ADVICE FOR INDIVIDUALS TRAVELLING TO HIGH ALTITUDE

Dr Lee Eng Sing, Dr Lee Meng Kam Richard, Dr Aw Lee Fhoon Lily

ABSTRACT

More people are traveling to remote places for leisure and business. It is not uncommon for patients to get medication and advice for travel to high altitudes. Although high altitude cerebral and pulmonary oedemas are more frequent at very high and extreme altitudes, they may sometimes occur at lower altitudes and lead to fatalities. Even though acute mountain sickness (AMS) is generally deemed benign, it can easily wreck a holiday. The Lake Louise Score Questionnaire is a useful screening tool for AMS and it can be self-administered during travel. Non-pharmacological means in the prevention and treatment of AMS, especially acclimatisation, are the most important. Pharmacological prevention and treatment strategies should be used as a useful adjunct. This paper provides an approach to the provision of education and advice for high altitude travel in the primary care setting.

Keywords: Acute Mountain Sickness; high altitude illness; prevention; treatment

SFP2013; 39(1): 48-54

INTRODUCTION

The ease of travel has allowed more people to pursue leisure activities at remote places. These destinations include places of high altitudes. The allure of the summit, picturesque sceneries, skiing and mountain trekking are some of the common reasons why equatorial Singaporeans are drawn to such destinations.

For the majority of people who travel to high altitude, most will return from their sojourn with no ill effects. Morbidities are common but rarely does fatality occur[1]. Most of the deaths reported were caused by accidents at extreme altitudes[2]. These accidents may be attributable to altitude-induced hypoxia causing misjudgments and disorientation.

As family physicians, we sometimes have healthy individuals or patients with chronic diseases coming to us for advice or medications for such travels. It is therefore imperative that we should get ourselves acquainted on the subject matter to give the most evidence-based and unbiased advice. Most of the time, all it needs is to warn patients of certain precautions or to assess for possible exacerbation of pre-existing illnesses. Infrequently, we may have to firmly advise a patient not to participate in such an activity.

This review aims to give an overview of the problems that individuals may encounter at high altitudes for short holidays or business trips. It provides a basic understanding of illnesses that can occur at high altitudes and recognition of these illnesses. The emphasis of this article is on the guidelines for prevention, the critical steps in the treatment and management of AMS. Appropriate advice in a primary care setting is included. High altitude destinations commonly visited by Singaporeans are summarised in Appendix 1. (This a personal search from the google search engine of individual countries and areas that Singaporeans commonly visit after interviewing a travel agent in Singapore)

METHODOLOGY

A PubMed search was conducted using keywords like "prevention", "treatment", "acute mountain sickness" and "high altitude illness". Relevant articles were selected from this list and from the references of the articles. UpToDate and The International Mountaineering and Climbing Federation (UIAA) website (http://www.theuiaa.org/medical_advice.html) were also consulted.

WHAT HAPPENS AT HIGH ALTITUDE?

At sea level, barometric pressure is 760 mmHg; atmospheric partial pressure of Oxygen (pO_2) is 159 mmHg; and inspired pO_2 is 150 mmHg or 21% of Oxygen[3]. The inspired Oxygen is primarily dependent on the barometric pressure. Barometric pressure decreases in a non-linear way with increasing elevation. As such, the availability of inspired pO_2 lowers as one ascends.

In this article, the following definition for altitudes are used:

Intermediate altitude	1,500-2,499m
High altitude	2,500-3,499m
Very high altitude	3,500-5,499m
Extreme altitude	> 5,500m

Table 1 summarises the notable changes of a human body at increasing altitude.

LEE ENG SING, Family Physician, Associate Consultant, National Healthcare Group Polyclinics

LEE MENG KAM RICHARD, Family Physician, Associate Consultant, National Healthcare Group Polyclinics

AW LEE FHOON LILY, Consultant Family Physician, Private Practice

Appendix 1: Some common high altitude destinations visited by Singaporeans

Country	Place of interest	Highest altitude
Singapore		0-166m (highest point is Bukit Timah Hill) - For reference
Himalaya		
Bhutan		Cultural tours do not reach altitudes higher than 3,500m. All treks reach at least 3,500m; some go as high as 5,000m
China	Tibet	
	Lhasa (Capital)	3,658m
	Lalung-La Pass	5,050m
	Gyatsola Pass	5,220m
	Karola Pass	5,010m
	Kambala Pass	4,974m
India	Sikkim	
	Gangtok (Capital)	1,780m
	Goechala Pass	5,000m
	Jammu	
	Kishtwar High Altitude National Park	The altitudinal level of the park ranges from 1,700 to 4,800m above sea level
Nepal	Kathmandu (Capital)	1,400m
	Jomson (City)	2,700m
	Langtang (City)	3,307m
	Trekking in Annapurna	Thorung La Pass at 5,416m
	Trekking in Muktinath	Muktinath Shrine at 3,170m
	Trekking in Everest	Mera Peak 6,476m; Tesi Lapcha Pass 5,755m; French Col 5,240m; Dhampus Pass 5,155m
	Phoksumdo Lake	3,627m
Ski Resorts		
Austria	Austrian Alps	Up to 3,800m
China	Jade Dragon Snow Mountain (Lijiang Yunan)	4,516-4,700m
	Duolemeidi Mountain Resort (Zhangjiakou Hebei)	1,500-2,174m
	Kanas International Ski Resort (Xinjiang)	1,000-2,000m
	Dagu Glacier (Sichuan)	3,617-4,843m
Japan	Happo-One (Hakuba, Nagano)	760-1,831m
South Korea	Yongpyong Resort	700-1,458m
Switzerland	Swiss Alps	Up to 2700m. The highest mountain in the Alps is Mont Blanc (4,810m)
China	Sichuan	Altitude of Jiuzhaigou ranges from 1,998 to 2,140m, at the mouth of Shuzheng Gully, to 4,558 - 4,764m on Mount Ganzigonggai at the top of Zechawa Gully.
	Jiuzhaigou	
	Huangshan	The Huangshan mountain range comprises many peaks, some more than 1,000m high. The three tallest and best-known peaks are *Lotus Peak* (Lian Hua Feng 1,864m, *Bright Summit Peak* (Guang Ming Ding 1,840m, and *Celestial Peak* (Tian Du Feng, literally *Capital of Heaven Peak* 1,829m)
Kyrgyzstan	Great Silk Road Tour	The average altitude is about 2,500m.
	Issyk-Kul Lake	1,607m (second largest mountain lake)
Malaysia	Mount Kinabalu	The summit (known as Low's Peak) is 4,095m.
Peru	Puno (City) - Lake Titicaca	3,827m
	Machu Picchu	2,430m. Usually travel from Cusco, the nearest city - 3,500m
	Arequipa - Colca Canyon	2,325m
USA (Colorado Springs)	Denver (City) (Rocky Mountain National Park)	1,570m. The Manitou and Pikes Peak Cog Railway will take one up to the summit of summit of Pikes Peak at 4,300m.

Table 1: Summary of the changes an individual undergo at increasing altitude[3, 6, 32]

Altitude	Changes
Intermediate (1500-2499m)	Physiological changes detectable. Arterial oxygen saturation > 90%. Altitude illness possible but rare. Equivalent in altitude to commercial aircraft pressurised cabin during flight.
High (2500-3499m)	Altitude illness common with rapid ascent. Decreased exercise performance and increased ventilation. Complex reaction time slows.
Very High (3500-5499m)	Altitude illness common. Arterial oxygen saturation < 90% (75-85%). Marked hypoxemia during exercise and sleep. Learning and special memory impaired. Psychomotor impairment detectable.
Extreme (>5500m)	Progressive deterioration of physiological function outstrips acclimatisation. Arterial oxygen saturation 58-75%. Memory retrieval impaired. MRI shows cortical atrophy above 7000m. 32% of climbers have hallucinations above 7500m. Altitude above 8000m is generally accepted as the death zone.

HIGH ALTITUDE ILLNESS

High Altitude Illness (HAI) describes the cerebral and pulmonary syndromes that occur after an initial climb to high altitude or following a new ascent while already at high altitude[4]. The full pathophysiology of HAI is yet to be elucidated[5]. It is characterised by three distinct clinical presentations[6]. These are namely Acute Mountain Sickness (AMS) that is the commonest and mildest form, High Altitude Cerebral Oedema (HACE) and High Altitude Pulmonary Oedema (HAPE) that are the more severe forms. The latter two can lead to fatalities if not treated early.

Another distinct clinical presentation – Chronic Mountain Sickness (CMS), occurs in people who stay at high altitude for long periods. This entity will not be discussed in this paper.

Acute Mountain Sickness (AMS)

Historical records as far back as 2000 years ago have reported symptoms very similar to AMS[7,8]. It affects 22-53% of travelers to altitudes between 1,850m-4,240m[9]. As one ascends, the atmospheric pO_2 lowers and therefore the risk of developing AMS increases. For example, AMS affects close to 25% of travelers at an altitude of 2500m but up to 75% of travelers at an altitude of 4500m[10].

AMS is defined as headache in an unacclimatised individual plus the presence of one or more of the following symptoms[11, 12,13]:

- Gastrointestinal (anorexia, nausea or vomiting)
- Lassitude or fatigue
- Dizziness or lightheadedness
- Insomnia

The headache commonly starts as a tension-like band that eventually generalises[1]. It may sometimes mimic a classical migraine. The headache worsens with movements and especially when lying supine. Vomiting usually relieves it.

Sleep is particularly disturbed at high altitude and is a dominant symptom of AMS[10]. Travelers often complain of abbreviated and restless sleep especially on the first night[14]. This is due to periodic breathing with apnoeic episodes, a form of Cheyne-Stokes respiration[4,15].

AMS is usually a benign condition that is unpleasant and self-limiting. When staying at the same altitude without further ascent, it commonly resolves within 24-48 hrs [6]. Any individual with persistent AMS that does not resolve should be considered with high suspicion of developing HACE or HAPE. A past history of AMS is a good predictor for development of AMS especially when the conditions of ascent are similar[4].

The Lake Louise Score Questionnaire (LLSQ) is commonly used for diagnosis of AMS. A score greater than 4 in the LLSQ has a sensitivity of 78% and a specificity of 93% for the diagnosis of AMS (Appendix 2). The LLSQ also has an additional clinical assessment score that registers change in mental status, ataxia and peripheral oedema on a severity scale[16].

High Altitude Cerebral Oedema (HACE)

HACE is often thought of as a continuum of AMS[4]. The headache is of a more severe form and worsens in the morning. The afflicted person may behave strangely before exhibiting detectable neurological signs. Without early intervention, an afflicted person develops globalised encephalopathy, becomes comatose and dies[11].

High Altitude Pulmonary Oedema (HAPE)

HAPE seems to be of a different entity altogether and causes higher mortality when compared to HACE[17]. Symptoms of HAPE include breathlessness with coughing of pinkish, frothy sputum[9]. It most commonly occurs within 48-120 hrs after exposure to a high altitude. It can develop without preceding AMS or HACE. Without early intervention, a person may progress to respiratory failure[18].

According to the Lake Louise Consensus[13], it is diagnosed as follows:

- At least two of the following symptoms
  a. Dyspnoea at rest
  b. Cough
  c. Weakness or decreased exercise performance
  d. Chest tightness or congestion
- At least two of the following signs:
  a. Crackles or wheezing in at least one lung field
  b. Central cyanosis
  c. Tachypnoea
  d. Tachycardia

OTHER ILLNESSES AT HIGH ALTITUDE

It is natural for doctors and potential travelers to dwell only on HAI. However, exposure to high altitude also carries other risks. Proximity to the sun causing heat stroke and ultraviolet keratitis can happen. Exposure to cold may cause hypothermia and frost bite. Other environmental changes at high altitude that potentially can pose hazards to an individual include irradiation and decrease in humidity.

PREVENTION OF AMS

Non-pharmacological means for prevention of AMS

Travel agencies commonly do not provide enough time for tourists to acclimatise. For example, most tour packages travelling to Lhasa in Tibet reach an altitude of 4000m in less than two days.

Giving enough time for acclimatisation is the most reliable method for prevention of AMS. Experts advise that at altitude of more than 2500m, progress should not be more than 300-500m per day for sleeping altitude and should include a rest day (no ascent and no vigorous activities) every 3-4 days[3,19].

Climb high and sleep low is the maxim for high altitude travel[20]. Avoid sleeping above 2800m on the first night of travel[4]. Residing or having brief climbs above 1500m in the weeks before a high-altitude trip may hasten acclimatisation[21]. Acclimatisation is not a permanent phenomenon even for dwellers who have their usual residence at high-altitude.[18] Oxygen supplementation can help to prevent AMS[22]. Heavy physical exertion at high altitude has been shown to increase the risk of sudden cardiac death[23].

Adequate rest, appropriate hydration, avoidance of alcohol and sedatives are also important preventive measures.

Pharmacological means for prevention of AMS

Acetazolamide and dexamethasone are commonly used for the prophylaxis of AMS. Other drugs for prevention of HAI have never been proven[24]. Gingko biloba was a major contender a few years ago but has recently been refuted[25].

Acetazolamide

Acetazolamide is safe and 60-80% effective for AMS[17,26]. Studies have shown that acetazolamide at a dosage of 125-250 mg twice daily can help to prevent AMS. However, complete understanding of its protection in AMS remains speculative.

Side effects of the drug include paraesthesia, altered taste and hangover feeling[27]. Uncommon adverse drug reactions are rashes and blood dyscrasias. Fatal drug reactions may include Toxic Epidermal Necrolysis, Stevens-Johnson syndrome and renal failure1. It may therefore be prudent to try out the drug many days before travel to ascertain that there are no side effects.

Although acetazolamide is generally safe for individuals with no chronic diseases, avoidance and special precautions with certain medical conditions or concomitant drugs should be practiced.

Dexamethasone

Dexamethasone minimises the effects of AMS without improving the acclimatisation process[28]. A return of the symptoms of AMS may occur and develop rapidly when the drug is abruptly terminated. Dexamethasone is useful for individuals who cannot tolerate acetazolamide as prophylaxis[6].

Caution is advised for diabetic patients who have poorly controlled glycemia. It is also prudent to avoid in individuals at risk for peptic ulcer disease or upper gastrointestinal bleed. For those who travel to rural places frequently, it may be prudent to avoid this drug as it may worsen amoebiasis and strongyloidiasis. Potential tendon rupture may occur especially when individuals are taking dexamethasone with fluroquinolones in the management of traveler's diarrhoea[28]. Side effects of steroids such as euphoria and mania may also occur[12].

TREATMENT OF AMS

Non-Pharmacological treatment of AMS

Measures like sleeping propped up[1], rest, proper hydration (not vigorous hydration), avoidance of alcohol are all that is required for simple headaches.

The best treatment for AMS is to stop further ascent, descend within 24 hrs if symptoms do not resolve or descend urgently if respiratory or neurological symptoms develop[6]. It is important that the rest of the tour members do not help carry the unwell for further ascent.

An individual afflicted with AMS should not descend alone in case symptoms worsen[17]. Debilitating illness, tough terrain and/or bad weather conditions can make descent difficult. Occasionally, the descending route may involve further ascent before eventually declining. An alternative route may have to be sought in such cases with a guide familiar with the local terrain. The Gamow bag (portable hyperbaric bag) and supplemental Oxygen may be useful in instances when descent is impossible.

Pharmacological treatment of AMS

Simple analgesia (non-narcotics) such as aspirin, paracetamol and ibuprofen may reduce headache caused by AMS. Antiemetics like metoclopramide and prochlorperazine may be used for nausea[6]. Short-acting benzodiazepines may be used for individuals bothered by insomnia[15]. Drugs should be used mainly to aid descent[6]. It should not be used as an aid for further ascent. Table 2 summaries the common drugs used for prevention and treatment of AMS.

Table 2: Summary of pharmacological agents for AMS prevention and treatment [6,16,27]

Prevention	Treatment
• Acetazolamide 125-250mg bd (taken one day before the ascent for at least 3-5 days for the first part of a trip or the full duration of ascent)	• Acetazolamide 250mg bd
• Dexamethasone 2mg qds or 4mg bd	• Dexamethasone 4mg qds

SPECIAL GROUPS OF INDIVIDUALS

It is generally safe for patients with chronic diseases such as diabetes, epilepsy, hypertension and stable ischaemic heart disease to travel provided their conditions are well-controlled[1,6]. The UIAA (The International Mountaineering and Climbing Federation or Union Internationale des Associations d'Alpinisme) has provided a helpful guide on this topic[29].

Patients with asthma or chronic obstructive pulmonary disease should be warned that, contrary to what is commonly believed, air quality might not be better at high altitude. Emissions from diesel trucks and wood burning especially in areas such as the Himalayas may cause poor air quality in the early mornings and evenings. Valleys within the mountains may also trap particulate air pollutants during temperature inversions.[9]

As long as one is physically fit, age is not an obstacle to high altitude travel[27]. Children are at the same risk of suffering from AMS as adults. However, recognition of symptoms in pre-verbal children may be delayed due to their inability to communicate effectively[6]. Excessive crying, poor appetite, lethargy and vomiting

in pre-verbal children should be assessed with AMS in mind[30].

There are not many studies on pregnant women travelling to high altitude. It may be wise to advise those with low-lying placenta, pre-eclampsia and pregnancy-induced hypertension to avoid such travel[27]. Both acetazolamide and dexamethasone are pregnancy class C drugs.

GENERAL ADVICE IN A PRIMARY CARE SETTING

Places at high altitude have always been held with mystique and there is an inexplicable lure of summits of mountains to mankind. With increased affluence and ease of travel, more Singaporeans will be travelling to such destinations. An approach to the provision of education and advice for high altitude travel in the primary care setting is proposed. It will be prudent to get the following information before dishing out advice to an individual intending to travel to high altitude:

1. Proposed rate of ascent and mode of transport
2. Previous history of HAI
3. Current and past medical history
4. Current medications and drug allergies
5. Purpose of ascent

The following proposal is not meant for adventurers who do competitive mountain climbing or skiing; or who ascend to extreme altitudes e.g., Mount Everest Expedition (altitude of 8850m); or people who have decided to migrate and stay long-term in high altitude.

1. Find out from the travel agency the exact itinerary. There should be contingency plans for travelers who suffer from AMS. Choose one that has a flexible itinerary to allow for days of rest if necessary.
2. Screen for medical conditions that are absolutely contraindicated e.g., pulmonary hypertension, etc.[9,18,29,31]
3. Profile the risk of individuals intending to travel to high altitude and provide the suggested advice as indicated in Table 3. This is an important step as a history of previous HAI, rapid ascent to a high altitude due to tight schedule in a travel itinerary and/or existence of cardio-pulmonary conditions will deem a potential traveler to be at high risk of developing HAI.
4. Explain that the level of fitness, gender and age of an individual are not reliable predictors of AMS.[5,32]
5. Provide a copy of LLSQ (Appendix 2) for self-assessment so that individuals may seek help early if indicated.
   a. If the score is between 3-5, mild AMS is present. Travelers are advised to rest and avoid further ascent. Non-pharmacological measures as described above are to be instituted. Serial evaluations of LLSQ are recommended to assess the condition.
   b. If symptoms resolve and the score is less than 3, further ascent may be appropriate. If symptoms do not resolve and the score is still within 3-5, descend within 24 hours.
   c. If analgesia, anti-emetics or short-acting benzodiazepines are used or the score is 6 or more on the LLSQ, dexamethasone (if not already started and not contraindicated) may be initiated to minimise the symptoms of AMS. Arrangements for immediate descent with medical attention from a doctor trained in high-altitude medicine should be made.
   d. If HACE or HAPE develop, arrangements for immediate descent and medical treatment from a doctor trained in high-altitude medicine should be made.
6. Reinforce non-pharmacological measures as first line.
7. A moderate degree of physical conditioning should be initiated before participating in unaccustomed physical activities e.g., skiing.
8. Common illnesses like traveler's diarrhoea and possible physical injuries should be discussed. It is important to entertain other possible diagnoses when AMS is presented e.g., hypoglycaemia, dehydration, exhaustion, or hypothermia.[3,17]
9. Get good travel insurance.
10. Finally, discuss prophylaxis and treatment. Prophylactic medication is only indicated in those with a known history of HAI or those who cannot avoid rapid ascent.

Table 3: Risk profiling and suggested advice for individuals travelling to high altitude for leisure[4]

Risk of HAI	Description	Suggested Advice
Low	• No history of HAI & initial destination < 2800m (sleeping altitude) • ≥ 2 days to reach destination • ≤ 500m/day of ascent once over 2500m	• Non-pharmacological measures • Education
Moderate	• Previous history of AMS & initia destination < 2800m (sleeping altitude) • No history of AMS & initial destination < 3000m in < 2 days • > 500m/day of ascent once over 2800m	• Non-pharmacological measures • Education • Consider acetazolamide or dexamethasone (if unable to tolerate the former)
High	• History of HACE or HAPE & initial destination > 3000m in < 2 days • History of AMS & < 3000m in < 2 days • >500m/day of ascent once over 3000m; rapid guided ascents • Predisposing medical conditions e.g. COPD, pulmonary hypertension etc.	• Non-pharmacological measures • Education • Discuss possibility of cancelling trip • Refer for further assessment e.g., treadmill ECG

Appendix 2: Lake Louise Score Questionnaire (LLSQ)

(Downloaded from www.treksafe.com.au/medical/documents/LakeLouisescore_001.pdf)

A diagnosis of AMS is based on:
1. A rise in altitude within the last 4 days
2. Presence of a headache

PLUS

3. Presence of at least one other symptoms
4. A total score of 3 or more from the questions below.

SELF-REPORT QUESTIONNAIRE

Add together the individual scores for each symptom to get the total score.

Headache	No headache	0
	Mild headache	1
	Moderate headache	2
	Severe headache, incapacitating	3
Gastrointestinal Symptoms	None	0
	Poor appetite or nausea	1
	Moderate nausea &/or vomiting	2
	Severe nausea &/or vomiting	3
Fatigue &/or Weakness	Not tired or weak	0
	Mild fatigue/weakness	1
	Moderate fatigue/weakness	2
	Severe fatigue/weakness	3
Dizziness/ Lightheadedness	Not dizzy	0
	Mild dizziness	1
	Moderate dizziness	2
	Severe dizziness, incapacitating	3
Difficulty Sleeping	Slept as well as usual	0
	Did not sleep as well as usual	1
	Woke many times, poor sleep	2
	Could not sleep at all	3
	TOTAL SCORE	

Total score of
3-5 : Mild AMS
6 or more : Severe AMS

NOTE:
- Do not ascend with symptoms of AMS
- Descend if symptoms are not improving or getting worse
- Descend if symptoms of HACE or HAPE develop

REFERENCES

1. Clarke C. Acute mountain sickness: medical problems associated with acute and subacute exposure to hypobaric hypoxia. Postgrad Med J 2006;82(973):748-53. doi: 10.1136/pgmj.2006.047662
2. Pollard AJ. Altitude induced illness. BMJ 1992;304(6838):1324-5. doi: 10.1136/bmj.304.6838.1324
3. Gallagher SA, Hackett PH. High-altitude illness. Emerg Med Clin North Am 2004;22(2):329-55, viii. doi: 10.1016/j.emc.2004.02.001
4. Gallagher SA, Hackett P, Rosen JM. High altitude illness: Physiology, risk factors, and general prevention. UpToDate 2010.
5. Roach RC, Hackett PH. Frontiers of hypoxia research: acute mountain sickness. J Exp Biol 2001;204(Pt 18):3161-70.
6. Barry PW, Pollard AJ. Altitude illness. BMJ 2003;326(7395):915-9. doi: 10.1136/bmj.326.7395.915
7. Gilbert DL. The first documented description of mountain sickness: the Andean or Pariacaca story. Respir Physiol 1983;52(3):327-47. doi: 10.1016/0034-5687(83)90089-0
8. Gilbert DL. The first documented report of mountain sickness: the China or Headache Mountain story. Respir Physiol 1983;52(3):315-26. doi: 10.1016/0034-5687(83)90088-9
9. Luks AM, Swenson ER. Travel to high altitude with pre-existing lung disease. Eur Respir J 2007;29(4):770-92. doi: 10.1183/09031936.00052606
10. McMurray SJ. High altitude medicine for family physicians. Can Fam Physician 1994;40:711-8.
11. Wilson MH, Newman S, Imray CH. The cerebral effects of ascent to high altitudes. Lancet Neurol 2009;8(2):175-91. doi: 10.1016/S1474-4422(09)70014-6
12. Bia FJ. Current prevention and management of acute mountain sickness. Yale J Biol Med 1992;65(4):337-41.
13. The Lake Louise Consensus on the Definition of Altitude Illness. http://www.high-altitude-medicine.com/AMS-LakeLouise.html [Last modified 8-May-2000 assessed 1 Sep 2012 2000.]
14. Weil JV. Sleep at high altitude. High Alt Med Biol 2004;5(2):180-9. doi: 10.1089/1527029041352162
15. Beaumont M, Batejat D, Pierard C, Van Beers P, Philippe M, Leger D, et al. Zaleplon and zolpidem objectively alleviate sleep disturbances in mountaineers at a 3,613 meter altitude. Sleep 2007;30(11):1527-33.
16. Maggiorini M, Muller A, Hofstetter D, Bartsch P, Oelz O. Assessment of acute mountain sickness by different score protocols in the Swiss Alps. Aviat Space Environ Med 1998;69(12):1186-92.
17. Schoene RB. Illnesses at high altitude. Chest 2008;134(2):402-16. doi: 10.1378/chest.07-0561
18. Maloney JP, Broeckel U. Epidemiology, risk factors, and genetics of high-altitude-related pulmonary disease. Clin Chest Med 2005;26(3):395-404, v. doi: 10.1016/j.ccm.2005.05.002
19. Hackett PH, Roach RC. High-altitude illness. N Engl J Med 2001;345(2):107-14. doi: 10.1056/NEJM200107123450206
20. British Mountaineering Council Information Service Information Sheets.
21. Muza SR, Beidleman BA, Fulco CS. Altitude preexposure recommendations for inducing acclimatization. High Alt Med Biol 2010;11(2):87-92. doi: 10.1089/ham.2010.1006
22. West JB. Oxygen enrichment of room air to relieve the hypoxia of high altitude. Respir Physiol 1995;99(2):225-32. doi: 10.1016/0034-5687(94)00094-G
23. Albert CM, Mittleman MA, Chae CU, Lee IM, Hennekens CH, Manson JE. Triggering of sudden death from cardiac causes by vigorous exertion. N Engl J Med 2000;343(19):1355-61. doi: 10.1056/NEJM200011093431902
24. Bartsch P, Bailey DM, Berger MM, Knauth M, Baumgartner RW. Acute mountain sickness: controversies and advances. High Alt Med Biol 2004;5(2):110-24. doi: 10.1089/152702904135210 8
25. Chow T, Browne V, Heileson HL, Wallace D, Anholm J, Green SM. Ginkgo biloba and acetazolamide prophylaxis for acute mountain sickness: a randomized, placebo-controlled trial. Arch Intern Med 2005;165(3):296-301. doi: 10.1001/archinte.165.3.296
26. Swenson ER, Teppema LJ. Prevention of acute mountain sickness by acetazolamide: as yet an unfinished story. J Appl Physiol 2007;102(4):1305-7. doi: 10.1152/japplphysiol.01407.2006

27. Rodway GW, Hoffman LA, Sanders MH. High-altitude-related disorders - Part II: prevention, special populations, and chronic medical conditions. Heart Lung 2004;33(1):3-12. doi: 10.1016/j.hrtlng.2003.08.003

28. Luks AM, Swenson ER. Medication and dosage considerations in the prophylaxis and treatment of high-altitude illness. Chest 2008;133(3):744-55. doi: 10.1378/chest.07-1417

29. Milledge JS, Kupper T. Consenses Statement of the UIAA Medical Commission. Vol. 13, People with Pre-Existing Conditions Going to the Mountains. 2008.

30. Samuels MP. The effects of flight and altitude. Arch Dis Child 2004;89(5):448-55. doi: 10.1136/adc.2003.031708

31. Higgins JP, Tuttle T, Higgins JA. Altitude and the heart: is going high safe for your cardiac patient? Am Heart J 2010;159(1):25-32. doi: 10.1016/j.ahj.2009.10.028

32. O'Connor T, Dubowitz G, Bickler PE. Pulse oximetry in the diagnosis of acute mountain sickness. High Alt Med Biol 2004;5(3):341-8. doi:10.1089/ham.2004.5.341

33. Imray C, Wright A, Subudhi A, Roach R. Acute mountain sickness: pathophysiology, prevention, and treatment. Prog Cardiovasc Dis 2010;52(6):467-84. doi: 10.1016/j.pcad.2010.02.003