CHAPTER e51

Altitude Illness

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Mountains cover one-fifth of the earth's surface; 38 million people live permanently at altitudes ≥2400 m, and 100 million people travel to high-altitude locations each year. Skiers in Aspen, religious pilgrims to Lhasa, trekkers and climbers to Kilimanjaro or Everest, and military personnel deployed to high-altitude locales are all at risk of developing acute mountain sickness (AMS), high-altitude cerebral edema (HACE), high-altitude pulmonary edema (HAPE), and other altitude-related problems. AMS is the benign form of altitude illness, whereas HACE and HAPE are life-threatening. Altitude illness is likely to occur above 2500 m but has been documented even at 1500–2500 m.

Ascent to a high altitude subjects the body to a decrease in barometric pressure that results in a decreased partial pressure of oxygen in the inspired gas in the lungs. This change leads in turn to less pressure driving oxygen diffusion from the alveoli and throughout the oxygen cascade. A normal initial "struggle response" to such an ascent includes increased ventilation, which is the cornerstone of acclimation. Hyperventilation may cause respiratory alkalosis and dehydration. Alkalosis may depress the ventilatory drive during sleep, with consequent periodic breathing and hypoxemia. During early acclimation, renal suppression of carbonic anhydrase and excretion of dilute alkaline urine combat alkalosis and tend to bring the pH of the blood to normal. Other physiologic changes during normal acclimation include increased sympathetic tone; increased erythropoietin levels, leading to increased hemoglobin levels and red blood cell mass; increased tissue capillary density and mitochondrial numbers; and higher levels of 2,3-bisphosphoglycerate, enhancing oxygen utilization. Even with normal acclimation, however, ascent to a high altitude decreases maximal exercise tolerance and increases susceptibility to cold injury due to peripheral vasoconstriction. Finally, if the ascent is made faster than the body can adapt to the stress of hypobaric hypoxemia, altitude-related disease states can result.

ACUTE MOUNTAIN SICKNESS AND HIGH-ALTITUDE CEREBRAL EDEMA

AMS is a neurologic syndrome characterized by nonspecific symptoms (headache, nausea, fatigue, and dizziness) with a paucity of physical findings developing 6–12 h after ascent to a high altitude. AMS must be distinguished from exhaustion, dehydration, hypothermia, alcoholic hangover, and hyponatremia. AMS and HACE are thought to represent opposite ends of a continuum of altitude-related neurologic disorders. HACE (but not AMS) is an encephalopathy whose hallmarks are ataxia and altered consciousness with diffuse cerebral involvement but generally without focal neurologic deficits. Progression to these signal manifestations can be rapid. Papilledema and, more commonly, retinal hemorrhages may also be seen. Retinal hemorrhages occur frequently at ≥5000 m, even in individuals without clinical symptoms of AMS or HACE. It is unclear whether retinal hemorrhage and cerebral hemorrhage at high altitude are caused by the same mechanism; however, one report revealed a correlation between HACE and retinopathy.

The most important risk factors for the development of altitude illness are the rate of ascent and a history of high-altitude illness. Exertion is a risk factor, but lack of physical fitness is not. An attractive but still speculative hypothesis proposes that AMS develops in people who have inadequate cerebrospinal capacity to buffer the brain swelling that occurs at high altitude. One protective factor in AMS is high-altitude exposure during the preceding 2 months; the explanation for this association is intriguing but remains uninvestigated. Children and adults seem to be equally affected, but people >50 years of age may be less likely to develop AMS than younger people. Most studies reveal no gender difference in AMS incidence. Sleep desaturation—a common phenomenon at high altitude—is associated with AMS. Debilitating fatigue consistent with severe AMS on descent from a summit is also an important risk factor for death in mountaineers.

Pathophysiology

The exact mechanisms causing these syndromes are unknown. Evidence points to a central nervous system process. MRI studies have suggested that vasogenic (interstitial) cerebral edema is a component of the pathophysiology of HACE. In the setting of high-altitude illness, the MRI findings shown in Fig. e51-1 are confirmatory of HACE, with increased signal in the white matter and particularly in the splenium of the corpus callosum. Quantitative analysis in a 3-tesla MRI study revealed that hypoxia is associated with mild vasogenic cerebral edema irrespective of AMS. This finding is in keeping with case reports of suddenly symptomatic brain tumors and of cranial nerve palsies without AMS at high altitudes. Vasogenic edema may become cytotoxic (intracellular) in severe HACE.

Impaired cerebral autoregulation in the presence of hypoxic cerebral vasodilatation and altered permeability of the blood-brain barrier due to hypoxia-induced chemical mediators like histamine, arachidonic acid, and vascular endothelial growth factor (VEGF)
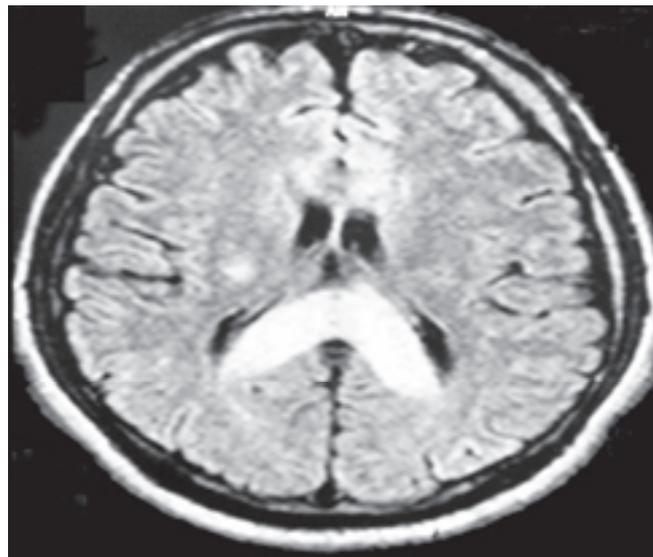

Figure e51-1   **T2 MRI image of the brain of a patient with HACE** showing marked swelling and a hyperintense posterior body and splenium of the corpus callosum (area with dense opacity). The patient, a climber, went on to climb Mount Everest about 9 months after this episode of HACE. *[With permission from Wilderness and Environmental Medicine, 15(1): 53-55, Spring 2004.]*

may all contribute to brain edema. In 1995, VEGF was first proposed as a potent promoter of capillary leakage in the brain at high altitude, and studies in mice have borne out this role. Although preliminary studies of VEGF in climbers have yielded inconsistent results and have revealed no association with altitude illness, indirect evidence of a role for this growth factor in AMS and HACE comes from the observation that dexamethasone, when used in the prevention and treatment of AMS and HACE, blocks hypoxic upregulation of VEGF. Other factors in the development of cerebral edema may be the release of calcium-mediated nitric oxide and neuronally mediated adenosine, which may promote cerebral vasodilation.

Increased sympathetic activity triggered by hypoxia may also contribute to blood-brain barrier leakage. Enhanced optic-nerve sheath diameter with increasing severity of AMS has been noted and suggests an important role for increased intracranial pressures in the pathophysiology of AMS. Finally, the effect of hypoxia on reactive oxidant species and the role of these species in clinical AMS are unclear.

The pathophysiology of the most common and prominent symptom of AMS—headache—remains unclear because the brain itself is an insensate organ; only the meninges contain trigeminal sensory nerve fibers. The cause of high-altitude headache is multifactorial; various chemicals and mechanical factors activate a final common pathway, the trigeminovascular system. In the genesis of high-altitude headache, the response to nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids provides indirect evidence for involvement of the arachidonic acid pathway and inflammation. Although the International Headache Society acknowledges that high altitude may be a trigger for migraine, it is unclear whether high-altitude headache and migraine share the same pathophysiology. However, sumatriptan (50 mg by mouth within 1 h of ascent) prevents AMS.

Prevention and treatment (Table e51-1)

Gradual ascent, with adequate time for acclimation, is the best method for the prevention of altitude illness. Above 3000 m, a graded ascent of ≤300 m from the previous day's sleeping altitude is generally recommended, and taking every third day of gain in sleeping altitude as an extra day for acclimation is helpful. Spending one night at an intermediate altitude before proceeding to a higher altitude may enhance acclimation and attenuate the risk of AMS. Clearly, a flexible itinerary that permits additional rest days will be helpful. Sojourners to high-altitude locations must be aware of the symptoms of altitude illness and should be encouraged not to ascend further if these symptoms develop. Any hint of HAPE (see below) or HACE mandates descent.

Pharmacologic prophylaxis at the time of travel to high altitudes is warranted for people with a history of AMS or when a graded ascent and acclimation are not possible—e.g., when rapid ascent is necessary for rescue purposes or when flight to a high-altitude location is required. Acetazolamide (125–250 mg twice a day), administered for 1 day before ascent and continued for 2 or 3 days, is effective. Higher doses generally are not required. Paresthesia and a tingling sensation are common side effects of acetazolamide. Dexamethasone (8 mg/d in divided doses) is also effective. A large-scale, randomized, double-blind, placebo-controlled trial in partially acclimated trekkers has clearly shown that *Ginkgo biloba* is ineffective in the prevention of AMS. To date, no trials of NSAIDs in the prevention of AMS have been reported.

TABLE e51-1 Management of Altitude Illness

Condition	Management
Acute mountain sickness (AMS), mild[a]	Discontinuation of ascent Treatment with acetazolamide (250 mg q12h) Descent[b]
AMS, moderate[a]	Immediate descent for worsening symptoms Use of low-flow oxygen if available Treatment with acetazolamide (250 mg q12h) and/or dexamethasone (4 mg q6h)[c] Hyperbaric therapy[d]
High-altitude cerebral edema (HACE)	Immediate descent or evacuation Administration of oxygen (2–4 L/min) Treatment with dexamethasone (8 mg PO/IM/IV; then 4 mg q6h) Hyperbaric therapy if descent is not possible
High-altitude pulmonary edema (HAPE)	Immediate descent or evacuation Minimization of exertion while patient is kept warm Administration of oxygen (4–6 L/min) to bring O_2 saturation to >90% Adjunctive therapy with nifedipine[e] (30 mg, extended-release, q12h) Hyperbaric therapy if descent is not possible

[a]Categorization of cases as mild or moderate is a subjective judgment based on the severity of headache and the presence and severity of other manifestations (nausea, fatigue, dizziness, insomnia).

[b]No fixed altitude is specified; the patient should descend to a point below that at which symptoms developed.

[c]Acetazolamide treats and dexamethasone masks symptoms. For prevention (as opposed to treatment), 125–250 mg of acetazolamide q12h or (when acetazolamide is contraindicated—e.g., in people with sulfa allergy) 4 mg of dexamethasone q12h may be used.

[d]In hyperbaric therapy, the patient is placed in a portable altitude chamber or bag to simulate descent.

[e]Nifedipine (30 mg extended release q12h) is also effective for the prevention of HAPE, as is salmeterol (125 μg inhaled twice daily), tadalafil (10 mg twice daily), or dexamethasone (8 mg twice daily).

For the treatment of mild AMS, rest alone with analgesic use may be adequate. Descent and the use of acetazolamide and (if available) oxygen are sufficient to treat most cases of moderate AMS. Even a minor descent (400–500 m) may be adequate for symptom relief. For moderate AMS or early HACE, dexamethasone (8 mg orally or parenterally) is highly effective. For HACE, immediate descent is mandatory. When descent is not possible because of poor weather conditions or darkness, a simulation of descent in a portable hyperbaric chamber is effective and, like dexamethasone administration, "buys time." Like nifedipine, phosphodiesterase-5 inhibitors have no role in the treatment of AMS or HACE.

■ HIGH-ALTITUDE PULMONARY EDEMA

Unlike HACE (a neurologic disorder), HAPE is primarily a pulmonary problem and therefore is not necessarily preceded by AMS. HAPE develops within 2–4 days after arrival at high altitude; it rarely occurs after more than 4 or 5 days at the same altitude, probably because of remodeling and adaptation that render the pulmonary vasculature less susceptible to the effects of hypoxia. A rapid rate of ascent, a history of HAPE, respiratory tract infections, and cold environmental temperatures are risk factors. Men are more susceptible than women. People with abnormalities of the cardiopulmonary circulation leading to pulmonary hypertension—e.g., patent foramen ovale, mitral stenosis, primary pulmonary hypertension, and unilateral absence of the pulmonary artery—are at increased risk of HAPE, even at moderate altitudes. For example, patent foramen ovale is four times more common among HAPE-susceptible individuals than in the general population. Echocardiography is recommended when HAPE develops at relatively low altitudes (<3000 m) and whenever cardiopulmonary abnormalities predisposing to HAPE are suspected.

The initial manifestation of HAPE may be a reduction in exercise tolerance greater than that expected at the given altitude. Although a dry, persistent cough may presage HAPE and may be followed by the production of blood-tinged sputum, cough in the mountains is almost universal and the mechanism is poorly understood. Tachypnea and tachycardia, even at rest, are important markers as illness progresses. Crackles may be heard on auscultation but are not diagnostic. HAPE may be accompanied by signs of HACE. Patchy or localized opacities (Fig. e51-2) or streaky interstitial edema may be noted on chest radiography. In the past, HAPE was mistaken for pneumonia due to the cold or for heart failure due to hypoxia and exertion. Kerley B lines or a bat-wing appearance are not seen on radiography. Electrocardiography may reveal right
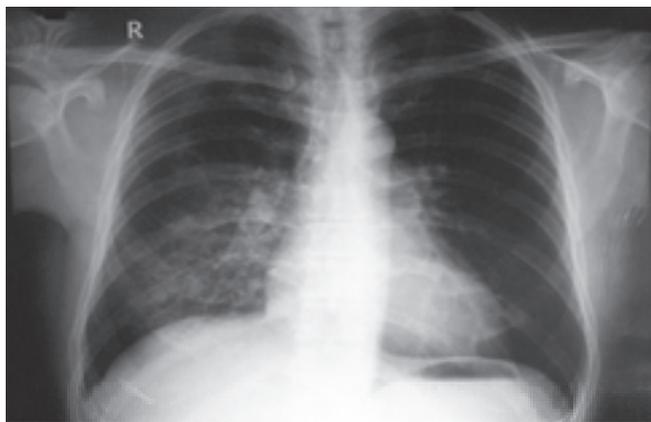

Figure e51-2 Chest radiograph of a patient with HAPE shows opacity in the right mid- and lower zones simulating pneumonic consolidation. The opacity cleared almost completely in 2 days with descent and oxygen.

ventricular strain or even hypertrophy. Hypoxemia and respiratory alkalosis are consistently present unless the patient is taking acetazolamide, in which case metabolic acidosis may supervene. Assessment of arterial blood gases is not necessary in the evaluation of HAPE; an oxygen saturation reading with a pulse oximeter is generally adequate. The existence of a subclinical form of HAPE probably has been suggested by an increased alveolar-arterial oxygen gradient in Everest climbers near the summit, but hard evidence correlating this abnormality with the development of clinically relevant HAPE is lacking.

Pathophysiology

HAPE is a noncardiogenic pulmonary edema characterized by patchy pulmonary vasoconstriction that leads to overperfusion in some areas. This abnormality leads in turn to increased pulmonary capillary pressure (>18 mmHg) and capillary "stress" failure. The exact mechanism for the vasoconstriction is unknown. Endothelial dysfunction due to hypoxia may play a role by impairing the release of nitric oxide, an endothelium-derived vasodilator. At high altitude, HAPE-prone persons have reduced levels of exhaled nitric oxide. The effectiveness of phosphodiesterase-5 inhibitors in alleviating altitude-induced pulmonary hypertension, decreased exercise tolerance, and hypoxemia supports the role of nitric oxide in the pathogenesis of HAPE. One study demonstrated that prophylactic use of tadalafil, a phosphodiesterase-5 inhibitor, decreases the risk of HAPE by 65%. In contrast, the endothelium also synthesizes endothelin-1, a potent vasoconstrictor whose concentrations are higher than average in HAPE-prone mountaineers. Bosentan, an endothelin receptor antagonist, attenuates hypoxia-induced pulmonary hypertension, but further field studies with this drug are necessary.

Exercise and cold lead to increased pulmonary intravascular pressure and may predispose to HAPE. In addition, hypoxia-triggered increases in sympathetic drive may lead to pulmonary venoconstriction and extravasation into the alveoli from the pulmonary capillaries. Consistent with this concept, phentolamine, which elicits α-adrenergic blockade, improves hemodynamics and oxygenation in HAPE more than do other vasodilators. The study of tadalafil cited above also investigated dexamethasone in the prevention of HAPE. Surprisingly, dexamethasone reduced the incidence of HAPE by 78%—a greater decrease than with tadalafil. Besides possibly increasing the availability of endothelial nitric oxide, dexamethasone may have altered the excessive sympathetic activity associated with HAPE: the heart rate of participants in the dexamethasone arm of the study was significantly lowered. Finally, people susceptible to HAPE also display enhanced sympathetic activity during short-term hypoxic breathing at low altitudes.

Because many patients with HAPE have fever, peripheral leukocytosis, and an increased erythrocyte sedimentation rate, inflammation has been considered an etiologic factor in HAPE. However, strong evidence suggests that inflammation in HAPE is an epiphenomenon rather than the primary cause. Nevertheless, inflammatory processes (e.g., those elicited by viral respiratory tract infections) do predispose persons to HAPE—even those who are constitutionally resistant to its development.

Another proposed mechanism for HAPE is impaired transepithelial clearance of sodium and water from the alveoli. β-Adrenergic agonists upregulate the clearance of alveolar fluid in animal models. In a double-blind, randomized, placebo-controlled study of HAPE-susceptible mountaineers, prophylactic inhalation of the β-adrenergic agonist salmeterol reduced the incidence of HAPE by 50%. Other effects of β agonists may also contribute to the prevention of HAPE, but these findings are in keeping with the concept that alveolar fluid clearance may play a pathogenic role in this illness.

GENETICS

Hypoxia-inducible factor, which is important in high-altitude adaptation, controls transcriptional responses to hypoxia throughout the body and is involved in VEGF release in the brain, erythropoiesis, and other pulmonary and cardiac functions at high altitudes. Hypoxia-inducible factor is regulated through oxygen-dependent proteasomal degradation and thus responds to variations in oxygen availability. Although gene polymorphism may influence susceptibility to HAPE, the data on this point are unclear. Endothelial nitric oxide synthase gene polymorphism has been associated with susceptibility to HAPE in Japan but not in Europe. Although angiotensin-converting enzyme gene polymorphism appears to confer a performance advantage at high altitude, an association with susceptibility to HAPE is lacking.

Prevention and treatment (Table e51-1)

Allowing sufficient time for acclimation by ascending gradually (as discussed above for AMS and HACE) is the best way to prevent HAPE. Sustained-release nifedipine (30 mg), given once or twice daily, prevents HAPE in people who must ascend rapidly or who have a history of HAPE. Other drugs for the prevention of HAPE are listed in Table e51-1 (footnote *e*). Although dexamethasone is listed for prevention, its adverse-effect profile requires close monitoring. Acetazolamide has been shown to blunt hypoxic pulmonary vasoconstriction, and this observation warrants further study in HAPE prevention. However, one study failed to show a decrease in pulmonary vasoconstriction in partially acclimated individuals given acetazolamide.

Early recognition is paramount in the treatment of HAPE, especially when it is not preceded by the AMS symptoms of headache and nausea. Fatigue and dyspnea at rest may be the only initial manifestations. Descent and the use of supplementary oxygen (aimed at bringing oxygen saturation to >90%) are the most effective therapeutic interventions. Exertion should be kept to a minimum, and the patient should be kept warm. Hyperbaric therapy in a portable altitude chamber may be used if descent is not possible and oxygen is not available. Oral sustained-release nifedipine (30 mg once or twice daily) can be used as adjunctive therapy. Inhaled β agonists, which are safe and convenient to carry, are useful in the prevention of HAPE and may be effective in its treatment, although no trials have yet been carried out. Inhaled nitric oxide and expiratory positive airway pressure may also be useful therapeutic measures but may not be available in high-altitude settings. No studies have investigated phosphodiesterase-5 inhibitors in the treatment of HAPE, but reports have described their use in clinical practice. The mainstays of treatment remain descent and (if available) oxygen.

In AMS, if symptoms abate (with or without acetazolamide), the patient may reascend gradually to a higher altitude. Unlike that in acute respiratory distress syndrome (another noncardiogenic pulmonary edema), the architecture of the lung in HAPE is usually well preserved, with rapid reversibility of abnormalities (Fig. e51-2). This fact has allowed some people with HAPE to reascend slowly after a few days of descent and rest. In HACE, reascent after a few days is not advisable.

■ OTHER HIGH-ALTITUDE PROBLEMS

Sleep impairment

The mechanisms underlying sleep problems, which are among the most common adverse reactions to high altitude, include increased periodic breathing, changes in sleep architecture with increased time in lighter sleep stages, and changes in rapid-eye-movement sleep. Sojourners should be reassured that sleep quality improves with acclimation. In cases where drugs do need to be used, acetazolamide (125 mg before bedtime) is especially useful as this agent decreases hypoxemic episodes and alleviates sleeping disruptions caused by excessive periodic breathing. Whether combining acetazolamide with temazepam or zolpidem is more effective than administering acetazolamide alone is unknown. In combinations, the doses of temazepam and zolpidem should not be increased by >10 mg at high altitudes. Limited evidence suggests that diazepam causes hypoventilation at high altitudes and therefore is contraindicated. For trekkers with obstructive sleep apnea who are using a continuous positive airway pressure (CPAP) machine lacking pressure compensation, set pressures may need to be adjusted.

Gastrointestinal issues

Because of decreased atmospheric pressure and consequent intestinal gas expansion at high altitudes, many sojourners experience abdominal bloating and distension and excessive flatus expulsion. In the absence of diarrhea, these phenomena are normal, if sometimes uncomfortable. Accompanying diarrhea, however, may indicate the involvement of bacteria or *Giardia* parasites, which are common at many high-altitude locations in the developing world. Prompt treatment with fluids and empirical antibiotics may be required to combat dehydration in the mountains. Finally, hemorrhoids are common on high-altitude treks; treatment includes hot soaks, application of hydrocortisone ointment, and measures to avoid constipation.

High-altitude cough

High-altitude cough can be very debilitating and is sometimes severe enough to cause rib fracture, especially above 5000 m. The etiology is probably multifactorial. Although high-altitude cough has been attributed to inspiration of cold dry air, this explanation appears not to be sufficient in itself; in long-duration studies in hypobaric chambers, cough has occurred despite controlled temperature and humidity. The implication is that hypoxia also plays a role. Exercise can precipitate cough at high altitudes, possibly because of water loss from the respiratory tract. Long-acting β agonists and glucocorticoids prevent bronchoconstriction that otherwise may be brought on by cold and exercise. In general, infection does not seem to be a common etiology. Anecdotal reports have described the efficacy of an inhaled combination of fluticasone and salmeterol in the treatment of high-altitude cough. Both salmeterol and glucocorticoids are known to prevent HAPE, which may be an underrecognized cause of cough.

High-altitude neurologic events unrelated to "altitude illness"

Transient ischemic attacks (TIAs) and strokes have been well described in high-altitude sojourners outside the setting of altitude sickness. However, these descriptions are not based on cause (hypoxia) and effect. The population that suffers strokes and TIAs at sea level is generally an older age group with other risk factors, whereas those so afflicted at high altitudes are generally younger and probably have fewer risk factors for atherosclerotic vascular disease. Other mechanisms (e.g., vasospasm, focal edema, hypocapneic vasoconstriction, hypoxia in the watershed zones of minimal cerebral blood flow, or cardiac right-to-left shunt) may be operative in TIAs and strokes at high altitude.

Subarachnoid hemorrhage, transient global amnesia, delirium, and cranial nerve palsies (e.g., lateral rectus palsy) occurring at high altitudes but outside the setting of altitude sickness have also been well described. Syncope is common at moderately high altitudes, generally occurs shortly after ascent, usually resolves without descent, and appears to be a vasovagal event related to hypoxemia. Seizures occur rarely with HACE, but hypoxemia and hypocapnia, which are prevalent at high altitudes, are well-known triggers that

may contribute to new or breakthrough seizures in predisposed individuals. However, the consensus among experts is that sojourners with well-controlled seizure disorders can ascend to high altitudes. Ophthalmologic problems, such as cortical blindness, amaurosis fugax, and retinal hemorrhage with macular involvement and compromised vision, are well recognized. Visual problems from previous refractive surgery and blurred monocular vision—due either to the use of a transdermal scopolamine patch (touching the eye after touching the patch) or to dry-eye syndrome—may also occur in the field at high altitudes and may be confused with neurologic conditions. Finally, persons with hypercoagulable conditions (e.g., antiphospholipid syndrome, protein C deficiency) who are asymptomatic at sea level may experience cerebral venous thrombosis (possibly due to the enhanced blood viscosity triggered by polycythemia and dehydration) at high altitudes. Proper history-taking, examination, and prompt investigations where possible will help define these conditions as entities separate from altitude sickness. Administration of oxygen (where available) and prompt descent are the cornerstones of treatment of most of these neurologic conditions.

■ PREEXISTING MEDICAL ISSUES

Because travel to high altitudes is increasingly popular, common conditions such as hypertension, coronary artery disease, and diabetes are more frequently encountered among high-altitude sojourners. This situation is of particular concern for the thousands of elderly pilgrims with medical problems who visit high-altitude sacred areas (e.g., in the Himalayas) each year. Although most of these medical conditions do not appear to influence susceptibility to altitude illness, they may be exacerbated by ascent to altitude, exertion in cold conditions, and hypoxemia. Advice regarding the advisability of high-altitude travel and the impact of high-altitude hypoxia on these preexisting conditions is becoming increasingly relevant, but there are no evidence-based guidelines. Personal risks and benefits must be clearly thought through before ascent.

Hypertension

At high altitudes, enhanced sympathetic activity may lead to a transient rise in blood pressure that rarely reaches dangerously high levels. Sojourners should continue to take their antihypertensive medications at high altitudes. Hypertensive patients are not more likely than others to develop altitude illness. Because the probable mechanism of high-altitude hypertension is α-adrenergic activity, anti-α-adrenergic drugs like prazosin have been suggested for symptomatic patients and those with labile hypertension. It is best to start taking the drug several weeks before the trip and to carry a sphygmomanometer. Sustained-release nifedipine may also be useful.

Coronary artery disease

Myocardial oxygen demand and maximal heart rate are reduced at high altitudes because VO_2 max decreases with increasing altitude. This effect may explain why signs of cardiac ischemia or dysfunction are not seen in healthy persons at high altitudes. Asymptomatic, fit individuals with no risk factors need not undergo any tests before ascent. For persons with ischemic heart disease, previous myocardial infarction, angioplasty, and/or bypass surgery, an exercise treadmill test is indicated. A strongly positive treadmill test is a contraindication for high-altitude trips; a negative treadmill test in an individual who leads an active life at sea level does not warrant the avoidance of high altitudes. Patients with poorly controlled arrhythmias should avoid high-altitude travel, but patients with arrhythmias that are well controlled with antiarrhythmic medications do not seem to be at increased risk.

Asthma

Although cold air and exercise may provoke acute bronchoconstriction, asthmatic patients usually have fewer problems at high than at low altitudes, possibly because of decreased allergen levels and increased circulating catecholamine levels. Nevertheless, asthmatic individuals should carry all their medications, including oral glucocorticoids, with proper instructions for use in case of an exacerbation. Severely asthmatic persons should be cautioned against ascending to high altitudes.

Pregnancy

In general, low-risk pregnant women ascending to 3000 m are not at special risk except for the relative unavailability of medical care in many high-altitude locations, especially in developing countries. Despite the lack of firm data on this point, venturing higher than 3000 m to altitudes at which oxygen saturation drops steeply seems unadvisable for pregnant women.

Obesity

Although living at a high altitude has been suggested as a means of controlling obesity, obesity has also been reported to be a risk factor for AMS, probably because nocturnal hypoxemia is more pronounced in obese individuals. Hypoxemia may also lead to greater pulmonary hypertension, thus possibly predisposing the trekker to HAPE.

Sickle cell disease

High altitude is one of the rare environmental exposures that occasionally provokes a crisis in persons with the sickle cell trait. Even when traversing mountain passes as low as 2500 m, people with sickle cell disease have been known to have a vasoocclusive crisis. Sickle cell disease needs to be considered when persons traveling to high altitudes become unwell and develop left-upper-quadrant pain. Patients with known sickle cell disease who need to travel to high altitudes should use supplemental oxygen and travel with caution.

Diabetes mellitus

Trekking at high altitudes may enhance sugar uptake. Thus, high-altitude travel may not pose problems for persons with diabetes that is well controlled with oral hypoglycemic agents. An eye examination before travel may be useful. Patients taking insulin may require lower doses on trekking/climbing days than on rest days. Because of these variations, diabetic patients need to carry a reliable glucometer and use fast-acting insulin. Ready access to sweets is also essential. It is important for companions of diabetic trekkers to be fully aware of potential problems like hypoglycemia.

Chronic lung disease

Depending on disease severity and access to medical care, preexisting lung disease may not always preclude high-altitude travel. A proper pretravel evaluation must be conducted. Supplemental oxygen may be required if the predicted PaO_2 for the altitude is <50–55 mmHg. Preexisting pulmonary hypertension may also need to be assessed in these patients. If the result is positive, patients should be discouraged from ascending to high altitudes; if such travel is necessary, treatment with sustained-release nifedipine (20 mg twice a day) should be considered. Small-scale studies have revealed that when patients with bullous disease reach ~5000 m, bullous expansion and pneumothorax are not noted. A handheld pulse oximeter can be useful to check for oxygen saturation.

Chronic kidney disease

Patients with chronic kidney disease can tolerate short-term stays at high altitudes, but theoretical concern persists about progression to

end-stage renal disease. Acetazolamide, the drug most commonly used for altitude sickness, should be avoided by anyone with pre-existing metabolic acidosis, which can be exacerbated by this drug. In addition, the acetazolamide dosage should be adjusted when the glomerular filtration rate falls below 50 mL/min, and the drug should not be used at all if this value falls below 10 mL/min.

■ CHRONIC MOUNTAIN SICKNESS AND HIGH-ALTITUDE PULMONARY HYPERTENSION

Chronic mountain sickness (also known as Monge's disease) is a disease of long-term residents of altitudes above 2500 m that is characterized by excessive erythrocytosis with moderate to severe pulmonary hypertension leading to cor pulmonale. This condition was originally described in South America and has also been documented in Colorado and in the Han Chinese population in Tibet. Migration to a low altitude results in the resolution of chronic mountain illness. Venesection and acetazolamide are helpful.

High-altitude pulmonary hypertension is also a subacute disease of long-term high-altitude residents. Unlike Monge's disease, this syndrome is characterized primarily by pulmonary hypertension (not erythrocytosis) leading to heart failure. Indian soldiers living at extreme altitudes for prolonged periods and Han Chinese infants born in Tibet have presented with the adult and infantile forms, respectively. High-altitude pulmonary hypertension bears a striking pathophysiologic resemblance to brisket disease in cattle. Descent to a lower altitude is curative.

FURTHER READINGS

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