



Acute Mountain Sickness (AMS)

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Conflict of Interest Statement

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GSK, Glenmark, Hermes Arzneimittel, Hoffmann LaRoche, India Serum
Institute, Medicago, Pfizer, r-biopharm, Sanofi Pasteur, MSD Sharp &
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May, 23rd, 2019



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EXPLORERSWEB

HOME BREAKING NEWS EXPEDITIONS SIZE

Everest's Lonely North Side Summited Today

May 23, 2019

By [unreadable]

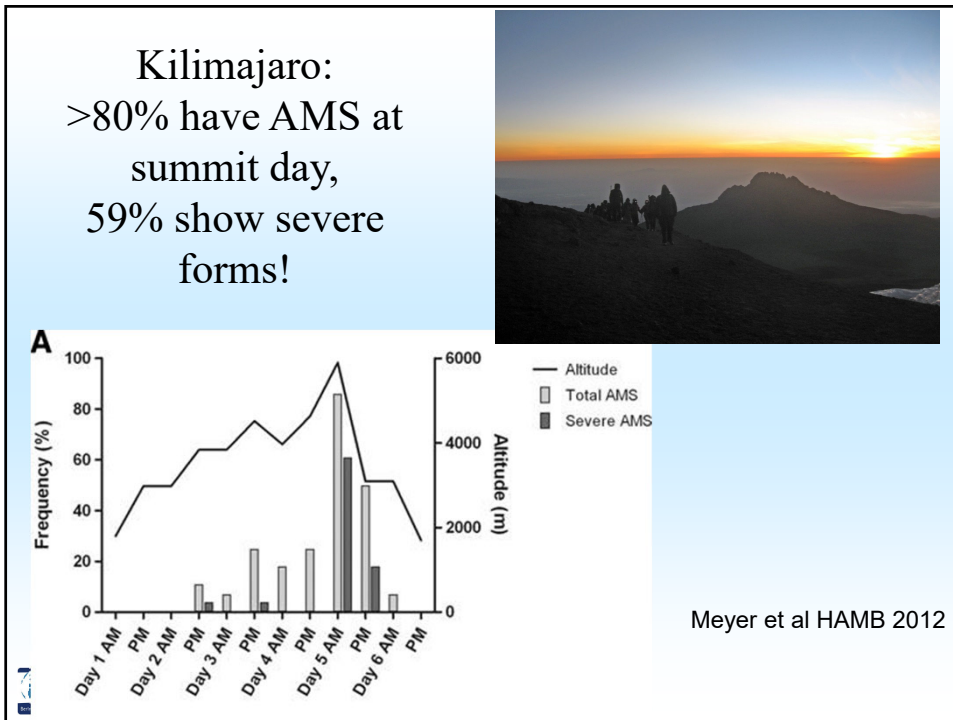


Climbing guide Mingma South on the summit of Everest. Photo: Expedition Adventure

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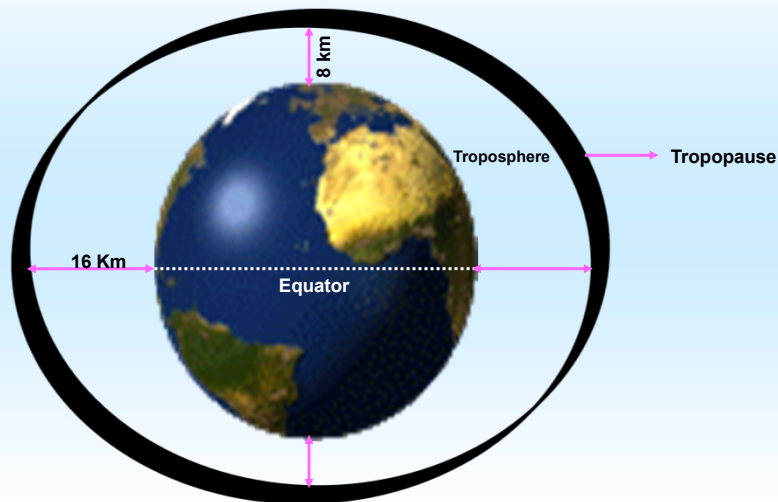
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Why do we develop altitude sickness?

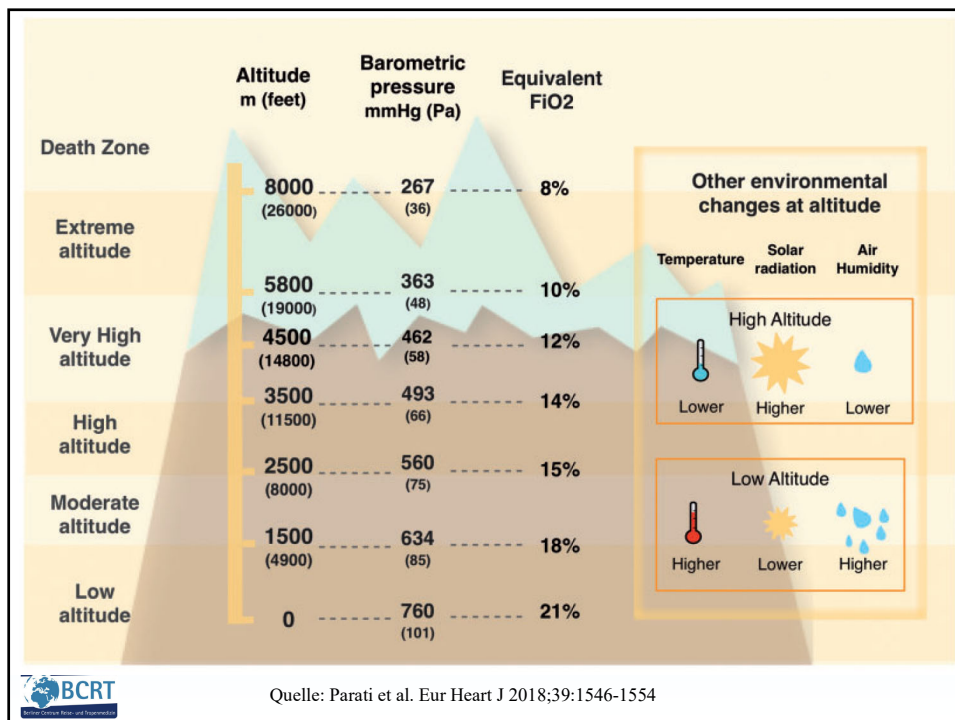


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Air Pressure in the Troposphere




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Hypoxia: Early Physiological Adaptation

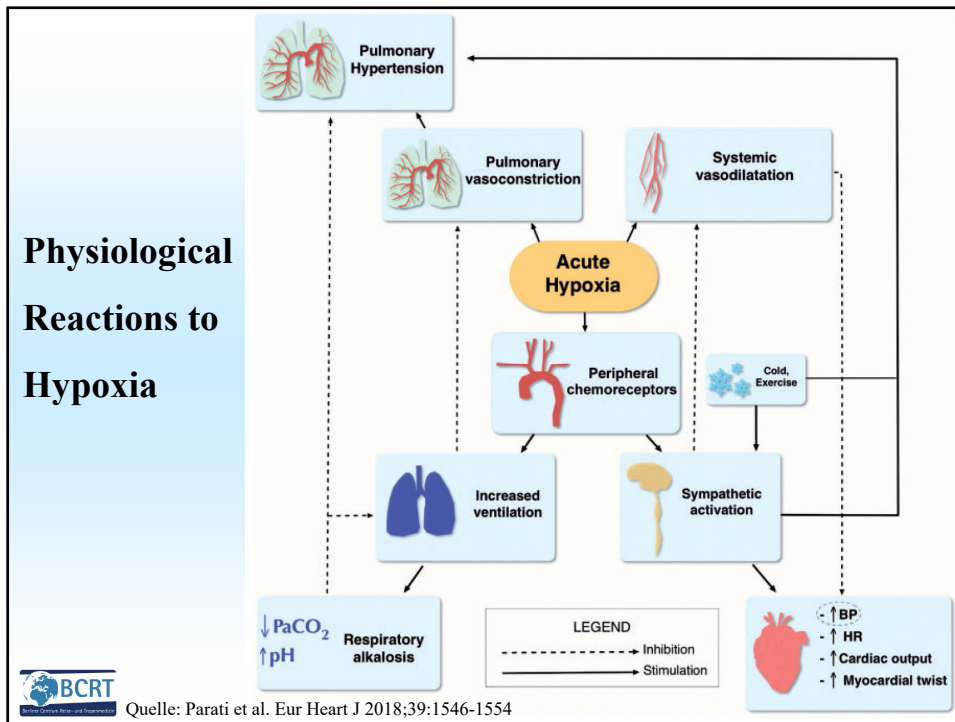
- Increase of Ventilation
(up to 200 l / min*, Resp. Rate 80 /min*)
- Pulmonary Hypertension
- Reduction of Pulmonal Shunts
- Increase Cardiac Output
- Splenic Contraction[§]
- Hb-Increase through
 - Erythropoietine-Increase[§]
 - Shifting of Oxygen Binding Curve



* West et al, 1983, J Appl Phy
§ Richardson et al, Eur J Appl Physiol 2007
SDe Brujin et al. Eur J Appl Physiol 2008

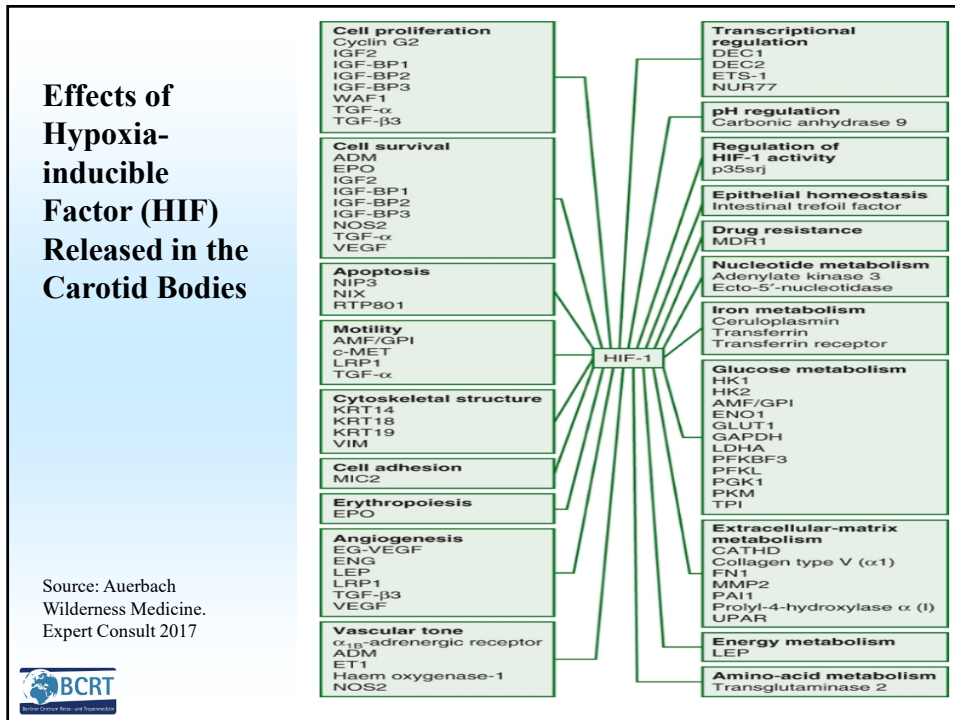
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Physiological Reactions to Hypoxia

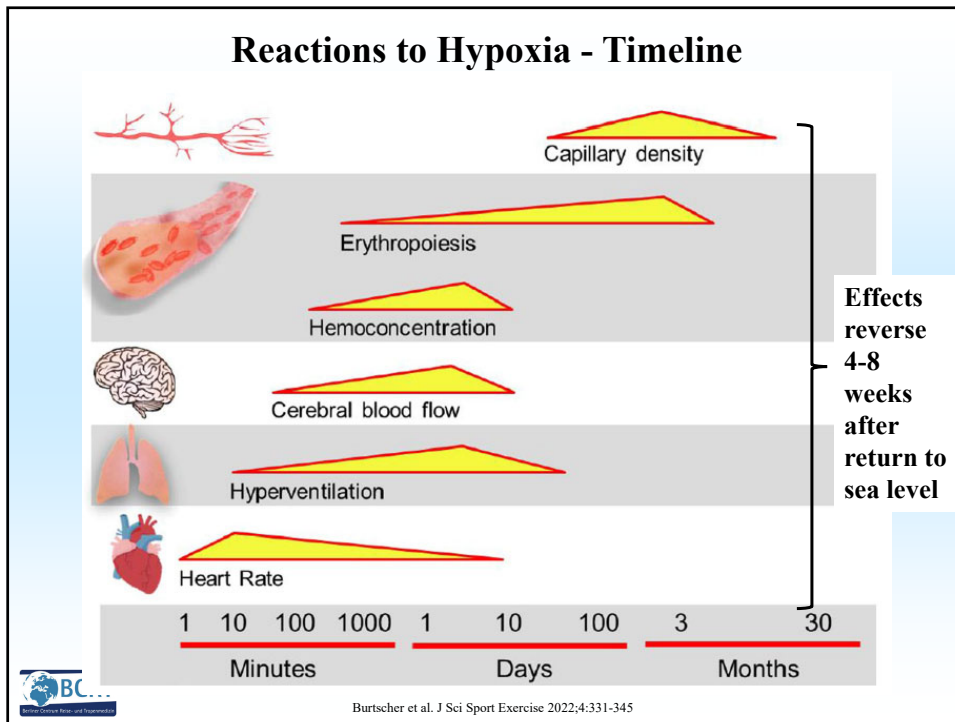


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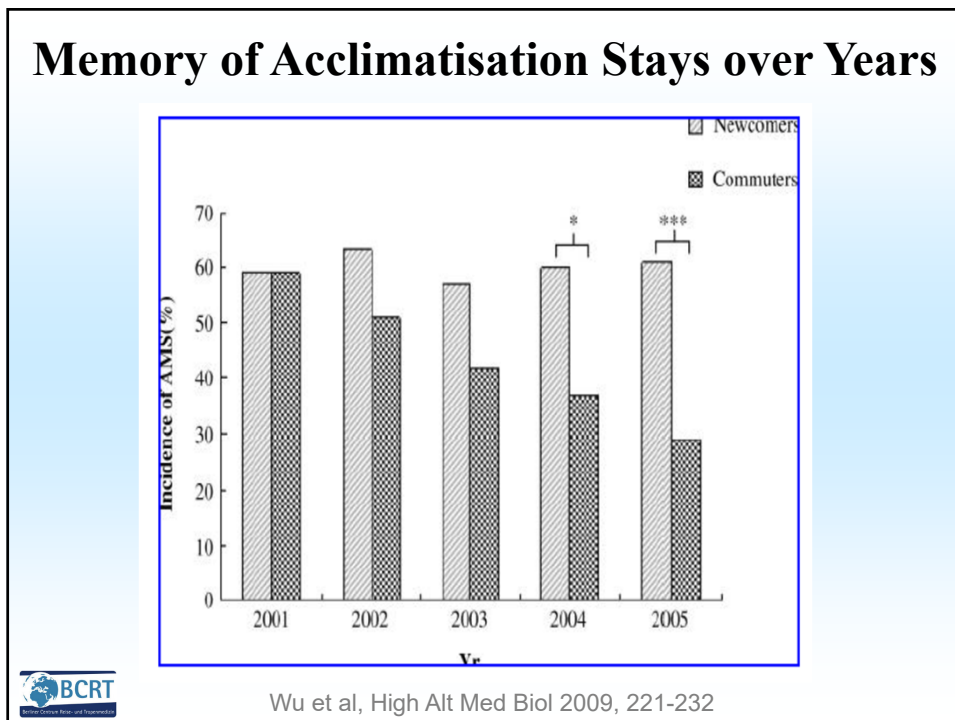
Effects of Hypoxia-inducible Factor (HIF) Released in the Carotid Bodies



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Forms of Acute Mountain Sickness

Cerebral Manifestations

Acute Mountain Sickness (AMS)

High Altitude Cerebral Edema (HACE)



Pulmonal Manifestations

High Altitude Pulmonary Edema (HAPE)

High Altitude Lymph Edema (HALE)

High Altitude Retinal Hemorrhages (HARH)



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AMS - Symptoms

- **Headache**
- Nausea
- Vomiting
- Fatigue
- Insomnia
- Loss of appetite
- Drowsiness



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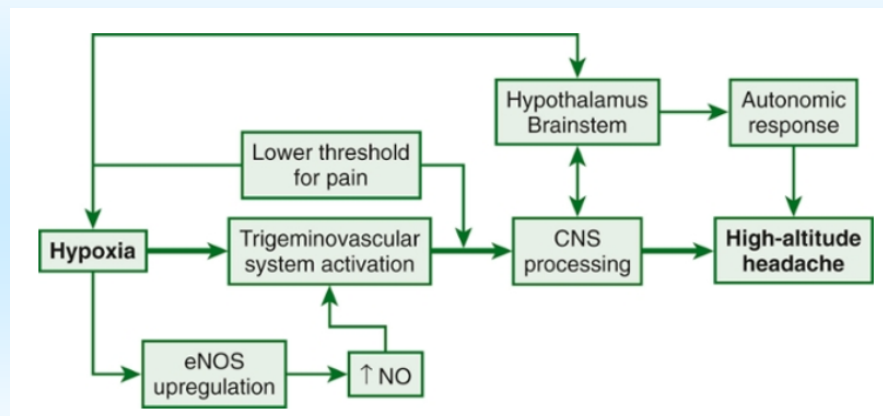
Reasons for AMS and HACE

- Hypoxia
- Increase of cerebral blood flow
- – Increased vascular permeability
- – Cerebral Edema



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Pathophysiology of High Altitude Headache



Source: Auerbach Wilderness Medicine, Expert Consult 2017

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Who is at Risk for AMS ?

- *No Correlation of AMS/HACE with*
 - Fitness
 - Smoking
 - Diet
 - Sex (maybe more frequent in woman?)
 - Cerebral blood flow
- *Correlation with*
 - SaO2 at arrival at altitude
 - Level of exercise
 - Age



Special Reports

The 2018 Lake Louise Acute Mountain Sickness Score

Robert C. Roach,¹ Peter H. Hackett,² Oswald Gatz,³ Peter Birtbeck,⁴ Andrew M. Laks,⁵ Martin J. MacInnis,⁶ J. Kenneth Kettle,⁷ and The Lake Louise AMS Score Consensus Committee.

Abstract

Roach, Robert C., Peter H. Hackett, Oswald Gatz, Peter Birtbeck, Andrew M. Laks, Martin J. MacInnis, J. Kenneth Kettle, and The Lake Louise AMS Score Consensus Committee. The 2018 Lake Louise Acute Mountain Sickness Score. *High Alt Med Biol*. 19(4): 2018. The Lake Louise Acute Mountain Sickness (AMS) scoring system has been a useful research tool since first published in 1991. Recent studies have shown that disturbed sleep at altitude, one of the five symptoms used for AMS, is more likely due to altitude hypoxia per se, and is not closely related to AMS. To address this issue, and also to update the Lake Louise AMS score to high altitudes of experience, experts in high altitude research met to revise the score. We have present an international consensus consensus involving 100 leading the symptoms and symptoms of the International Society of Mountain Medicine World Congress in Bergamo, Italy, in May 2018 and all the International Hypoxia Symposium in Lake Louise, Canada, in February 2015. The consensus group has revised the score to estimate a standard score in questionnaire form, and has defined instructions for use of the score.

Keywords: AMS; high altitude; illness; history; Lake Louise; symptom scores

Consensus members: Edw. Achter, United States; Edw. Achter, Australia; Jan S. Andrew, United States; James D. Faulkner, United States; Mohammad Jafar Jafari, Iran; Paul Armstrong, United States; Judith Berman, Nepal; Beth A. Bealman, United States; R. B. Bealman, The Netherlands; Mark Berman, Austria; Khaled F. Black, Switzerland; Peter Birtbeck, Italy; Mustafa Ceylan, Italy; Donald Cook, Austria; Alan Coombs, United Kingdom; Alexey O. Davydenko, United States; Eyal D. DeGroot, Slovenia; Cameron Duncan, United Kingdom; David Durrant, United States; Joseph P. Evans, Slovakia; Michael Fagan, Switzerland; Matt Gaudin, United States; Prasad Ganapathi, India; Michael P.W. Geary, United Kingdom; Debra Hackett, Canada; David Hall, United Kingdom; David Hillbrand, United Kingdom; Markus Hutter, Switzerland; George Hwang, India; Benjamin Hurn, United States; Scott Jacobson, United States; Joseph Kasper, Switzerland; Erika Kaye, United States; Michel Kienast, Canada; Kanaoka Koji, India; Arnon Kuper, United Kingdom; Benjamin D. Lester, United States; Matt Lofthouse, Switzerland; James MacInnis, United Kingdom; Marka Madsen, Italy; Maria Magagnoli, Switzerland; Daniel Martin, United Kingdom; Sagar Mawanya, Japan; John McCall, Canada; Scott M. Mitchell, United States; Gregor Miska, Switzerland; Timothy Moya, Chile; Craig Osborne, United Kingdom; Stephen R. Olson, United States; Norman Owen, United Kingdom; Gopal Pooni, India; Roger Poyser, United States; Lutz Phillips, United States; Anthony Ryan, France; Phillip A. Parker, Germany; Maurizio Pini, Canada; Martin Rink, India; Praveen Ramesh, United States; G. H. Li, P.R. China; Steve Rice, Canada; Steven Vetter, France; Fatima Rifaat, Canada; Scott Rennie, United States; Giovanni Sgarbi, Italy; Andrew W. Seaballs, United States; Erik Swenson, United States; A. A. Bigger Thompson, United Kingdom; Robert Tovey, United States; Bruce Topping, Canada; Silvio Trevisan, United States; David Vanderschueren, United States; Robert Walker, United States; Mark Wilson, United States; Robert Wilkes, United Kingdom; Gabriel Williams, Germany; Michael Yarn, United States; Ron Zolton, United States.

TABLE 1. 2018 LAKE LOUISE ACUTE MOUNTAIN SICKNESS SCORE

Headache	0—None at all
	1—A mild headache
	2—Moderate headache
	3—Severe headache, incapacitating
Gastrointestinal symptoms	0—Good appetite
	1—Poor appetite or nausea
	2—Moderate nausea or vomiting
	3—Severe nausea and vomiting, incapacitating
Fatigue and/or weakness	0—Not tired or weak
	1—Mild fatigue/weakness
	2—Moderate fatigue/weakness
	3—Severe fatigue/weakness, incapacitating
Dizziness/light-headedness	0—No dizziness/light-headedness
	1—Mild dizziness/light-headedness
	2—Moderate dizziness/light-headedness
	3—Severe dizziness/light-headedness, incapacitating

AMS Clinical Functional Score

Overall, if you had AMS symptoms, how did they affect your activities?

0—Not at all
1—Symptoms present, but did not force any change in activity or itinerary
2—My symptoms forced me to stop the ascent or to go down on my own power
3—Had to be evacuated to a lower altitude

3-5 points: mild AMS
 6-9 points: moderate AMS
 10-12 points: severe AMS

Assessment not earlier than 6 hours after reaching altitude

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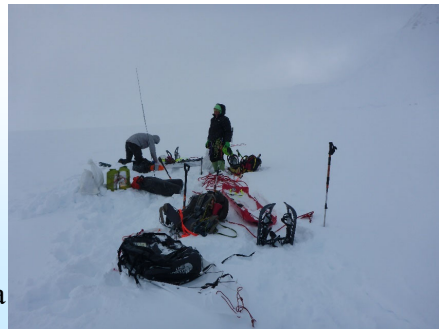
HAPE and HACE

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High Altitude Pulmonary Edema (HAPE)

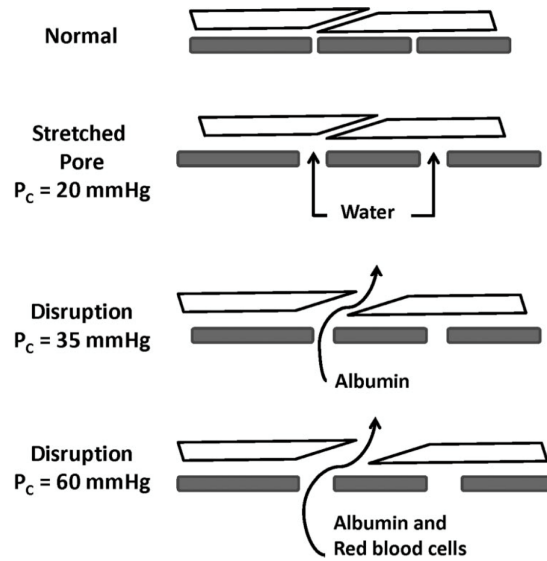
Symptoms

- Resting **dyspnoea** / orthopnoea
- Sudden drop in performance
- Fine- to coarse-bubbling rales
- Severe cough with foamy reddish sputum
- Severe cyanosis
- Fever (!), Cave DDX pneumonia/infection
- AMS not a necessary preliminary stage (negative in 20-25%)
- Rapid re-ascent possible after symptoms disappear



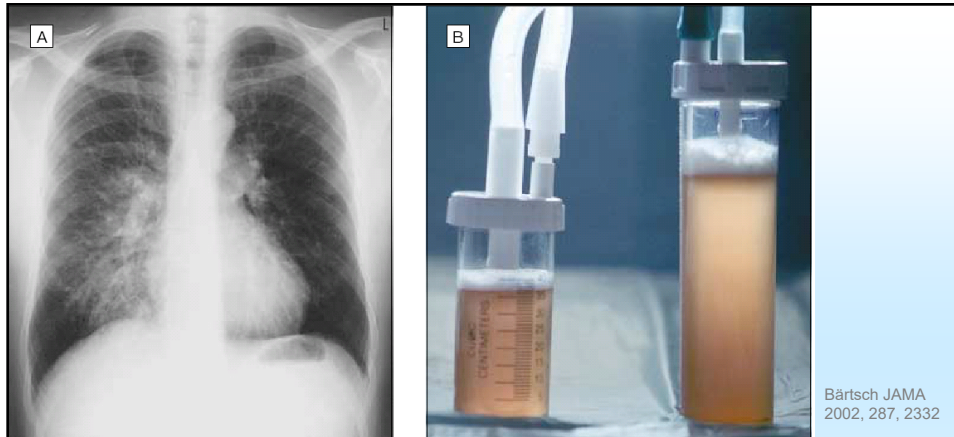
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Disruption of alveo-capillary barrier



Swenson E, Maggiorini M, Mongovin S, et al. Pathogenesis of high-altitude pulmonary edema, inflammation is not an etiologic factor. JAMA 2002;287:2228-35.

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Bärtsch JAMA 2002, 287, 2332

Table 1. Arterial Blood Gas Measurements and Chest Radiograph Scores at Low and High Altitude on Bronchoalveolar Lavage*

	Mean (SD)				
	490 m		4559 m		
	Resistant (n = 6)	Susceptible (n = 10)	Resistant (n = 6)	Susceptible Well (n = 7)	Susceptible III (n = 3)
PaO ₂ , mm Hg	88 (4)	92 (3)	40 (2)†	33 (2)‡	29 (2)§
SaO ₂ , %	97 (1)	97 (1)	78 (2)†	66 (2)‡	57 (3)§
Paco ₂ , mm Hg	38 (2)	37 (2)	28 (2)†	29 (2)†	29 (3)†
Chest radiograph score	0	0	0	1.5 (4.2)	12.7 (1.2)¶

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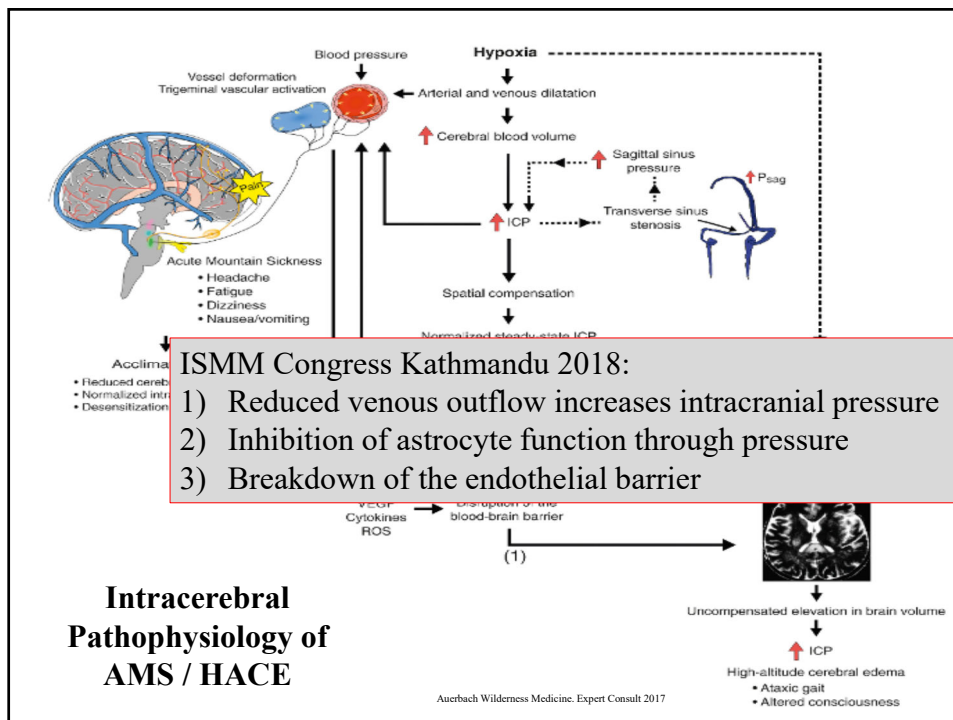
High Altitude Cerebral Edema HACE



- Symptoms:
 - Severe headache
 - **Ataxia**
 - Visual Disturbances
 - Hallucination
 - Nausea
 - Vomiting
 - **Unreasonable behaviour**
 - Loss of consciousness to coma



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HACE

- Severe hypoxia at high altitude leads directly to HACE
- Hypoxia at medium altitude initially leads to HAPE, then to HACE
- Remission after descent often delayed (>14 days), re-ascent not advisable
- Often residual damage (e.g. microhaemorrhages in the corpus callosum (bars) visible on MRI up to 50 months after HACE)



ISMM Congress Kathmandu 2018

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High Altitude Lymph Edema (HALE)

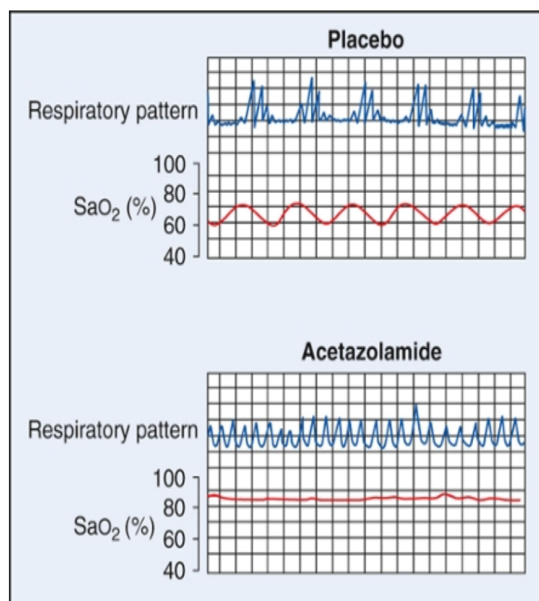
- Frequent phenomenon, women >>men
- Increase with AMS
- Mainly feet, hands, face
- Warning signs for HAPE and HACE!



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Sleep Disturbances

- Cheyne-Stokes
respiration starts early
- Leads to poorer
oxygenation
- Remedy with
acetazolamide and
benzodiazepines



Source: Auerbach
Wilderness Medicine.
Expert Consult 2017



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High Altitude Cough

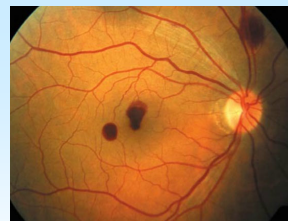
- Almost universal problem above 5500m
- Lack of oxygen triggers coughing
- Main cause inhalation of dry, cold air through the mouth:
leads to dehydration of the mucous membranes, viscous mucus in the airways, eventually coughing, also tendency to infection
- Massive coughing irritation up to rib fractures
- Prevention:
breathing through balaclava, nospapine drops,
inhaled β -mimetics, steroids,
antihistamines (ketotifen)



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High Altitude Retinopathy (HAR)

- Often an incidental finding, rarely visual disturbances, visual field defects
- More common in older climbers, often delayed
- Caused by increased blood flow in retinal vessels
- Good regression
- Incidence of HAR around 60%
- 28 soldiers up to 4120m:
81.5% central retinal vein occlusion,
18.7% lateral branch occlusion, all reversible
(Mukhtar et al. 2017)



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Thrombosis

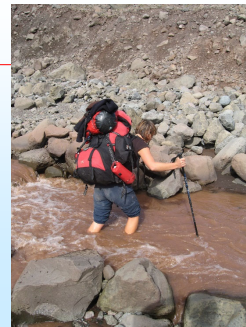
- Fibrinolysis tends to increase at high altitudes
- But still tendency to thrombosis due to dehydration, inactivity, polycythaemia
- Increased fibrin production with HAPE
- Risks with hereditary tendency to thrombosis (e.g. factor V Leiden) unknown



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Immunosuppression

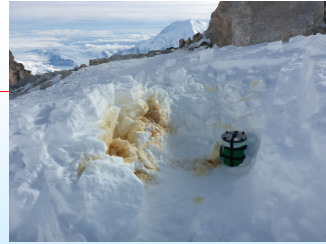
- Poor wound healing, poor response to antibiotics
- Improvement on descent
- Suppression of T-lymphocyte function in animal experiments
- B-lymphocytes not restricted - higher susceptibility to bacterial infections
- Probably caused by high levels of stress hormones, possibly also due to high UV exposure



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Diarrhea and ARI

- Diarrhea rate at Denali 34%,
in Nepal 80%
- Variable pathogens
- Reduced hygiene
- No water for hand washing
- URTI triggered by
 - Cold air
 - Lack of oxygen
 - High altitude cough



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High-Altitude Deterioration

- Starts at approx. 5500m, very visible from 8000m
- Weight loss through loss of appetite and limited resorption
(fat -49%, protein -33%, carbohydrates -24%)
- Performance weakness, fatigue
- Organic psycho-syndrome in 35%
of mountaineers above 7000m
- Alitude psychosis?



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Hormones at High Altitude: Stress and Sex



Swiss Himlung Himal Expedition 2013:
24 subjects, >1000 blood samples, >6000 hormone measurements

- Stress hormones inhibited up to 5,000m, normalisation through acclimatisation
- Stress hormones massively increased from 5,000m, no adaptation
- Testosterone and oestrogen decrease steadily with altitude



Source: von Wolff M, Interview in Die Alpen 4/2017

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Mountain Sickness – Emergency Medication

- Oxygen
- Pressure Bag
- Ibuprofen
- Acetazolamide
- Nifedipine
- Dexamethasone



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Pressure Bag (Gamow, Certec, DEBEL)



Real Altitude [m]	Simulated Altitude
4000	1650
5000	2450
6000	3100
7000	3850
8000	4500

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AMS Therapy

- Mild symptoms:
 - Rest day at the same level
 - Fluids!
 - Symptomatic therapy (Ibuprofen)
- Severe symptoms:
 - Descent to the last campsite, never alone
 - Oxygen administration / hyperbaric chamber
 - Symptomatic therapy
 - Acetazolamide 125-250 mg 3 x daily
 - Dexamethasone 4 - 8 mg p.o. (up to 3 x daily)
- Consider DDx



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Therapy of Severe High Altitude Disease

Sequence of Measures in Severe Manifestations:

- **Decrease Altitude** „descent – descent – descent !!“
- Oxygen
- Drug Therapy
- Pressure Bag



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HAPE - Therapy

- **Descent at least 1000m**
- Oxygen
- Pressure Bag Roach et al. 1993
- **Decrease PA-pressure**
 - Nifedipine (Oelz et al. 1989) 20 mg ret. +
 - Salmeterol (Salbumatol) 125 µg 2x/die (Sartori et al, NEJM 2002)
 - Sildenafil 50mg (ISMM World Congress 2018)
 - Phentolamin (Hackett et al. 1992)
 - Acetazolamide (Teppema et al 2007)
 - Sildenafil, Tadalafil (Olschewski 2004, Richalet 2004, Bärtzsch, 2006)



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HACE - Therapy

- Immediate, if possible passive descent
- Oxygen administration
- Dexamethasone orally/iv/im, at least 4 mg, preferably 8 mg every 6 h
- Acetazolamide (protects endothelial barrier, reduces cerebrospinal fluid production)
- Hyperbaric chamber



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Drugs for Prophylaxis of AMS

- ✗ Acetazolamide
- ✗ Prednisone
- ✗ Nifedipine
- ✗ Sildenafil
- ✗ Tadalafil
- ✗ Salmeterol (Spray)
- ✗ ASS
- ✗ Ibuprofen



- ✗ Intake of betablockers reduces altitude adaptation!
- ✗ Lots of fluid!



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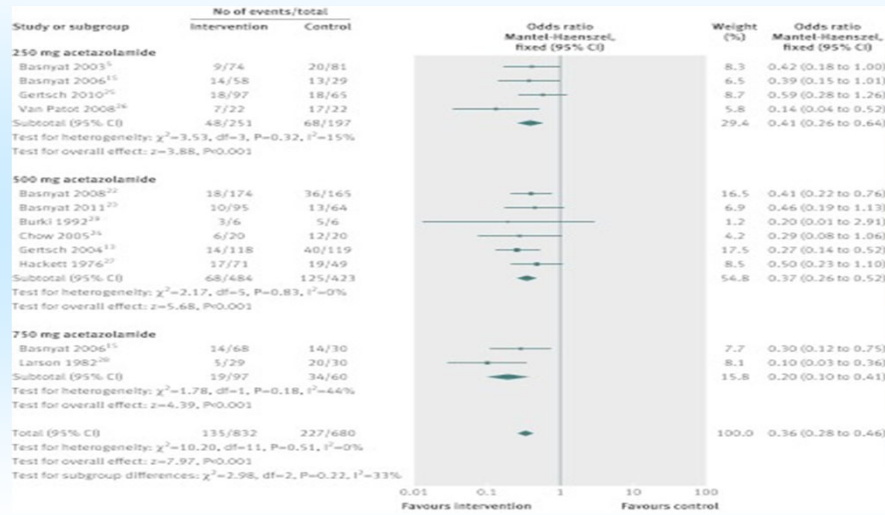
Acetazolamide

- Characteristics
 - Diuretic - enough fluid!
 - Sulfonamide - Allergies?
 - Dosage for prophylaxis 2 x ½ tablet (=125 mg) per day, if necessary only 2 x ¼ tablet/day
 - Start: individually / 1 day before ascent > 2500m
 - End: usually from the start of the descent
- Side effects
 - Frequent: paraesthesia, change in taste, urge to urinate
 - Rare: Fatigue, dizziness, calf cramps
 - Sy overdose: tachycardia and -pnoea, Kussmaul respiration (acidosis), hypotension, muscle cramps
 - DDX AMS (!), but SO₂ remains good



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Meta-analysis: efficacy of acetazolamide prophylaxis



Low EV et al. BMJ 2012;345:e6779.

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Self Medication in Trekking Tourists at Thorong-La

Journal of Wilderness Medicine 2, 110-117 (1991)

ORIGINAL ARTICLE

Acute mountain sickness in western tourists around the Thorong pass (5400 m) in Nepal

B. KAYSER*

Himalayan Rescue Association, Nepal

1986: 1% acetazolamide

HIGH ALTITUDE MEDICINE & BIOLOGY
Volume 3, Number 4, 2004
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Awareness, Prevalence, Medication Use, and Risk Factors of Acute Mountain Sickness in Tourists Trekking around the Annapurnas in Nepal: A 12-Year Follow-up

SAMUEL GAILLARD,¹ PASCALE DELLASANTA,¹ LOUIS LOUTAN,¹ and BENGT KAYSER²

1998: 12% acetazolamide

WILDERNESS & ENVIRONMENTAL MEDICINE, 25, 152-159 (2014)

ORIGINAL RESEARCH

Risk Determinants of Acute Mountain Sickness in Trekkers in the Nepali Himalaya: a 24-Year Follow-Up

Marion McDevitt, DO, MPH, Scott E. McIntosh, MD, MPH, George Rodway, PhD, APRN, Jitsupa Peelay, MS, Doug L. Adams, MSat, Bengt Kayser, MD, PhD

2010: 44% acetazolamide



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Alternatives to Acetazolamide

- **Dexamethasone**
 - 4 mg every 12 hours
 - Limited to 5 days
 - For rapid ascents – rescue missions
- **Nifedipine**
 - 20 mg every 8 hours, especially for persons at risk of AMS complications
- **Salmeterol**
 - 125 µg every 12 hours, additionally to Nifedipine
- **Tadalafil**
 - 10 mg every 12 hours

Not effective

- **Ginkgo- and Coca-Preparations**

Bates M et al. High Alt Med Biol 2011;12:207-14.
Luks AM et al. Wilderness Environ Med 2010;21:146-55.
Maggiorini M. Prog Cardiovasc Dis 2010;52:500-6.
Maggiorini M et al. Ann Intern Med 2006;145:497-506.
Chow T et al. Arch Intern Med 2005;165:296-301.

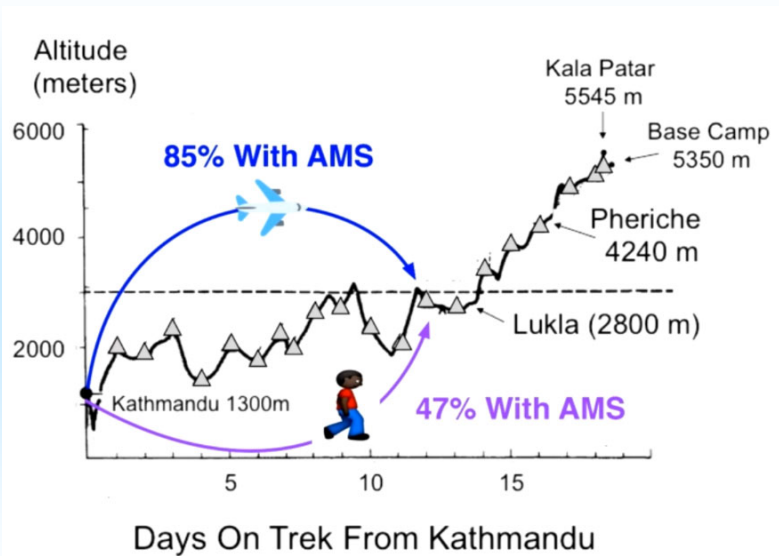


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We know since a long time that speed of ascent makes a big difference



Hackett et al. Lancet 1976. 2(7996): 1149

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Acclimatisation to Altitude

„dont go too high too fast“
„dont go up until symptoms go down“
„climb high - sleep low“



- No anaerobic efforts
- Sleep as low as possible
- Daily sleep elevation gain 300 - 500m
- One additional rest day every 1000m



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Pre-Acclimatisation



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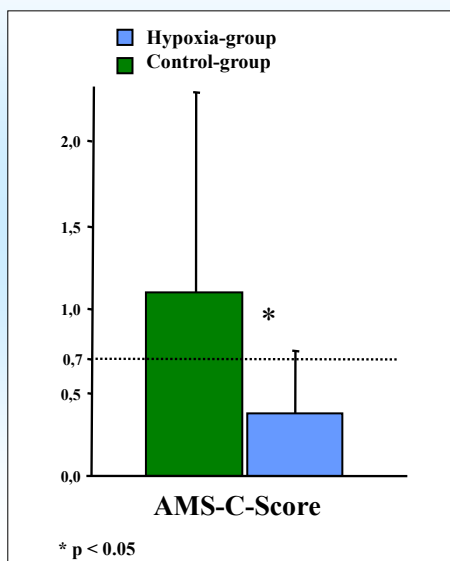


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**Sleeping in Moderate Hypoxia at Home for Prevention of Acute Mountain Sickness (AMS):
A Placebo-Controlled, Randomized Double-Blind Study**



AMS Definition:
AMS-C-Score > 0.7

	AMS +	AMS -
Control (< 800 m)	52%	48%
Hypoxia (> 2200 m)	14%	86%

Chi²-test, p = 0.022

Dehnert, Wilderness Med 2014

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Journal of Travel Medicine, 2020, 1-7
doi: 10.1093/jtm/taaa099
Advance Access Publication Date: 24 June 2020
Review

Journal of Science in Sport and Exercise (2022) 4:311–345
https://doi.org/10.1007/s42978-021-00150-9

REVIEW ARTICLE

Check for updates

Journal of Travel Medicine
International Society of Travel Medicine
Promoting healthy travel worldwide

Review

Rapid ascents of Mt Everest: normobaric hypoxic preacclimatization

Markus Tannheimer¹ Assoc Prof. Dr med^{1,*} and Raimund Lechner Dr med²

¹University of Ulm, Department of Sport and Rehabilitation Medicine, Leimgrubenweg 14, 89089075 Ulm/75 Ulm, Germany and ²Department of Anaesthesiology and Intensive Care, Bundeswehr Hospital Ulm, Oberer Eselsberg 40, 89081 Ulm, Germany

*To whom correspondence should be addressed. Fax: +49 (0)7344 1710-4301, Tel: +49 (0)7344 1710-4305, Email: markus.tannheimer@barco.de

The study was presented at the seventh Sport Orthopaedic Winter Symposium on the Feldberg Freiburg, Germany on 15 February 2020. The study was presented as scientific lecture required as part of the habilitation procedure of the University of Ulm, Germany on 22 February 2019. The opinions expressed in this article are those of the authors and do not necessarily reflect the views of the German Armed Forces.

Submitted 24 February 2020; Revised 22 March 2020; Accepted 11 June 2020

Abstract
Background: Acclimatization to high altitude is time consuming. An expedition to Mt Everest (8848 m) requires roughly 8 weeks. Therefore it seems very attractive to reach the summit within 3 weeks from home, which is currently promised by some expedition tour operators. These rapid ascent expeditions are based on two main components, normobaric hypoxic training (NHT) prior to the expedition and the use of high flow supplemental oxygen (HF_{SO}₂). We attempted to assess the relative importance of these two elements.
Methods: We evaluated the effect of NHT on the basis of the available information of these rapid ascent expeditions and our experiences made during an expedition to Manaslu (8162 m) where we used NHT for preacclimatization. To evaluate the effect of an increased O₂ flow rate we calculated its effect at various activity levels at altitudes of 8000 m and above.
Results: So far rapid ascents to Mt Everest have been successful. The participants carried out 8 weeks of NHT, reaching sleeping altitudes > 7100 m and spent at least 300 h in NH. At rest a flow rate of 2 l O₂/min is sufficient to keep the partial pressure of inspired oxygen (P_{IO}₂) close to 50 mm Hg even at the summit. For activities of ~80% of the maximum rate of oxygen consumption (V_O_{2max}) at the summit 6 l O₂/min are required to maintain a P_{IO}₂ above 50 mm Hg.
Discussion: NHT for preacclimatization seems to be the decisive element of the offered rapid ascent expeditions. An increased O₂ flow rate of 8 l/min is not mandatory for climbing Mt Everest.
Conclusions: Preacclimatization using normobaric hypoxia (NH) is far more important than the use of HF_{SO}₂. We think that NHT will be widely used in the future. The most effective regimen of preacclimatization in NH, the duration of each session and the optimal P_{IO}₂ are still unclear and require further study.

Key words: Mount Everest, pre-acclimatization, normobaric hypoxia, AMS, high altitude, artificial altitude, supplemental oxygen





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Oxygen Systems:

Poisk, TopOut and Summit Oxygen

- ✓ Constant Flow max. 2-8 l/h
- ✓ No On-Demand
- ✓ Regulator usually in backpack
- ✓ Problems with icing

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International Society of Travel Medicine

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Kathmandu: Oxygen Bottles of an Everest-Expedition



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Five Golden Rules of the Himalayan Rescue Association

1. Everybody can get AMS, but nobody has to die from it !
2. Any health disorder at altitude must be considered altitude sickness until proven otherwise
3. No further ascent with symptoms of AMS
4. Descent immediately, if symptoms increase
5. A person with AMS must never be left alone



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How to Travel Safe at High Altitude

1. Don't go
2. If you absolutely have to go: go slow
3. Consider pre-acclimatisation
4. Sleep low
5. Check yourself and your partner
6. Drink a lot
7. Don't get diarrhea or ARI
8. Carry emergency medication
9. Consider prophylactic medication
10. Consider oxygen
11. Stay only briefly at high altitude
12. Descent immediately if sick
13. Despite all of this: try to enjoy yourself!



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Africa: Kilimanjaro 5895m



Asia: Everest 8850m



Europe: Elbrus 5642m



Oceania: Carstensz Pyramid 4884m



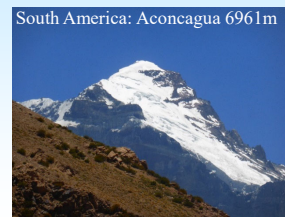
North America: Denali 6190m



Antarctica: Vinson 4892m



South America: Aconcagua 6961m



Questions?

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