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An Advisory Committee Statement (ACS)

Committee to Advise on Tropical Medicine and Travel (CATMAT)*

STATEMENT ON HIGH-ALTITUDE ILLNESSES

Introduction

Many Canadians travel to recreational areas which are located at high altitude (> 1,500 m). As altitude increases, the total pressure and partial pressure of oxygen decreases, resulting in hypoxia which may be associated with decreased exercise performance, increased ventilation, and symptoms of lightheadedness, fatigue, altered perceptions, and sleep disorders. Although the risk increases with altitude, some susceptible individuals may experience symptoms of altitude-related illness beginning as low as 2,500 m.

Specific altitude illnesses include acute mountain sickness (AMS), high-altitude pulmonary edema (HAPE), high-altitude cerebral edema (HACE), and a number of other medical problems (Table 1). Travel to altitiude may also aggrevate underlying illnesses, particularly cardiopulmonary diseases. On the basis of increasing risk of health problems, altitudes can be subclassified into high (1,500 to 3,500 m), very high (> 3,500 to 5,500 m) and extreme (> 5,500 m)[1]. The risk of altitude illness increases directly with the rate of ascent and the altitude reached. Rapid ascent to altitudes > 5,500 m, even for brief exposures, may be associated with severe or fatal illness. The barometric pressure at 5,500 m is one-half of that at sea level. In addition, the temperature drops an average of 6.5° C per 1,000 m of elevation and penetration of ultraviolet (UV) light increases about 4% per 300 m gain in altitude [1]. The combination of cold and hypoxia enhances the risk of cold injuries and altitude problems. The extra UV penetration increases the risk of sunburn, skin cancer, and snow-blindness. Furthermore, in the absence of wind, the reflection of sunlight on flat glaciers can lead to intense radiation with a paradoxical temperature elevation of up to 40° C. Heat exhaustion or dehydration may thus go unrecognized. Acclimatization is the process by which climbers gradually adjust to hypoxia. This enhances performance and ultimately survival at extreme altitudes.

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Table 1 Potential medical problems associated with high-altitude ascent[1]
Acute hypoxia†
Acute mountain sickness†
High-altitude cerebral edema†
High-altitude pulmonary edema†
Cerebrovascular syndromes
Peripheral edema
Retinopathy†
Thromboembolism
Sleep disorders and periodic breathing†
High-altitude pharyngitis and bronchitis
Ultraviolet exposure and keratitis (snowblindness)
Exacerbation of pre-existing illness
† Covered in this statement

Table 2 Strength and quality of evidence summary sheet[2]	
Categories for the strength of each recommendation	
CATEGORY	DEFINITION
A	Good evidence to support a recommendation for use.
B	Moderate evidence to support a recommendation for use.
C	Poor evidence to support a recommendation for or against use.
D	Moderate evidence to support a recommendation against use.
E	Good evidence to support a recommendation against use.
Categories for the quality of evidence on which recommendations are made	
GRADE	DEFINITION
I	Evidence from at least one properly randomized, controlled trial.
II	Evidence from at least one well designed clinical trial without randomization, from cohort or case-controlled analytic studies, preferably from more than one centre, from multiple time series, or from dramatic results in incontrolled experiments.
III	Evidence from opinions or respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees.

Recommendations

Table 2 presents evidence-based medicine categories for the strength and quality of the evidence for the recommendations that follow.

Acute Hypoxia

Acute profound hypoxia may occur during rapid ascent, or when there is an abrupt decline in oxygenation. The latter may be due to overexertion, carbon monoxide poisoning, pulmonary edema, sleep apnea, or failure of the system used to deliver oxygen. Symptoms include fatigue, weakened sensory perceptions, vertigo, sleepiness, hallucinations, and ringing in the ears. The ultimate consequence of acute hypoxia is loss of consciousness, which occurs in the non-acclimatized person at an arterial oxygen saturation (SaO_2) of 40% to 60% or an arterial PO_2 of < 30 mm Hg[1].

Recommendations for the treatment of acute hypoxia

1. Treatment of acute hypoxia includes immediate administration of oxygen, rapid pressurization, or descent[3] (**A II**).
2. Whenever possible, secondary causes of hypoxia such as overexertion, apnea, or failure of the system to deliver oxygen should also be corrected (**B II**).
3. Hyperventilation should be considered; it may increase the minute ventilation and thereby increase the amount of time of consciousness (**B II**).

Acute Mountain Sickness

Table 3 summarizes the 1993 Lake Louise Consensus Committee definition of AMS. AMS symptoms may be assessed with the use of a self-administered questionnaire, and supplemented by a clinical assessment that evaluates changes in mental status, ataxia, and peripheral edema. AMS is now considered to be primarily due to the body's response to modest hypoxia and has a different pathophysiology from simple acute hypoxia, being associated with fluid shifts not seen with hypoxia alone. In some cases, AMS may occur even with modest increases in altitude. Incidence of AMS decreases with advancing age[4], and occurs in up to 25% of adults ascending from sea level to 2,000 m[5] and 28% of children at 2,835 m[6]. AMS is unrelated to physical fitness, weight of luggage carried, gender, or recent respiratory infection.

Table 3
The Lake Louise Consensus Committee definition of acute mountain sickness[4]

To diagnose AMS, all of criteria 1 to 3 and one of symptoms a to d are required:

Criteria

1) a recent gain in altitude

2) at least several hours at the new altitude, and

3) the presence of headache

Symptoms

a) gastrointestinal upset (anorexia, nausea, or vomiting)

b) fatigue or weakness

c) dizziness or lightheadedness

d) difficulty sleeping

AMS can be classified as mild, moderate or severe based on the symptoms present[4]. The cardinal symptoms of moderate to severe AMS are headache, fatigue, dizziness, anorexia, nausea, vomiting, dyspnea on exertion, and ataxia[7]. The headache is typically a throbbing one most pronounced in the bitemporal or occipital areas, worse in the morning and at night, and aggravated with the Valsalva maneuver. In moderate to severe AMS, there is relative hypoventilation[8], retention of fluid[9], raised intracranial pressure[10], impaired gas exchange, and interstitial edema[11]. An early finding is the lack of diuresis normally observed at high altitude, with a decreased urine output and fluid retention. This may be related to the failure of decrease in aldosterone. Alderstoerone usually decreases with ascent but this may not occur in severe AMS. Furthermore, the renin-angiotensin system is less suppressed at altitude in persons with AMS compared to those without, and the glomerular filtration rate is diminished[12]. The net fluid retention and subsequent over-hydration of brain cells, combined with increased permeability of the blood-brain barrier (vasogenic edema) leads to increased intracranial pressure in severe AMS, with coma as the end result. Increased levels of carbon monoxide secondary to the use of small, windproof shelters or cooking in such confined shelters at high altitude can aggravate or precipitate AMS.

Differential diagnosis of acute mountain sickness

The differential diagnosis of AMS includes influenza-like viral illness, alcoholic hangover, exhaustion and dehydration, and high-altitude cerebral edema.

Recommendation for management of acute mountain sickness

The most important aspect of AMS management is early recognition because initial clinical presentation does not predict its eventual severity.

Recommendations for the treatment of acute mountain sickness

1. Stop ascent, with rest and acclimatization at the same altitude; acclimatization may require 12 hours to 4 days (**A II**).
2. Decend immediately if
   - there are symptoms of severe AMS: neurologic abnormalities (ataxia or altered level of consciousness) and/or pulmonary edema (**A II**), and/or
   - symptoms progress at the same altitude during acclimatization or treatment (**A II**).

   Descent to an altitude at least 500 m lower than where the symptoms began will usually reverse AMS.
3. Specific therapeutic drugs
   - Acetazolamide (250 mg orally within 24 hours of onset of symptoms and 250 mg orally 8 hours later): a carbonic anhydrase inhibitor that hastens acclimatization and shortens duration of AMS through its action on acid-base balance[11]. It causes renal excretion of bicarbonate, leading to metabolic acidosis, a compensatory hyperventilation, and improved oxygenation (**A I**).

     Side effects of acetazolamide include paresthesias, polyuria, nausea, drowsiness, impotence, and myopia. The taste of carbonated beverages, including beer, can be altered because the carbon dioxide they contain can be tasted. Because it is a sulfa drug, acetazolamide is contraindicated in persons known to be allergic to these compounds. Rarely, acetazolamide causes crystalluria and bone marrow suppression.
   - Furosemide (80 mg orally twice a day): a diuretic which was found to be useful in treatment in one case series, but cannot be recommended without further evaluation[9] (**C III**).
   - Dexamethasone (4 mg to 8 mg intravenous, intramuscular, or oral loading dose followed by 4 mg every 6 hours): a steriod that is effective for moderate AMS[13-15] and leads to marked improvement within 12 hours, but should be reserved for patients with progressive neurologic symptoms, or ataxia. Discontinuation of dexamethasone without descent usually leads to recurrence of symptoms, so it should not be used alone to treat AMS. It should be used either in combination with descent or with acetazolamide to hasten acclimatization (**A I**).
4. Hyperbaric therapy

   The main goal of hyperbaric therapy is to simulate descent and to give symptomatic improvement within a few hours as a temporizing measure while awaiting descent. Lightweight (7 kg) manual air-pump, fabric pressure bags (Gamow bags) are now effectively used on mountaineering expeditions and in mountain clinics as temporizing measures. Two randomized controlled trials have examined the effect of short-term treatment of AMS at high altitude. The first study demonstrated that the use of hyperbaric therapy was of similar efficacy to oxygen therapy[16]. The other showed that hyperbaric therapy was superior to bed rest[17]. However, neither study showed a benefit compared to controls after 12 hours. Therefore, this treatment should be considered as a temporizing measure only, and descent is still the treatment of choice (**A I**).
5. Symptomatic treatments that may be considered include

   Analgesics
   - Ibuprofen (single 400 mg oral dose) was shown to be superior to placebo in reducing high-altitude headache severity and increased

speed of relief among military service personnel going from base camp at sea level to 5,000 m altitudes in a randomized controlled crossover design trial[18]. It is postulated that prostaglandin-mediated increase in cerebral microvascular permeability may contribute to the pathophysiology of AMS , and treatment with prostaglandin synthetase inhibitors may reduce this response. The main potential side effects of ibuprofen are gastrointestinal bleeding and easy bruising (**A I**).

- Acetaminophen: some experts recommend this analgesic for mild headaches (**C III**).
- Sumatriptan, a selective agonist of 5-hydroxytryptamine receptor used for migraine headaches. was shown to be inferior to ibuprofen in a randomized controlled trial[18] and is not recommended (**E I**).

Prochlorperazine (5 mg to 10 mg intramuscularly) or *promethazine* (50 mg by rectum or orally) may be beneficial for nausea and vomiting (**B III**).

6. Sedatives and alcohol should be avoided and exertion should be minimized (**D III**).
7. Low-flow oxygen (if available) at 0.5 L/min to 1 L/min at night is useful especially for high-altitude headaches and is suggested for mild AMS[2] (**A I**).

Note: Anecdotal reports from experienced physicians and climbers suggest that descent is more effective and oxygen should not be used alone for moderate or severe AMS.

Prevention of Acute Mountain Sickness

General measures

1. The safest method is graded ascent[4]. Graded ascent means that climbers, especially persons without altitude experience, should
   - avoid rapid ascent to sleeping altitudes > 3,000 m
   - spend 2 to 3 nights at 2,500 m to 3,000 m before going higher
   - spend an extra night for acclimatization every 600 m to 900 m if continuing ascent.

   Day trips to higher altitude, with a return to lower altitude for sleep, aid in acclimatization. A general rule of thumb is that > 3,000 m, each night should be spent not > 300 m above the last, with a rest day (2 nights at the same altitude) every 2 or 3 days (**B III**).
2. Alcohol and sedative-hypnotics should be avoided (**D III**).
3. A high carbohydrate diet (> 70%) reduced AMS symptoms by 30% in soldiers taken quickly to near the summit of Pike's Peak (4,300 m) and should be considered as an adjunctive preventative measure[20,21] (**A II**).
4. Overexertion (activities involving more than walking around or tending to camp chores) contributes to illness, and should be avoided. Mild exercise aids in acclimatization but severe heavy exercise should be avoided (**B III**).

Pharmacologic measures

5. Specific Preventative Drugs
   - Acetazolamide: a carbonic anhydrase inhibitor (see under **Treatment of AMS** above) which, in numerous randomized controlled studies, has been shown to be effective in preventing AMS in persons transported rapidly to altitudes of 4,000 m to 4,500 m [22-28]. Small doses of 125 mg to 250 mg orally twice a day, starting 24 hours prior to ascent, have been reported to be as effective as higher doses[29]. One 500 mg tablet of sustained release acetazolamide taken orally every 24 hours has also been shown in one randomized trial to be of equivalent effectiveness with fewer side effects due to lower peak serum levels[30]. Acetazolamide should be continued only for the first 2 days at high altitude while acclimatization occurs (**A I**).

     Indications: rapid ascent (≤ 1 day) to altitudes > 3,000 m, a rapid gain in sleeping altitude (e.g. moving camp from 4,000 m to 5,000 m in one day), and a past history of AMS or HAPE (**A I**).

     The side effects of acetazolamide have been discussed (see under **Treatment of AMS** above) and should be considered.
   - Methazolamide: one randomized trial involving 20 climbers (19 males, one female) showed equal efficacy of this carbonic anhydrase inhibitor (150 mg orally once a day, starting 1 week prior to ascent) in preventing AMS symptoms. Compared with acetazolamide, fewer patients developed paraesthesias on methazolamide[31] (**B II**).
   - Spironolactone (25 mg orally 4 times a day): one randomized study showed spironolactone to be of similar efficacy to acetazolamide, but this has not been confirmed[26] (**B II**).
   - Dexamethasone: many randomized studies have shown dexamethasone to have similar efficacy to acetazolamide in reducing the incidence of AMS[24, 32-36]. One randomized trial of 32 healthy backpackers climbing at between 3,650 m to 4,050 m on the Sierra Nevada Mountains found that the combination of dexamethasone acetate (4 mg orally four times a day) with acetazolamide (250 mg orally twice a day) was superior to dexamethasone or acetazolamide alone[37]. In another study, a dose as low as 4 mg dexamethasone every 12 hours was effective in reducing AMS symptoms[34]. However, because most cases only have mild AMS, the availability of an effective alternative in acetazolamide, and the potential for rebound and other serious side effects from dexamethasone, we recommend restricting the use of dexamethasone only for treatment of AMS, or for prophylaxis as necessary in intolerant persons or those allergic to acetazolamide (**A I**).
   - Nifedipine: in the only randomized trial for AMS prevention, this calcium channel inhibitor was shown to be beneficial in lowering the pulmonary arterial pressures during rapid ascent to 4,559 m, but had no effect on gas exchange and symptoms of AMS[38]. Although nifedipine may be of help in HAPE, it has not been found to be helpful in AMS (**D I**).

High-Altitude Cerebral Edema

HACE is usually recognized when a person with AMS or HAPE develops symptoms of encephalopathy. HACE can be viewed as the extreme end of the spectrum of AMS, and it rarely occurs without HAPE[39]. It is characterized by ataxia, extreme lassitude, and altered level of consciousness in the form of confusion, impaired thinking, drowsiness, stupor, and coma. Other possible symptoms and signs include cyanosis or grayish colour, headaches, nausea and vomiting, hallucinations, cranial nerve palsy, hemiparesis, hemiplegia, seizures, retinal hemorrhages, and focal neurologic signs. Examination of blood gases or pulse oximetry shows severe hypoxemia. A chest x-ray usually reveals signs of pulmonary edema. Progression to HACE from mild AMS

varies from 12 hours to the more common duration of between 1 and 3 days. The pathophysiologic mechanisms underlying HACE are similar to those of AMS and result in cerebral edema and raised intracranial pressure, but are more pronounced[40].

Recommendations for the treatment of high-altitude cerebral edema

1. Early recognition is most important in the treatment of HACE. In order to prevent death, descent must be undertaken as soon as ataxia or altered level of consciousness begins (**A II**).
2. Hyperbaric therapy (Gamow bag) combined with oxygen should be started if descent can not be initiated immediately. If oximetry is available, the oxygen delivered should be titrated to keep the SaO_2 at > 90%.
3. Dexamethasone (4 mg to 8 mg intravenous, intramuscular, or orally loading dose followed by 4 mg every 6 hours), and oxygen (2 L/min to 4 L/min given by mask or nasal cannula) have also been shown to be beneficial in addition to descent (**A II**).
4. The comatose patient
   - A secure airway should be ensured and the bladder may need drainage. Other mangement components include intubation and hyperventilation, and careful use of diuretics such as furosemide (**B III**).
   - There are no controlled trials on the use of steroids in the setting of coma, but there is anecdotal evidence of good response if started early in the course of HACE (**C III**), but a poor response if started after unconsciousness has set in (**D III**).
   - Data to support the use of mannitol, saline, or urea for coma are limited (**C III**).

   Coma may persist for days, even with descent to lower altitude, and other causes need to be ruled out if this occurs.

Prevention of high-altitude cerebral edema

The prevention of HACE is the same as for AMS. The non-fatal complications may last for several weeks.

High-Altitude Pulmonary Edema

HAPE, described as a unique clinical syndrome in 1960[41], is the most common cause of fatality due to high altitude. Up to 20 deaths are reported annually[42]. The incidence of this condition varies with the rate of ascent, altitude reached, temperature, physical exertion, use of sleeping pills, and other factors. Whereas 1 in 10,000 skiers in the Rocky Mountains (maximum altitude 3,500 m) develop HAPE[43], up to 1.6% of trekkers to Mount Everest base camp 5,150 metres, 3% of adults trekking in Peru at 3,782 m[44], and 5.2% of Swiss climbers at 4,559 m[45] developed it. Furthermore, up to 15% of Indian soldiers develop this syndrome when airlifted from sea level to altitudes between 3,500 m and 5,500 m[10]. Younger persons and men may be more susceptible[42,44]. Persons with HAPE tend to have a low hypoxic ventilatory drive and a raised pulmonary vasoconstrictor response to hypoxia[46].

HAPE usually occurs within 2 to 4 days of ascent to altitudes > 2,500 m, most commonly on the second night. The earliest symptoms may include persistent cough, decreased exercise performance, and increased recovery time from exercise. Other common symptoms include fatigue, weakness, shortness of breath on exertion, and the signs of AMS (headache, anorexia, lassitude). As the condition progresses, dry cough, central and peripheral cyanosis, tachycardia, and tachypnea occur at rest. The mortality rate is affected by many variables, especially prompt diagnosis and treatment.

Differential diagnosis of high-altitude pulmonary edema

The differential diagnosis of HAPE includes: pneumonia, pulmonary embolism, pulmonary infarct, and hyperactive airway disease. In addition, HAPE may be complicated by super-infection, cerebral edema, pulmonary thrombosis, frostbite, or trauma from pressure points during immobilization.

Laboratory findings for high-altitude pulmonary edema

Laboratory findings for HAPE include: mild elevation of hematocrit and hemoglobin, mild elevation of the white blood cell count, and elevated creatinine phosphokinase levels. Arterial blood gases reveal respiratory alkalosis and severe hypoxemia. Chest x-ray findings are consistent with non-cardiogenic pulmonary edema (patchy bilateral interstitial and air space infiltrate with prominence of the lower lobes).

HAPE is a non-cardiogenic form of pulmonary edema. Although the mechanism of HAPE is unknown, pulmonary hypertension is always present, and is usually accompanied by a high protein permeability leak and normal left ventricular function.

Recommendations for the treatment of high-altitude pulmonary edema

1. Successful treatment of HAPE requires early recognition. Evacuation to a lower altitude is critical (**A II**).

   For mild HAPE, early descent of only 500 to 1,000 m leads to rapid recovery. Affected individuals may be able to re-ascend slowly 2 to 3 days later.
2. High-flow oxygen, if available, delivered by face mask or nasal cannulae can be lifesaving[1] (**A II**).

   In some high-altitude situations, bed rest with oxygen may be enough for mild HAPE (symptoms only on strenuous activity) if frequent observations are made to ascertain that clinical improvement is occurring[47].
3. Exertion should be minimized. The patient should be warmed to avoid cold stress which may elevate the pulmonary arterial pressures (**B III**).
4. Positive pressure masks have recently been shown to improve gas exchange, but should not replace descent[48] (**B II**).
5. Medications play only a small secondary role in the management of HAPE, because of effective results of descent and treatment with oxygen. Drug therapy should be considered only as an adjunct to these two modalities and not as a replacement.
   - Nifedipine (30 mg slow-release capsule orally every 12 to 24 hours or 10 mg sublingually repeated as necessary) reduces pulmonary vascular resistance, and pulmonary arterial pressures[49] and should be considered for adjunctive therapy (**B III**).
   - Nitric oxide: in a recent randomized controlled trial, inhalation of 40 ppm of nitric oxide was shown to produce a significant decrease

in mean systolic pulmonary-artery pressure and improve arterial oxygenation in subjects who were prone to HAPE, but not in those who were resistant to this condition[50] (**B I**).

This form of therapy should also be considered as adjunctive to descent in at risk individuals. However, it may be impractical to administer, e.g. in skiers.

- Furosemide (80 mg either intravenously or orally every 12 hours, with 15 mg of intravenous morphine sulphate added to the first dose): this treatment remains controversial. One study suggested that it improved diuresis and clinical status[9]. A subsequent report indicated adverse effects of furosemide in subjects brought to 5,340 m on Mount Logan[51]. Thus, more research is needed with furosemide prior to recommendation (**C III**).
- Morphine: morphine reduces dyspnea, improves oxygenation and comfort and reduces the heart and respiratory rates. However, concerns have been raised about the respiratory depression, hypovolemia, and hypotension that may occur with this therapy combined with furosemide[52] (**C III**).

6. After descent, ongoing treatment for severe cases of HAPE consists of bed rest, and administration of oxygen to maintain SaO_2 at > 90%. Most patients recover rapidly with this simple form of therapy, and intubation and ventilation are rarely needed. Pneumonia should be treated with antibiotics. Patients may be discharged when there is clinical improvement, and an arterial PO_2 of 60 mm Hg or SaO_2 > 90%. They should be warned to resume normal activities slowly[1]. Advice about prevention should also be given (see below).

Prevention of high-altitude pulmonary edema

The same preventive measures as for AMS apply, i.e. graded ascent, slow acclimatization, low sleeping altitudes, and avoidance of alcohol and sleeping pills. In addition, overexertion should be avoided, especially during the first 2 days at altitude.

1. Clinical experience (but no studies) suggests that acetazolamide may prevent HAPE in persons with a history of recurrent episodes, especially in children [53] (**C III**).
2. In one randomized controlled clinical trial, nifedipine (20 mg of slow-release capsule orally every 8 hours) prevented HAPE in subjects with a history of repeated episodes who rapidly ascended (within 22 hours) from a low altitude to 4,559 m[54]. However, use of the drug in this fashion is limited because of potentially harmful side effects including hypotension, headache, nausea, vomiting, fatigue, dizziness, and pedal edema. Nifedipine should thus be restricted for use in persons with known susceptibility to HAPE who nevertheless go to altitudes where supplemental oxygen supplies and opportunities for descent may be limited[55] (**B I**).

   Such persons should be warned that in no way does nifedipine replace graded ascent, and slow acclimatization. Descent should be immediate if symptoms occur.
3. Individuals who have experienced HAPE should have a cardiac assessment to rule out undetected cardiovascular conditions (**C III**).

Table 4 summarizes the key evidence-based medicine recommendations for each of AMS, HACE, and HAPE.

High-Altitude Sleep Disturbance and Periodic Breathing

Normal sleep is often impairmed at high altitudes. At about 3,048 m, some individuals will report poor sleep while the majority of persons sleeping > 4,300 m have marked sleep disturbance[56,57]. In a study of six men during 2 nights at sea level and four non consecu- tive nights at 4,301 m at the high altitude, all had disturbed sleep as measured by sleep electroencephalogram[58]. This was characterized by a significant decrease in sleep stages three and four, and a trend toward more time spent awake. The men complained of poor sleep but there was only a small reduction in total sleep time. Five also had periodic breathing, but arousals from sleep were not always associated with this breathing pattern. The mechanism of arousal is not certain, but may be related to hypoxia.

Periodic breathing occurs mainly at night, and is characterized by hyperpnea followed by apnea. Persons with a high hypoxic ventilatory response (HVR) have higher rates of periodic breathing[59], while persons with low HVR may have periods of extreme hypoxemia during sleep that are unrelated to periodic breathing[61-63]. There is evidence that arousal is protective in preventing severe oxygen deprivation[63-65].

Table 4
Evidence-based management of altitude sickness

	Acute Mountain Sickness		High-Altitude Cerebral Edema		High-Altitude Pulmonary Edema	
MODALITY	**Prevent**	**Treat**	**Prevent**	**Treat**	**Prevent**	**Treat**
Descent	–	A II	–	A II	–	A II
Hyperbaric therapy	–	A I*	–	–	–	
Oxygen	–	A I*	–	A II*	–	A II†
THERAPEUTIC DRUGS						
Acetazolamide	A I	A I†	A I	–	C III	
Methazolamide	B II	–	B II	–	–	
Spironolactone	B II	–	B II	–	–	
Furosemide	–	C III	–	B III*	–	C III
Dexamethasone	A I¶	A I**	A I¶	A II*	–	
Nifedipine	D I	–	D I	–	B I	A II*
SYMPTOMATIC TREATMENTS						
Analgesics						
Ibuprofen	–	A I‡	–	–	–	–
Acetaminophen	–	C III‡	–	–	–	–
Anti-emetics						
Prochloperazine	–	C III§	–	–	–	–
Promethazine	–	C III§	–	–	–	–

* Must be used as temporizing measure while awaiting descent or in addition to descent only

** Use with descent or in combination with acetazolamide only

† Must be given within early (< 24 hours) of mild symptoms: descent mandatory if symptoms progress

‡ For high-altitude headaches

§ For nausea and vomiting

¶ Suggest restrict for treatment alone or for prophylaxis in at risk persons who are intolerant or allergic to acetazolamide

Prevention and treatment of high-altitude sleep disorders

1. Acetazolamide (125 mg orally at bedtime) has been shown to decrease periodic breathing and apnea, improve oxygenation compared to placebo and almitrine, and is safe for use as a sleeping aid[61] with consideration of the side effects previously discussed (see under **Treatment of AMS** above) (**A I**).
2. Temazepam (10 mg orally): a short-acting benzodiazepine that has also been recently shown to be superior to placebo in decreasing the number and severity of changes in saturation during sleep and improving the quality of sleep[66] (**A 1**).

   This was achieved without a significant drop in mean arterial saturation values during sleep that may have been anticipated with the longer acting benzodiazepines.

High-Altitude Retinal Hemorrhage

Retinal hemorrhages are very common > 5,200 m[67-69]. These are not necessarily related to AMS and are more related to hypoxemia. They are symptomatic only if found over the macula. While retinal haemorrhages may lead to blindness, the majority resolve on descent within 7 to 14 days. Although there is no evidence that the location of a hemorrhage will be the same on repeat ascent to high altitude, most experts would consider this to be a contraindication for future ascents. Hemorrhages not affecting vision are not known to have any clinical significance and do not warrant descent. Hemorrhages have been induced by strenuous exercise which increases blood pressure and decreases the arterial oxygen saturation levels[67]. Below 5200 m, hemorrhages are more likely due to high-altitude illnesses and these should be managed according to the syndrome involved.

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