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Acute Medical Problems in the Himalayas Outside the Setting of Altitude Sickness

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ABSTRACT

Basnyat, Buddha, Tom A. Cumbo, and Robert Edelman. Acute medical problems in the Himalayas outside the setting of altitude sickness. *High Alt Med Biol* 1:167–174, 2000.—Well-recognized medical threats at high altitude (>2500 m) include acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), and high altitude cerebral edema (HACE). Thousands of travelers in the Himalayas are exposed annually to these often life-threatening syndromes. Their recognition and treatment has advanced considerably in recent years. In the Himalayas, we frequently see acute medical problems outside the setting of AMS and the two types of altitude edemas. Many of these other conditions are also hypoxia related and sometimes may mimic the classic high altitude illnesses of AMS, HAPE, and HACE. Although the vast majority of these medical problems are neurological, pulmonary and other organ system dysfunction also occur. These "non-high altitude sickness" disease entities in persons who sojourn to remote mountainous environments are reviewed in this paper to enhance their recognition, diagnosis, and treatment.

Key Words: acute mountain sickness; high altitude cerebral edema; high altitude pulmonary edema; "non-high altitude sickness" diseases of altitude; Himalayas

INTRODUCTION

ACUTE MOUNTAIN SICKNESS (AMS), high altitude cerebral edema (HACE) and high altitude pulmonary edema (HAPE) are well-known syndromes encountered at high altitude (>2500 m), which are commonly referred to as "altitude sickness." AMS may present with headache, nausea, dizziness, fatigue, and insomnia (Lake Louise consensus, 1992). AMS may worsen and progress to HACE, characterized by mental changes and/or ataxia. HAPE (cough, chest discomfort, breathlessness on minimal exertion, tachypnea, and tachycardia) can result from the complications of AMS, or it may present independently (Hackett, 1997). These well-recognized medical problems at altitude have been extensively discussed and reviewed (Zafren and Honigman, 1997; Harris et al., 1998; Klocke et al., 1998). In places like the

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Khumbu Valley in the Everest region of Nepal, many thousands of Western travelers saunter around every spring and fall for days to weeks at hypoxic altitudes of 4300 m and higher. At such altitudes, medical ailments in addition to AMS, HAPE, and HACE are reported more frequently. To our knowledge, this is the first, comprehensive, published review of these acute medical problems outside the setting of altitude sickness experienced in the Himalayas. Some of these may mimic the classic high altitude disease entities. These illnesses are manifested by neurological, visual, pulmonary, and other organ system signs and symptoms. Many of the hypoxia-related conditions to be discussed are encountered less often in the European Alps and in the Rocky Mountains of North America, because in these areas, most travelers quickly ascend and descend without spending a night at high altitude or they trek and sleep at lower altitudes than in the Himalayas or Andes of South America. Most, but not all of the conditions discussed in this review are associated with hypoxia. Some simply share similar epidemiological characteristics rather than similar pathophysiology, and may sometimes need to be considered in the differential diagnosis of altitude sickness in a remote setting.

Neurological conditions

Neurological malfunctions are by far the most common group of problems that may mimic altitude sickness, and may therefore need to be considered in the differential diagnosis of HACE (Table 1). An important point to remember is that in most instances of HACE, the neurological presentation is global, and focal neurological findings are less common (Hackett and Roach, 1995). The neurological conditions described below present with focal signs (with the possible exception of subarachnoid hemorrhage), which generally help to differentiate them from HACE.

Subarachnoid hemorrhage. Subarachnoid hemorrhage has been reported in an autopsy series of high altitude-related deaths (Dickinson et al., 1983) and in a recent clinical case occurring in the Himalayas (Litch et al., 1997), and thus it needs to be considered in the differential of HACE. With increased cerebral blood flow (Severinghaus et al., 1966) and decreased barometric pressure at high altitude (Jehle et al., 1994) preexisting cerebral aneurysms and arterial venous malformations may rupture more readily in a process akin to the common retinal hemorrhages detected at high altitude. Because a subarachnoid hemorrhage surrounds the brain and does not flow from within it, global impairment of consciousness rather than focal neurological impairment is characteristic of subarachnoid hemorrhage and HACE. A key difference is the history of a sudden intense headache in subarachnoid hemorrhage, which is usually absent in HACE, the latter condition being characterized by gradual loss of mental clarity without the initial warning of an intense headache.

Transient global amnesia. Global amnesia is characterized by confusion and bewilderment lasting for hours with no motor or sensory weakness (Adams and Victor, 1989). Global

Table 1. Documented Neurological, Visual, Pulmonary, and Miscellaneous Conditions at High Altitude Outside the Setting of AMS, HAPE, or HACE

Neurological problems:
Strokes and transient ischemic attacks, seizures, migraine, high altitude syncope, subarachnoid hemorrhage, and transient global amnesia.
Suddenly symptomatic brain tumor.
Visual problems:
Retinal hemorrhage, lateral rectus palsy, radial keratotomy causing long-sightedness, cortical blindness, and amaurosis fugax.
Pulmonary problems:
Pulmonary embolism, respiratory tract infection, and pneumonia.
Miscellaneous problems:
Drug- and alcohol-related problems, hypothermia and dehydration, carbon monoxide poisoning, psychological problems, gastrointestinal and other infections, asthma and myocardial infarctions, and language barrier.

amnesia has been reported in the high altitude literature (Litch and Bishop, 1999), but the abrupt onset and the lack of other symptoms of AMS (e.g., headache, nausea, dizziness, insomnia, and fatigue) should make it possible to differentiate it from HACE. Because global amnesia may be precipitated by ischemia of the brain secondary to hypoxia (Adams and Victor, 1989), descent to low altitude is advisable. Fortunately, this syndrome is usually benign and carries none of the underlying central nervous system (CNS) pathology associated with transient ischemic attacks.

Stroke and transient ischemic attacks (TIA). Strokes at high altitude may be exacerbated by polycythemia, dehydration, and increased intracranial pressure, which are common in high altitude sojourners (Hackett and Roach, 1995). Other factors operative at high altitude that may cause ischemia or infarction of the brain include cerebrovascular spasm, increased cerebrovenous pressure (Hackett and Roach, 1995), thrombosis (Boulos et al., 1999), focal edema of the brain (Basnyat, 1997), and coagulation abnormalities (Maher et al., 1976). TIAs at high altitude are well described (Wohns, 1986; Basnyat, 1997), and may occur suddenly without the warning signs typical of AMS. Management would include descent to low altitude and subsequent diagnostic workup. On many occasions, descent alone will eliminate further TIAs, which suggests that hypoxia is an important trigger.

Seizures. Focal or grandmal seizures are among the most common neurological presentation at any altitude. Hyperventilation (which is the cornerstone of acclimatization) and hypoxia may precipitate seizure activity in seizure-prone individuals (Hackett, 1997). Seizures at altitude may be noted outside the setting of AMS (Basnyat, 1997, 1998). Studying electroencephalograms (EEGs) of persons prone to epilepsy taken in a hypobaric chamber may help to prove their susceptibility to an anoxic stimulus. A seizure usually prompts the patient to be evacuated out of the Himalayas for proper medical help.

Brain tumors. Shlim et al. (1991) have described silent brain tumors that suddenly became symptomatic with headache and nausea at altitude, most likely caused by the increased brain volume that occurs in the Himalayas (Hackett, 1997). Thus, altitude may play the role of an acute "stress test" exacerbating the underlying pathophysiological changes associated with space occupying lesions of the brain. The confusion with HACE is a possibility, but as in the case of the brain edema of high altitude (Ferrazzni, 1987), the response to steroids may be gratifying.

Migraine. Migraine attacks may be more common at high altitude and thus probably provocated by hypoxia. The high prevalence of migraine headache in South American high altitude populations suggests that hypoxia may be at fault (Arregui et al., 1991), although in our experience migraine is not a common complaint of Himalayan Sherpas. However, chronic mountain sickness, which is relatively more common in South America compared with the Himalayas, may itself cause headache in the South American population. Migraine with aura and focal neurological deficits in the mountains have also been reported (Jenzer and Bartsch 1993; Murdoch, 1995a).

High altitude syncope. Syncope, occurring most commonly shortly after arriving at altitude, is usually benign and unrelated to AMS (Houston, 1998).

Guillain–Barré syndrome. Guillain–Barré syndrome can occur spontaneously or linked to an infectious etiology, such as *Campylobacter jejuni* diarrhea (Blaser, 1998). *C. jejuni* is a common cause of gastroenteritis in Nepal (Hoge et al., 1996), and Guillain–Barré syndrome has been documented in a trekker (Shlim and Cohen, 1989). A common presenting sign is a drunken gait, which is commonly associated with HACE in the Himalayas. A careful history and physical findings of muscle weakness and areflexia of the lower limbs, intact sensation, and cerebrospinal fluid (CSF) cell-protein dissociation may help to distinguish Guillain-Barré syndrome from HACE. The patients obviously needs medical evacuation to a larger center.

Visual conditions

Cortical blindness. Cortical blindness is transient blindness affecting both eyes. Pupillary reflexes are intact. In the Himalayas, Hackett (1987) first described cortical blindness among a group of trekkers. The pathophysiolgy may be compromised blood supply in the visual cortex, possibly due to focal edema or vascular spasm. The reported cases have not been accompanied by symptoms of altitude sickness. The patients improved with oxygen inhalation and, in some cases, by rebreathing carbon dioxide. Both treatments induce increased cerebral blood flow. Descent was accompanied by rapid recovery of vision.

Amaurosis fugax. This transient monocular blindness has been noted at high altitude, but not described in any detail (Shlim et al., 1995b).

Lateral rectus palsy. Although cranial nerve palsies can be associated with AMS or HACE, single cranial nerve palsies can occur without accompanying symptoms of altitude sickness (Shlim et al., 1995a). In the late 1970s, high altitude trekkers with diplopia secondary to unilateral lateral rectus palsy were admitted to the old Shanta Bhawan hospital in Kathmandu, even though they would have no other abnormalities, including AMS or diabetes. Case reports of trekkers with similar sixth cranial nerve palsy confirm the generally benign outcome of this condition, although diplopia and muscle palsy last for several weeks or months (Murdoch, 1994). Theoretically, the palsy may be caused by altitude-induced increased intracranial pressure, or vascular lesions affecting the long sixth nerve trunk (Walton, 1985) precipitated by hypoxia, dehydration, coagulation defects, polycythemia, or vascular spasms. Whatever the cause, descent to low altitude is strongly recommended.

Retinal hemorrhage. Retinal hemorrhage occurs frequently at 5000 m and higher, even in individuals without AMS. Experts of high altitude medicine say descent is not necessary in most instances because the hemorrhage resolves spontaneously in about 2 weeks (Hackett, 1997). However, if the macula is involved more severe visual loss occurs, and the patient needs to descend for further evaluation by an opthalmologist. In addition, a recent publication revealed a correlation of AMS symptoms and retinopathy (Weidman and Tabin, 1999). Hence, this is a controversial area. The cause of retinal hemorrhage is ill-defined; trauma induced by increased cerebral blood flow at high altitude could be one possibility.

Radial keratotomy at high altitude. The cornea receives oxygen directly from the air by diffusion through the liquid covering it. When the eyes are closed in sleep the corneal pO_2 falls significantly, and at altitude the resultant hypoxia causes the cornea to swell. For individuals who have not had radial keratotomy for nearsightedness, corneal swelling produces no visual changes because the swelling is symmetrical. However, for patients who have had radial keratomy, corneal swelling results in a flattening of the central part of cornea, and patients become farsighted (Mader and White, 1996). Although vision may be compromised at altitude, the effect can be variable and unpredictable. The alternative form of surgery, photo-refractive keratatomy using a laser knife, does not seem to cause visual aberration. People with radial keratotomy may need to carry lenses for the correction of farsightedness when venturing to high altitude.

Pulmonary conditions

Pulmonary embolism. Because the symptoms and signs of pulmonary embolism are so similar to HAPE, the correct diagnosis may be difficult (Shlim and Paperfus, 1995b). Dyspnea, cough, chest discomfort, tachypnea, and tachycardia are common to both entities, except that HAPE usually presents slowly while pulmonary embolism usually presents suddenly. In the wilderness, the history and physical exam are critical to make the distinction so that the correct therapy can be initiated. For example, trekking and expedition parties often carry low-molecular-weight heparin for suspected deep vein thrombosis or pulmonary embolism (Goldhaber, 1999), which is easy to administer and may be lifesaving.

Respiratory tract and other infections. Respiratory tract infections, which are common at high

altitude (Basnyat et al., 1999a), may predispose to AMS (Murdoch, 1995b) and may themselves simulate AMS because of the shared, nonspecific symptoms of headache, nausea, fatigue, and dizziness. Infectious pharyngitis and bronchitis, which are common and distressing problems in mountain climbers, by themselves are not suggestive of HAPE. The irritation caused by intensely cold, dry air is thought to exacerabate respiratory symptoms. Himalayan trip leaders suggest keeping the head covered and using a soft porous scarf around the nose and mouth to warm the air to avoid the "khumbu cough."

As recently reviewed (West, 1998), HAPE was slowly recognized as a distinct entity because it was confused with pneumonia, probably the most common mimic of HAPE. HAPE was first recognized to be a separate disease process by Hultgren and Sprickard (1960) and then by Houston (1960). Nevertheless, HAPE may be complicated by a chest infection, and in this setting antibiotics are therapeutic (Ward, 1995). Concurrent or primary pulmonary tuberculosis must always be suspected in Himalayan and other indigenous mountain people who develop signs and symptoms of HAPE. Pulmonary tuberculosis in such individuals is as common today as it was in Welsh coal miners who lived in the early 1900 (Cronin, 1935).

Rheumatic heart disease and its complication pulmonary hypertension may predispose to the development of HAPE in local Nepalese porters and guides who accompany tourists to high altitude. Mitral stenosis and mitral regurgitation are still the most common heart murmurs in the clinics of Nepal.

Periodic breathing. Periodic breathing, characterized by alternating apnea and hyperpnea spells during sleep, is a normal and common phenomenon at altitude (Hackett and Roach, 1995). However, many travelers say that periodic breathing during sleep is extremely disturbing and anxiety-producing because it causes "suffocating and claustrophobia." The treatment for individuals without sulpha allergy is to take 125 mg of acetazolamide in the evening to decrease the hypoxemic spells that trigger the periodic breathing (Hackett, 1997).

Miscellaneous conditions

Drugs and alcohol. Trekking up to high altitude is an enjoyable sport, and some travelers will take recreational drugs and alcohol in an attempt to enhance their enjoyment. Abuse of these stimulants can cause headache, nausea, mental confusion and ataxia, and one can easily confuse these symptoms with HACE, particularly if the patient surreptitiously ingested them in his or her tent unbeknownst to the rest of the group.

Hypothermia and dehydration. Many travelers with reckless behaviors and overly romantic notion of high altitude are not suitably dressed for mountain climbs. They may suffer gradual hypothermia, which mimics the headache, fatigue, and mental status changes associated with AMS and HACE. Hence, thermal underwear and insulated jackets are critical in the Himalayas, where balmy temperatures fall to subfreezing cold when the sun sets.

Dehydration occurs rapidly at high altitude, and together with physical exertion, sweating and hyperventilation, presents with fatigue, nausea, and headache like AMS. Furthermore, if the kidneys must choose between the two possibilities of bicarbonate diuresis (an important factor in high altitude acclimatization), and fluid conservation (to correct dehydration), they may choose the latter and thus compromise acclimatization (Basnyat et al., 1999a). Hence, adequate fluid consumption is essential.

Carbon monoxide poisoning. Under certain housing conditions in the Himalayas, patients may present with the headache, nausea, drowsiness, and coma associated with carbon monoxide poisoning rather than with HACE. Fortunately, carbon monoxide poisoning is rarely seen in tea houses where many tourists sleep, because these smoke-filled rooms are too porous to allow accumulation of toxic concentrations of carbon monoxide generated by open fires and lack of chimneys. By contrast, in snow caves and tents at high altitude where stoves are used, carbon monoxide poisoning is always a possibility. The commonly used pulse oximeters, which examine only two wavelengths of light, may give a false reading of adequate oxy-

gen saturation in these patients and should not be used to diagnose carbon monoxide poisoning (Weinberger and Drazen, 1998).

Psychological problems. Unrelated to AMS, predisposed trekkers may undergo a psychotic breakdown due to the psychological stress brought on by the harsh, often poverty-stricken environment. Careful history obtained from close contacts of the patient and physical examination may help confirm the diagnosis. The two individuals who developed acute disorientation and violent behavior while trekking, which one of us (B.B.) witnessed, recovered rapidly and completely after they returned to their home environment. Acute anxiety (perhaps triggered by excessive periodic breathing and insomnia), voluntary hyperventilation, and mental depression are other psychological problems at altitude that might be encountered and need to be differentiated from altitude sickness.

Gastrointestinal infections. Infectious diarrhea is the most common medical problem among Himalayan tourists (Steffen, 1986). Consequently, it is not surprising that many high altitude trekkers are plagued by diarrhea, and sometimes have to abandon their trip because of it. Clearly, however, diarrhea is not a symptom of AMS. Because the symptoms of headache, nausea, vomiting, and dizziness are seen in patients with infectious gastroenteritis and with AMS, it is important to decide if the diarrhea is the primary problem. Bacteria, giardia, and amebas in that order (Hoge et al., 1996) are the usual etiological agents of diarrhea in Nepal, with viral agents and cyclospora being seasonal causes. If there is any doubt whether the symptoms are caused by altitude sickness or by intestinal infection, it is best to assume altitude sickness and descend.

Other infections. Dengue fever, meningitis, Japanese encephalitis, cerebral malaria, typhoid fever, and staphylococcal sepsis are often seen in developing countries, including Nepal (Centers for Disease Control and Prevention, 1999–2000). Because headache and mental changes accompany these infections, they may be confused with altitude sickness. High fever and myalgia, which frequently characterize most of these illnesses, are not features of altitude sickness. Immunization history against typhoid and Japanese encephalitis may be used to narrow the diagnostic possibilities.

Asthma and myocardial infarction. Asthma (Cogo et al., 1997) and myocardial infarction (Hutchison and Litch, 1998), common medical problems often triggered by cold, hypoxia, and exertion, are conspicuous by their relative absence in the Himalayas. Obviously, persons with a history of myocardial infarction or asthma should consult with a knowledgeable physician or travel medicine specialist before venturing to high altitude.

Language barriers. Because tourists of so many different nationalities and backgrounds visit the Himalayas, the caregiver may not be able to obtain a proper medical history or communicate a crucial message, such as the need to descend, to someone with HAPE or HACE. The inability to communicate under such stressful conditions often thwarts the correct diagnosis, aggravates the patient's symptoms, and stymies medical management. Under such conditions, it is crucial to seek help from other people in the patient's party who may be multilingual. Above all else, a patient with altitude sickness should never be left alone with a porter or another person who does not speak the patient's language, while the remainder of the patient's party climbs the mountain (Basnyat et al., 1999b).

CONCLUSION

Medical problems not directly related to classical high altitude cerebral and pulmonary edema need to be recognized. These many and varied acute medical problems at altitude summarized in this review need to be considered for the proper diagnosis and management of travelers who become ill in the Himalayas and other high altitude mountainous environments. Some of these may be medical mimics of altitude sickness. In most instances, and es-

pecially when the diagnosis is uncertain, it is best to descend.

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