



Innere Medizin VII / Sportmedizin

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Hypoxic Conditions: Impact on Health

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○○ Overview over Diseases at High Altitude

Acute exposure:

- High altitude diseases
 - Acute mountain sickness (AMS)
 - High altitude cerebral edema (HACE)
 - High altitude pulmonary edema (HAPE)
- First manifestation or deterioration of pre-existing illness

Chronic exposure

- Sub-acute mountain sickness
(2-4 months > 5000 m)
- Chronic mountain sickness
(living at > 3500 - 4000 m)

AMS: Clinical Picture



- Symptoms:
 - Headache
 - Loss of appetite, nausea, vomiting
 - Dizziness
 - Sleep disturbance
 - Peripheral edema
- Delayed onset: 4-8 hours
- Definition of AMS:
Headache + 1 additional symptom





AMS: Time Course and Prevalence

- Maximum: day 2 - 3 at given altitude
- Spontaneous remission within 3 – 4 days, rarely persistence of symptoms
- Progression to HACE: possible when no adequate therapy, usually not below 3000 – 3500 m
- Threshold altitude: between 2100 and 2400 m

Prevalence:	Alpine Mountaineers	Tourists
at 2100 m	5 %	18 – 25 %
at 3000 m	13 %	27 – 42 %
at 3600 m	34 %	?
at 4500 m	52 %	?



Major Risk Factors for AMS at a Given Altitude

Mountaineers

- Previous history of AMS
- Pre-acclimatization
- Rate of ascent
- Exertion (most likely)

Schneider, Med Sci Sports Exerc 2002

Tourists

- Previous history of AMS
- Living altitude > 900 m
- Obesity (BMI > 30)
- Chronic lung disease

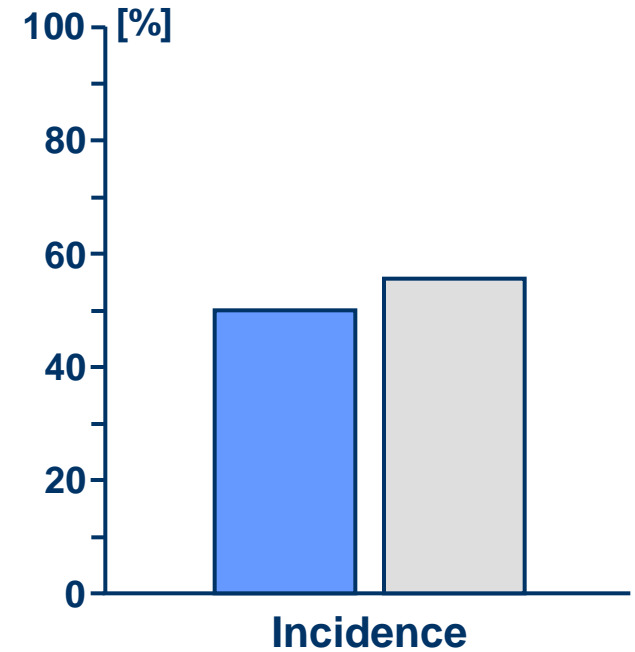
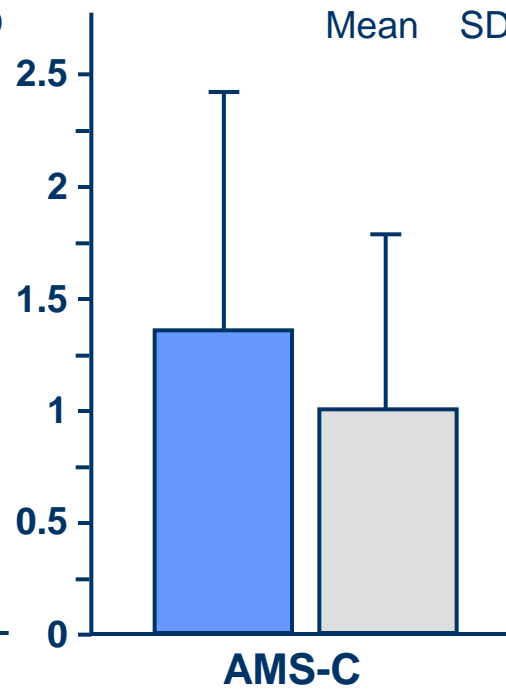
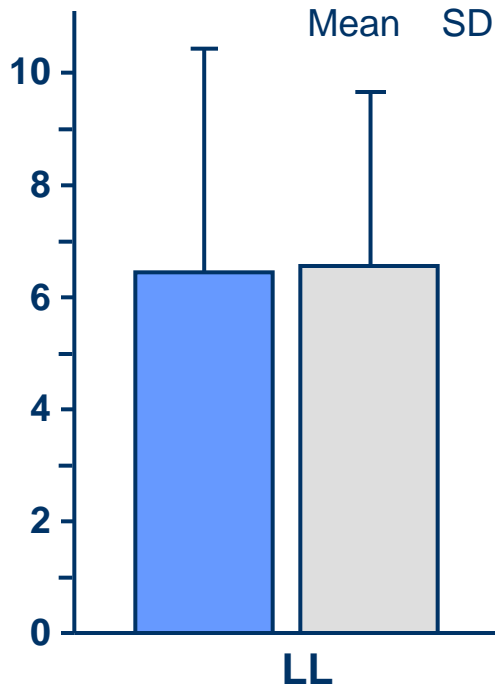
Honigman, Ann Intern Med 1993



Pathophysiology of AMS

- Activation of trigemino-vascular system by a hypoxia-triggered mechanism
- Normobaric vs hypobaric hypoxia:
 - slight difference in fluid balance
 - slight difference in ventilatory response
 - same symptoms and similar incidence of AMS in normobaric hypoxia and field studies with comparable ambient pO₂

AMS in hypobaric vs normobaric hypoxia



 Field



(18h at 4559m; n=15)

Schommer HAMB in press

 Chamber



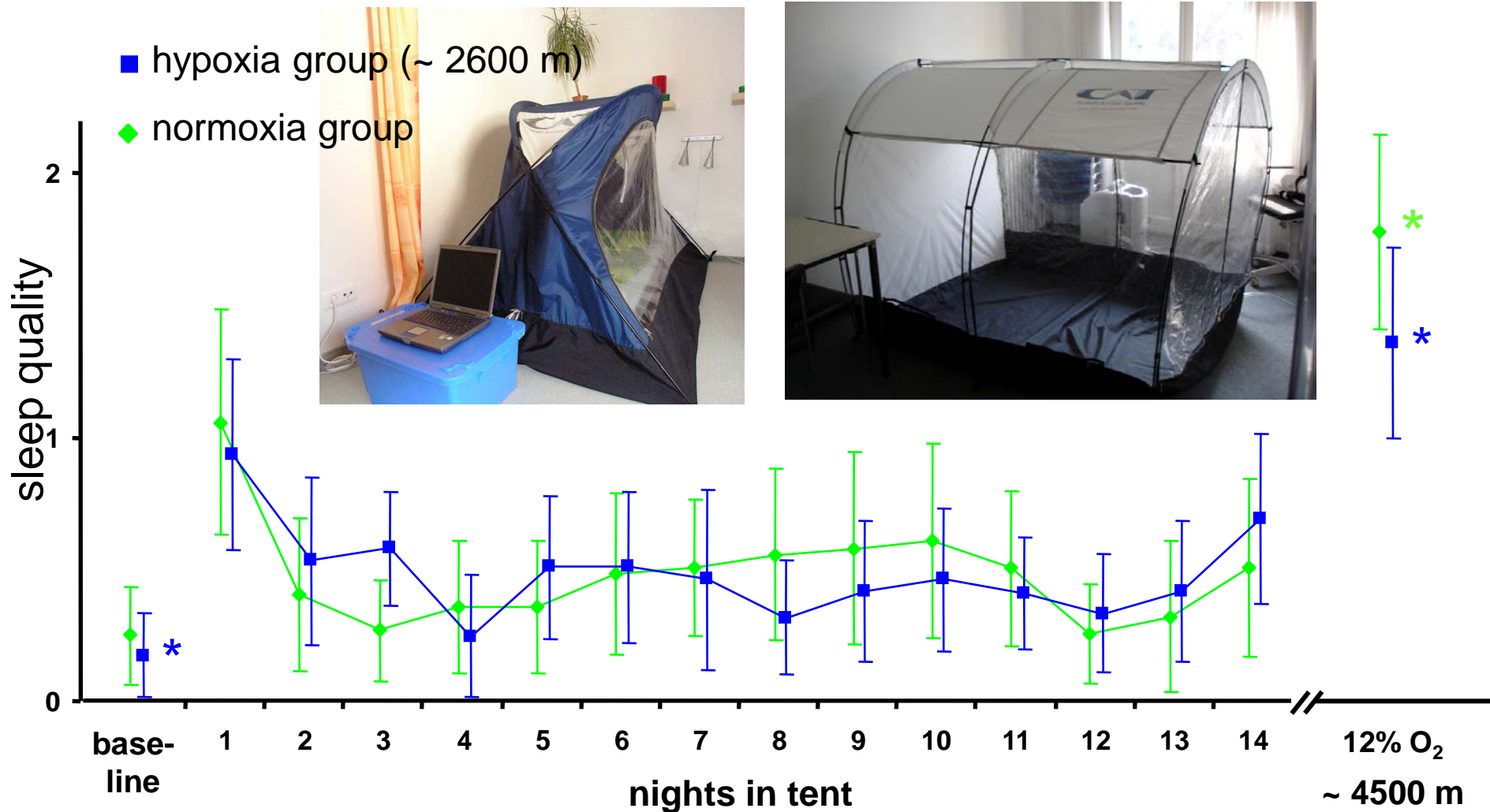
(15h at 12%O₂; n=22)

Bailey JCBFM 2005;

○ ○ AMS and Sleep with Live High Train Low

- $n = 41$ (cross country skiers, swimmers, runners),
 $VO_{2max} \sim 60 \text{ ml/kg/min}$
- 2500 m (6 nights) \rightarrow 3000 m (6 - 12 nights)
 \rightarrow 3500 m (6 nights)
- Duration of daily exposure: 11- 14 - 16 hrs
- No AMS at all
- Only symptoms: Fatigue and sleep disturbance,
but equal between groups
- Lowest average SaO_2 at night: 91 – 90 – 89 %

○ Sleep Quality with Sleep High-Train Low



0 = as usual; 1 = not so good; 2 = bad; 3 = did not sleep at all

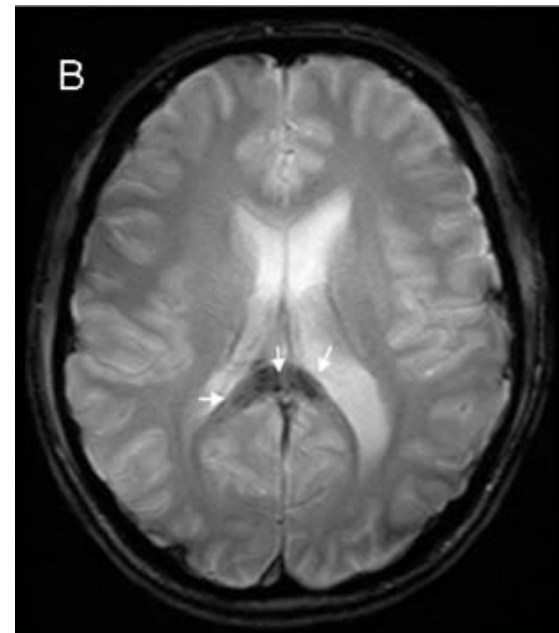
* Significantly different from mean value of nights 4 to 14

Summary AMS

- AMS is no threat to health and life → transient impairment of well-being
- Below 3000 m mild and involves a minority, above 4000 m relevant for about 50 % of the people, comparable to a migraine attack or hangover
- Self limiting when adequate measures are taken
- Preventable by slow ascent or repeated exposures or by acetazolamide (Diamox)
- No clinically relevant difference between normobaric and hypobaric hypoxia

HACE on Kilimanjaro (5895 m)

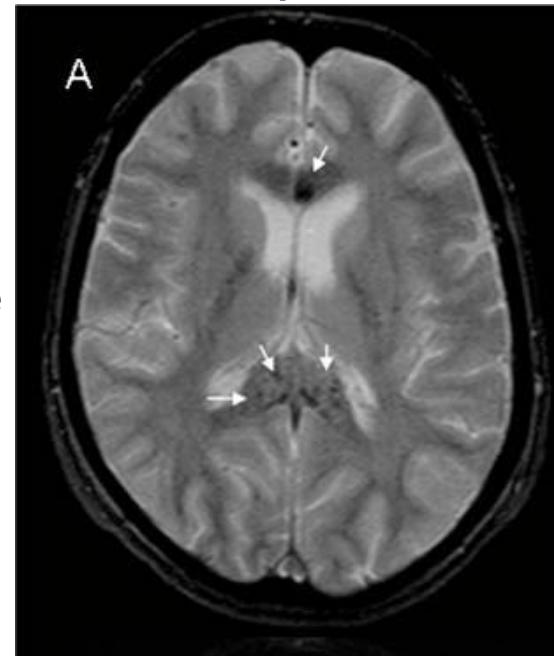
- 26 y, male, often AMS above 3000 m, climbs in 3 days to 5700 m on Kilimanjaro
- day 2 AMS, day 3 ataxia and tunnel vision before arrival in camp
- falls unconscious at night, is carried down to hospital at 1540 m and recovers within 4 days, after 4 weeks completely well



Kallenberg,
JCBFM 2008

Case report of HACE

- 65-year-old woman, 68 kg/168 cm, never > 3000 m, hypertension treated with ACE inhibitor and indapamide
- after 2 days in Arequipa (2300 m) flight to 3825 m
- 8 hours later in Puno headache, dizziness and vomiting. BP 160/70 mmHg, 20 min O₂ and medication, slept well
- day 2 in hotel, somnolent, AMS and ataxia
- day 3 coma, evacuation by air plane to Lima, CT scan: brain edema, after 2 months mild ataxia,
- cognitive deficit and weakness, after 9 months complete recovery



Kallenberg, JCBFM 2008

Summary HACE

Symptoms and signs:

- progressive AMS (not compulsory!)
- ataxia (assistance for walking)
- clouded consciousness → coma
- often fever > 38°C and CSF pressure

Prevalence:

- rarely below 4000 m,
- at 4500 m 0,5 - 1%

Clinical course:

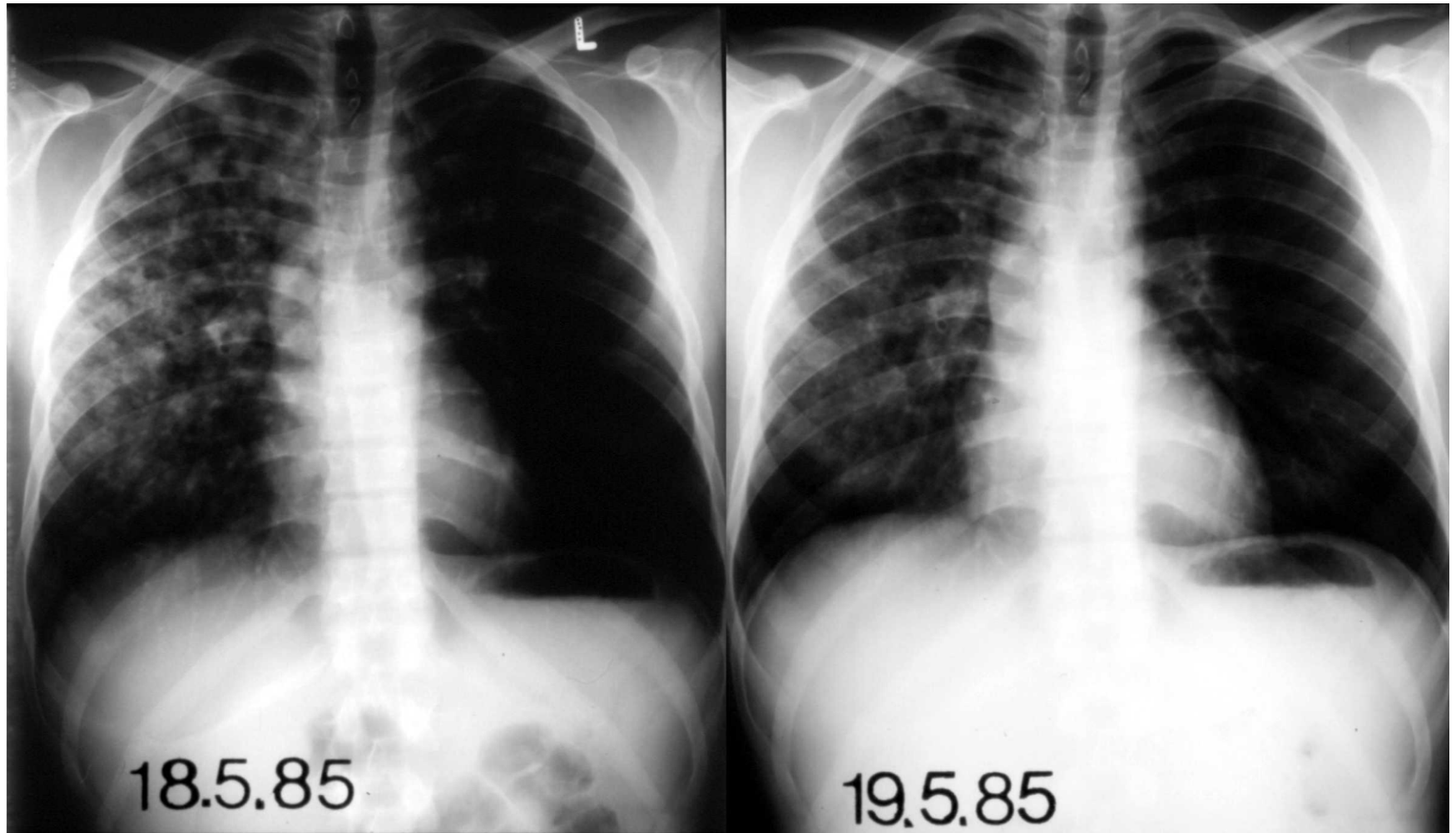
- usually rapid deterioration
- death within 1-2 days if untreated
- recovery can be delayed at LA

Therapy: descent, supplemental O₂,
dexamethasone

HAPE



High Altitude Pulmonary Edema



25-year-old healthy mountaineer



High Altitude Pulmonary Edema (HAPE)

- Setting: - rapid ascent above 3000 - 4000 m
- Symptoms: - often preceded by AMS
 - dyspnea, decreased exercise performance, cough
 - orthopnea, gurgling, pink frothy sputum
 - ataxia, decreased consciousness
- Prognosis: - rapid complete resolution after descent
 - high mortality without treatment
- Incidence: - variable, individual susceptibility



Incidence of HAPE

	Altitude	Ascent	Incidence
Rocky Mountains (tourism)	3000 m	1-2 days	0.01%
Alps (mountaineers)	4559 m	2-4 days	< 0,2%
Himalaya (trekking)	5450 m	6 days	1.6%
Alps (non-susceptible individuals)	4559 m	22 hours	6 %
Himalaya (soldiers)	5400 m	flight/car	15,5%
Alps (susceptible individuals)	4559 m	22 hours	62%



Pathophysiology of HAPE

- Exaggerated hypoxic pulmonary vasoconstriction
- Normal wedge pressure, increased capillary pressure
- BAL: erythrocytes and proteins \uparrow , no markers of inflammation

→ pressure induced, non inflammatory leak



Prevention and treatment

- No HAPE in susceptible individuals up to 7000 m when ascent rate is 300 - 350 m/day above 2000m
- Pulmonary vasodilators (nifedipine or PDE-5 inhibitors) prevent HAPE with rapid ascent
- Successful treatment lowers pulmonary artery pressure:
 - descent (increase of ambient pO_2)
 - supplemental O_2
 - nifedipine or PDE-5 inhibitors



Chronic Repeated Exposure to 3000-4000 m

No negative effects on health in:

- Mountain guides (except for increased risk for skin cancer because of UV-radiation)
- Personnel in Alpine tourist facilities
- Workers commuting between sea level and mines in the Andes
- Workers in normobaric hypoxic environment for fire protection, archives or storage

○○ Oxidative Stress in Hypoxia and Exercise

Findings:

- Exercise at 3000 m: oxidative stress↓, anti-oxidative capacity↓
(Pialoux, Eur J Clin Nutr 2006; Int J Sports Med 2009)
- Live high, train low for 18 days: antioxidative capacity↓
(Pialoux, Eur J Appl Physiol 2009)

Clinical significance of reactive oxygen species not clear:

- Role of oxidative stress in atherosclerosis, but increased mortality under long-term supplementation with anti-oxidative vitamins (Bjelakovic, JAMA 2007) and no preventive effect on coronary artery disease (Sesser, JAMA 2008)
- Increased risk for some forms of cancer
(NEJM 1994;330:1029-1094, Lippman, JAMA 2009)
- Decreased response to training under antioxidants
(Ristow, PNAS 2009)

○○ Summary: Impact of hypoxic conditions in healthy individuals

- Delayed onset of illness:
 - after 4 - 8 h for AMS
 - after 2 to several days for HACE or HAPE
- Level of altitude:
 - AMS: minor impact below 3000 m for majority
 - HACE: rarely below 3500 - 4000 m (no data)
 - HAPE: seldom below 3000 - 3500 m ($\approx 0,01\%$)
- Prevention by staged ascent or repeated exposure
- Treatment is effective and easy to install

○○ Conclusion: Impact of hypoxic conditions in healthy individuals

Level of altitude/hypoxia used by athletes:

- high altitude training: 2 - 3 weeks at 2000 – 2500 m
- live or sleep high: 8 – 20 h/day at 2500 – 3000 m
- hypoxic training: 12 min - 2 h/day at 2250 – 5700 m
(average of 21 studies 3300m)
- hypoxia at rest: 6-9 x 4-5 min/day (4500 – 6000 m)

→ No danger for healthy athletes with common modalities of using altitude or applying hypoxia at rest or during training