

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.

Prevention and Treatment (Table 476e-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 476e-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 in animal models, and this observation warrants further study in HAPE prevention. However, one large 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. 476e-2). This fact has allowed some people with HAPE to reascend slowly after a few days of descent and rest. In HACE, reascend after a few days may not be advisable during the same trip.

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 because 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, the addition of acetazolamide, which will decrease centrally mediated sleep apnea, may be helpful. There is evidence to show that obstructive sleep apnea at high altitude may decrease and “convert” to central sleep apnea.

Gastrointestinal Issues High-altitude exposure may be associated with increased gastric and duodenal bleeding, but further studies

are required to determine whether there is a causal effect. Because of decreased atmospheric pressure and consequent intestinal gas expansion at high altitudes, many sojourners experience abdominal bloating and distension as well as 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 debilitating and is sometimes severe enough to cause rib fracture, especially at >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 by 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; however, a placebo-controlled, randomized trial failed to support this beneficial effect. Furthermore, anecdotal evidence supports the utility of the proton pump inhibitor omeprazole in preventing gastroesophageal reflux in some trekkers and climbers. In most situations, cough resolves upon descent.

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. In general, symptoms of AMS present gradually, whereas many of these neurologic events happen suddenly. 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., migraine, vasospasm, focal edema, hypocapnic 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. Nevertheless, 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)