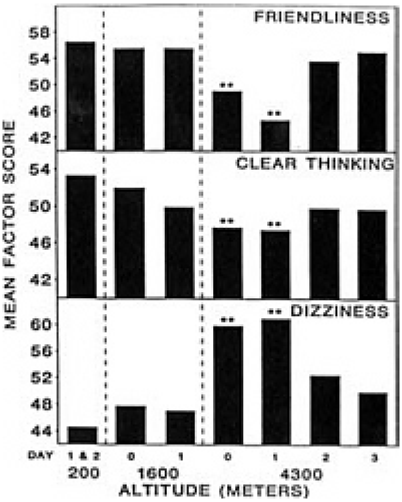

FIGURE 22-1 Factor scores for friendliness, clear thinking, and dizziness at 200; 1,600; and 4,300 m (656; 5,250; and 14,110 ft). ** indicate a significant difference ($P < 0.01$) from 200 m (656 ft). SOURCE: Shukitt and Banderet (1988), used with permission.

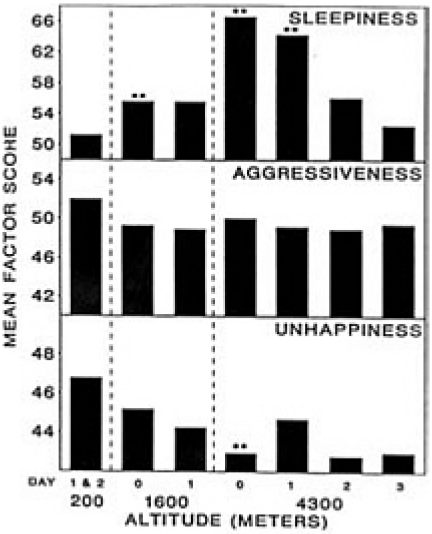

FIGURE 22-2 Factor scores for sleepiness, aggressiveness, and unhappiness at 200; 1,600; and 4,300 m (656; 5,250; and 14,110 ft). ** indicate a significant difference ($P < 0.01$) from 200 m 656 ft). SOURCE: Shukitt and Banderet (1988), used with permission.

tested over a period of 7 days during a climb to 3,630 m (11,909 ft). The subjects were tested five times,twice at 2,225 m (7,300 ft); then at 2,530 m (8,300 ft); 3,080 m (10,105 ft); and 3,630 m (11,909 ft).

Two mood states were found to be adversely affected over time by the changes in altitude. At 3,080 m (10,105 ft) and 3,630 m (11,909 ft), the subjects were less vigorous and more fatigued (Figure 22-3). These changes were different from those on day 2 at 2,225 m (7,300 ft). The fewer adverse effects seen on day 2 at 2,225 m (7,300 ft) show that some degree of acclimatization may have taken place from day 1 to day 2 at this altitude.

It is interesting to note from this study that even though the climb to the moderate altitude of 3,630 m (11,909 ft) was relatively slow (less than 300 m/d [984 ft/d]), adverse changes were still evident. Exercise promotes a greater demand for oxygen, so a climber can become more hypoxic under these conditions. These data imply that factors other than just the level of altitude can affect mood states, such as physical exertion (or exercise) associated with a climb.

COGNITIVE PERFORMANCE

As with mood changes, the research on cognitive functioning at altitude is somewhat limited. Most investigations have shown decrements in cognitive

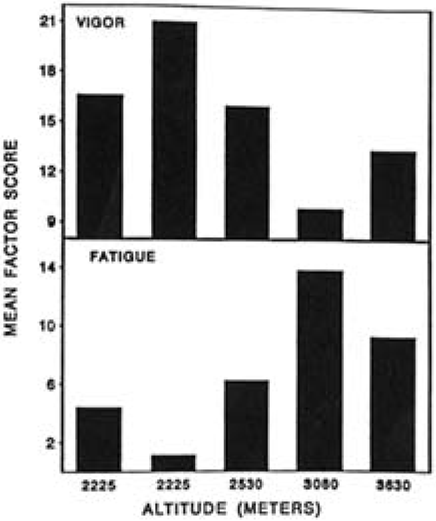

FIGURE 22-3 Profile of Mood States (POMS) factor scores for vigor and fatigue at 2,225; 2,225; 2,530; 3,080; and 3,630 m (7,300; 7,300; 8,300; 10,105; and 11,909 ft). SOURCE: Shukitt-Hale et al. (1990), used with permission.

performance beginning at an altitude of 3,000 m (9,843 ft) (Bahrke and Shukitt-Hale, 1993; Tune, 1964). Interestingly, a few studies have even reported that some of the changes in performance after exposures to extreme altitudes persist for up to a year or longer after return to lower altitudes, although much debate surrounds this issue (Bahrke and Shukitt-Hale, 1993).

High altitude produces substantial impairments in a number of cognitive performances. Changes in psychomotor performance, mental skills, reaction time, vigilance, memory, and logical reasoning have all been measured at altitudes above 3,000 m (9,843 ft) (Bahrke and Shukitt-Hale, 1993). Cognitive performance is usually more vulnerable to altitude than psychomotor performance, and it has been suggested that complex tasks are typically affected before simple tasks (Cudaback, 1984). Impaired performance at altitude can manifest itself in increased errors, slowing of performance, or a combination of these factors (Banderet and Burse, 1991).

Because human cognitive function is sensitive to changes in oxygen availability, exposure to hypoxia should produce a continuum of effects as altitude level and duration increase. One study (Lieberman et al., 1991) evaluated the behavioral effects of hypoxia as a function of time of exposure and altitude level with various standardized tests of cognitive performance. Twenty-three males were tested in an altitude chamber during a 4.5-h exposure to hypobaric hypoxia. The tests (Banderet and Lieberman, 1989) were administered using paper and pencils as well as lap-top computers. All subjects were exposed to two levels of hypoxia, the equivalent of 4,206 m (13,800 ft) and 4,725 m (15,500 ft), as well as a near sea level control condition (549 m [1,800 ft]). During exposure, tests were given from one to three times. Prior to simulated altitude exposure, subjects practiced all tests extensively to insure that performance was stable and near-maximal.

Cognitive performance was significantly impaired on 8 out of the 10 performance measures. Even on relatively simple performance tasks—such as simple and choice reaction time—as well as complex tests of cognition—such as the addition test—impairments occurred in a graded manner. The number of hits on the Bakan vigilance task (Banderet and Lieberman, 1989) decreased with increasing hypoxia (or simulated altitude) (Figure 22-4). Additionally, simple reaction time increased as a function of increased hypoxia (Figure 22-5) as did the percent errors on the four-choice reaction time test. The number of correct responses on the addition (Figure 22-6), coding (Figure 22-7), number comparison (Figure 22-8), pattern recognition, and Tower of Hanoi optimal tests decreased with increasing simulated altitude and time at altitude. Therefore, adverse changes in cognitive performance increased with higher altitudes and longer durations.

As part of this study, mood states were also evaluated at the equivalent of 4,206 (13,800 ft) and 4,725 m (15,500 ft), using the POMS and the Clyde Mood Scale. Data from the POMS showed increased anger, confusion, fatigue, tension, and vigor, while data from the Clyde Mood Scale showed increased

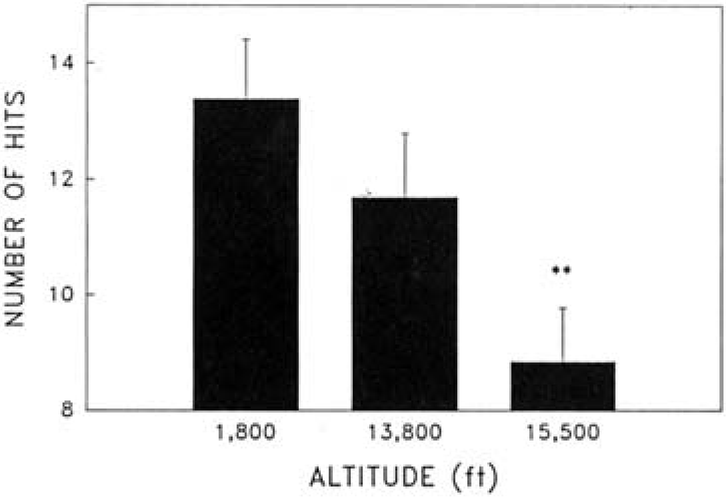

FIGURE 22-4 Effects of simulated altitude (549; 4,206; and 4,725 m [1,800; 13,800; and 15,500 ft]) on number of hits on the Bakan vigilance task. ** indicate a significant difference ($P < 0.01$) from 549 m (1,800 ft). SOURCE: Lieberman et al. (1991), used with permission.

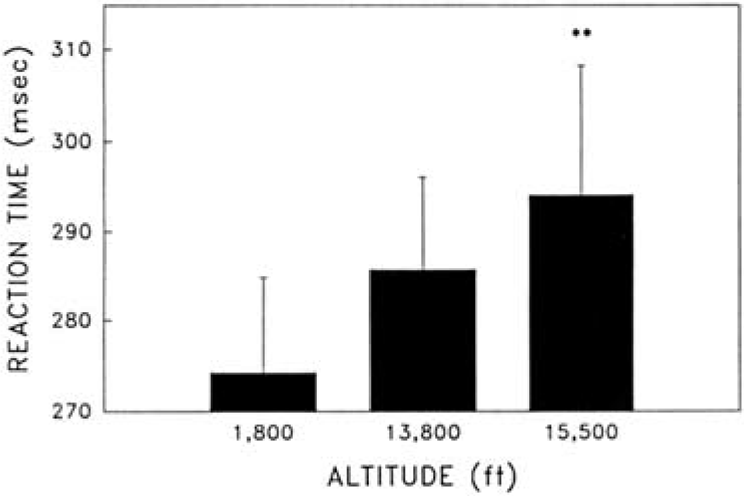

FIGURE 22-5 Effects of simulated altitude (549; 4,206; and 4,725 m [1,800; 13,800; and 15,500 ft] on reaction time on the simple reaction time task. ** indicate a significant difference ($P < 0.01$) from 549 m (1,800 ft). SOURCE: Lieberman et al. (1991), used with permission.

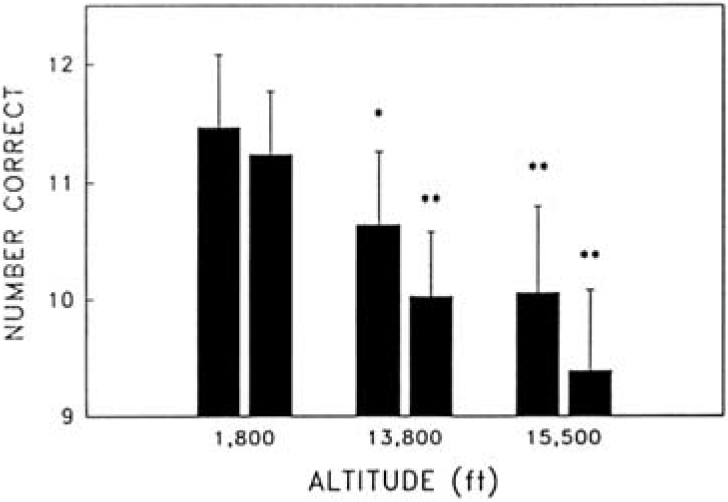

FIGURE 22-6 Effects of simulated altitude (549; 4,206; and 4,725 m [1,800; 13,800; and 15,500 ft]) and time of exposure on number correct for the addition task at two time points. Asterisks indicate a significant difference (*, $P < 0.05$; **, $P < 0.01$) from 549 m (1,800 ft). SOURCE: Lieberman et al. (1991), used with permission.

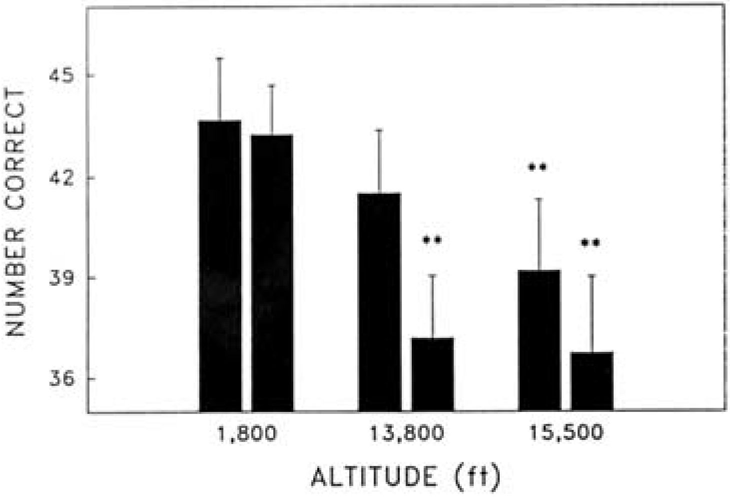

FIGURE 22-7 Effects of simulated altitude (549; 4,206; and 4,725 m [1,800; 13,800; and 15,500 ft]) and time of exposure on number correct for the coding task at two time points. ** indicate a significant difference ($P < 0.01$) from 549 m (1,800 ft)

SOURCE: Lieberman et al. (1991), used with permission.

sleepiness and dizziness as well as decreased friendliness. Again, the changes observed were a function of both exposure duration and altitude level. A more detailed discussion of these results can be found in Shukitt-Hale et al. (Unpublished manuscript, "Elevation-dependent symptom, mood, and performance changes produced by exposure to hypobaric hypoxia," B. Shukitt-Hale, L. E. Banderet, and H. R. Lieberman, 1996).

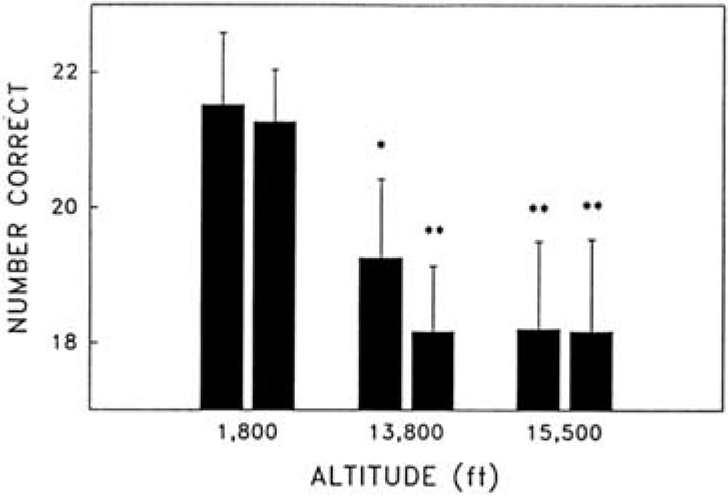

FIGURE 22-8 Effects of simulated altitude (549; 4,206; and 4,725 m [1,800; 13,800; and 15,500 ft]) and time of exposure on number correct for the number comparison task at two time points. Asterisks indicate a significant difference (*, $P < 0.05$; **, $P < 0.01$) from 549 m (1,800 ft). SOURCE: Lieberman et al. (1991), used with permission.

TIME COURSE OF EFFECTS

Because adverse changes in mood and cognitive performance occur at altitude, one interesting question is, What is the time course of these effects, and are they related to increases in the incidence of acute mountain sickness (AMS)? The number, severity, rapidity of onset, and duration of symptom, mood, and performance changes vary from person to person and are related to both level of altitude and rate of ascent (Hansen et al., 1967; Shukitt-Hale et al., 1991a). It is usually assumed that individuals afflicted with AMS will be more susceptible to changes in these other parameters. However, previous studies have suggested that their time courses are different (Banderet and Burse, 1991).

AMS symptoms begin to appear after 6 hours, increase from 6 to 24 hours, and reach maximum severity after 30 to 40 hours of exposure (Carson et al., 1969; Hackett, 1980). The time courses of other symptoms and mood states appear similar to that of AMS symptomatology, although these changes are not as well documented (Shukitt and Banderet, 1988). The time course of performance impairments, however, appears somewhat different. One study (Banderet et al., 1986) found decreased levels of performance on all seven tasks administered 1 or 6 hours after ascent to 4,600 m (15,092 ft). At 14 or 19 hours, only four tasks were still impaired, and by 38 or 42 hours, only two were still impaired (Figure 22-9). Therefore, changes in performance were most severe at 1 to 6 hours, the time when AMS symptoms are only beginning to appear. Additionally, performance changes return to baseline when AMS symptoms are most severe (after 30 to 40 hours).

Shukitt-Hale et al. (1991a) conducted a study to determine whether individuals afflicted with initial symptoms of AMS would be more susceptible to adverse changes in other symptoms, moods, and performance, since they may be differentially affected at this point in time. The AMS-Cerebral (AMS-C) factor of the Environmental Symptoms Questionnaire (ESQ) was chosen as the best measure of altitude sickness, since it is a standard index of the degree of illness. Other measures were chosen to assess symptoms, moods, and performance.

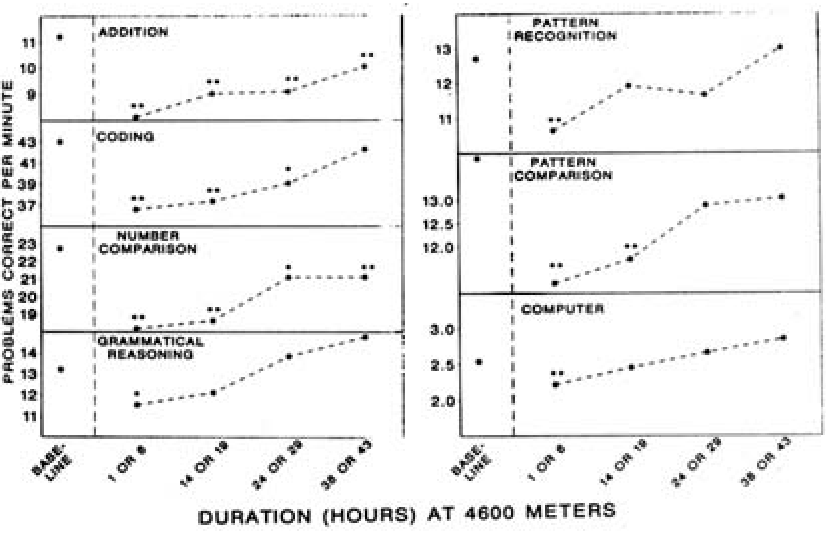

FIGURE 22-9 Performance on cognitive tasks at simulated 4,600 m (15,092 ft) after varied durations of altitude exposure. Performance impairments, significantly different from baseline, are indicated with asterisks above each data point.
SOURCE: Banderet et al. (1986), used with permission.

Twenty subjects were evaluated on 11 symptom, 13 mood, and 14 cognitive-motor performance measures after exposure in the hypobaric chamber to simulated altitudes of 4,725 m (15,500 ft) for 5 to 7 hours. The AMS-C score was significantly correlated with the composite measures of symptoms (*r* = 0.90), moods (*r* = 0.77), and performance (*r* = 0.59) (Figure 22-10). Individuals afflicted with AMS appear to be more susceptible to changes in symptoms, then moods, and finally performance at an altitude of 4,725 m (15,500 ft) for 5 to 7 hours, since the time courses are different. Therefore, it is important to measure a variety of parameters during altitude studies because they are not affected similarly.

BEHAVIOR AND NEUROCHEMISTRY

Because mood and cognitive performance are adversely affected by hypoxia, the question becomes, What is responsible for these effects? The central mechanisms responsible for the effects of hypoxia on behavior and cognitive

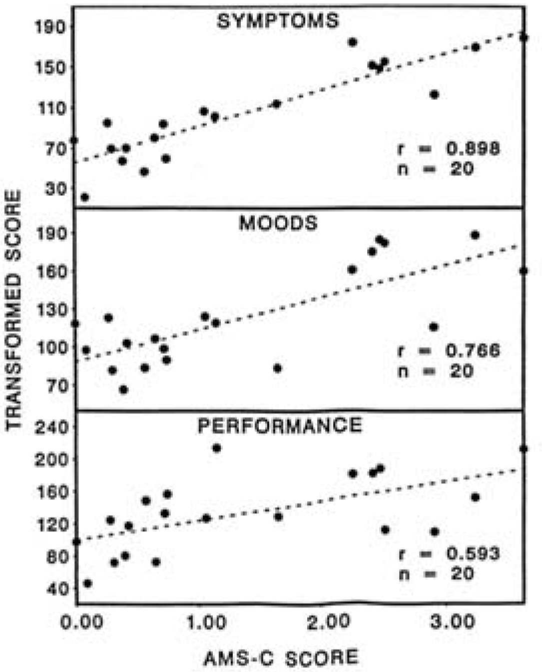

FIGURE 22-10 Correlation with acute mountain sickness-cerebral (AMS-C) score for symptoms, moods, and performance at simulated 4,725 m (15,500 ft). SOURCE: Shukitt-Hale et al. (1991a), used with permission.

performance are not known. It is likely that the direct effects of mild transient hypoxia on the brain are variations in the level of specific neurotransmitters. Because the synthesis of several neurotransmitters is oxygen dependent, abnormalities of neurotransmitter metabolism may mediate the early functional changes due to acute hypoxia (Gibson and Duffy, 1981). It is likely that some of the behavioral decrements caused by hypoxia are attributable to changes in neurotransmitter utilization and concentration (Freeman and Gibson, 1988).

The cholinergic system is particularly vulnerable to hypoxia, and it appears that acetylcholine (ACh) is the neurotransmitter primarily affected (Gibson and Duffy, 1981). ACh is a neurotransmitter involved in the regulation of learning and memory processes (Freeman and Gibson, 1988). The rates of synthesis of other neurotransmitters (e.g., dopamine, serotonin, and the amino acids) are also sensitive to hypoxia, but perhaps less so than the rate of ACh synthesis (Freeman et al., 1986). To determine the effect and influence of acetylcholine on learning and memory performance at altitude, this laboratory undertook a variety of studies using the rat as an experimental model (Shukitt-Hale et al., 1991b, 1993a, 1993b, 1994, in press).

The first series of studies sought to determine the effects of various levels of hypobaric hypoxia on spatial memory in rats and to develop a model to test drug and nutrient interventions. Although deficits in human cognitive performance are well established, few studies have measured cognitive changes in animals exposed to hypoxia.

The Morris water maze (MWM) was used to assess behavior in these studies (Shukitt-Hale et al., 1993b, 1994). The MWM is a standardized test of spatial learning and memory that has been shown to be sensitive to decrements in hippocampal cholinergic function. The maze is a circular black pool filled with water, in which a circular black escape platform is located. The platform is kept below the surface of the water so that the rat must use distal cues to locate it. Numerous extramaze cues were located on the walls of the altitude chamber. Accurate navigation is rewarded with escape from the water onto the platform. The MWM does not rely on food as a reward like other tests of spatial memory (e.g., radial maze or T-maze). Because food consumption is suppressed under hypoxia (discussed below), this is an advantage of using the MWM to assess learning at altitude.

Rats were tested at 2 and 6 hours while exposed to a range of simulated altitudes: sea level, 5,500 m (18,045 ft); 5,950 m (19,521 ft); and 6,400 m (20,997 ft). At the beginning of each trial the rat was gently immersed in the water so that it was facing and touching the wall of the pool. Each rat was allowed 120 seconds to escape onto the platform (Trial 1: termed reference or long-term memory). If the rat failed to escape within this time, it was guided to the platform. Once the rat reached the platform, it remained there for 10 seconds. Trials were given in pairs, with the second trial using the same starting location as the first (Trial 2: termed working or short-term memory).

Pairs of trials were given every 20 minutes until all four starting locations had been used.

Hypobaric hypoxia adversely affected performance in the Morris water maze in an elevation-dependent fashion; as the simulated altitude increased above 5,500 m (18,045 ft), the decrement in performance also increased. Exposure to simulated altitudes of 5,950 and 6,400 m (19,521 and 20,997 ft) produced deficits in both the reference (Figure 22-11) and working memory (Figure 22-12) components of this task as indicated by the significant increase in latency. Also at these altitudes, path lengths increased and swim speeds decreased compared to sea level values. Performance at 6,400 m (20,997 ft) was inferior to that at 5,950 m (19,521 ft), while at 5,500 m (18,054 ft) there were no differences from sea level.

These results agree with human studies that demonstrate elevation-dependent impairments in spatial memory performance during exposure to hypobaric hypoxia. It is important to establish that these decrements in performance exist in animals because numerous treatment strategies can then be evaluated. Also the theory that these deficits may be attributable to changes in hippocampal cholinergic function or other central neurotransmitter systems can be more easily tested. A later chapter (see Lieberman and Shukitt-Hale, Chapter 23 in this volume) will discuss the neurochemical studies done to explore this hypothesis.

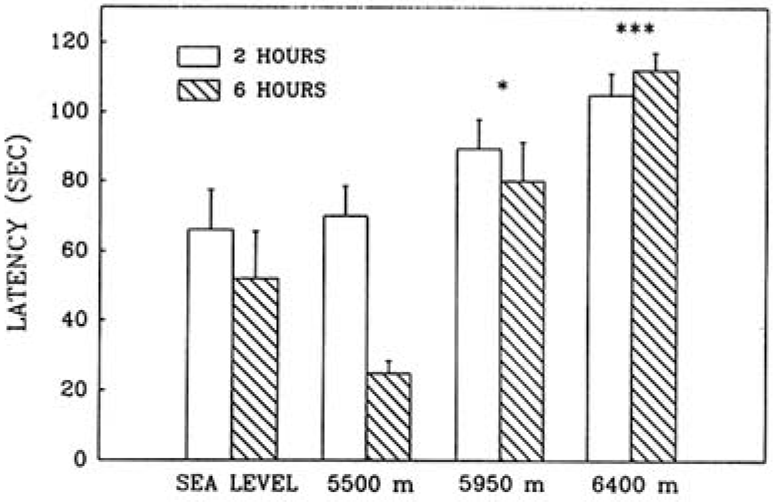

FIGURE 22-11 Effect of simulated altitude (5,500; 5,950; and 6,400 m [18,045; 19,521; and 20,997 ft]) exposure on Morris water maze performance (latency) for Trial 1-reference memory. Asterisks indicate significant group differences between sea level and altitude (*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$).
SOURCE: Shukitt-Hale et al. (1993b), used with permission.

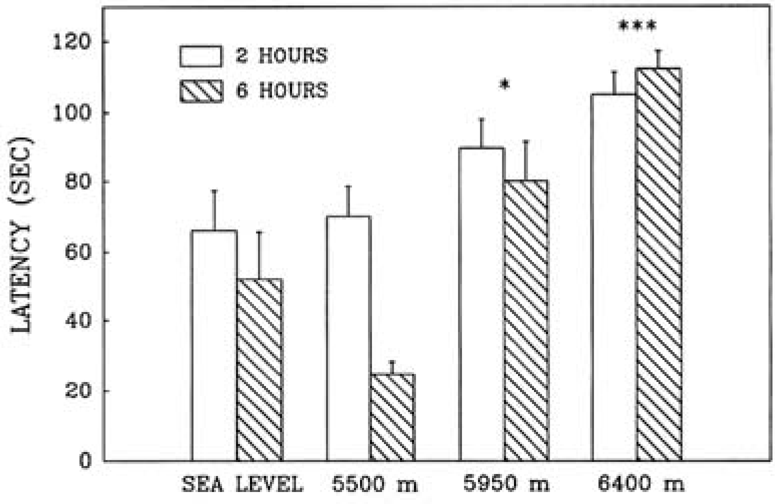

FIGURE 22-12 Effect of simulated altitude (5,500; 5,950; and 6,400 m [18,045; 19,521; and 20,997 ft]) exposure on Morris water maze performance (latency) for Trial 2—working memory. Asterisks indicate significant group differences between sea level and altitude (*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$). SOURCE: Shukitt-Hale et al. (1993b), used with permission.

NUTRITION

High-altitude conditions cause anorexia, a self-induced starvation (Banderet and Burse, 1991). When this laboratory evaluated the effect of prolonged exposure to hypobaric hypoxia in the rat (Shukitt-Hale et al., 1991b, in press), one portion of the study evaluated the effect of long-term exposure to hypoxia on growth and feeding rates. Weight loss and food consumption were measured in three different groups of rats (termed "morphology" or "behavior" groups) after a simulated 4-d exposure to sea level; 5,500 m (18,045 ft); or 6,400 m (20,997 ft).

Long-term exposure to simulated altitude had an adverse effect on weight. Rats at altitude lost significantly more weight than did animals at sea level (Figure 22-13). They also consumed significantly less food than rats at sea level (Figure 22-14). These data show that rats exposed to prolonged altitude only consumed approximately one-quarter of what a normal rat would eat.

These results corroborate previous findings that animals and humans lose body weight when exposed to low oxygen conditions, due to reduced daily food intake and perhaps other factors. Rose et al. (1988) found similar results

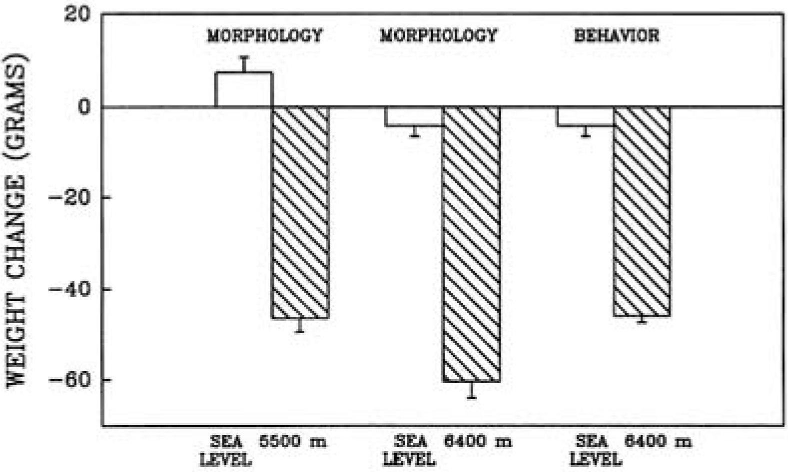

FIGURE 22-13 The effect of simulated altitude (5,500 or 6,400 m [18,045 or 20,997 ft]) on weight loss in three groups of rats.
SOURCE: Shukitt-Hale et al. (1991b), used with permission.

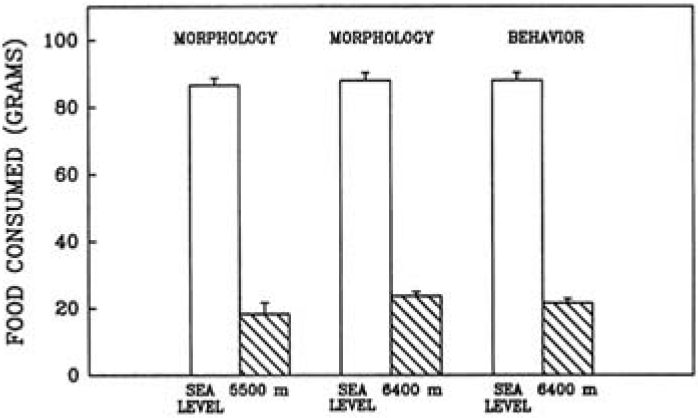

FIGURE 22-14 The effect of simulated altitude (5,500 or 6,400 m [18,045 or 20,997 ft]) on food consumption in three groups of rats.
SOURCE: Shukitt-Hale et al. (1991b), used with permission.

during their investigation of six men fed a palatable diet during a 40-d simulated ascent of Mount Everest to 8,850 m (29,035 ft) (Operation Everest II) (Houston et al., 1987). Prolonged exposure to increasing hypoxia was associated with a reduction in body weight, particularly due to a decrease in carbohydrate preference, despite access to ample varieties and quantities of food. This study (Rose et al., 1988) suggested that hypobaric hypoxia rather than the combined stresses of the mountain environment can be sufficient cause for the weight loss and decreased food consumption reported by major mountain expeditions.

AUTHORS' CONCLUSIONS AND RECOMMENDATIONS

The studies reviewed here show that altitude produces adverse alterations in human mood states, behavior, and cognitive functioning. Human performance, including many critical behavioral functions such as memory, reasoning, and vigilance are significantly impaired initially. Behavioral impairments caused by ascent to high altitude can thus degrade military operations, since both rate of performance and judgment are affected. If the elevation is high enough, complete acclimatization is not possible. The adverse behavioral consequences of hypoxia are dependent on both the level of altitude and the duration at altitude, and they have distinct and measurable time courses. Limited research seems to indicate that some performance decrements induced by extreme altitudes may persist for up to a year or longer after individuals return to lower elevations. These issues need to be considered when military operations at altitude are planned and undertaken.

The neurochemical basis for mood and performance changes needs to be further explored since behavioral decrements at altitude may be attributable to changes in neurochemistry. Strategies, including drugs and nutrients, to facilitate psychological coping and improve performance and functioning in high-altitude environments need to continue to be evaluated. Both animal and human models need to be developed to test the efficacy of these strategies. These treatment strategies may one day be useful in high-altitude military operations to prevent performance decrements and mood changes caused by this environment.

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23

Food Components and Other Treatments That May Enhance Mental Performance at High Altitudes and in the Cold

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INTRODUCTION

High-altitude exposure that results in hypobaric hypoxia can produce significant decrements in human mental performance (see Shukitt-Hale and Lieberman, Chapter 22 in this volume). Although these adverse effects are reduced by the acclimatization process, only partial adaptation occurs at extreme terrestrial altitudes. Furthermore, when soldiers are rapidly deployed to mountainous regions, their performance of required critical duties upon arrival, including offensive or defensive operations, may be impaired. The adverse effects of cold exposure on human behavior can also be significant and can exacerbate the physical consequences of exposure to extreme cold. Because mountainous regions are frequently cold, the adverse effects of both stressors on soldier performance—cold and high altitudes—may be additive. Cold and hypoxia are not the only stressors that soldiers experience. Other common

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stressors include heat, psychological stress (which can be extraordinarily intense in combat operations), and sleep loss. Because soldiers are typically exposed to multistressor environments, the optimal treatment for any individual stressor might also have beneficial effects that generalize across other stressors. However, there is no reason to believe that if a treatment is effective in one environment it will also work in others.

Cold, heat, and hypoxia have different physiological effects. In the case of heat and cold, some of the effects, at least on the peripheral nervous system, are in opposition (Murphy and Redmond, 1975). Therefore, it may be likely that treatments for the adverse peripheral consequences of exposure to various stressors will not have common positive effects across stressors. In fact, treatments that have beneficial effects in one environment could even have adverse effects in other environments. It is also possible however, that enhancement of certain critical metabolic or physiological functions such as energy utilization or cardiovascular function would generalize across different stressors. Appropriate nutritional supplements might, in theory, be good candidates for producing beneficial effects in various environments and in situations in which multistressor exposure occurs. In addition, if there are common elements in the response of the central nervous system (CNS) to different types of stressors, modulation of these mechanisms could be a generic treatment for the adverse effects of stress. Treatments that are less stressor-specific might have significant advantages over strategies that are targeted at specific metabolic functions associated with individual stressors.

If it can be determined what underlying brain mechanisms are responsible for the adverse CNS response to stress, assuming there are some, it may be possible to find practical interventions—nutritional or other—to treat some of the adverse symptoms associated with the CNS components of the stress response. At the U.S. Army Research Institute of Environmental Medicine (USARIEM), a comprehensive program has been initiated to evaluate the neurochemical and behavioral effects of various stressors on brain function. One of the key objectives of this program is to specify which neurochemical changes are responsible for the adverse behavioral effects of stressors. With this basic information, researchers at USARIEM hope to determine how to treat adverse behavioral effects of stress appropriately by preventing or mitigating the underlying neurochemical deficits with nutrient and drug treatment. To date, two environmental stressors have been studied in some detail: cold and high altitude. Researchers hope to extend the research to various other stressors. In addition, two neurochemical systems have been studied that are believed to be intimately involved either in the response of the organism to stress (specifically the catecholaminergic system), or in critical behavioral functions such as learning and memory (specifically the cholinergic system).

STRESS AND CENTRAL CATECHOLAMINES

A great deal of evidence from the animal literature, and to a limited extent from the human clinical literature, supports the idea that there are common elements, across a variety of stressors, of the CNS response to acute stress (Gray, 1982). Furthermore, this response seems to have some common neurochemical substrates and involves, in particular, the activation of catecholaminergic systems (Lieberman, 1994; Murphy and Redmond, 1975; Stone 1975). An increase in the release of specific brain neurotransmitters may initially lead to an increased ability to cope, but if the stress is severe enough, these homeostatic regulatory mechanisms can be overwhelmed. When this situation occurs, the organism cannot effectively respond to the environment, and a syndrome characterized by lethargy and helplessness results (Gray, 1982; Maier and Seligman, 1976). A more detailed discussion of this hypothesis and the supporting evidence is provided by Wurtman and Lieberman (1989) and Lieberman (1994).

Central catecholaminergic stores are depleted by exposure to various types of stress, including both environmental and psychological stressors. Heat, cold, and electrical shock all produce significant increases in brain catecholaminergic activity (Stone, 1975). The neurotransmitter norepinephrine (NE) appears to be particularly critical in the brain's response to stress, although the other important brain catecholamine, dopamine, also appears to be involved. It is probably not coincidental that the classic performance-enhancing drugs are catecholamine (CA-) agonists that seem to have beneficial effects on a variety of stressors. The most widely recognized CA-agonist is the potent drug amphetamine, which also has beneficial effects on certain types of performance in unstressed organisms (Gray, 1982; Murphy and Redmond, 1975).

Tyrosine is a nutrient precursor of the catecholamines, and therefore, it has been studied as part of the Performance Enhancing Ration Component Program, a joint U.S. Army Research Institute of Environmental Medicine/Natick Research Development and Engineering Center program. Tyrosine appears, in certain situations, to enhance catecholaminergic function and to prevent certain stress-induced decrements in performance (Lieberman, 1994). Such beneficial effects were predicted because when catecholaminergic neurons are highly active (which occurs during exposure to many acute stressors), the amount of neurotransmitter they release increases if more tyrosine is made available (Wurtman et al., 1981). Because increased catecholamine release appears to be associated with an effective response of the organism to acute stress, the provision of supplemental tyrosine (precursor for the synthesis of catecholamines) might enhance the ability of the organism to respond appropriately to stress (Lehnert et al., 1984; for reviews see Lieberman, 1994; Owasoyo et al., 1992; Salter, 1989).

Since the mid-1980s, a series of animal and human studies have been conducted at USARIEM and elsewhere to examine this phenomenon, because the results could have practical implications for treatment of stress-induced decrements of mental performance and even ration design (Lieberman, 1994). As part of this program, the authors have employed various techniques to assess changes in animal brain function and in animal and human behavior associated with acute stress. Furthermore, the authors have studied the effects of tyrosine administration on neurotransmitter release and behavior in acutely stressful scenarios.

Microdialysis is one of the techniques used at USARIEM to examine the effects of various stressors on brain function. This technique permits continuous monitoring of neurotransmitter release in vivo (Ungerstedt et al., 1982) by sampling extracellular fluid from a small brain region to assess neurotransmitter and metabolite levels. A specially manufactured guide cannula is implanted stereotaxically onto the skull of an anesthetized animal and above a specific brain region of interest. After the animal has recovered from the effects of the surgery and anesthesia, a microdialysis probe can be inserted through the cannula into the predesignated brain region. The probe consists of two separate inflow and outflow tubes connected at the end by a closed loop of dialysis membrane. The tip of the probe is typically 1 to 3 mm in length. When the probe is inserted into the brain, it is perfused with artificial cerebrospinal fluid (CSF) at a flow rate of 2 μl/min. Although no fluid is added or removed from the brain, by perfusing the probe with a solution that does not contain brain metabolites, a concentration gradient is established across the dialysis membrane. Therefore, brain metabolites move from the brain extracellular space across the dialysis membrane into the artificial CSF due to this gradient. The collected artificial CSF is then assayed for the concentration of the brain neurotransmitter(s) and metabolites of interest. It typically takes 10 to 20 minutes to collect a sample large enough for analysis. For assay of brain catecholamines, high performance liquid chromatography with electrochemical detection (Lehnert et al., 1994) is the method of choice.

Using this technique, researchers at USARIEM have assessed NE release during exposure of rats to cold water stress and to restraint stress and have reported substantial changes in levels of hippocampal NE (Luo et al., 1993). Microdialysis guide cannulae have been implanted in Fischer rats to assess the release of NE in the hippocampus. This brain region plays a key role in learning and memory function. In addition, NE collected in the hippocampus is released only by afferents from the locus coeruleus, the only brain region providing noradrenergic input to the hippocampus. The locus coeruleus is a very small but critical region of the brain, which plays an important role in regulating aspects of the acute response of animals to stressors (Stone, 1975). This midbrain region provides noradrenergic innervation to large areas of the brain, including the cerebral cortex, and probably plays an important role in the regulation of arousal level and attention (Gray, 1982).

The rats tested in this study were treated with either 400 mg of tyrosine per kg body weight, administered intraperitoneally (i.p.), or with a saline placebo treatment (Luo et al., 1993) (Figure 23-1). Simply exposing the saline-treated control animals to 10 minutes of restraint stress caused a massive increase in the release of NE, greater than 100 percent, as assessed by in vivo microdialysis (Figure 23-1). However, an additional stressor, cold, begun 30 minutes into the experiment, caused no additional increase in NE release. Treatment with tyrosine increased the release of NE over 500 percent above baseline levels, 20 minutes after the beginning of exposure to stress. Higher rates of NE release were maintained in tyrosine-treated animals throughout the exposure to the multiple stressors. It appears that by supplying additional neurotransmitter precursor to the brain by peripheral administration of tyrosine, which readily crosses the blood-brain barrier, substantial additional NE is released during exposure to acute stress.

Changes in the release of particular brain neurotransmitters, while of theoretical interest, are by themselves difficult to interpret. Because an increase in neurotransmitter release could either have positive or negative behavioral consequences, it is essential to study the behavioral correlates of neurochemical phenomena. Several laboratories have conducted such studies (for a review see Lieberman, 1994), including the authors'. In particular, this lab has attempted to determine whether tyrosine administration has beneficial behavioral effects when animals or humans are exposed to various stressors, alone and in combination.

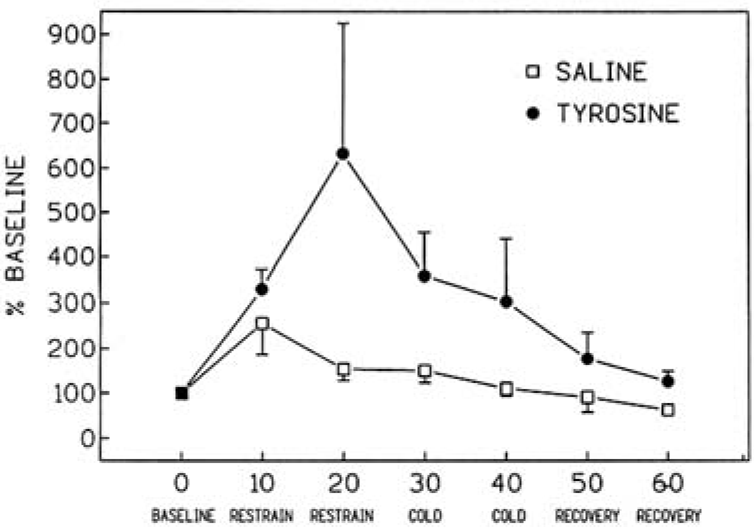

FIGURE 23-1 Effect of immobilization stress alone and in combination with cold stress on hippocampal norepinephrine release in tyrosine- (400 mg/kg; intraperitoneally [i.p.]) and placebo-treated rats. Testing conditions, in 10-min intervals, are specified on the x-axis. SOURCE: Adapted from Luo et al. (1993).

In a series of animal studies, the authors have attempted to develop a paradigm that consistently detects the effects of tyrosine on stress-related coping behavior. The test employed, the Porsolt swim test, was previously reported to be sensitive to other catecholaminergic agonists and has been used as a screening test to help in the selection of new antidepressant drugs (Porsolt et al., 1978). The Porsolt swim test was also reported to detect the effects of various neurotransmitter precursors, including tyrosine, in relatively nonstressed animals (Gibson et al., 1982). The test is simple to administer; a rat is placed in a glass beaker filled with water for several minutes, and the amount of time it spends actively attempting to escape is assessed. An animal who is actively attempting to escape is judged to be more appropriately responding to the environment than one who is inactive and helpless. Of course, other behavioral tests are necessary to confirm and extend the results of the Porsolt test, but it has usually proven to be a reliable indicator of the potency and selectivity of many experimental treatments (Porsolt et al., 1978). Furthermore, the authors have found it to be consistently sensitive to the effects of tyrosine on animals exposed to acute cold stress (Luo et al., 1992; Rauch and Lieberman, 1990). In one study, tyrosine, when administered in a dose of 400 mg/kg, significantly increased the amount of time animals were active in the Porsolt swim test following a brief exposure to cold water stress (Rauch and Lieberman, 1990). More recently, the authors found that tyrosine in lower doses (200 mg/kg) also improved performance in the Porsolt test. As would be predicted, tyrosine is less potent when administered in this dose than the higher dose (Luo et al., 1992) (Figure 23-2).

The authors have also seen beneficial effects of tyrosine using behavioral tasks that require more cognitive performance than the Porsolt swim test. For example, a recently conducted series of studies examined some of the neurochemical, behavioral, and morphologic consequences of acute and chronic exposure to hypobaric hypoxia (Shukitt-Hale and Lieberman, Chapter 22 in this volume; Shukitt-Hale et al., 1993, 1994, in press a, in press b). Unfortunately, the authors were unable to assess noradrenergic function during exposure to hypobaric hypoxia because NE release fell to undetectable levels soon after the start of exposure. However, it was possible to study cholinergic function using microdialysis. When rats were exposed to a simulated altitude of 18,000 ft (5,486 m), hippocampal acetylcholine levels significantly decreased (Shukitt-Hale et al., 1993) (Figure 23-3). Exposure to an altitude of 19,500 ft (5,944 m) also adversely affected learning and memory (Shukitt-Hale et al., 1994). However, upon administering a drug (the calcium channel blocker, nimodipine), which restored acetylcholine to normal levels (Figure 23-3), performance on a test of learning and memory (the Morris water maze [MWM]) was not restored (Unpublished observations, B. Shukitt-Hale and H. R. Lieberman, U.S. Army Research Institute of Environmental Medicine, Natick, Mass., 1994).

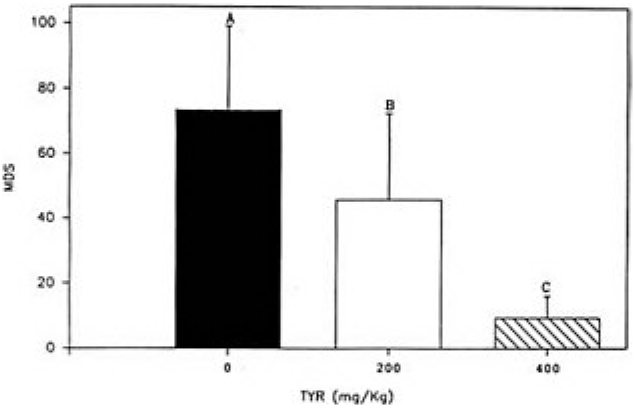

FIGURE 23-2 The effect of two doses of tyrosine (TYR) (200 and 400 mg/kg; i.p.) on duration of immobility in the Porsolt swim test. Prior to testing, core body temperature was lowered to 86°F (30°C). These data demonstrate that the effects of tyrosine on cold-stressed animals are dose dependent. Values are expressed as mean difference scores (MDS), which equal hypothermia immobility time minus normothermia immobility time. A lower score indicates better performance. Treatment means that are labeled with different letters are significantly different. Results are expressed as mean + SEM.
SOURCE: Adapted from Lieberman (1994) and Luo et al. (1992).

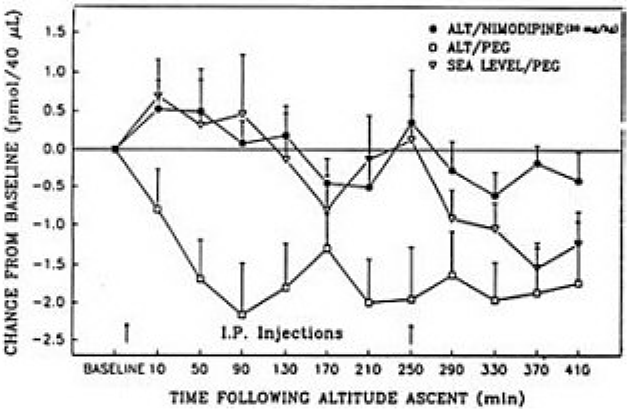

FIGURE 23-3 Changes in extracellular hippocampal acetylcholine levels under three conditions: ALT/NIMODIPINE, a simulated altitude of 18,000 ft (5,486 m) and treatment with the drug nimodipine (20 mg/kg); ALT/PEG, an altitude of 18,000 ft and treatment with a placebo; SEA LEVEL/PEG, sea level altitude and treatment with a placebo. Arrows above the x-axis indicate times of drug or placebo injection. SOURCE: Adapted from Shukitt-Hale et al. (1993).

The authors have also conducted a study in which tyrosine was administered twice (400 mg/kg on each occasion) to rats exposed to hypobaric hypoxia, with the result that it significantly improved spatial learning performance on the MWM (Lieberman et al., 1992; Shukitt-Hale et al., in press b) (Figure 23-4). These studies support the conclusion that, at least for some of the behavioral symptoms of hypobaric hypoxia, the cholinergic system may play a less-important role or may be more difficult to modify than the catecholaminergic system. That beneficial effects of tyrosine were detectable by very different behavioral tests, such as the MWM and the Porsolt swim test, is encouraging with regard to the generalization of tyrosine's effects. Furthermore, that tyrosine's effects are present when animals are exposed to very different types of stress also supports its potentially comprehensive effects.

The authors have also conducted several studies to determine whether tyrosine protects humans from the adverse effects of the combined stressors of cold and high altitudes. In two separate but similar studies, tyrosine given orally in doses of 85 to 170 mg/kg protected humans from some of the adverse effects of these stressors on symptoms, mood, and performance (Banderet and Lieberman, 1989; Lieberman et al., 1990). In these studies, mood, performance, and symptoms associated with cold and hypoxia were partially mitigated

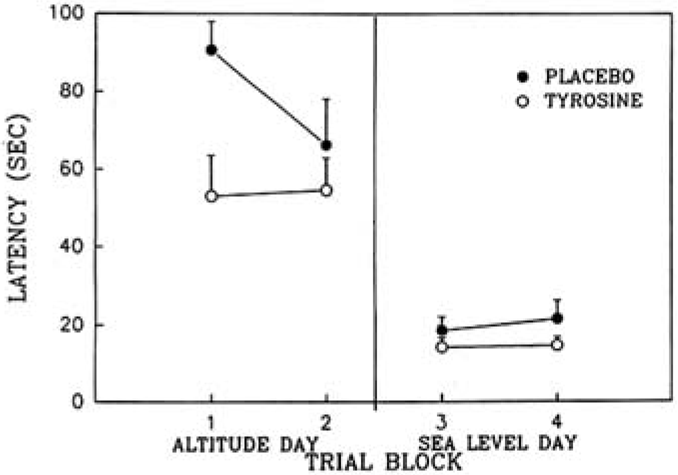

FIGURE 23-4 Effect of tyrosine and placebo on working (short-term) memory as assessed by the Morris water maze. Rats were exposed to hypobaric hypoxia (equivalent to 19,500 ft [5,944 m]) or sea-level conditions. Four hundred mg/kg of tyrosine was administered i.p. on two occasions: 1.5 hours and 5.5 hours after the start of exposure to hypoxia. Hypoxia clearly impaired performance on this task, and tyrosine reduced the decrements in performance as assessed by latency to locate the hidden platform on the first trial block. There were no residual effects of tyrosine on the next day (sea-level day). Results are expressed as mean + SEM. Tyrosine significantly different from placebo ($p <$ 0.04). SOURCE: Adapted from Lieberman et al. (1992).

in many individuals who were treated with tyrosine. Research conducted by the Navy Medical Research Laboratory in humans and animals exposed to cold stress have confirmed and extended these findings (Ahlers et al., 1994; Shurtleff et al; 1992).

STRESS AND THE CHOLINERGIC SYSTEM

As noted above, the cholinergic system is considered to be especially critical with regard to regulation of certain types of learning and memory. To better understand the neurochemical and behavioral consequences of stress on this key brain system, this lab has studied the effects of several stressors on brain cholinergic function and behavior. As discussed above, hypobaric hypoxia was observed to cause substantial reductions in the release of acetylcholine in the rat hippocampus (Figure 23-3 above) and to impair learning and memory (Shukitt-Hale et al., 1993, 1994). The authors have also studied the effects of cold stress and restraint stress on hippocampal acetylcholine and choline levels. As shown in Figure 23-5, restraint stress causes significant reductions in acetylcholine release in the rat hippocampus. The combination of restraint and cold stress causes a somewhat larger reduction in acetylcholine release then restraint alone (Lieberman et al., 1994; Stillman et al., 1993). In addition, when only restraint stress is employed, there is a

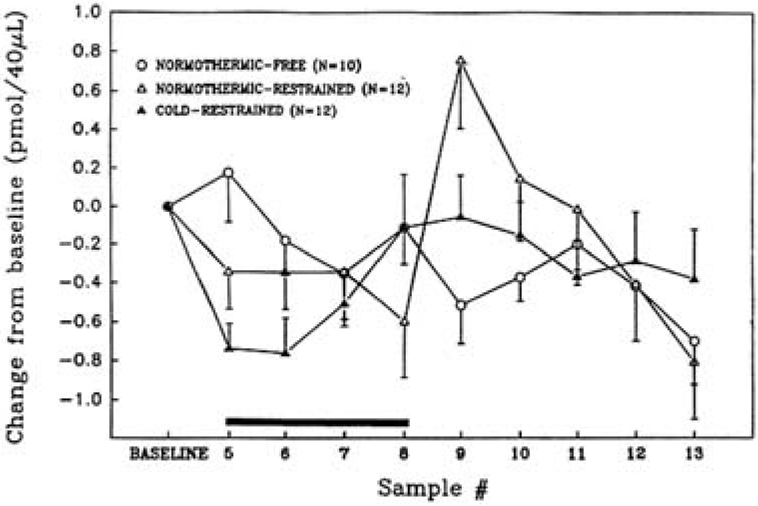

FIGURE 23-5 Effects of restraint stress alone and in combination with cold stress on hippocampal acetylcholine levels. An unrestrained normothermic group was also tested. Samples were taken every 20 minutes. Bar denotes duration of acute stress exposure for cold-restraint and normothermic-restraint conditions. SOURCE: Adapted from Lieberman et al. (1994) and Stillman et al. (1993).

large burst of acetylcholine release following removal from stress. This phenomenon does not occur in animals exposed to the more severe combination of both stressors. When learning and memory performance are assessed with the eight-arm radial maze after exposure to these stressors, animals exposed to the combination of stressors are the most severely impaired (Lieberman et al., 1994; Stillman et al., 1994) (Figure 23-6). These results support the idea that the surge in acetylcholine release among animals that are only exposed to a single stressor may contribute to behavioral recovery from stress exposure.

AUTHORS' CONCLUSIONS

As noted above, exposure to different stressors, particularly those as physiologically different in their consequences as hypoxia and cold stress, may require different types of treatment. However, if there are common CNS elements to the response of organisms to stress, common treatment strategies may be useful for a wide range of dissimilar stressors. For soldiers who are exposed to multiple stressors, a common approach to treating the adverse effects of stress would be particularly appropriate. Use of catecholaminergic agonists like tyrosine appear to be one such strategy with considerable promise. This laboratory and other research groups have reported in both animal

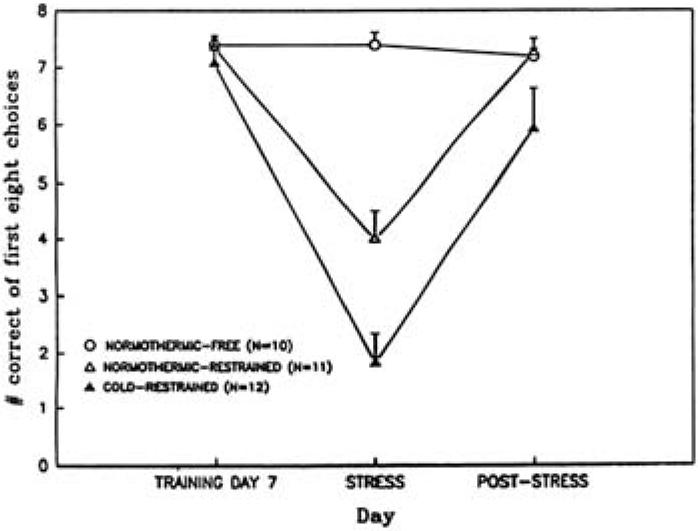

FIGURE 23-6 Effects of restraint stress alone and in combination with cold stress on learning as assessed with the eight-arm radial maze. A control, unstressed group was also tested. SOURCE: Adapted from Lieberman et al. (1994) and Stillman et al. (1993).

and human studies that tyrosine, a food constituent, has beneficial effects under conditions of hypoxia and cold, both separately and in combination. However, considerable basic research must be conducted to specify further the neurochemical mechanisms underlying various types of stress. In addition, behavioral studies that assess performance and symptoms associated with particular stressors and a variety of different treatment strategies are necessary. Whenever possible, such applied studies should be based on an understanding of the underlying neurochemical mechanisms responsible for the adverse effects of each stressor. In addition to tyrosine, certain other food constituents, particularly caffeine, should also be considered for their potential to treat some of the adverse effects of cold or altitude exposure.

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General Discussion

ROBERT SCHOENE: I would like to bring out a point that COL Schumacher made with respect to making the troops or expedition members more aware, so they know what to expect. Education about the cold has been pretty well emphasized, but I would like to make a plea for better education about high-altitude operations.

When the troops are operating in the Sierras at 7,000 to 8,000 ft (2,134–2,439 m), the problems are not generally serious. They are acclimatized and are probably at full physical capacity at that point. However, when they get higher than 8,000 ft (2,439 m), the omnipresent hypoxia exerts a subtle, mysterious effect on people, their energy, and their psychological energy. I think the troops need to know about altitude illness and what to expect when they get some of those symptoms, so they do not think they are dying. They also need to know that they will need to make extra efforts to overcome the lack of spontaneity and vigor that is inevitable at 11,000 to 14,000 ft (3,354–4,268 m).

I say this from personal experience and from my own sense of what happens. When collecting data at 20,000 ft (6,098 m), I really had to make an effort. At Denali, at 14,000 ft (4,268 m) for months, I had to make an effort. The troops must know about these effects. Perhaps there should be a more complete educational system with respect to altitude. As is often said, the commanders know this, but the troops also need to know what to expect.

MURRAY HAMLET: Physiologically, the first change that occurs is physiological vasoconstriction, resulting from both cold and high altitude. Many studies define the impact of altitude on cold injury, and clearly physiological vasoconstriction has an impact. It is essentially a mediated constrictor response. We understand a little bit about how it works.

Decreased thirst also seems to be common to both cold and high altitude. But there is a concomitant increased water requirement for some reason. Therefore, not only are you not drinking as much as you need, you need more. These two things may be synergistic in cold and high altitude.

Regarding fatigue, clearly people become more tired in cold and altitude than they would under other conditions. There is also probably an increased caloric requirement in cold and high altitude.

Therefore peripheral constriction and its relation to the ability to perform certain tasks—to do things with one's hands, for example—affects a mission. Other examples of impaired tasks are preparing food and taking one's clothes on and off.

ROBERT NESHEIM: Is there any evidence that the fatigue you are talking about can be overcome if people take in an adequate amount of calories? Is that fatigue a result of inadequate caloric intake, or is there some other physiological activity going on?

RUSSELL SCHUMACHER: Anecdotally, I would say no. I think they are getting all the calories they need. I do not think anyone suffers in that regard below 12,000 ft (3,659 m). But fatigue over time drags you down. The physical nature of the cold in conjunction with the altitude is the cause.

ROBERT SCHOENE: Sleep is a problem. I think the problem of sleep needs to be addressed, particularly above 10,000 ft (3,049 m). Periodic breathing and all the things that take place that alter the sleep patterns might be very important factors.

A. J. DINMORE: The big problem at high altitude is the fatigue upon exertion. You perception of what can be done is actually much greater than what you are physically able to do. As soon as you try to do something, you immediately hit this fatigue barrier. I think over the long term, that is very worrying.

MURRAY HAMLET: It is both a physical and mental fatigue. It is a combination of "I know I have got to do this," "I might be able to drive myself to do it," but psychologically "I do not think I want to bother."

Regarding meal preparation, ease of preparing meals is absolutely critical in cold and high altitude. If it is difficult to prepare, you are not going to do it. If it is too hard to fix, you go to bed.

A. J. DINMORE: There is a conflicting requirement here. When you go to altitude, you want to carry a very light-weight ration. When you are climbing and going on a long-range mission, carrying everything on your back, that is significantly different from a mission in cold, when the location is more static and there is more logistical backup. The conflicting requirement is between ease of preparation and trying to get light-weight rations that can be carried in the field.

NICOLE HOTSON: Has anybody ever tested how your taste is affected by high altitude?

ROBERT REYNOLDS: Yes, I think there have been a number of anecdotal studies. One study that we will be going over next month is from Mount Everest, where they are looking at changes in perception and threshold of taste as a function of altitude. Those of us who have been at high altitude know that taste perception goes down. To overcome this we added more spices. McCormick Spice was one of our sponsors, and they gave us 5 lb (2.3 kg) of cayenne pepper. It was gone within a matter of weeks.

Colonel, you mentioned flavoring agents, such as garlic, pepper, and the more subtly flavored things that will make the food more palatable, acceptable, or desirable at altitude.

ELDON W. ASKEW: Certainly taste at altitude goes out the window if you are taking Diamox (acetazolamide, a cerebral vasodilator), at least in my experience.

ROBERT NESHEIM: What I am hearing here is a common need to push water at both high altitude and cold, and when you are at altitude usually you are also experiencing cold. There is a common need to push calories in those areas, but you are not likely to overcome the difficulties of caloric intake by pushing them.

GAIL BUTTERFIELD: In the exercise community, it is pretty well accepted that you can maintain the thirst mechanism in an individual who has lost a significant amount of water as a result of heavy exercise by replacing the fluid with a fluid and electrolyte potion rather than plain water. I wonder if anybody has ever tried that to maintain a better thirst mechanism.

ALLISON YATES: Do you mean that the voluntary consumption is higher with a beverage replacement that has electrolytes?

GAIL BUTTERFIELD: Yes.

ROBERT NESHEIM: I was thinking of it not so much as a response to the thirst mechanism, but that maybe people are voluntarily willing to take in more.

GAIL BUTTERFIELD: If you take in plain water, you dilute the electrolytes that are present in the body. Therefore, you turn off the thirst mechanism more quickly than if you replace with water and electrolytes, because the electrolytes then add to the electrolytes in the body and keep the osmolarity slightly higher and promote the thirst mechanism longer.

I. SIMON-SCHNASS: I have some anecdotal data. I had some friends who were convinced they had to take electrolytes. They forced themselves to drink up to 4 liters of electrolyte-containing sport drinks at high altitude. They became sick because they lost most of the fluid by the lung (through respiration), which is distilled water. They did not sweat a lot, so they were actually overdosing. They were convinced it was good for them, even though they felt sick. I think you need to teach people what kind of fluid loss is taking place, whether it is vapor from the lungs or sweating. Then they can decide for themselves what they need to replace.

RUSSELL SCHUMACHER: I would like to address the comment on pushing food and water. The converse is that at altitude and in the cold, the failure to do so is catastrophic. The failure at sea level and with exertion does not even compare. Not just individuals are lost, but whole units, companies, and platoons. That is what is really scary about the fluid scenario from my personal experience.

ROBERT REYNOLDS: With respect to the electrolytes, I would like to suggest caution in pushing them. On our On Top Everest '89 expedition, we took zero salt. Where possible, we had a low-salt alternative for a number of the freeze-dried or the retort-pouched entrees. The first 2 weeks, there were great objections to the taste, but after 2 weeks, they were totally acceptable. People went for the spices, and I think we had lower fluid retention as a result. The acceptability of the food went up because of the additional spices.

WILLIAM BEISEL: The matter of salt and water balance is not clear to me. We heard stories about why we need to push fluid intake, as well as stories about edema and fluid in the wrong places as a major cause of catastrophe. I wonder if the committee could address this paradox in more depth?

A. J. DINMORE: From the mountaineer's point of view, the question is one of acclimatization and then chronic altitude state. During the acclimatization phase, normally there is diuresis, which is beneficial to the body in getting to high altitude. However, in any prolonged stay at high altitude, you must have that immediate increase in water intake.

MURRAY HAMLET: The endothelial cells are incapable of holding water in the vascular space. When they drop below 30 in an acid medium—in hypothermia, for example—the sodium pump dies, so they do not hold fluid in the vascular space. Thus one of the problems in resuscitation and one of the things killing hypothermics today is trying to raise their central venous pressures too fast and too early in resuscitation, resulting in fluid leaking out. Until they are warmed up to the point where those sodium pumps and endothelial cells start, they are unable to hold fluid.

Something is wrong with the endothelial cells' ability to do that at altitude. So when you are thinking about where the fluid is, you have to think about where it is going next and what kind of damage it is going to cause. Recall the pitting edema that we saw. Many people get a small amount in their hands or their feet, and I think I have seen it more in women than in men. The edema is transient; it lasts a day or two and then goes away. It is related to endothelial cell function somewhere in the extremities, but it is not clear what is wrong with them, why, and what we can do about it.

We do not know what to do about it in resuscitation, other than warming them up.

ROBERT SCHOENE: I think Bill's point is a very good one. You hear us say, push fluids with increasing altitude, and you heard me say this morning that all the pathological effects are due to fluid in the wrong place. I think Murray is right that the endothelium is the culprit.

In my view, if we can maintain optimal intervascular volume, optimal cardiac output, and optimal oxygen delivery in a hypoxic situation, we will minimize whatever the effect of hypoxia is on making the endothelium leak. It happens in the intensive care unit all the time. Endotoxins may play a role, but there is something about hypoxia that triggers permeability in the vascular endothelium. So if we can optimize oxygen delivery and minimize hypoxia during acclimatization, then I think we will minimize altitude dysfunction.

Once it is leaking, I do not know what the solution is. The point is, you do not want to volume deplete people at altitude.

ALLEN CYMERMAN: I wanted to talk about sleep at altitude. I think once you get over the illness stage and you still have the troops in a high-altitude situation, sleep is paramount. Sleep disturbances continue for a long period of time after that. If the committee could come up with something like a hot glass of milk as a solution, it would be perfect. In that sense, if Harris has done something with serotonin or any of the serotonin analogs, where there are no aftereffects on both mental and physical performance the next day, I think we would go a long way toward helping the soldier at high altitude.

WILLIAM BEISEL: I worked on the original studies in the late 1950s that solved the problems with fluid electrolytes and cholera, so fluid and electrolytes have been in my field for a long time. You are saying we have to worry about something that does not follow the rules, like capillary leak problems. If we are going to anticipate capillary leak problems, perhaps we should be thinking about it during indoctrination and training, at least for a certain period of time, to anticipate it and protect our troops in some way. I do not see this in any of the written guidelines. Do we need a new set of guidelines that anticipate the problems of cerebral edema and other conditions that can be life threatening?

MURRAY HAMLET: There is not enough predictability in those conditions to be able to warn anybody ahead of time. However, there are certain people who are going to get cerebral edema, and others who are going to get pulmonary edema. We know there is some past history that would affect their susceptibility. But I do not think there is a general statement we can make that is a prognosticator of edema in the extremities, or cerebral edema, for example, other than prior exposure or prior injury. It would be nice if there were; it would solve a lot of our problems.

We have looked at cold-induced dilation of the extremities to see if that might be a predictor of people who get sick at altitude. We did not pursue it, but we wondered if someone whose peripheral sympathetic system really constricts badly at high altitude or at moderate altitude may be the one who is going to get sick first.

WILLIAM BEISEL: Is acute mountain sickness or acute edema strictly a phenomenon of the first few days, or can it occur any time?

ROBERT SCHOENE: Any time. Most commonly it occurs in the first 6 to 40 hours, but I have seen it occur after a couple of weeks at high altitude.

ALLEN CYMERMAN: Change in altitude is what does you in with cerebral edema and pulmonary edema, but they are probably not the same.

WILLIAM BEISEL: These are life- threatening conditions. My first thought as a physician is, take care of the life-threatening things, and the other things can be solved later.

ROBERT SCHOENE: It can occur at any time. That is why I emphasized this morning that education and knowledge where HAPE (high-altitude pulmonary edema) can occur will prevent any fatalities.

WILLIAM BEISEL: Part of the training of the soldiers and leaders should be the recognition of the early symptoms. We must prepare the leadership and the soldiers to pick it up in each other—a buddy system kind of management.

RUSSELL SCHUMACHER: In the Marine Corps, it is.

MURRAY HAMLET: Fortunately we have a quick treatment in place, so there is a built-in process. But the one that scares me is when people who develop pulmonary edema go down, recover, and then climb again. I grip my chest on that one. I would not want to be the doctor on that trip. That is scary.

JOHN VANDERVEEN: Is there enough training for physicians in this area? Do the military programs and other programs cover this well?

RUSSELL SCHUMACHER: The Navy does. The Navy has a cold-weather medicine program that covers the subject in total. They do it at my base.

JOHN VANDERVEEN: Is it your experience in dealing with physicians in this area that they are knowledgeable enough in how to treat acute cases?

ROBERT SCHOENE: In general, no. Two years ago when I was in Colorado, helping to run the Colorado Altitude Research Institute, many of the physicians at high altitude were not good with altitude illnesses, let alone the doctors who would call from low altitudes and ask whether their patient with a particular condition could tolerate high altitude. I think the education is very thin.

JOHN VANDERVEEN: Specialization might be an area that we could consider suggesting as a follow-on.

DAVID SCHNAKENBERG: Two years ago when the Ration, Cold Weather (RCW) was developed, the Army Surgeon General was asked for recommendations on nutritional composition. We went to the committee for advice. We were advised that for a cold-weather ration for use by troops during operations, we should minimize the sodium and protein contents (compared to the Meal, Ready-to-Eat) because it would reduce somewhat the obligatory water requirements of the soldiers in an environment where liquid water could be scarce. Thus the Ration, Cold Weather was designed so that even if you eat the 4,500 kcal, there are only about 4,500 mg of sodium, that is, 1 mg of sodium per calorie. It contains approximately 90 g of protein in those 4,500 kcal, which is considerably less than the MRE, which would be over 150.

Based on what we have heard today and during this meeting, are those levels still appropriate for a cold-weather operation? Is that ration appropriate for the first few days of an altitude operation, relative to the electrolytes question that was asked, so that the troops must drink water along with it?

Should we have less sodium the first few days, or should we have a carbohydrate-electrolyte supplement during the first few days of altitude operation to address the issue of trying to maintain the body's hydration in the appropriate compartments?

That is a complicated question, but I think it is a practical one that comes back to the Surgeon General giving advice to Irv Taub and his colleagues in putting together this ration.

MURRAY HAMLET: You lose palatability quickly.

ROBERT NESHEIM: Is there any risk of hyponatremia with the RCW? Anecdotally, I think I heard somebody report that.

ELDON W. ASKEW: I have a letter from a member of the Special Forces —a medic—who had been on a climb in Alaska. He had been working hard, sweating quite a bit, even though it was a cold-weather climb. Several members of the team had become exhausted, and in his opinion, they were salt depleted. He had to start intravenous salines to bring them around. He stated that there ought to be more sodium in the Ration, Cold-Weather.

This is the one dissenting opinion we have had so far. Nevertheless, if he is correct, it is significant. I think maybe he had exhaustion, glycogen depletion, and dehydration more than sodium depletion, but I would be interested in hearing a comment on this.

ELSWORTH BUSKIRK: I think David has raised the issue of timing. Because the troops are going in under conditions where early on they will be sweating heavily, they do need some sodium under many circumstances. But I do not think they need as much sodium as some of these rations contain.

HARRIS LIEBERMAN: I would like to comment on behavioral problems and what can be done about them. Someone brought up the issue of sleep. Clinically, there are medicines that help people sleep. You can get a prescription from your physician, take a benzodiazepine, and you will sleep better at high altitude. The question is, can you perform adequately the next day? There is a complicated answer to that question. It depends on the half-life of the benzodiazepine prescribed, the dose taken, and the person's sensitivity to the drug.

There are also a series of other drugs that are less potent than benzodiazepines, will not help your sleep as much, but clearly do not have the next-day aftereffects. For example, antihistamines are reasonably potent sedatives. In fact, one can buy a lot of over-the-counter sleep aids, which are nothing but antihistamines, and they work to a certain degree. In that same potency range, between antihistamines and benzodiazepines is a hormone, melatonin, which seems to have clear sleep-promoting effects at very low doses, and which does not seem to have the next-day aftereffects. It is in the process of being developed by a number of drug companies and will probably be available in the next few years.

Then the final issue and maybe the one that is most interesting here—the nutrient and amino acid, tryptophan. We had to stop working on tryptophan when contaminated tryptophan was being sold by one company. We need to consider whether people are interested in having some kind of nutrient that will help them sleep.

Tryptophan does not have aftereffects. It is not nearly as potent as benzodiazepines and not as potent as melatonin, but it is a nutrient.

Finally, I want to comment on the converse: The issue of being too tired during the day. Part of that fatigue is probably attributable to poor sleep—the interrupted sleep that produces next-day fatigue. However, I believe that there is a malaise syndrome present at high altitude, and the way to deal with that is probably not nutritionally. I think you could treat maybe 20 or 30 percent of the problem with proper use of caffeine during the day. Timing the caffeine consumption is important to avoid interfering with sleep. But it is a viable option for increasing mental performance during the day at altitude.

PARTICIPANT: How much tryptophan do you have people take?

HARRIS LIEBERMAN: We have given people 50 mg/kg.

ROBERT SCHOENE: Regarding the sleep issue, 10 years ago, Dalmane was being used, which did have prolonged effects and did give people a hangover the next day. That happened on Mount Everest. Someone almost fell off the south face because he was very ataxic.

A couple of other considerations. You want to make sure that whatever you give, it is not a respiratory depressant. Some of the benzodiazepines in larger doses are respiratory depressants, and you want to avoid that. Halcyon has been used in low doses. It is probably short-acting enough that there will not be a next-day aftereffect, and it does not suppress ventilation.

One of the things that will interrupt sleep is periodic breathing. In a very low dose, Diamox or acetazolamide is recommended for sleep, not because it is a sedative, but because it stops periodic breathing and allows people to sleep comfortably through the night.

RUSSELL SCHUMACHER: No commander in his right mind is going to give his front-line troops any kind of sleep inducer. If you have that kind of problem, you will pull your forces off that line and replace them. At high altitude, you are using special operation-type forces, and in those cases, maybe you would do that. But whether you are in the United States or Bosnia, Iran, Turkey—places in the world where there might be problems with high altitude but the altitudes still are not high enough to produce the level of sleep loss that could necessitate sleep inducers.

ROBERT NESHEIM: Your point is well taken. Most of the altitudes we are dealing with are in the more moderate ranges.

ROBERT POZOS: Some of us are caught up in the euphoria of some of these nutrients. I want to caution the entire group about glycerol. This idea of hydration and glycerol is a very debatable issue. Whether it promotes some kind of intracellular or extracellular movement of fluids and enhances performance is extremely debatable. What always bothers me is that some of these notions get into the folklore very fast and then are implemented with disastrous consequences.

Regarding the issue of salt and hydration, millions of corporate dollars have been spent looking at this specific issue. Yet there is no clear answer to it. The question you raise is excellent, but we do not have a scientific basis for electrolyte drinks and their effectiveness in these kinds of unique environments. I think we must be very cautious. We do not want COL Schumacher's successor coming down on us later because we made recommendations that were not solidly based on scientific fact.

A. J. DINMORE: I have a specific question for Dr. Taub about fluid intake and working in cold environments. As pointed out earlier, you normally melt your water in the morning. You make your food and then you fill up a hot flask, which you carry with you during the day so you can drink from it. I was surprised that your Ration, Cold Weather doesn't have any liter-sized beverages in it. How are soldiers able to make and carry a liter of fluid when they only have a few fluid ounces of drink mix in the ration?

ROBERT NESHEIM: Colonel, I think you commented on that. You indicated that you do not encourage people to melt snow or ice.

RUSSELL SCHUMACHER: No, snow or ice is not a problem. We do encourage that. But they must make sure it boils. All our forces have vacuum flasks in their kits.

A. J. DINMORE: That is the point I am making. They use a vacuum flask, which is 1 liter in size, and they heat water from whichever source in the morning to make this hot drink. But they do not actually have a liter of hot drink mix in their cold-weather rations. It comes in much smaller cup sizes.

RUSSELL SCHUMACHER: That is a good point.

GAIL BUTTERFIELD: Until we adequately nourish people and see what the differential effect of high altitude is, we will not know what is going to happen with salt and fluid. With adequate nourishment, we may eliminate some of the problems we have been talking about. That is a lot simpler then making a potion that has something artificial in it, such as glycerol or a high-caffeine drink that puts people on a jag.

ROBERT NESHEIM: What you are saying is get the calories into them that are more correspondent to their expenditure.

GAIL BUTTERFIELD: And then see what falls out as being additional needs. Until the basic needs are met, I think we are shooting around.

HARRIS LIEBERMAN: I do not agree with that. When we deprive people of food under normal conditions, we have to make them severely calorie deficient for long periods of time before we see any performance decrements. So a couple of days of inadequate nutrition are simply not going to have any effects on mental performance, although it may on physical performance. As far as mental performance is concerned, if you want 100 percent performance, you have to consider that you may not get it simply with adequate nutrition.

JOËL GRINKER: If you have knowledgeable subjects as opposed to naive subjects, are they aware of these performance effects?

HARRIS LIEBERMAN: Which effects, Joël?

JOËL GRINKER: In terms of their being able to show less of a decrement in performance. Are they able to verbalize that?

HARRIS LIEBERMAN: That is a good question. The question is, if you produce performance improvements by giving people things, can you ask them if they have improved performance? Can they detect it themselves? The answer is, it depends how potent the substance is that you give them.

In general, the kind of improvements we get with nutrients are of a magnitude where it is difficult to detect the improvement, with the possible exception of caffeine. I am talking about mental performance.

ROBERT NESHEIM: We have a real challenge as a committee now to sort through all of this excellent information, largely physiological in nature, and then translate it into nutritionally-related recommendations as applied to cold weather and high altitude.

APPENDIXES

A

Environmental Stress Management at High Altitudes by Adaptogens

Summary of Unpublished Manuscript Presented by
K. K. Srivastava[1]

Several crude plant and animal preparations, which are generally ill-defined chemically, have been used for ages in many oriental systems of medicine for managing stress and increasing endurance. Such products have been called adaptogens. However, evidence for the efficacy of such medicines, despite their age-old and world-wide use, in well-controlled experiments is lacking. Therefore, such preparations and their effects are considered largely unsubstantiated and unfounded.

An experimental animal model for evaluating adaptogens and their antistress effect was described. In this model, the physiological response monitored under multiple stresses was the capacity of the homeothermic animal (rat) to maintain core body temperature in a hypobaric cold chamber. Any antistress effect of a preparation observed in this model would presumably represent a general antistress effect. A composite Indian herbal preparation (the crude drug powder, a commercial preparation of CIHP available in India called

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Geriforte) was tested with this model, and it was found to be a strong antistress adaptogen. The long-term administration of CIHP to rats (6 weeks) at a dose of 1 mg/g body weight increased the duration of time to reach a core temperature of 23°C (73°F) by 72 percent and decreased the recovery time by 46 percent. Results obtained with this experimental animal model suggest that CIHP administration induces significant thermoregulatory tolerance to cold and hypoxia.

In a subsequent placebo-controlled, double-blind trial of CIHP, human male volunteers, who remained at extreme altitudes (4,800 to 6,000 m [15,748 to 19,684 ft]) for a period of 3 or 6 months, were tested for various indices at 3,050 m (10,007 ft) prior to their induction to higher altitudes (4,800 to 6,000 m [15,748 to 19,684 ft]) and again 6 months after their return to the plains after the high-altitude stay. Environmental stresses at the higher altitudes consisted of hypobaric hypoxia (420 to 335 mm Hg), low temperature (-40° to 0°C [-40° to 32°F]), high-velocity winds (0 to 150 km/h), and sunlight, which created intense heat, blinding reflection on the snow, and increased ultraviolet and ionizing radiation. The psychological stresses consisted of isolation, uncertainty of weather conditions, and enhanced physical exertion.

A randomly assigned group of 14 men remained and worked in the high mountains for a period of 3 months, and a second group of 30 men remained for 6 months. Each group was further divided at random into two subgroups. The subgroups were given placebo or CIHP tablets. The volunteers were examined a second time at 3,050 m (10,007 ft) within 7 days of their descent from the high mountains. The third set of data was recorded 6 months after returning to the plains from altitude.

During the human subjects' prolonged stay and work for 3 months in the high mountains (4,800 to 6,000 m), the placebo-administered group lost 3.3 percent of their body weight. The group given CIHP lost 2.67 percent of their body weight. After returning from high altitude and staying 6 months in the plains, subjects gained body weight, which exceeded their initial body weight by 1.65 percent and 4.75 percent in placebo and CIHP groups, respectively. These data show that the administration of adaptogens in a high-altitude environment helped to maintain subjects' body weight and, on returning to the plains, helped further to increase body weight, even though the administration of adaptogen was discontinued after the return from high altitude. However, in subjects who stayed 6 months at high altitude, the loss in body weight could not be arrested by CIHP administration. Gain in body weight during their stay in the plains also did not exceed significantly their initial body weight.

The effect of high altitude on some of the higher cognitive functions of humans indicated that the perception and concentration functions deteriorated after a stay of 3 months in the high mountains. These functions recovered fully on return to lower altitude within 6 months. In those subjects who were given CIHP at high altitude, a deterioration in perception was not observed. Deterioration in concentration was observed in subjects give CIHP ($p < 0.05$).

CIHP was able to restore the deterioration in perception and concentration functions in subjects who stayed in the high mountains for 6 months, but the vigilance function deteriorated to the same extent both in subjects given placebo and those given CIHP. Upon return to the plains, all of the higher functions of the brain described above recovered fully in the placebo group, as well as in the adaptogen group.

The oxygen consumption during rest and on maximal exercise before and after exposure to extreme altitudes in the plains had been studied. The maximal exercise oxygen consumption did not show any significant difference between placebo- and CIHP-administered volunteers at the end of 3 and 6 months of stay at extreme high altitudes. However, on return to the plains the oxygen consumption on maximal exercise was significantly elevated in CIHP-given volunteers as compared with the placebo group, suggesting an increased exercise tolerance and endurance capacity. The increase in creatine phosphokinase in circulation on prolonged stay at extreme high altitudes (125 percent) was found to be restricted (30 percent only) in CIHP-given volunteers, suggesting improved skeletal muscle and/or neural tissue oxygenation.

Evidence of adequate heart oxygenation in adaptogen-administered subjects in the high mountains was obtained from the electrocardiographic observations of subjects. In placebo-administered subjects 42.8 percent (three out of seven) showed a right axis shift of 10° to 30°. The CIHP-administered subjects did not show any electrocardiographic abnormalities. After 6 months of stay at high altitudes, CIHP administration had reduced the magnitude of axis shift and T-wave changes. The reduced incidence and magnitude of right axis shift in CIHP-administered subjects is suggestive of decreased right ventricular load. This might have occurred due to the decrease in high altitude-induced pulmonary hypertension in adaptogen-administered men.

The observations on human subjects exposed to a high-altitude environment of 4,800 to 6,000 m (15,748 to 19,684 ft) for a prolonged stay of 3 or 6 months suggest that remaining at these altitudes was accompanied by a loss in body weight, deterioration in mental and physical performance, cellular oxygenation, and cardiac stress. Administering the adaptogen CIHP arrested either partially or fully such changes when the stay was restricted to 3 months. CIHP was not able to reverse the high altitude-induced deterioration in most of the functions when the stay was prolonged to 6 months. However, the changes were fully reversed upon returning to the plains within a period of six months. The changes in $\dot{V}_{o2}$ max showed improvement in the adaptogen-administered group as compared with the placebo-administered group upon return to the plains.

In conclusion, the animal and human studies described herein suggest that CIHP administration is effective in maintaining and assisting thermoregulation in a challenging cold and hypoxic environment. Furthermore, CIHP can arrest the altitude-induced physiological deterioration to some extent in humans. These studies have proven, to a reasonable extent, that CIHP has antistress and adaptogenic action. CIHP is representative of a large number of formulations described as rasayan in ayurveda and several preparations of other oriental systems of medicine. These drugs or food supplements have the potential to act as rejuvenators and vitalizers for the strengthening of healthy humans. A large trial of CIHP, with a view to reducing cold- and hypoxia-induced injuries and diseases in extreme cold and high-altitude areas beyond 5,000 m (16,404 ft), is indicated.

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B

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C

Abbreviations

α-TE	α-tocopherol equivalent
ACTH	adrenocorticotropic hormone
ADH	antidiuretic hormone
AFFS	Army Field Feeding System
AGARD	Advisory Group for Aerospace Research and Development
AMS	acute mountain sickness
AMS-C	acute mountain sickness-cerebral
ANF	atrial natriuretic factor
ANP	atrial natriuretic peptide
APRE	U.K. Army Personnel Research Establishment
AR 40-25	Army Regulation 40-25
BMR	basal metabolic rate
BTPS	body temperature pressure saturated
BV	blood volume
CID	cold-induced diuresis
CMNR	Committee on Military Nutrition Research
CNS	central nervous system
CRTC	U.S. Army Cold Regions Test Center
CSF	cerebrospinal fluid

CSIR	Council for Scientific and Industrial Research
DCIEM	Defence and Civil Institute of Environmental Medicine, Department of National Defence, Canada
DISCOM	Division Support Command
DLW	doubly labeled water
DoD	Department of Defense
DSA	Division Support Area
ECV	extracellular volume
ECWCS	U.S. Army Extended-Cold-Weather Clothing System
EEG	electroencephalogram
EMG	electromyogram
EOG	electrooculogram
ERPF	effective renal plasma flow
ESADDI	Estimated Safe and Adequate Daily Dietary Intake
ESQ	Environmental Symptoms Questionnaire
FAO/WHO/UNU	Food and Agricultural Organization/World Health Organization/United Nations University
FAD	flavine adenine dinucleotide
FEV_1	forced expiratory volume in 1 second
FFM	fat-free mass
FIO_2	fraction of inspired oxygen
FNB	Food and Nutrition Board
GFR	glomerular filtration rate
GPX	glutathione peroxide
HACE	high-altitude cerebral edema
HAPE	high-altitude pulmonary edema
HPVR	hypoxic pulmonary vasoconstrictive response
HVR	hypoxic ventilatory response
ICV	intracellular volume
IOM	Institute of Medicine
ISA	iodinated serum albumin
IU	international unit
KCLFF	Kitchen Company Level Field Feeding equipment
LLRP	Long-Life Ration Packet
LRP I	Long-Range Patrol, Improved
LRP II	Long-Range Patrol II
MIG	micronutrient intake goal
MKT	Mobile Kitchen Trailer
MRDA	Military Recommended Dietary Allowance
MRE	Meal, Ready-to-Eat
MWM	Morris water maze
NAD	nicotinamide adenine dinucleotide
NE	norepinephrine
NMR	nuclear magnetic resonance

NRC	National Research Council
NRDEC	U.S. Army Natick Research, Development and Engineering Center
P_B	barometric pressure
P_{O2}	partial pressure of oxygen
PERC	Performance Enhancing Ration Component Program
PL	pyridoxal 5'-pyridoxal
PLP	pyridoxal 5'-phosphate
POMS	Profile of Mood States
PRA	plasma renin activity
PV	plasma volume
RBF	renal blood flow
RCW	Ration, Cold Weather
RDA	Recommended Dietary Allowances
RE	retinol equivalent
REM	rapid eye movement
RER	respiratory exchange ration
RLW	Ration, Lightweight
SAD	seasonal affective discord
SL	sea level
SUSV	Small Unit Support Vehicle
TBARS	thiobarbituric acid reactive substances
$TBNa_E$	total body exchangeable sodium
TBW	total body water
TEC	thermogenic effect of cold
TEE	thermogenic effect of exercise
TEF	thermogenic effect of feeding
TEMPER	Tent, Expendable, Module, Personnel
TISA	Troop Issue Subsistence Activity
TOC	Tactical Operations Center
TO&E	Table of Organization and Equipment
T Ration	Tray Ration
T_{re}	rectal core temperature
TRH	thyrotropin-releasing hormone
TSH	thyroid-stimulating hormone
T_{sk}	skin temperature
USARIEM	U.S. Army Research Institute of Environmental Medicine
$\dot{V}_{O2}$ max	maximal oxygen uptake

D

Factors Related to Nutritional Needs in Cold and in High-Altitude Environments—A Selected Bibliography

On the following pages is a selection of references dealing with the factors related to nutritional needs in cold and high altitude environments. This bibliography was compiled from the joint reference lists of the 23 chapters in this report, selected references from a limited literature search, and references recommended by the invited speakers as background reading for the workshop participants. As a result, references that are historical in nature are included in this listing with the most current studies on factors related to cold and high altitude environments.

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