

*Current Concepts***HIGH-ALTITUDE ILLNESS**

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THE term “high-altitude illness” is used to describe the cerebral and pulmonary syndromes that can develop in unacclimatized persons shortly after ascent to high altitude. Acute mountain sickness and high-altitude cerebral edema refer to the cerebral abnormalities, and high-altitude pulmonary edema to the pulmonary abnormalities. Because millions of visitors travel to high-altitude locations each year, acute mountain sickness is a public health problem and has economic consequences, especially for the ski industry. High-altitude pulmonary edema and high-altitude cerebral edema, though uncommon, are potentially fatal. High-altitude illness also provides a useful model for studying the pathophysiological process of hypoxia in an otherwise healthy population.

EPIDEMIOLOGIC PROCESS AND RISK FACTORS

Whether high-altitude illness occurs is determined by the rate of ascent, the altitude reached, the altitude at which an affected person sleeps (referred to as the sleeping altitude), and individual physiology. In 1991 in Summit County, Colorado, the incidence of acute mountain sickness was 22 percent at altitudes of 1850 to 2750 m (7000 to 9000 ft)¹ and 42 percent at altitudes of 3000 m (10,000 ft).² Risk factors include a history of high-altitude illness, residence at an altitude below 900 m,¹ exertion,³ and certain preexisting cardiopulmonary conditions.⁴ Persons over 50 years of age are somewhat less susceptible to acute mountain sickness than younger persons,^{1,5,6} whereas the incidence in children appears to be the same as that in adults.⁷ Women seem less susceptible to high-altitude pulmonary edema than men, but equally prone to acute mountain sickness.^{1,5} Physical fitness is not protective against high-altitude illness.⁸ Common con-

ditions such as hypertension, coronary artery disease, mild chronic obstructive pulmonary disease, diabetes, and pregnancy do not appear to affect the susceptibility to high-altitude illness.^{4,6} Diverse interactions between genetic factors and the environment most likely explain individual susceptibility or relative resistance to these hypoxia-induced illnesses.

ACUTE MOUNTAIN SICKNESS AND HIGH-ALTITUDE CEREBRAL EDEMA**Clinical Presentation and Diagnosis**

Acute mountain sickness is a syndrome of nonspecific symptoms and is therefore subjective. The Lake Louise Consensus Group defined acute mountain sickness as the presence of headache in an unacclimatized person who has recently arrived at an altitude above 2500 m plus the presence of one or more of the following: gastrointestinal symptoms (anorexia, nausea, or vomiting), insomnia, dizziness, and lassitude or fatigue.⁹ Rarely, acute mountain sickness occurs at altitudes as low as 2000 m. The symptoms typically develop within 6 to 10 hours after ascent, but sometimes as early as 1 hour. There are no diagnostic physical findings except in the few cases that progress to cerebral edema.

High-altitude cerebral edema is a clinical diagnosis, defined as the onset of ataxia, altered consciousness, or both in someone with acute mountain sickness or high-altitude pulmonary edema. Clinically and pathophysiologically, high-altitude cerebral edema is the end-stage of acute mountain sickness. In those who also have high-altitude pulmonary edema, severe hypoxemia can lead to rapid progression from acute mountain sickness to high-altitude cerebral edema. Associated findings of high-altitude cerebral edema may include papilledema, retinal hemorrhage (a common incidental finding), and occasionally, cranial-nerve palsy as a result of elevated intracranial pressure. However, global encephalopathy rather than focal findings characterizes high-altitude cerebral edema. Drowsiness is commonly followed by stupor. Seizures are rare. Usually, the illness progresses over a period of hours or days.¹⁰ The cause of death is brain herniation.

Many conditions mimic acute mountain sickness and high-altitude cerebral edema. The onset of symptoms more than three days after arrival at a given altitude, the absence of headache, a rapid response to fluids or rest, and the absence of a response to descent, oxygen, or dexamethasone all suggest other diagnoses. Table 1 lists conditions sometimes confused with acute mountain sickness and high-altitude cerebral edema.¹¹⁻¹³

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TABLE 1. DIFFERENTIAL DIAGNOSIS OF HIGH-ALTITUDE ILLNESSES.**Acute mountain sickness and high-altitude cerebral edema**

Acute psychosis
 Arteriovenous malformation
 Brain tumor
 Carbon monoxide poisoning
 Central nervous system infection
 Dehydration
 Diabetic ketoacidosis
 Exhaustion
 Hangover
 Hypoglycemia
 Hyponatremia
 Hypothermia
 Ingestion of toxins, drugs, or alcohol
 Migraine
 Seizures
 Stroke
 Transient ischemic attack
 Viral or bacterial infection

High-altitude pulmonary edema

Asthma
 Bronchitis
 Heart failure
 Hyperventilation syndrome
 Mucus plugging
 Myocardial infarction
 Pneumonia
 Pulmonary embolus

Pathophysiological Process

In both the brain and the lungs, hypoxia elicits neurohumoral and hemodynamic responses that result in overperfusion of microvascular beds, elevated hydrostatic capillary pressure, capillary leakage, and consequent edema (Fig. 1).

The exact process of acute mountain sickness is unknown. The hypoxia-induced cerebral vasodilatation or its effectors, such as nitric oxide, most likely produce the headache, perhaps through the activation of the trigeminovascular system.¹⁵ The headache itself can cause other symptoms, such as nausea and malaise, and thereby account for mild acute mountain sickness. An alternative hypothesis is that early acute mountain sickness is due to mild cerebral edema.^{10,16}

New evidence suggests that on ascent to high altitudes, all people have swelling of the brain.^{17,18} The magnetic resonance imaging techniques used for these studies, however, could not differentiate between vasodilatation-induced hyperemia and edema. An interesting hypothesis, supported by preliminary data, is that acute mountain sickness might be related to a person's ability to compensate for the swelling of the brain.^{10,19} Those with a greater ratio of cranial cerebrospinal fluid to brain volume are better able to compensate for swelling through the displacement of cerebrospinal fluid, and may therefore be less likely to have acute mountain sickness. This theory could ex-

plain the random nature of acute mountain sickness and deserves further study.

In those with moderate-to-severe acute mountain sickness or high-altitude cerebral edema, neuroimaging demonstrates vasogenic edema.^{20,21} Hemodynamic factors such as sustained vasodilatation,²² impaired cerebral autoregulation,²³ and elevated cerebral capillary pressure²⁴ most likely contribute to the formation of edema but cannot entirely explain the process.¹⁰ Hypoxia-induced biochemical alteration of the blood-brain barrier may also be important. Possible mediators, some triggered by endothelial activation, include vascular endothelial growth factor, inducible nitric oxide synthase, and bradykinin.²⁵⁻²⁷

Treatment and Prevention

Management of acute mountain sickness or high-altitude cerebral edema follows three axioms: further ascent should be avoided until the symptoms have resolved, patients with no response to medical treatment should descend to a lower altitude, and at the first sign of high-altitude cerebral edema, patients should descend to a lower altitude. Table 2 suggests management and prevention options for four common clinical scenarios. Table 3 lists useful therapeutic agents.^{5,28-39} A few points are worth emphasizing. Descent and supplementary oxygen are the treatments of choice, and for severe illness, the combination provides optimal therapy. Remarkably, a descent of only 500 to 1000 m usually leads to resolution of acute mountain sickness; high-altitude cerebral edema may require further descent. Simulated descent with portable hyperbaric chambers, now commonly used in remote locations, is also effective. With the use of these chambers at a pressure of 2 psi (13.8 kPa), the equivalent altitude is roughly 2000 m lower than the ambient altitude (Table 3).

When descent is not possible or supplementary oxygen is unavailable, medical therapy becomes crucial. A small, placebo-controlled study showed that the administration of acetazolamide reduced the severity of symptoms by 74 percent within 24 hours.²⁸ Multiple studies have demonstrated that dexamethasone is as effective as or superior to acetazolamide and works within 12 hours.^{30,31,40} Whether the combination of acetazolamide and dexamethasone, because of their different mechanisms of action, is superior to the use of either agent alone is unknown. In two studies, a single dose of 400 mg or 600 mg of ibuprofen ameliorated³⁶ or resolved⁴¹ high-altitude headaches. The success of sumatriptan for high-altitude headache has been inconsistent.⁴¹⁻⁴³ Antiemetics are indicated for nausea and vomiting. For insomnia requiring treatment, acetazolamide, which reduces periodic breathing and improves nocturnal oxygenation, is the safest agent. Because of the risk of respiratory depression, sedative hypnotic agents should be avoided in those with acute mountain sickness unless

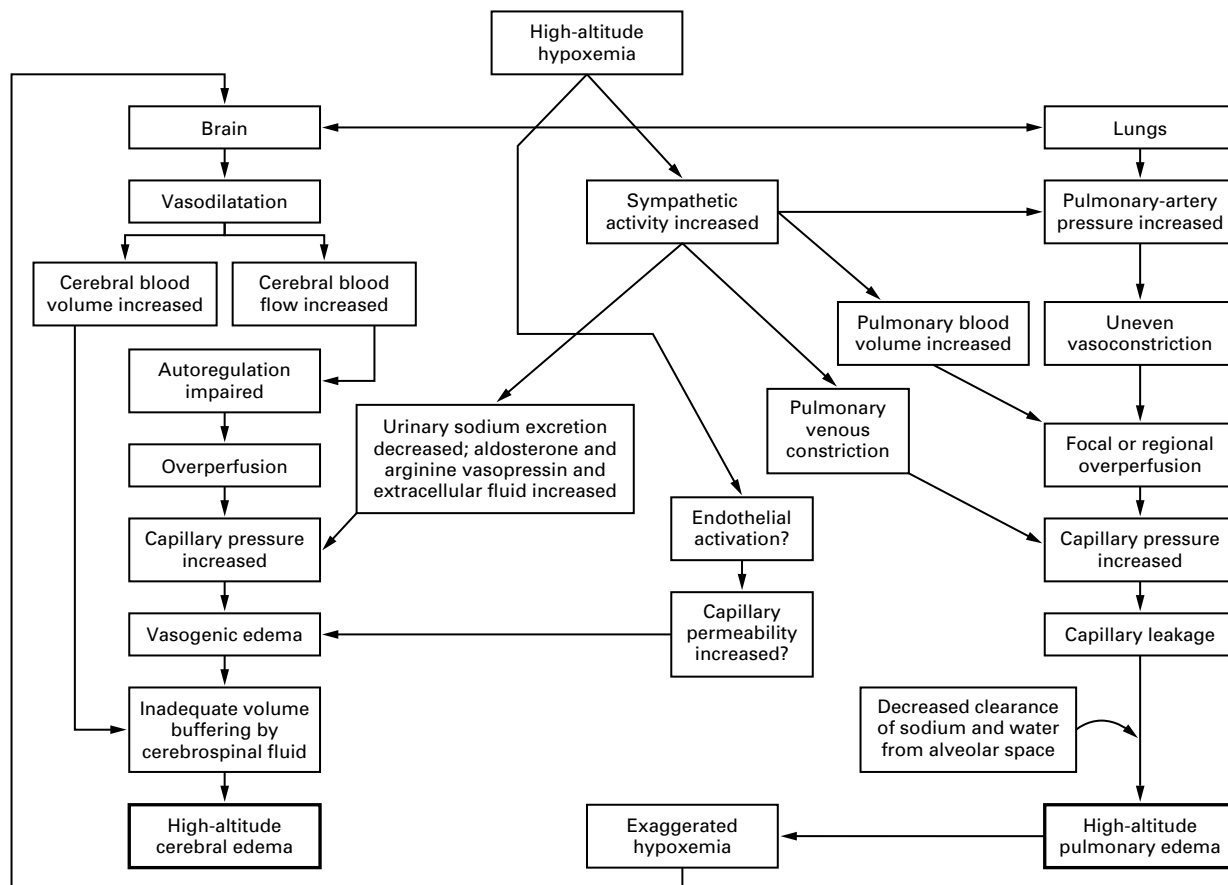


Figure 1. Proposed Pathophysiological Process of High-Altitude Illness.

At high altitudes hypoxemia can lead to overperfusion, elevated capillary pressure, and leakage from the cerebral and pulmonary microcirculation.^{10,11,14} Increased sympathetic activity has a central role in this process, and increased permeability of capillaries as a result of endothelial activation (inflammation) may also have a role.

they are combined with acetazolamide.⁴⁴ Zolpidem does not depress ventilation at high altitudes and may therefore be a safe treatment for insomnia in persons with acute mountain sickness, but it has not been studied in clinical trials.³⁹ After acute mountain sickness has resolved, any further ascent should be made with caution, perhaps with acetazolamide prophylaxis.

For the prevention of high-altitude illness, the best strategy is a gradual ascent to promote acclimatization. The suggested guidelines are that once above an altitude of 2500 m, the altitude at which one sleeps should not be increased by more than 600 m in 24 hours and that an extra day should be added for acclimatization for every increase of 600 to 1200 m in this altitude. For example, as compared with ascent to an altitude of 3500 m in a one-hour period, a gradual ascent over a period of four days reduced the incidence and severity of acute mountain sickness by 41 percent.⁴⁵ Most experts recommend prophylaxis

for those who plan an ascent from sea level to over 3000 m (sleeping altitude) in one day and for those with a history of acute mountain sickness. Acetazolamide is the preferred drug, and dexamethasone is an alternative; both are unequivocally effective; the dosages vary.^{5,29,31,46-48} The combination was more effective than either alone.⁴⁹ Although controversial, small doses of acetazolamide (125 mg twice a day in adults) appear empirically to be as effective as larger doses, with fewer side effects; the minimal effective dose remains uncertain.⁵⁰ In two controlled trials, *Ginkgo biloba* prevented acute mountain sickness during a gradual ascent to 5000 m³⁸ and reduced both the symptoms and the incidence of acute mountain sickness by 50 percent during an abrupt ascent to 4100 m.³⁷ With respect to headache, prophylactic aspirin (325 mg every four hours for a total of three doses) reduced the incidence from 50 percent to 7 percent.³⁵ Reports suggest various Chinese herbal

TABLE 2. OPTIONS FOR THE MANAGEMENT AND PREVENTION OF HIGH-ALTITUDE ILLNESS.

CLINICAL PRESENTATION	MANAGEMENT	PREVENTION
Mild acute mountain sickness Headache with nausea, dizziness, and fatigue during first 12 hr after rapid ascent to high altitude (>2500 m)	Descend 500 m or more; or stop, rest, and acclimatize; or speed acclimatization with acetazolamide (125 to 250 mg twice daily); or treat symptoms with analgesics and antiemetics; or use a combination of these approaches.	Ascend at a slow rate; spend a night at an intermediate altitude; avoid overexertion; avoid direct transport to an altitude of more than 2750 m; consider taking acetazolamide (125 to 250 mg twice daily) beginning 1 day before ascent and continuing for 2 days at high altitude.
Moderate acute mountain sickness Moderate-to-severe headache with marked nausea, dizziness, lassitude, insomnia, fluid retention at high altitude for 12 hr or more	Descend 500 m or more; if descent is not possible, use a portable hyperbaric chamber or administer low-flow oxygen (1 to 2 liters/min); if descent is not possible and oxygen is not available, administer acetazolamide (250 mg twice daily), dexamethasone (4 mg orally or intramuscularly every 6 hr), or both until symptoms resolve; treat symptoms; or use a combination of these approaches.	Ascend at a slow rate; spend a night at an intermediate altitude; avoid overexertion; avoid direct transport to an altitude of more than 2750 m; consider taking acetazolamide (125 to 250 mg twice daily) beginning 1 day before ascent and continuing for 2 days at high altitude; treat acute mountain sickness early.
High-altitude cerebral edema Acute mountain sickness for 24 hr or more, severe lassitude, mental confusion, ataxia	Initiate immediate descent or evacuation; if descent is not possible, use a portable hyperbaric chamber; administer oxygen (2 to 4 liters/min); administer dexamethasone (8 mg orally, intramuscularly, or intravenously initially, and then 4 mg every 6 hr); administer acetazolamide if descent is delayed.	Avoid direct transport to an altitude of more than 2750 m; ascend at a slow rate; avoid overexertion; consider taking acetazolamide (125 to 250 mg twice daily) beginning 1 day before ascent and continuing for 2 days at high altitude; treat acute mountain sickness early.
High-altitude pulmonary edema Dyspnea at rest, moist cough, severe weakness, drowsiness, cyanosis, tachycardia, tachypnea, rales	Administer oxygen (4 to 6 liters/min until condition improves, and then 2 to 4 liters/min to conserve supplies); descend as soon as possible, with minimal exertion, or use a portable hyperbaric chamber; if descent is not possible or oxygen is not available, administer nifedipine (10 mg orally initially and then 30 mg of extended-release formulation orally every 12 to 24 hr); add dexamethasone if neurologic deterioration occurs.	Ascend at a slow, graded rate; avoid overexertion; consider taking nifedipine (20 to 30 mg of extended-release formulation every 12 hr) in persons with repeated episodes.

preparations might prevent high-altitude illness, but controlled studies are lacking.⁵¹ The notion that overhydration prevents acute mountain sickness has no scientific basis.

HIGH-ALTITUDE PULMONARY EDEMA

Clinical Presentation and Diagnosis

High-altitude pulmonary edema accounts for most deaths from high-altitude illness.¹¹ As is the case for acute mountain sickness, the incidence of high-altitude pulmonary edema is related to the rate of ascent, the altitude reached, individual susceptibility, and exertion; cold, which increases pulmonary-artery pressure by means of sympathetic stimulation, is also a risk factor.⁵² Abnormalities of cardiopulmonary circulation increase the risk of high-altitude pulmonary edema.^{4,53} High-altitude pulmonary edema commonly strikes the second night at a new altitude and rarely occurs after more than four days at a given altitude, owing to adaptive cellular and biochemical changes in pulmonary vessels.⁵⁴

Early diagnosis is critical. In the proper setting, decreased performance and a dry cough should raise suspicion of high-altitude pulmonary edema. Only late

in the illness does pink or bloody sputum and respiratory distress develop. Resting tachycardia and tachypnea become more pronounced as high-altitude pulmonary edema progresses.⁵⁵ Orthopnea is uncommon, as is frank hemoptysis. Cerebral signs and symptoms are common: 50 percent of those with high-altitude pulmonary edema have acute mountain sickness, and 14 percent have high-altitude cerebral edema.⁵⁶ Of those whose condition deteriorates and who die, 50 percent have high-altitude cerebral edema at autopsy. Fever (a temperature of up to 38.5°C) is common. Rales typically originate in the right axilla and become bilateral as the illness progresses. Upper respiratory tract infection or bronchitis may be precipitating factors, especially in children.⁵⁷ The differential diagnosis of high-altitude pulmonary edema is listed in Table 1. Electrocardiography demonstrates sinus tachycardia and, often, right ventricular strain, right-axis deviation, right bundle-branch block, and P-wave abnormalities. Chest radiography typically reveals a normal-sized heart, full pulmonary arteries, and patchy infiltrates, which are generally confined to the right middle and lower lobes in mild cases and are found in both lungs in more severe cases. Measurements of

TABLE 3. MEDICAL THERAPY FOR HIGH-ALTITUDE ILLNESS.*

AGENT	INDICATION	DOSE	MECHANISM OF ACTION	ADVERSE EFFECTS	COMMENTS†
Oxygen	All high-altitude illnesses	2–4 liters/min by cannula or mask initially, then 1–2 liters/min or titrate dose until SaO ₂ >90%	Increases PaO ₂ ; reduces cerebral blood flow, cerebral blood volume, and pulmonary-artery pressure	None	Lifesaving for HAPE; improves headache within minutes in AMS
Portable hyperbaric chamber	All high-altitude illnesses	Depends on model; 2–4 psi for a minimum of 2 hr; continued as long as necessary	Simulates descent; increases PaO ₂	Potential rebound effect after removal of patient from chamber; limits access to airways	Effects equivalent to the administration of low-flow oxygen; can be lifesaving; does not require oxygen; can add supplemental oxygen by cannula or mask if necessary
Acetazolamide ^{5,28,29}	Prevention of AMS	125–250 mg orally twice a day 24 hr before ascent and first 2 days at high altitude	Carbonic anhydrase inhibitor; causes bicarbonate diuresis and respiratory stimulation; increases PaO ₂ ; reduces formation of CSF; promotes ion transport across blood–brain barrier	Paresthesias; alters taste of carbonated beverages; polyuria	Sulfonamide reactions possible; should be avoided by breast-feeding women; can be taken episodically for symptoms; no rebound effect; pregnancy category C
	Treatment of AMS Pediatric AMS	250 mg twice a day orally until symptoms resolve 5 mg/kg of body weight/day, given orally in divided doses every 8–12 hr			
Dexamethasone ^{29,31}	Prevention of AMS	2 mg every 6 hr or 4 mg every 12 hr orally	Unknown; may reduce brain–blood volume; may prevent blood–brain barrier leak (blocks VEGF, inducible nitric oxide, lipid peroxidation)	Mood changes; hyperglycemia; dyspepsia; rebound effect on withdrawal	Can be lifesaving for AMS or HACE; effects evident in 2–8 hr; no effect on acclimatization; no value in HAPE; preferably avoided by women who are pregnant or breast-feeding
	Treatment of AMS HACE	4 mg every 6 hr orally, IM, or IV 8 mg initially, then 4 mg every 6 hr orally, IM, or IV			
	Pediatric AMS or HACE	0.15 mg/kg every 6 hr orally, IM, or IV			
Furosemide ³²	AMS or HACE	80 mg orally every 12 hr for a total of 2 doses‡	Diuresis; decreases extracellular fluid; causes venodilatation	Hypovolemia; hypotension; hypokalemia	Currently out of favor; not recommended for prevention; not established for use in HAPE
Nifedipine ^{33,34}	Prevention of HAPE	20–30 mg of extended-release formulation orally every 12 hr	Calcium-channel blocker; reduces pulmonary-artery pressure	Reflex tachycardia; hypotension (uncommon)	No value in AMS or HACE; pregnancy category C; not necessary if supplemental oxygen available
	Treatment of HAPE	10 mg orally initially, then 20–30 mg of extended-release formulation orally every 12 hr			
Nonsteroidal anti-inflammatory drugs			Inhibit prostaglandins	Dyspepsia; gastrointestinal bleeding	No clinical trials of aspirin for treatment or of ibuprofen for prevention; naproxen ineffective
Aspirin ³⁵	Prevention of headache	325 mg orally every 4 hr for a total of 3 doses			
Ibuprofen ³⁶	Treatment of headache	400 or 600 mg orally once; may be repeated			
<i>Ginkgo biloba</i> ^{37,38}	Prevention of AMS	80–120 mg orally twice daily	Unknown; may block inducible nitric oxide; an antioxidant oxygen radical scavenger; may block platelet-activating factor	Occasional headache; rare episodes of bleeding	Requires further study; preparations vary; should not be used with antithrombotic agents; may be used by women who are pregnant or breast-feeding
Antiemetics	Nausea; vomiting		Phenothiazine; centrally acting	Extrapyramidal reactions; cause sedation	Pregnancy category C; use diphenhydramine intramuscularly for extrapyramidal reactions
Prochlorperazine		10 mg orally or IM every 6–8 hr			
Promethazine		25–50 mg orally, IM, or rectally every 6 hr			
Zolpidem ³⁹	Insomnia	10 mg orally	Nonbenzodiazepine modulator of γ -aminobutyric acid receptors	Rare, short-acting	Does not depress ventilation at high altitude; pregnancy category B

*Further information on hyperbaric therapies, oxygen systems, and protocols is available at <http://www.ismmed.org>. SaO₂ denotes arterial oxygen saturation, PaO₂ partial pressure of arterial oxygen, HAPE high-altitude pulmonary edema, AMS acute mountain sickness, CSF cerebrospinal fluid, IM intramuscularly, IV intravenously, HACE high-altitude cerebral edema, and VEGF vascular endothelial growth factor.

†Agents in pregnancy category C have had toxic effects in studies in animals, but the results of studies in humans are inadequate; the agent should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Agents in pregnancy category B have not been associated with an increased risk to the fetus in studies in animals and have not been adequately studied in well-controlled trials of pregnant women or have had an adverse effect in studies in animals but not in adequate and well-controlled studies of women in the first trimester of pregnancy; there is no evidence that these agents pose a risk when given in the second or third trimester.

‡This dose is the only one studied in clinical trials. If the drug is used at all, we recommend using a lower dose (20 to 40 mg orally or parenterally) in order to avoid adverse effects.

arterial blood gas reveal severe hypoxemia (a partial pressure of arterial oxygen of 30 to 40 mm Hg) and respiratory alkalosis, but not respiratory acidosis.^{34,58}

Pathophysiological Process

High-altitude pulmonary edema is a noncardiogenic pulmonary edema associated with pulmonary hypertension and elevated capillary pressure.⁵⁹ The usual pulmonary hypertension on ascent to high altitude is excessive in those with high-altitude pulmonary edema, as a result of exaggerated hypoxic pulmonary vasoconstriction.⁶⁰ The mechanisms for this response include sympathetic overactivity, endothelial dysfunction, and greater hypoxemia resulting from a poor ventilatory response to hypoxia.⁶¹ In addition, the increased sympathetic activity⁶² probably raises capillary pressure as a result of pulmonary venous constriction.⁵⁹ Supporting this notion, α -adrenergic blockade improved hemodynamics and oxygenation in high-altitude pulmonary edema.⁶³

Another possible explanation for elevated capillary pressure is uneven hypoxic pulmonary vasoconstriction.⁵⁵ Hultgren proposed that the microcirculation is protected in vasoconstricted areas but that less constricted areas are overperfused, causing elevated capillary pressure and capillary leakage.⁵⁵ The results of radioisotope perfusion studies in patients with high-altitude pulmonary edema bolstered this concept.⁵⁸ In addition, the dramatic increase in susceptibility to high-altitude pulmonary edema in persons with congenital or acquired pulmonary circulation abnormalities supports the idea that edema resulting from overperfusion in a restricted pulmonary vascular bed is a cause.^{53,56,64}

Stress failure of pulmonary capillaries as a result of high microvascular pressure is the presumed final process leading to extravasation of plasma and cells⁶⁵ (Fig. 1). On the basis of recent research,^{59,66} the inflammation reported in high-altitude pulmonary edema^{67,68} is most likely a nonspecific response to stress-induced failure of capillaries and alveolar flooding, rather than part of the pathophysiological process. The dramatic response to oxygen therapy can be explained by the finding that the microcirculation rapidly returns to normal when capillary pressure drops.⁶⁹ A new concept in the pathophysiological process of high-altitude pulmonary edema is that impaired clearance of fluid from the alveolar space has a role⁶¹ (Fig. 1).

Susceptibility

Persons with a prior episode of high-altitude pulmonary edema may have a risk of recurrence as high as 60 percent if they abruptly ascend to an altitude of 4559 m.³³ These persons are healthy but have a reduced ventilatory response to hypoxia^{60,70} and an exaggerated pulmonary pressor response to hypoxia and exercise.^{60,71,72} There is substantial overlap in these measured values between susceptible and nonsuscep-

tible groups, however, and it is not possible to predict exactly which healthy persons are at increased risk. In addition, in susceptible persons endothelial function might be impaired, with overexpression of constrictors (such as endothelin-1) or underexpression of vasodilators (such as nitric oxide), or both, in response to hypoxia.^{61,73} Persons who are susceptible to high-altitude pulmonary edema have a genetic difference in the amiloride-sensitive sodium channel, which reduces the ability to transport sodium and water from the alveolar space.⁶¹ Susceptible persons also have a higher incidence of HLA-DR6 and HLA-DQ4 antigens, suggesting that there may be an immunogenetic basis for susceptibility to high-altitude pulmonary edema.⁷⁴

Treatment and Prevention

Increasing alveolar and arterial oxygenation is the highest priority in patients with high-altitude pulmonary edema. Breathing supplemental oxygen reduces pulmonary-artery pressure 30 to 50 percent,^{34,63,75} which is sufficient to reverse the effects of the illness rapidly. Supplemental oxygen (as well as descent) increases arterial oxygen pressure and benefits the brain as well. Descent, supplemental oxygen, or both are nearly always successful. Reports of death during descent are probably related to the additional exertion involved, which exacerbates high-altitude pulmonary edema by increasing cardiac output and pulmonary hypertension. At ski resorts or other such facilities with medical care, mild-to-moderate high-altitude pulmonary edema can be treated with rest and supplemental oxygen for 48 to 72 hours.⁵⁶ Portable oxygen concentrators are convenient for outpatient treatment. Monitoring of arterial oxygen saturation by pulse oximetry is adequate to guide therapy. Patients with severe high-altitude pulmonary edema, indicated by the failure of arterial oxygen saturation to improve to more than 90 percent within five minutes after the initiation of high-flow oxygen, and those with concomitant high-altitude cerebral edema must be moved to a lower altitude and possibly hospitalized. If supplemental oxygen is unavailable, then descent, the use of a portable hyperbaric chamber, or both become lifesaving. Medication (nifedipine) is necessary only when supplemental oxygen is unavailable or descent is impossible (Tables 2 and 3). In clinical studies, nifedipine reduced pulmonary-artery pressure approximately 30 percent but barely increased the partial pressure of arterial oxygen.^{34,63}

A recent study suggested that inhaled beta-agonists might be useful in the prevention of high-altitude pulmonary edema, and by extension, for treatment as well.⁷⁶ Beta-agonists appreciably increase the clearance of fluid from the alveolar space and might also lower pulmonary-artery pressure.⁷⁶ Although this finding requires confirmation, these agents are safe and convenient and should be considered. Positive end-expira-

tory pressure delivered by means of a mask helps improve gas exchange and can be a temporizing measure. Antibiotics are indicated if there is evidence of infection. Endotracheal intubation, mechanical ventilation, and pulmonary-artery catheterization are rarely necessary. Complications of high-altitude pulmonary edema other than high-altitude cerebral edema are unusual. The detection of heart murmur should lead to echocardiography to rule out intracardiac shunt, especially in children. Before leaving the hospital, patients should have an arterial oxygen saturation of more than 90 percent while breathing room air and distinct clinical and radiographic evidence of improvement.

After an episode of high-altitude pulmonary edema, a person should be advised subsequently to ascend to high altitudes more slowly, recognize symptoms of high-altitude illness early, and consider nifedipine prophylaxis, especially after multiple episodes. Patients who have recurrent high-altitude pulmonary edema or high-altitude pulmonary edema at altitudes below 2500 m may require an evaluation to rule out intracardiac or intrapulmonary shunts, preexisting pulmonary hypertension, mitral-valve stenosis, and other conditions that increase pulmonary vascular resistance.

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