

0.0 SUMMARY

0.1 CRITICAL FOCUS

A. GENERAL:

1. ALL MANIFESTATIONS: Descent, rest, oxygen.
2. SERIOUS COMPLICATIONS: Mechanical ventilation, Swan-Ganz monitoring, decrease intracranial pressure.
3. PREVENTION: Acetazolamide, acclimatization.

B. ACUTE MOUNTAIN SICKNESS:

1. DESCENT: 3000 to 4000 feet (1000 to 1500 meters) usually adequate.
2. OXYGEN: For more severe symptoms; useful for all forms of altitude illness, including AMS (but often not available); give 2 to 3 L/min.
3. ACETAZOLAMIDE: 250 mg PO Q8H (children: 5 mg/kg/day PO in 3 divided doses) for 48 hours.
4. DEXAMETHASONE: 4 mg PO or IM Q6H in patients with neurologic deterioration (eg, ataxia, change in level of consciousness) or severe headache and/or vomiting.
5. ASPIRIN OR ACETAMINOPHEN: 650 mg (children: 10 to 15 mg/kg) PO Q4-6H for headache.
6. PROCHLORPERAZINE: 10 mg IM or PO Q6-8H (children >2 years: 0.4 mg/kg/day PO or 0.2 mg/kg/day IM in 3 to 4 divided doses) for nausea and vomiting.

C. HIGH ALTITUDE PULMONARY EDEMA:

1. BED REST/WARMTH: To decrease pulmonary artery pressure; avoid exertion.
2. OXYGEN: If available, give 6 to 12 L/min by nasal cannula or face mask (1 to 2 L if O₂ is a problem).
3. DESCENT: As rapidly as possible but preferably with little exertion by the victim; 1000 to 3000 feet may be adequate.
4. AIRWAY MANAGEMENT: CPAP by tight-fitting mask in awake patients; intubation, mechanical ventilation, and PEEP for severe cases.
5. FUROSEMIDE: 20 to 40 mg (children: 1 to 2 mg/kg) IV may be needed if intravascular volume is increased (rarely necessary); must be given under medical supervision.
6. NIFEDIPINE (Emergency treatment when descent or evacuation is impossible and supplemental oxygen is not available): 10 mg SL plus 20 mg PO of slow-release nifedipine. If systolic BP does not decrease ≥ 10 mmHg within 10 min, repeat SL dose after 15 min, then give 20 mg of slow-release nifedipine Q6H for entire time at altitude.
7. MORPHINE: 2 to 10 mg IV if no cerebral involvement (children: 0.1 to 0.2 mg/kg/dose IV); rarely necessary.

D. HIGH ALTITUDE CEREBRAL EDEMA:

1. DESCENT.
2. OXYGEN: 2 to 4 L via nasal cannula.
3. AIRWAY MANAGEMENT: Intubation and hyperventilation for patients in coma (mechanical ventilation for long-term management).
4. FUROSEMIDE: 20 to 40 mg IV (children: 1 to 2 mg/kg/dose IV).
5. DEXAMETHASONE: 10 mg IV initially, then 4 mg Q6H (children: 0.25 to 0.5 mg/kg/dose IV Q6H).
6. FOLEY CATHETER: For bladder drainage if comatose.

E. PROPHYLAXIS:

1. ACCLIMATIZATION: Graded exercise and slow ascent (300 m/day over 3000 m) avoid abrupt ascent from sea level to sleeping altitude over 10,000 ft; stay at intermediate altitude for one night.
2. ACETAZOLAMIDE: 250 mg PO BID, or one sustained-action 500-mg capsule PO Q24H (children: 5 mg/kg/day PO in 2 divided doses) beginning 3 days before ascent and continuing for 2 to 3 days at altitude.

0.2 CLINICAL PRESENTATION

- A. ETIOLOGY: Relative or absolute hypoxia secondary to low oxygen content of air at altitudes above 7200 feet (2000 meters); HAPE and HACE rarely occur below 2500 m.
- B. CLASSIFICATION: Primary clinical syndromes are acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), high altitude cerebral edema (HACE); may occur singly or in combination.

- C. PREDISPOSING FACTORS: Rapid ascent, lack of sufficient time for acclimatization, increased physical activity, prior episodes, underlying pulmonary disease, drugs that depress ventilation.
- D. CLINICAL FINDINGS: Onset usually within first 48 hours of arrival at a higher altitude.
 - 1. AMS: Headache (most common and usually most prominent symptom), nausea, vomiting, anorexia, lethargy, sleep disturbance, vertigo or dizziness, palpitations, difficulty in concentrating; symptoms often worse on second and third day, especially on awakening.
 - 2. HAPE: Mild fever, tachypnea, tachycardia, dry cough, rales, cyanosis, fatigue; occasionally, wheezing, orthopnea, hemoptysis (late), chest pain (tightness); confusion, ataxia, coma possible; symptoms often preceded by strenuous exercise; victim often awakes with it; may be confused with bronchitis or pneumonia early in course.
 - 3. HACE: Severe headache; confusion, delirium, lassitude, hallucinations, emotional lability progressing to coma; gait ataxia common early finding; possible focal neurologic signs; papilledema.
- E. COMPLICATIONS: Anoxic encephalopathy (rare); death (HACE, HAPE) if unrecognized and untreated.

0.3 DIAGNOSTICS

A. LABORATORY:

- 1. AMS: No laboratory tests generally required; usually lower SaO₂ than normal for that altitude and widened A-a O₂ difference.
- 2. HAPE: ABGs (hypocapnic alkalosis; severe hypoxemia (PaO₂ <30 to 40)).
- 3. HACE: ABGs; drug toxicology screen if diagnosis uncertain; electrolyte panel not useful.

B. RADIOLOGY:

- 1. AMS: Not indicated.
- 2. HAPE: Chest film - patchy alveolar infiltrates with sparing of bases and prominent pulmonary arteries.
- 3. HACE: Chest film, CT scan.

C. DIAGNOSTIC AIDS:

- 1. HAPE: EKG (signs of acute pulmonary hypertension); pulmonary artery catheterization if patient fails to improve with oxygen therapy, rest, descent.

0.4 DIFFERENTIAL DIAGNOSIS

- A. AMS: Gastroenteritis, head trauma, hypothermia, dehydration, drug ingestion, exhaustion, carbon monoxide poisoning, alcohol "hangover"; usually can be differentiated on basis of history.
- B. HAPE: Any respiratory infection or inflammation; history, x-rays, and failure to improve with oxygen therapy and descent should suggest another entity.
- C. HACE: Any entity producing cerebral edema and neurologic findings; failure to improve with oxygen therapy and descent suggests another entity; electrolyte levels, LFTs, CT scan, lumbar puncture may be necessary to rule out other causes of coma.

1.0 CLINICAL PRESENTATION

1.1 INTRODUCTION

1.1.1 ETIOLOGY

A. DEFINITION:

- 1. Relative or absolute hypoxia secondary to low oxygen content of air at altitudes above 2000 meters (7200 feet); HAPE and HACE rarely occur below 2500 m (8200 ft) (Hackett, 1992; Yaron, 1994; Pigman, 1990).
- 2. Requires several physiologic adaptations, some of which are advantageous (elevated hematocrit and increased breathing), while others are disadvantageous (respiratory alkalemia and decreased stroke volume).
- 3. Severity of symptoms influenced by level of altitude, rate of climb, terrain, and environment on mountain (Shukitt-Hale, 1980; Ergun, 1994).

B. ALTITUDES (Hackett, 1992; Ergun, 1994):

- 1. HIGH ALTITUDE: 1500 to 3500 m (4900 to 11,500 ft) above sea level; decreased exercise performance and increased ventilation occur, without major impairment in arterial O₂ transport. Altitude illness common with abrupt

ascent to >2500 m (8200 ft).

2. VERY HIGH ALTITUDE: 3500 to 5500 m (11,500 to 18,000 ft); maximum arterial O₂ saturation falls to <90%; extreme hypoxemia may occur during sleep, exercise, altitude illness. Abrupt ascent may be dangerous; requires period of acclimitization.
3. EXTREME ALTITUDE: >5500 m (>18,000 ft); accompanied by severe hypoxemia and hypocapnia; abrupt ascent almost always precipitates altitude illness.

1.1.2 CLASSIFICATION

A. OVERVIEW

1. HYPOXIC SYNDROMES (Hackett, 1992):
 - a. Problems of primary concern are those attributable directly to hypoxia, including acute hypoxia, acute mountain sickness (AMS), high altitude pulmonary edema (HAPE), high altitude cerebral edema (HACE), retinopathy, peripheral edema, sleeping problems, and group of nerurologic syndromes.
 - b. Share fundamental mechanism, occur in setting of rapid ascent in unacclimatized person, and respond to same essential therapy (oxygen, descent).
2. NONHYPOXIC SYNDROMES: Thromboembolic events (may be attributable to dehydration, prolonged incapacitation, polycythemia, cold), high altitude pharyngitis/bronchitis, ultraviolet keratitis (Hackett, 1992).

B. MOUNTAIN SICKNESS, ACUTE

1. EPIDEMIOLOGY:

- a. INCIDENCE: 20% to 50%, depending on altitude and rate of ascent (Hackett, 1992; Montgomery, 1989; Honigman, 1993; Theis, 1993).
- b. AGE:
 - (1) Younger persons are at higher risk than are older persons, although no age group is immune (Hackett, 1976; Roach, 1995; Theis, 1993). However, a study of AMS occurring at intermediate altitude (2000 to 4000 m) reported no association between age and number of symptoms (Montgomery, 1989).
 - (2) Older persons, including those with underlying asymptomatic cardiopulmonary disease, can safely visit moderate altitudes (Roach, 1995).

2. CLINICAL PRESENTATION:

- a. Manifested by headache, dyspnea, dizziness, anorexia, nausea, vomiting, fatigue, and insomnia; physical findings may include cyanosis, pallor, periorbital edema, tachycardia (Montgomery, 1989; Pigman, 1991; Hackett, 1992).
- b. Symptoms may begin during ascent but more typically occur 6 to 48 h later. With avoidance of overexertion, they usually decrease in 1 to 7 days, even when staying at the same altitude (Montgomery, 1989).

C. EDEMA, PULMONARY, HIGH ALTITUDE

1. INCIDENCE:

- a. 0.5% to 6%, depending on altitude (uncommon at <10,000 ft), speed of ascent, and individual susceptibility (Hackett, 1992; Hsia, 1994; Yaron, 1994; Hultgren, 1978).
- b. Subclinical form above 14,000 ft is common, noted in 15% to 23% of trekkers (Hackett, 1979; Houston, 1975).

2. CLINICAL PRESENTATION: Most lethal syndrome.

- Manifested by marked shortness of breath, undue fatigue, a persistent, progressive, nonproductive cough, tachypnea, tachycardia, cyanosis, fever, chest discomfort; symptoms often worsen with sleep (Rabold, 1989; Hsia, 1994).
3. RECURRENCES: Common; reported after rapid ascent to 4559 m in two thirds of adult residents of low altitude with history of HAPE (Vock, 1989).
- ##### D. EDEMA, CEREBRAL, HIGH ALTITUDE
1. DEFINITION: Presence of progressive neurologic deterioration in person with AMS or HAPE (Hackett, 1992).
 2. INCIDENCE: Least common form of altitude illness (Hackett, 1992; Yaron, 1994). Incidence in Mt Everest

trekkers is 1% (Hackett, 1976).

3. CLINICAL PRESENTATION: Characterized by altered mental status, ataxia, stupor, and progression to coma if untreated; headache, nausea, and vomiting may or may not be present; may be focal neurologic signs, eg, 3rd and 6th cranial nerve palsies, associated with increased ICP (Hackett, 1992).

E. RETINOPATHY, HIGH ALTITUDE

1. Include retinal edema, tortuosity and dilatation of retinal veins, disc hyperemia, retinal hemorrhages, and cotton wool exudate (rare) (Hackett, 1992).
2. Retinal hemorrhages common above sleeping altitude of 5000 m and occur at lower altitudes in persons with altitude illness; usually asymptomatic; resolves spontaneously in 10 to 14 days (Hackett, 1992; Shuping, 1993).

F. BRONCHITIS, HIGH ALTITUDE

1. Common entity at altitudes >14,000 ft and may be confused with HAPE. Symptoms range from mild dry cough to production of copious yellow/green sputum and hemoptysis; cough occurs primarily at rest. Patient may complain of exertional (but not resting) tachypnea; fever is absent. Lungs may have coarse rhonchi, but more commonly are clear. Symptoms worsen on ascent and improve on descent (Rabold, 1989).
2. Appears to be due to sterile bronchial inflammation caused by chronically high minute volume of cold and dry air (Rabold, 1989).

G. KERATITIS, ULTRAVIOLET

1. Symptoms delayed for 6 to 12 h postexposure. Characterized by severe eye pain, foreign body or gritty sensation, photophobia, tearing, marked conjunctival erythema, chemosis, lid edema. Generally self-limited and heals within 24 hours (Hackett, 1992).

H. MOUNTAIN SICKNESS, CHRONIC

1. GENERAL: May develop after variable length of residence in both long-term high altitude residents and lowlanders who relocate to high altitude; incidence higher in males and increases with age (Hackett, 1992).
2. CLINICAL PRESENTATION: Characterized by excessive polycythemia for given altitude (Hgb >20 to 22 g/dL); causes headache, difficulty thinking and sleeping, impaired peripheral circulation, drowsiness, chest congestion (Hackett, 1992).

1.1.3 EPIDEMIOLOGY

A. AMS:

1. Incidence is 20% to 40%, depending on altitude and rate of ascent (Hackett, 1992; Montgomery, 1989; Roach, 1995; Theis, 1993).
2. Younger persons are at higher risk than are older persons, although no age group is immune (Hackett, 1976; Roach, 1995; Theis, 1993). However, a study of AMS occurring at intermediate altitude (2000 to 4000 m) reported no association between age and number of symptoms (Montgomery, 1989).
3. Older persons, including those with underlying asymptomatic cardiopulmonary disease, can safely visit moderate altitudes (Roach, 1995).
4. Occurrence of altitude illness does not appear to be related to previous altitude experience (Hackett, 1976).

B. HAPE:

1. Incidence is 0.5% to 6% (Hackett, 1992; Yaron, 1994; Hultgren, 1978). Subclinical form above 14,000 ft is common, noted in 15% to 23% of trekkers (Hackett, 1979; Houston, 1975).
2. Recurrences common; reported after rapid ascent to 4559 m in two thirds of adult residents of low altitude with history of HAPE (Vock, 1989).
3. Mortality is 4% to 27%, depending on rapidity of descent and evacuation (Rabold, 1989).

C. HACE:

1. Least common form of altitude illness (Hackett, 1992; Yaron, 1994).
2. Incidence in Mt Everest trekkers is 1% (Hackett, 1976).

- D. MORTALITY: Altitude accounts for 10% to 15% of deaths among trekkers; persons in organized trekking groups are at a higher risk than those traveling on their own (Shlim, 1992).
- 1.1.4 PATHOPHYSIOLOGY
- A. GENERAL:
1. Illnesses associated with altitude have fluid retention, fluid compartment shifts, and leaky microvascular beds secondary to the hypoxemia as the basic underlying pathophysiologic mechanism (Ergun, 1994; Reeves, 1991).
 2. Hypoxemia results from decreasing barometric pressure and partial pressure of O₂ with altitude. Decreasing O₂ tension stimulates peripheral chemoreceptors to increase alveolar ventilation; this blows off CO₂, leading to respiratory alkalosis (Reeves, 1991).
 3. All types caused by a lack of oxygen. These entities rarely exist alone, and the victim usually presents with a predominance of signs and symptoms of one condition, as well as with several findings associated with the other entities (Hackett, 1976, 1979; Pigman, 1990; Montgomery, 1989; Hackett, 1992; Yaron, 1994; Ergun, 1994).
- B. CLINICAL SETTING:
1. Syndromes occur singly or in combination almost exclusively within the first 96 hours of arrival at high altitude (7500 feet or 2710 meters) or after ascending to a new, higher altitude before acclimatization has occurred. AMS may occur at altitude as low as 2000 m (Montgomery, 1989; Pigman, 1990; Ergun, 1994).
 2. HAPE:
 - a. Seen almost exclusively in persons who ascend to elevations >2740 m (Rabold, 1989). May occur in high altitude residents upon return to elevation after a visit to lower altitude.
 - b. Characterized by marked pulmonary vasoconstriction; may involve increased alpha adrenergic activity (Hackett, 1992). Appears to be caused by stress failure of pulmonary capillaries (West, 1992). Can occur in susceptible persons despite the presence of a normal or high ventilatory response to hypoxia (Selland, 1993).
 3. HACE: Hypoxic cerebral vasodilatation appears to be involved in pathogenesis of HACE but not of AMS. Prolonged increased capillary pressure in vasodilated areas could lead to vasogenic cerebral edema (Lassen, 1992).
- 1.1.5 PREDISPOSING FACTORS
- A. Travel to mountains from altitudes <900 m; fast rate of ascent (eg, arrival to altitude by airplane, ascent on foot >300 m/day above 3000 m) (Honigman, 1993).
 - B. Strenuous exercise (Honigman, 1993; Bartsch, 1992); not always correlation between physical fitness and susceptibility to AMS (Milledge, 1991; Pigman, 1990).
 - C. Unilateral pulmonary artery (congenital).
 - D. Underlying respiratory, cardiac, or neurologic disease (Honigman, 1993). (However, older persons with underlying asymptomatic cardiopulmonary disease, can safely visit moderate altitudes (Roach, 1995).)
 - E. Prior episodes (Vock, 1989; Honigman, 1993).
 - F. Use of respiratory depressants, eg, alcohol, codeine, barbiturates, diazepam. Alcohol inhibits initial stages of adequate acute ventilatory adaptation to mild hypoxia at moderate altitude (Roeggla, 1995).
 - G. Adolescent and preadolescent high altitude residents who return to altitude following a visit to sea level.
 - H. Low vital capacity (eg, kyphosis, pneumonectomy).
 - I. Fluid retention.
 - J. Pulmonary hypertension.
 - K. Sleep apnea syndromes (Normand, 1992; Goldenberg, 1992); however, periodic breathing may be help adaptation to altitude (Goldenberg, 1992).
 - L. Blunted hypoxic ventilatory response (carotid body function) (Rathat, 1992).
 1. However, this is controversial, as several studies have shown no correlation between HVR and subsequent

- susceptibility to AMS (Milledge, 1991) or that low HVR alone is critical factor for HAPE (Matsuzawa, 1989; Selland, 1993).
2. Persons with a more vigorous ventilatory response to hypoxia appear to have more residual neurobehavioral impairment after returning to lower elevations (Hornbein, 1989).
- M. Intracardiac shunting across patent foramen ovale (present in 10% to 30% of normal adults) (Levine, 1991).
- 1.2 ASSOCIATED CONDITIONS
- A. HYPOTHERMIA
1. Because high altitude is a frequent accompaniment of wintertime activities (eg, skiing), concomitant illnesses due to cold exposure, hypothermia, or frostbite may be present and should be sought.
- B. TRAUMA
1. May be a frequent cause of trauma, eg, falls or injuries caused by poor judgement or ataxia.
- 1.3 VITAL SIGNS
- A. TEMPERATURE
1. TEMPERATURE, INCREASED
 - a. Low-grade fever may accompany the cough of early HAPE. This has led to the erroneous diagnosis of underlying infection as the cause of the respiratory complaint (Hackett, 1992; Yaron, 1994; Rabold, 1989).
 2. TEMPERATURE, DECREASED
 - a. Hypothermia may occur secondary to environmental exposure.
- B. BLOOD PRESSURE
1. BLOOD PRESSURE, DECREASED
 - a. HAPE: BP usually low. In a study of 21 patients in Peru, the mean arterial BP was 106/69 mmHg (Hackett, 1992; Yaron, 1994).
 - b. Acute (short-term) exposure to moderate altitude does not seem to affect BP; 36 hours of exposure at 3000 m produces a small reduction (5 mmHg). Significant changes in BP (>10 mmHg) follow hypoxic and physical stress with intermediate high altitude exposure (2 to 7 weeks) (Brinchmann-Hansen, 1989).
 2. BLOOD PRESSURE, INCREASED
 - a. Altitude travel may lead to hypertension secondary to catecholamine release (Palatini, 1989).
 - b. Incidence of pregnancy-induced hypertension is increased at altitude (Moore, 1982).
- C. RESPIRATIONS
1. RESPIRATIONS, INCREASED
 - a. May be a presenting sign of AMS (Pigman, 1992; Ergun, 1994).
 - b. Increases in HAPE; rate usually 20 to 30/minute (Hackett, 1992; Yaron, 1994; Rabold, 1989).
 2. RESPIRATIONS, CHEYNE-STOKES
 - a. May occur on arrival to high altitude and may be observed by witnesses, especially at night (Fletcher, 1979).
 - b. May be normal in high altitude sojourners.
- D. HEART RATE
1. TACHYCARDIA
 - a. Generally occurs in persons with HAPE. In severe hypoxia, pulse rate may be as high as 160 beats/minute (Hackett, 1992; Yaron, 1994; Rabold, 1989).
 - b. Also may be a presenting sign in AMS (Pigman, 1990; Ergun, 1994).
 - c. Patients with underlying COPD may develop further hypoxemia because of a lack of sensitivity of the chemoreceptors to this hypoxemia.
- 1.4 PRESENTATION BY BODY SYSTEM
- 1.4.2 DERMATOLOGIC PRESENTATION
- A. CYANOSIS
1. Central cyanosis may be present due to hypoxemia (Raybold, 1989).
- 1.4.3 HEENT PRESENTATION
- A. ASYMMETRY, FACIAL
1. May occur secondary to specific muscle weakness in patients with HACE (Hackett, 1992; Yaron, 1994).

- B. EDEMA, FACIAL
 - 1. Occurs more commonly in females; usually accompanies more serious forms of altitude illness (Hackett, 1992; Yaron, 1994).
 - 2. There was a 4% incidence of periorbital edema in 200 trekkers examined at 4243 meters. It occurs more commonly in patients with other symptoms of AMS (Hackett, 1992; Yaron, 1994).
- C. SCOTOMA
 - 1. Paracentral scotoma may occur in 50% of patients with retinal hemorrhage (Hackett, 1992; Yaron, 1994).
- D. VISION, BLURRED
 - 1. Clouding of vision may be present in patients with retinal hemorrhage (Hackett, 1992; Yaron, 1994).
- E. FUNDUSCOPIC CHANGES
 - 1. HEMORRHAGE, RETINAL
 - a. Increased vessel engorgement and disc hyperemia were found in all patients studied at altitude (McFadden, 1981). Appears related to physical exertion during high altitude exposure (Brinchmann-Hansen, 1989; McFadden, 1981).
 - b. Occurs in 30% to 40% of persons at altitudes >4500 meters (Hackett, 1992; Yaron, 1994) and in 50% of climbers at altitudes over 5300 meters. Not necessarily a sign of either impending cerebral edema or a need for descent (Hackett, 1992).
 - c. Unless over macula, usually asymptomatic and resolve spontaneously; probably related to increased retinal blood flow and dilatation of vessels (Hackett, 1992).
- F. TINNITUS
 - 1. Rare finding in AMS (Hackett, 1992; Yaron, 1994). also may result from prophylactic treatment with acetazolamide.
- 1.4.4 NECK PRESENTATION
 - A. NUCHAL RIGIDITY
 - 1. Rarely present even when CSF pressure is markedly elevated (Hackett, 1992; Yaron, 1994).
- 1.4.5 RESPIRATORY PRESENTATION
 - A. COUGH
 - 1. Persistent nonproductive cough may be early manifestation of HAPE; often mistaken for an underlying pneumonia or bronchitis (Rabold, 1989).
 - 2. Patients with high-altitude bronchitis may have a mild dry cough or cough productive of copious yellow-green sputum; occurs primarily at rest (Rabold, 1989).
 - B. HEMOPTYSIS
 - 1. Late manifestation of HAPE; necessitates aggressive therapy (Hackett, 1992; Yaron, 1994).
 - C. DYSPNEA
 - 1. AMS: Dyspnea on exertion occurs in all visitors to high altitude (Hackett, 1992; Yaron, 1994; Pigman, 1990; Montgomery, 1989; Ergun, 1994). May be present due to marginally low PO₂ when combined with other symptoms (Hackett, 1992; Yaron, 1994).
 - 2. HAPE:
 - a. Nocturnal dyspnea or dyspnea at rest is a sign of HAPE and mandates aggressive management (Hackett, 1992; Yaron, 1994; Rabold, 1989).
 - b. A contributing factor to the "leaky capillaries" of HAPE is increased pulmonary artery pressure, occurring during exercise. Dyspnea at rest when pulmonary pressures are low is a sign of advanced disease.
 - D. BREATH SOUND CHANGES
 - 1. RALES
 - a. Occur in 23% of visitors to heights above 14,000 feet and are frequently associated with peripheral edema, AMS, and retinal hemorrhages (Hackett, 1979).
 - b. Once rales are heard, more acclimatization is recommended before ascending higher; these persons should be observed for symptoms of HAPE (Rabold, 1989).
 - c. In one series, rales were present in only 50% of patients whose chest films showed evidence of HAPE; even extensive lung edema was accompanied by discrete rales only. Conversely, rales in absence of

radiographic evidence of HAPE were observed in >50% of patients who developed radiographic evidence later during stay at high altitude (Vock, 1989).

E. RETRACTIONS, INTERCOSTAL

1. Nonspecific sign of severe respiratory distress; may be present in patients with HAPE as a result of increased airway resistance due to interstitial or intra-alveolar fluid.

1.4.6 CARDIOVASCULAR PRESENTATION

A. PAIN, CHEST

1. Dull pain and discomfort in the muscles of the posterolateral chest wall, which is at times described as a "tightness", is a common complaint in HAPE (Hackett, 1992; Yaron, 1994; Rabold, 1989).
2. Rarely, may be indicative of underlying coronary artery disease, which may be aggravated by hypoxemia at high altitude. However, in physically fit older men, strenuous exercise (eg, skiing) at high altitude does not appear to pose a greater coronary stress than does comparable exercise at low altitude (Hackett, 1992; Yaron, 1994).

B. ORTHOPNEA

1. May occur in patients with no previous history of underlying cardiac disease (Hackett, 1992; Yaron, 1994).

C. PALPITATIONS

1. Palpitations on effort may be noted (Hackett, 1992; Yaron, 1994; Ergun, 1994).

D. ARRHYTHMIAS

1. May occur secondary to hypoxia.

E. HEART SOUND CHANGES

1. HEART SOUND, THIRD
 - a. Unusual finding in HAPE; reflects right ventricular failure due to severe pulmonary hypertension.

F. EDEMA, PERIPHERAL

1. Noted in 18% of 200 trekkers at 4243 meters; more common when other signs of AMS were present. More common in women than in men (Hackett, 1992).
2. Mechanism not understood; when present signs of HAPE or HACE should be carefully sought (Hackett, 1992).

1.4.7 GASTROINTESTINAL PRESENTATION

A. ANOREXIA

1. Characteristic in visitors to high altitudes who are experiencing AMS (Hackett, 1979; Pigman, 1990; Montgomery, 1989; Ergun, 1994).

B. NAUSEA

1. Nausea, with or without vomiting, is a common accompaniment of AMS and seems to be more common in children (Hackett, 1992; Yaron, 1994; Pigman, 1990; Ergun, 1994).
2. Common feature of HACE (Hackett, 1992; Yaron, 1994).

C. VOMITING

1. May occur in victims of AMS (Pigman, 1990; Ergun, 1994).
2. Common feature of HACE (Hackett, 1992; Yaron, 1994).

1.4.8 GENITOURINARY PRESENTATION

A. POLYURIA

1. AMS: Diuresis (up to 5 L/day) has been reported during high altitude trekking; correlates negatively with severity (Delamare, 1979).

B. OLIGURIA

1. AMS: Present in moderate to severe cases; must be differentiated from dehydration.

1.4.9 MUSCULOSKELETAL PRESENTATION

A. WEAKNESS, MUSCLE

1. Uncommonly, specific and localized motor weakness, eg, amblyopia, difficulty with finger motions, facial asymmetry, and dysarthria, may be associated with HACE (Hackett, 1992; Yaron, 1994).
2. Supraspinal dysfunction producing mild alterations in motor function may occur in AMS as result of hypoxia-induced cerebral edema (Hamilton, 1991).

B. RIGIDITY, MUSCLE

1. HACE: Muscle rigidity has been reported (Hackett, 1992; Yaron, 1994).

C. FLACCIDITY, MUSCLE

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1. HACE: May present with muscle flaccidity (Hackett, 1992; Yaron, 1994).
- D. TREMOR
 1. HACE: Tremors have been reported (Hackett, 1992; Yaron, 1994).
- 1.4.10 NEUROLOGIC PRESENTATION
 - A. HEADACHE
 1. AMS:
 - a. Most common symptom; frequently present in the morning; occurs in nonacclimated visitors 6 to 96 hours after arrival to altitudes over 2000 meters.
 - b. Throbbing, bilateral, and frontal and associated with sensation of fullness of the head; worse in morning and with strenuous exercise; often not relieved by aspirin or acetaminophen (Pigman, 1991; Montgomery, 1989).
 - c. Migraineurs are likely to experience a migraine attack upon reaching high altitude.
 2. HACE: Headache, especially when occipital and associated with other neurologic symptoms, occurs and mandates immediate descent (Hackett, 1992; Yaron, 1994).
 - B. INSOMNIA
 1. Sleep is difficult at high altitude, especially for the first few nights. Frequent periods of wakefulness and strange dreams often occur (Hackett, 1992; Yaron, 1994; Pigman, 1990; Montgomery, 1989; Ergun, 1994).
 2. Disturbances of sleep are often secondary to periodic breathing and intermittent brain hypoxia, resulting in increasing CO₂ levels (Sutton, 1979).
 - C. DIZZINESS
 1. May be a symptom of AMS (Hackett, 1992; Yaron, 1994; Pigman, 1990; Ergun, 1994).
 - D. NEUROLOGIC SIGNS, FOCAL
 1. ATAXIA
 - a. HACE:
 - (1) Common; frequently one of the more reliable warning signs. At first, affected persons show a slight clumsiness in walking or using hands or fingers, but soon walking or even standing become difficult (Sutton, 1992; Tso, 1992).
 - (2) These symptoms are most likely due to the particular sensitivity of the cerebellum to hypoxia; often attributed initially to cold weather, rough terrain, or other environmental factors (Hackett, 1992; Yaron, 1994).
 - b. AMS: Occasionally, patients may have ataxic gait with poor finger-to-nose and heel-to-shin coordination tests (Pigman, 1990; Ergun, 1994).
 - E. ALTERED MENTAL STATUS
 1. OVERVIEW
 - a. Altered consciousness and CNS dysfunction may be related to profound hypoxia in severe HAPE (Hackett, 1992; Yaron, 1994) or may be a manifestation of HACE (Houston, 1975; Hackett, 1992; Yaron, 1994).
 2. CONFUSION
 - a. HACE: As the condition progresses, typical changes in mental status include mental confusion, irritability, emotional lability, and hallucinations. Progression to obtundation, coma, and death may occur if descent is not accomplished rapidly (Hackett, 1992; Yaron, 1994).
 3. LETHARGY
 - a. Lethargy may occur in AMS, HACE, and HAPE (Hackett, 1992; Yaron, 1994).
 4. COMA
 - a. HACE/HAPE: Mental status alterations may progress to obtundation, coma, and death if descent is not accomplished rapidly (Hackett, 1992; Yaron, 1994).
 - F. SEIZURES
 1. Convulsions associated with HACE have been reported (Hackett, 1992; Yaron, 1994).
 - G. COGNITIVE IMPAIRMENT
 1. Persistent cognitive impairment, particularly involving short-term memory, may occur following exposure to extremely high altitudes (Cavaletti, 1990; Regard, 1991; White, 1984; Hornbein, 1989).

2. Short-term memory impairment is most sensitive indicator of AMS; subclinical development appears to be heralded by decrement in ability to retrieve new information. Subclinical hypoxia in AMS may interfere with cognition, either directly or via secondary changes (eg, subclinical cerebral edema or alterations in cerebral blood flow) (Regard, 1991).
3. Persons who developed AMS with a 24- to 48-hour stay at high altitude were mildly impaired in short-term memory but improved in conceptual tasks. Persons who remained healthy had a better short-term memory but no improvement in cognitive flexibility (Regard, 1991).
4. Most likely explanation for memory impairment is sensitivity to hypoxia of anatomic structures known to be involved in memory tasks, ie, those situated in the temporal lobe (Cavaletti, 1990).
5. Persons with a more vigorous ventilatory response to hypoxia appear to have more residual neurobehavioral impairment after returning to lower elevations (Hornbein, 1989).

H. SYNCOPE

1. May occur following short-term exposure to moderate altitude. Typically occurs in otherwise healthy persons who have recently arrived (<24 h) at altitude, have a meal, and stand up and faint. Recovery usually is immediate, with no further symptoms (Nicholas, 1992).
2. Mechanism is unknown; role of hypoxia is uncertain (Nicholas, 1992). Does not appear to be related to poor physical conditioning or lack of fitness (Nicholas, 1993).

1.4.14 PSYCHIATRIC PRESENTATION

A. HALLUCINATIONS

1. Rare manifestation of HACE (Houston, 1975).

B. EMOTIONAL CHANGES

1. Rare manifestation of HACE (Houston, 1975).

C. CONCENTRATION, DECREASED

1. May be a symptom of AMS, HAPE, or HACE (Hackett, 1992; Yaron, 1994).

D. JUDGEMENT, IMPAIRED

1. HACE: Victims may become so paranoid and irrational that their behavior threatens both themselves and others, or judgement and dexterity may become so impaired that they are unable to perform necessary mental and physical tasks (Hackett, 1992; Yaron, 1994; Sutton, 1992; Tso, 1992).

1.4.15 MISCELLANEOUS SYMPTOMS

A. MALAISE

1. Lassitude with a general feeling of indisposition is characteristic of AMS (Hackett, 1992; Yaron, 1994; Montgomery, 1989).

1.5 COMPLICATIONS

A. ENCEPHALOPATHY, ANOXIC

1. Only long-term but rare complication of either HACE or HAPE; due to prolonged hypoxemia, (Hackett, 1992; Yaron, 1994).

B. BLINDNESS

1. Cortical blindness may occur at high altitude, probably secondary to cerebrovascular spasm, and is not necessarily associated with altitude illness (Hackett, 1987).
2. Permanent visual impairment due to retinal hemorrhage over the macula is a rare complication (Hackett, 1992; Yaron, 1994).

C. HIGH ALTITUDE ILLNESS, RECURRENT

1. HAPE: Recurrences common; reported after rapid ascent to >4550 m in two thirds of adult residents of low altitude with history of HAPE (Vock, 1989).

2.0 LABORATORY DATA

2.2 HEMATOLOGIC

A. HEMATOCRIT

1. HEMATOCRIT, INCREASED

- a. Persons who live at high altitude may show a chronic hematocrit elevation secondary to erythropoietic stimulation due to hypoxia. This occurs over a 2- to

- 3-week period in the acclimatization of sea level dwellers to high altitude.
- b. May be present secondary to dehydration and hemoconcentration.
- 2. HEMATOCRIT, DECREASED
 - a. Intravascular hemolysis associated with HAPE has been reported (Lovlin, 1980).
- B. WHITE BLOOD CELLS
 - 1. WHITE BLOOD CELLS, INCREASED
 - a. No distinct white cell abnormalities in HAPE, but leukocytosis when present resembles a pneumonic process (Hackett, 1992; Yaron, 1994).
 - 2. Hypothesized to be due to the resorption of blood and protein-rich exudate from the alveoli (Hackett, 1992; Yaron, 1994).
- C. PLATELET ADHESION
 - 1. Increased platelet adhesion may be causative in the pathogenesis of high altitude illness (Sharma, 1978).
- D. COAGULATION TESTS
 - 1. Shortened PTT, depressed fibrinogen, and depressed factor VIII values have all been associated with HAPE (Maher, 1976).
 - 2. Although some of these findings are consistent with DIC, other laboratory evidence of DIC (thrombocytopenia, prolonged protime, increased FDP) is lacking.
- 2.5 URINALYSIS
 - A. SPECIFIC GRAVITY, URINE
 - 1. SPECIFIC GRAVITY, URINE, INCREASED
 - a. High urine specific gravity represents antidiuresis and inappropriate fluid retention, or may be due to intravascular volume depletion (Hackett, 1992) and dehydration.
 - B. HEMATURIA
 - 1. Microscopic hematuria has been reported during high altitude trekking (Houston, 1975).
 - C. CATECHOLAMINES, URINE
 - 1. CATECHOLAMINES, URINE, INCREASED
 - a. Elevated urinary catecholamines levels have been reported in a majority of patients with symptomatic altitude illness and HAPE. The increase occurs immediately on arrival and peaks on day 10 (Hoon, 1976).
- 2.6 ARTERIAL BLOOD GASES
 - A. HYPOXIA
 - 1. GENERAL:
 - a. Consistent finding in HAPE, with arterial saturations ranging from 55% to 75% (Hultgren, 1978).
 - b. Hypoxemia is probably secondary to ventilation/perfusion mismatches, diffusion problems secondary to alveolar fluid accumulation, or shunting.
 - 2. PATHOPHYSIOLOGY: Many theories have attempted to explain the phenomenon of leaky capillaries in HAPE, including marked pulmonary hypertension, uneven hypoxic vasoconstriction, increased pulmonary blood flow, and platelet thrombi-induced damage to capillaries (Hackett, 1992; Yaron, 1994). HAPE is a high-protein permeability edema (Schoene, 1986).
 - B. ALKALOSIS, RESPIRATORY
 - 1. Typically, arterial PCO₂ is either normal for the altitude or decreased secondary to profound hypoxemia and hyperventilation (Hackett, 1992; Yaron, 1994).
- 3.0 RADIOLOGIC DATA
 - 3.2 PLAIN FILMS
 - A. RADIOGRAPHY, CHEST
 - 1. INDICATIONS: Suspected HAPE; helpful in detecting HAPE in patients with normal auscultation (Vock, 1989).
 - 2. FINDINGS:
 - a. Dilation of central pulmonary arteries and patchy alveolar infiltrates with sparing of the bases and prominent pulmonary arteries are characteristic of HAPE (Hackett, 1992; Yaron, 1994; Rabold, 1989; Vock, 1989). However, there is no single characteristic radiomorphologic condition of HAPE; appears to change with time, beginning as patchy opacities in periphery, progressing to more homogenous and diffusely distributed

lesions later on (Vock, 1991).

- b. Heart usually normal size.
- c. Rarely, with congenital absence of the right pulmonary artery, left-sided alveolar infiltrates, absent right pulmonary artery shadow, small right hemithorax, and shift of the mediastinum to the right (Hackett, 1992; Yaron, 1994).
- d. With appropriate therapy, the alveolar shadows clear in a few hours, with complete clearing in 3 to 5 days (Hackett, 1992; Yaron, 1994).

4.0 DIAGNOSTIC AIDS

4.1 ELECTROCARDIOGRAM

- A. Sinus tachycardia is the most consistent EKG finding; right ventricular hypertrophy by voltage; right axis deviation.
- B. There has been one report of transient atrial flutter associated with HAI (Hackett, 1992; Yaron, 1994).
- C. EKG abnormalities usually return to normal when HAPE resolves, although in a study of 10 follow-up EKGs, two showed persistent evidence of right heart strain, possibly due to pulmonary hypertension (Hackett, 1992; Yaron, 1994).

5.0 DIFFERENTIAL DIAGNOSIS

5.2 TRAUMA

A. TRAUMA, HEAD, BLUNT

- 1. HACE may mimic head trauma, but a history for trauma will be lacking.
- 2. Physical exam in high altitude cerebral edema will reveal no signs of trauma.
- 3. Focal neurologic findings may be present in both entities.
- 4. CT-scan and cerebral angiography may be normal in mild cases of HACE; however, severe cases may display cerebral edema on CT-scan.

(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: BLUNT HEAD TRAUMA)

B. CONTUSION, PULMONARY

- 1. Pulmonary contusion and HAPE may produce similar symptoms; however, history for trauma will be absent in high altitude pulmonary edema.
- 2. HAPE will not be associated with signs of trauma (flail chest, contused chest wall, crush injury, pneumothorax).
- 3. Pulmonary contusion and HAPE may be radiographically indistinguishable.

(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: PULMONARY CONTUSION)

5.3 INFECTIOUS

A. MENINGITIS

- 1. Most forms of meningitis preceded by a history of respiratory tract illness.
- 2. Patients with HACE usually are afebrile and have a supple neck.
- 3. Focal neurologic abnormalities and/or altered mental status may be present with both entities.
- 4. Meningitis will not improve with oxygen and descent.
- 5. Lumbar puncture is the only definite way to differentiate the two entities.

(FOR FURTHER INFORMATION, SEE CLINICAL REVIEWS: BACTERIAL MENINGITIS, VIRAL MENINGITIS)

B. ABSCESS, CEREBRAL

- 1. Abscess most often presents with headache, fever, and focal neurologic findings.
- 2. Abscess will not improve without definite therapy.
- 3. CT-scan or brain scan should be used to differentiate brain abscess from HACE and/or meningitis.

(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: BRAIN ABSCESS)

C. PNEUMONIA

- 1. Purulent sputum is more common and fever generally higher with pneumonia.
- 2. Radiographic appearance of HAPE may be indistinguishable from infectious pneumonitis (fungal, bacterial, or viral etiologies must always be considered). In infectious pneumonitis, x-rays rarely show improvement following

- oxygen therapy and descent.
3. Transtracheal aspiration, percutaneous needle biopsy, or bronchoscopy may be necessary to differentiate HAPE from infectious pneumonia.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEWS: BACTERIA PNEUMONIA, ATYPICAL PNEUMONIA)
- D. GASTROENTERITIS
1. Abdominal cramping and vomiting are rarely severe and fever is usually absent in AMS.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: GASTROENTERITIS)
- 5.4 INFLAMMATORY
- A. CEREBRITIS, LUPUS ERYTHEMATOSUS
1. Lupus cerebritis rarely is the first manifestation of SLE but may be clinically indistinguishable from HACE.
 2. Failure to improve with oxygen and descent should suggest the possibility of another etiology. Antinuclear antibodies test, erythrocyte sedimentation rate, and tissue biopsy may be necessary.
- B. POLYARTERITIS NODOSA
1. DESCRIPTION: Characterized by segmental inflammation and necrosis lesions of blood vessels, especially small to medium sized arteries in major organs, with secondary ischemia of tissue supplied by affected vessels. Kidneys, muscles, joints, heart, nerve, GI tract common sites; occasionally may be cutaneous and pulmonary involvement
 2. ETIOLOGY: Unknown; hypersensitivity appears to be involved.
 3. EPIDEMIOLOGY: All ages affected from infancy to old age, with peak incidence in 5th and 6th decades; male predominance.
 4. CLINICAL PRESENTATION: Variable, depending on severity and location of arteritis. Course may be acute, subacute, or chronic.
 - a. Most common initial complaints are fever, abdominal pain, symptoms of peripheral neuropathy (often mononeuritis multiplex), weakness, weight loss.
 - b. Other findings may include hypertension, edema, and oliguria and uremia (renal involvement); GI hemorrhage; precordial pain; headache, seizures, organic psychosis (CNS involvement); muscle and joint pain; dermal lesions, including palpable subcutaneous nodules along course of affected artery; cotton-wool spots occur with occlusion of retinal vessels.
 5. LABORATORY FINDINGS: Most frequently leukocytosis (WBC 20,000 to 40,000/microL), proteinuria, hematuria; also anemia due to blood loss or renal failure, elevated ESR, thrombocytosis
 6. DIAGNOSIS: Confirmed by biopsy of typical lesions or angiographic display of typical aneurysms of medium-sized vessels. Differentiated from other causes of necrotizing vasculitis by absence of extravascular granulomas, sparing of pulmonary arteries, failure of venous involvement except by contiguous spread, and predilection for medium-sized arteries.
- 5.5 METABOLIC
- A. KETOACIDOSIS, DIABETIC
1. HACE may need to be differentiated from diabetic ketoacidosis.
 2. Laboratory determinations, especially of blood glucose level and the presence or absence ketones, will be diagnostic. The blood pH is alkaline in HACE.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: DIABETIC KETOACIDOSIS)
- B. RENAL FAILURE, CHRONIC
1. HACE may need to be differentiated from uremia.
 2. Laboratory determinations will be diagnostic, especially creatinine clearance and BUN level.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
- C. ENCEPHALOPATHY, HEPATIC

1. DEFINITION: Reversible neuropsychiatric syndrome occurring in patients with liver disease. One of most characteristic features of liver failure; may be acute or chronic. Also known as hepatic coma or portal-systemic encephalopathy.
 2. ETIOLOGY: Biochemical abnormalities associated with hepatocellular deficit or hepatic bypass or portal vein blood into the systemic circulation.
 3. PRECIPITATING FACTORS:
 - a. Severe liver damage from any cause or acute decompensation of a chronic liver disease (usually cirrhosis) that is associated with portal-systemic shunting of intestinal venous blood and the pressure of an excessive systemic load of ammonia and mercaptans.
 - b. Common precipitants include:
 - (1) Anesthesia/surgery
 - (2) Azotemia
 - (3) Constipation
 - (4) Deterioration in hepatic function.
 - (5) Drugs
 - (a) Sedative, hypnotics, narcotics
 - (b) Potentially hepatotoxic agents
 - (c) Diuretics
 - (d) Ammonium or amino compounds
 - (6) GI hemorrhage
 - (7) Hypokalemia
 - (8) Hypoxia
 - (9) Increased dietary protein.
 - (10) Infection (systemic or hepatic)
 - (11) Paracentesis (with attendant hypovolemia)
 4. CLINICAL PRESENTATION:
 - a. Diagnosis based on presence of compatible neurologic signs and symptoms in a patient with advanced liver disease and exclusion of other possible causes of neurologic abnormalities. Signs and symptoms may be subtle, consisting initially of a personality change, mild confusional state, or lethargy. In advanced cases, almost any form of neurologic abnormality may be present, including seizures, lateralizing signs, and abnormal posturing.
 - b. Diagnosis should be suspected in any patient with liver disease who presents with changes in behavior, mentation, or neuromuscular status, including:
 - (1) BEHAVIOR CHANGES: Restlessness or aimless wandering, euphoria or garrulousness, irritability, agitation or apathy, sullenness or paranoia, inappropriate behavior and decreased inhibitions, confusion followed by disorientation, lethargy leading to somnolence or stupor.
 - (2) NEUROLOGIC ABNORMALITIES: Impaired handwriting, incoordination, asterixis, deliberate movements, picking, yawning or blinking, abnormal muscle tone, resistance to passive movements and muscle rigidity, hyperactive reflexes, abnormal toe signs. Asymmetric neurologic findings are unusual, and brain stem reflexes typically are preserved.
 - c. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
 5. DIAGNOSTIC STUDIES:
 - a. Routine laboratory studies (eg, electrolytes, chemical survey, liver function tests) are helpful primarily in excluding other causes of metabolic encephalopathy and evaluating presence and severity of liver disease.
 - b. Toxicologic screening may be appropriate when ingestion of sedatives or toxins capable of altering neurologic function is suspected.
 - c. Blood ammonia and CSF glucose levels usually are of limited value.
 - d. EEG changes are sensitive indicators of hepatic encephalopathy (present in most patients with subclinical disease) but are not specific for this disorder.
- D. REYE'S SYNDROME
1. Reye's syndrome should be considered in the differential

diagnosis in children, especially in the presence of a viral prodrome.

2. Laboratory determinations, eg, liver function tests and serum ammonia level, will be diagnostic.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: REYE'S SYNDROME)
- E. HYPERNATREMIA
1. Certain electrolyte abnormalities, eg, hypernatremia, may present with ataxia and/or focal neurologic deficits, but headache is rarely present.
 2. Laboratory determinations will be diagnostic.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: HYPERNATREMIA)
- G. HYPONATREMIA
1. Hyponatremia may present with ataxia and/or focal neurologic deficits, but headache is rarely present.
 2. Laboratory determinations will be diagnostic.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: HYPONATREMIA)
- G. HYPERCALCEMIA
1. Hypercalcemia may present with ataxia and/or focal neurologic deficits, but headache is rarely present.
 2. Laboratory determinations will be diagnostic.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: HYPERCALCEMIA)
- 5.6 VASCULAR
- A. HEMORRHAGE, SUBARACHNOID
1. Subarachnoid hemorrhage (SAH) and HACE may both present with severe headache and altered mental status.
 2. CSF in SAH is generally bloody but is clear in HACE.
 3. CT-scan with such findings as blood in the ventricles will be diagnostic in SAH (this may not be apparent initially). Findings in HACE include generalized cerebral edema and decreased ventricular size.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: SUBARACHNOID HEMORRHAGE)
- B. CEREBROVASCULAR ACCIDENT
1. Focal neurologic deficits may be present in both CVA and HACE, but headache is rare in CVA.
- C. HEADACHE, MIGRAINE
1. Visual scotomata of migraine may mimic those caused by retinal hemorrhage of high altitude.
 2. Migraine headache can usually be differentiated from HACE by history.
 3. Headache of migraine and HACE may both improve with oxygen.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: MIGRAINE HEADACHE)
- D. ANEURYSM, INTRACRANIAL
1. When large enough, cerebral aneurysm may cause severe headache.
 2. Angiography or CT-scan may be necessary to differentiate high altitude cerebral edema from cerebral aneurysm if symptoms fail to improve with oxygen and descent.
- E. EMBOLISM, PULMONARY
1. HAPE may mimic or be associated with PE. Differentiated by history (calf pain, sudden onset of chest pain and dyspnea) and physical exam (calf tenderness, edema, or cords and absence of prominent rales).
 2. If PE is suspected, the patient should not be allowed to ambulate. Modest improvement on adequate descent is more indicative of PE; in HAPE, victims should have substantial improvement with oxygen and descent as edema resolves (Rabold, 1989).
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: PULMONARY EMBOLISM)

5.7 NEOPLASTIC

A. NEOPLASM, CEREBRAL

1. TYPES:

- a. PRIMARY: Include gliomas (50%), meningiomas, pituitary adenomas, and neurofibromas.
- b. METASTATIC: Most common source is carcinoma of the lung; other primary sites are breast, kidney, and GI tract.

2. CLINICAL PRESENTATION: Characterized by generalized or focal disturbances of cerebral function, or both, and signs and symptoms of increased ICP.

a. GENERALIZED:

- (1) May include personality changes, intellectual decline, emotional lability, seizures, headache, nausea, malaise, slowly progressive weakness on one side, visual changes, aphasia, vomiting, mental changes. Papilledema occurs in 25% of patients and may not be early sign; vital signs are normal.
- (2) Increased ICP may cause herniation, most commonly tentorial, characterized by ipsilateral pupillary dilatation, followed by stupor, coma, decerebrate posturing, and respiratory arrest.

- b. FOCAL: Due to localized destruction or compression of nerve tissue or to altered endocrine function; depend on tumor location.

3. DIAGNOSIS: Neuroradiologic evidence of space-occupying lesion. CT or MRI may detect lesion and also may define its location, shape, and size; extent to which normal anatomy is distorted; and degree of any associated cerebral edema or mass effect.

5.8 TOXICOLOGIC

A. EDEMA, PULMONARY, NONCARDIOGENIC

1. Noncardiac pulmonary edema due to drugs or toxins may be indistinguishable from HAPE.

2. Following drugs or toxins cause pulmonary edema: heroin or methadone, Darvon(R), Placidyl(R), Librium(R), thiazides, paraquat, Demerol(R), salicylates, smoke inhalation, fat embolism, inhaled toxin, industrial exposure, or aspiration of gastric contents.

3. Drug levels may be necessary to document acute drug ingestion.

4. Both drug-induced pulmonary edema and HAPE may respond to high flow oxygen.

(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: NONCARDIAC PULMONARY EDEMA)

B. DRUG ABUSE

1. Coma secondary to HACE must be differentiated from coma due to drug ingestion.

2. Preceding history of the state of health immediately prior to loss of consciousness may be helpful.

3. Physical examination may reveal signs of acute drug toxicity, eg, pinpoint pupils, respiratory depression, dilated pupils, and flushing.

4. Drug levels, ABGs, and toxicology screens should be obtained when indicated by clinical history or physical findings.

5.9 PHYSICAL AGENTS

A. POISONING, TOXIC INHALATION

1. ETIOLOGY: Produced by combustion of household or industrial products in accidental fires (eg, CO, phosgene) or as byproducts of work activity (eg, welding). Exposure to toxic gases (eg, arsine, chlorine) may occur during an accidental leak or spill.

2. CLASSIFICATION:

a. SIMPLE ASPHYXIANTS:

- (1) TOXINS/SOURCE: Methane and propane (cooking gas); inert gases (argon, nitrogen; industry, esp welding); CO₂ (all fires).
- (2) CLINICAL EFFECTS:

- (a) Cause toxicity by lowering ambient O₂ concentration.
- (b) Symptoms of hypoxemia, without airway irritation.

b. CHEMICAL ASPHYXIANTS & SYSTEMIC POISONING:

- (1) TOXINS/SOURCE: CO₂ (fires); hydrocyanic acid (industry; burning plastics, furniture, fabrics);

hydrogen (liquid manure pits, decaying organic materials).

- (2) CLINICAL EFFECTS: These substances possess intrinsic systemic toxicity that is manifested after absorption into the circulation.
 - (a) CO: Forms carboxyhemoglobin; inhibits O₂ transport. Headache earliest symptom.
 - (b) HYDROCYANIC ACID: Highly toxic cellular asphyxiant.
 - (c) HYDROGEN SULFIDE: Highly toxic cellular asphyxiant similar to cyanide; causes sudden collapse; ability to smell characteristic rotten eggs odor is rapidly fatigued.
- c. IRRITANTS & CORROSIVES:
 - (1) TOXINS/SOURCE:
 - (a) HIGHLY WATER-SOLUBLE: Chlorine gas, hydrochloric acid; ammonia (industry; swimming pool chemicals; bleach mixed with acid at home).
 - (b) POORLY WATER-SOLUBLE: Nitrogen dioxide (burning cellulose; fabrics; grain silos (acrid red gas)); ozone (inert gas arc welding industry); phosgene (burning of chlorinated organic material).
 - (c) ALLERGENIC: Toluene diisocyanate (mfg of polyurethanes).
 - (2) CLINICAL EFFECTS: Cause cellular destruction and inflammation when they come into contact with the tracheobronchial tree, usually by producing acids or alkali upon contact with moisture.
 - (a) HIGHLY WATER SOLUBLE: Cause immediate irritation, mainly of upper airway and conjunctiva. Early onset of lacrimation, sore throat, stridor, tracheobronchitis; with heavy exposure, may progress to pulmonary edema in 2 to 6 h.
 - (b) POORLY WATER SOLUBLE: May be more deeply inhaled, producing delayed onset (12 to 24 h) of lower airway destruction with chemical pneumonitis and pulmonary edema; late chronic bronchitis. Has sweet "electric" smell.
 - (c) ALLERGENIC: Reactive bronchoconstriction; may have long-term effects (COPD) in susceptible persons.
- d. METAL FUMES:
 - (1) TOXIN/SOURCE: Zinc, copper, tin, Teflon (welding, esp galvanized metal welding); arsine (burning arsenic-containing ores; electronics industry); mercury, lead (industry; welding).
 - (2) CLINICAL EFFECTS:
 - (a) ZINC, COPPER, TIN, TEFLON: "Metal fume fever" (chills, fever, myalgia, headache, nonproductive cough, leukocytosis (4-8 h postexposure); self-limited course (12 to 24 h).
 - (b) ARSINE: Highly toxic; hemolysis, pulmonary edema, renal failure, chronic toxicity.
3. DIAGNOSIS: Usually is history of exposure.
 - a. Clinical presentation varies depending on toxin. In an accidental fire, combinations of all classes of toxic inhalants may be causing symptoms (eg, burning in eyes/mouth, sore throat, brassy cough, dyspnea, headache).
 - b. Physical findings may include singed nasal hairs, carbonaceous deposits on nose/face, upper airway swelling/obstruction, wheezing/signs of pulmonary edema, manifestations of systemic toxicity.
 - c. Diagnostic tests include ABGs, COHB level, chest x-ray.
4. DIFFERENTIATION:
 - a. Patients may develop headache at high altitudes as a result of toxic inhalations or exposure to a variety of physical agents.
 - b. The following should be differentiated from AMS and/or HACE: inhalation of carbon monoxide, natural gas, or hydrocarbons (especially cyclic compounds); high intensity sun exposure; or alcohol consumption (ie, "hangover").

B. HYPOTHERMIA

1. HACE may need to be differentiated from hypothermia, although both may be present due to cold exposure at high

- altitude.
2. Body temperature will be diagnostic.
 3. Metabolic causes of encephalopathy rarely improve with oxygen and descent alone.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: HYPOTHERMIA)
- 5.10 MISCELLANEOUS
- A. RESPIRATORY DISTRESS SYNDROME, ADULT
 1. The following disorders may present with ARDS, a clinical picture resembling HAPE: pancreatitis, near-drowning, uremia, shock lung, neurogenic pulmonary edema, infection-associated ARDS, ketoacidosis, pulmonary embolism, and leukoagglutinin hypersensitivity.
 2. Historical data or appropriate laboratory analysis will aid in the diagnosis.
(FOR FURTHER INFORMATION, SEE CLINICAL REVIEW: NONCARDIAC PULMONARY EDEMA)
- 6.0 TREATMENT
- 6.1 TREATMENT SUMMARY
- A. GENERAL:
 1. ALL MANIFESTATIONS: Descent, rest, oxygen.
 2. SERIOUS COMPLICATIONS: Mechanical ventilation, Swan-Ganz monitoring, decrease intracranial pressure.
 3. PREVENTION: Acetazolamide, acclimatization.
 - B. ACUTE MOUNTAIN SICKNESS:
 1. DESCENT: 3000 to 4000 feet (1000 to 1500 meters) usually adequate.
 2. OXYGEN: For more severe symptoms; useful for all forms of altitude illness, including AMS (but often not available); give 2 to 3 L/min.
 3. ACETAZOLAMIDE: 250 mg PO Q8H (children: 5 mg/kg/day PO in 3 divided doses) for 48 hours.
 4. DEXAMETHASONE: 4 mg PO or IM Q6H in patients with neurologic deterioration (eg, ataxia, change in level of consciousness) or severe headache and/or vomiting.
 5. ASPIRIN OR ACETAMINOPHEN: 325 to 650 mg (children: 10 to 15 mg/kg) PO Q4-6H for headache.
 6. PROCHLORPERAZINE: 10 mg IM or PO Q6-8H (children >2 years: 0.4 mg/kg/day PO or 0.2 mg/kg/day IM in 3 to 4 divided doses) for nausea and vomiting.
 - C. HIGH ALTITUDE PULMONARY EDEMA:
 1. BED REST/WARMTH: To decrease pulmonary artery pressure; avoid exertion.
 2. OXYGEN: If available, give 6 to 12 L/min by nasal cannula or face mask (1 to 2 L if O₂ is a problem).
 3. DESCENT: As rapidly as possible but preferably with little exertion by the victim; 1000 to 3000 feet may be adequate.
 4. AIRWAY MANAGEMENT: CPAP by tight-fitting mask in awake patients; intubation, mechanical ventilation, and PEEP for severe cases.
 5. FUROSEMIDE: 20 to 40 mg (children: 1 to 2 mg/kg) IV may be needed if intravascular volume is increased (rarely necessary); must be given under medical supervision.
 6. NIFEDIPINE (Emergency treatment when descent or evacuation is impossible and supplemental oxygen is not available): 10 mg SL plus 20 mg PO of slow-release nifedipine. If systolic BP does not decrease ≥ 10 mmHg within 10 min, repeat SL dose after 15 min, then give 20 mg of slow-release nifedipine Q6H for entire time at altitude.
 7. MORPHINE: 2 to 10 mg IV if no cerebral involvement (children: 0.1 to 0.2 mg/kg/dose IV); rarely necessary.
 - D. HIGH ALTITUDE CEREBRAL EDEMA:
 1. DESCENT.
 2. OXYGEN: 2 to 4 L via nasal cannula.
 3. AIRWAY MANAGEMENT: Intubation and hyperventilation for patients in coma (mechanical ventilation for long-term management).
 4. FUROSEMIDE: 20 to 40 mg IV (children: 1 to 2 mg/kg/dose IV).
 5. DEXAMETHASONE: 10 mg IV initially, then 4 mg Q6H (children: 0.25 to 0.5 mg/kg/dose IV Q6H).
 6. FOLEY CATHETER: For bladder drainage if comatose.

E. PROPHYLAXIS:

1. ACCLIMATIZATION: Graded exercise and slow ascent (300 m/day over 3000 m) avoid abrupt ascent from sea level to sleeping altitude over 10,000 ft; stay at intermediate altitude for one night.
2. ACETAZOLAMIDE: 250 mg PO BID, or one sustained-action 500-mg capsule PO Q24H (children: 5 mg/kg/day PO in 2 divided doses) beginning 3 days before ascent and continuing for 2 to 3 days at altitude.

6.2 NON-PHARMACOLOGIC TREATMENT

A. DESCENT

1. Moving the patient to a lower altitude is the first and single most therapeutic measure for all forms of altitude illness and should begin immediately in severe cases. Dramatic improvement can occur with only a 300-meter descent (Yaron, 1994; Pigman, 1991; Hackett, 1992; Ergun, 1994).
2. MECHANISM: Because the patient is on the steep portion of the oxygen-dissociation curve when at altitude, it is felt that descent will improve oxygen partial pressures and relieve some underlying hypoxia.

B. AIRWAY MANAGEMENT

1. VENTILATION, POSITIVE PRESSURE, NONINVASIVE

a. CONTINUOUS POSITIVE AIRWAY PRESSURE:

- (1) INDICATIONS: Improves gas exchange in HAPE. For patients requiring increased oxygenation in early respiratory distress and who:
 - (a) Are alert, cooperative, and breathing spontaneously.
 - (b) Have low or normal PCO₂ levels.
 - (c) Are in no danger of emesis.
- (2) MECHANISM: CPAP applies the principles of PEEP in nonintubated patients with spontaneous respirations (Gregory, 1971). It utilizes low levels of end-expiratory pressure (5-15 cmH₂O) and a tight-fitting face mask to administer oxygen (Covelli, 1982, 1984; Zamost, 1981; Wilson, 1974).
- (3) ADVANTAGES: Eliminates the need for intubation, has no associated decrease in cardiovascular hemodynamics, and does not further increase the work of breathing.
- (4) DISADVANTAGES:
 - (a) Requires an alert, cooperative, spontaneously-breathing patient. It may cause rising levels of PCO₂ since it has no effect on ventilation. May cause skin irritation and anxiety because of the seal of the mask on the face. If emesis occurs, aspiration may result.
 - (b) A small, prospective, randomized, controlled trial involving 27 ED patients with acute respiratory failure found use of noninvasive positive pressure ventilation (NPPV) delayed tracheal intubation and mechanical ventilation. A nonsignificant increase noted in inhospital mortality and multiorgan derangement in patients initially treated with NPPV (Wood, 1998).
 - (c) Further studies needed to define role of NPPV in the treatment of acute respiratory failure in ED (Wood, 1998).

2. EXPIRATORY POSITIVE AIRWAY PRESSURE

- a. In the field, EPAP has been used to increase hemoglobin saturation and decrease respiratory rate without supplemental oxygen. Mask is light, small, and does not require supplemental oxygen to work, although it does have an oxygen port (Larson, 1985; Schoene, 1985).
- b. Improves arterial O₂ saturation by 10% to 20% in subjects with HAPE in trials of 10 minutes' duration; however, clinical studies of long-term effects are needed before EPAP can be recommended as initial emergency treatment of HAPE (Bartsch, 1992).

3. INTUBATION, ENDOTRACHEAL

- a. GENERAL: The decision to intubate is extremely complex and is based mainly on patient's course. The method chosen should be the one that will permit the most rapid attainment of the best possible airway while minimizing the potential for adverse events.

- b. INDICATIONS:
 - (1) Failure to maintain an adequate airway.
 - (2) Failure to protect airway against aspiration.
 - (3) Failure of oxygenation.
 - (4) Failure of ventilation.
 - (5) A condition is present (elevated intracranial pressure), or a therapy is required (pulmonary toiletting) that mandates intubation.
 - c. PREREQUISITES TO INTUBATION: Emergent airway management, if necessary, should not be delayed for any reason. However, procurement of the following is highly desirable:
 - (1) IV access.
 - (2) ECG monitoring.
 - (3) Pulse oximetry.
 - (4) Removal of foreign bodies, food, or teeth in mouth or posterior pharynx.
 - (5) Preoxygenation with 100% oxygen.
 - d. RECOMMENDED APPROACH:
 - (1) PREPARATION:
 - (a) Prepare patient with explanations and ensure that patient is well oxygenated.
 - (b) Assemble all necessary equipment.
 - (2) SEDATION:
 - (a) Midazolam 1 to 2 mg IV.
 - (b) Fentanyl 50 to 100 mcg IV may be given concurrently with midazolam if analgesia is desired.
 - (3) AIRWAY ANESTHESIA:
 - (a) If time is not an issue, can use a standard respiratory nebulizer with a solution of 4% lidocaine (4 cc) and 1/2% phenylephrine (1 cc). Airway anesthesia will be achieved in about 5 to 10 minutes.
 - (b) Standard method is to spray the mouth, tongue, oropharynx, and then the larynx with lidocaine spray using a laryngeal spray device.
 - (4) Perform the laryngoscopy and insert the ETT.
 - (5) Obtain chest radiograph.
 - e. ADULT TUBE SIZE: The ETT should have a high volume/low pressure cuff. The largest tube size possible always should be used, especially in patients with chronic lung disease. ETT sizes are typically 7.0 to 8.0 internal diameter for females and 8.0 to 8.5 for males.
 - f. PEDIATRIC TUBE SIZE: Several methods and formulas have been devised for estimating tube size. A visual estimation can be made by choosing an ETT with an outside diameter approximating the diameter of the child's little finger. For children >1 year, the following formula may be used: internal diameter = (16 + patient's age in years) divided by 4.
 - g. NASOTRACHEAL TUBE:
 - (1) Although easier to secure, more comfortable, and less traumatizing to the vocal cords, NT intubation has higher failure and complication rates and requires smaller tube sizes.
 - (2) May still be preferable in certain settings:
 - (a) When paralysis poses an excessive relative risk (ie, when intubation is not emergent or when oral intubation after paralysis may be difficult).
 - (b) When patient is sitting upright.
 - (c) When spontaneous breathing is desired or serial physical examinations are anticipated.
 - (d) When the NT route is preferred long-term for patient comfort.
 - (3) The cuff should be inflated to a pressure less than 25 mmHg and should allow a small air leak during peak inspiration.
 - h. TUBE PLACEMENT: After intubation, it is mandatory to check for equal breath sounds over the lateral chest, especially on the left. Tube placement must be confirmed via chest x-ray; the tip should be 1 to 2 cm above the carina.
4. INTUBATION, RAPID SEQUENCE
- a. DEFINITION: Definitive airway management technique in which a potent sedative or induction agent is

- administered virtually simultaneously with a paralyzing dose of a neuromuscular blocking agent to facilitate rapid tracheal intubation.
- b. CAUTION: Physicians performing RSI must possess training, knowledge, and experience in the techniques and pharmacologic agents used to perform RSI.
(FOR DETAILED REVIEW, SEE CLINICAL REVIEW: RAPID SEQUENCE INTUBATION)
5. VENTILATION, MECHANICAL
- a. INITIAL ADULT SETTINGS
- (1) RESPIRATORY RATE: 8 to 20 breaths/minute (Oakes, 1994).
- (a) Manipulate with tidal volume to achieve desired minute volume (PaCO₂).
- (b) Slower rates allow for larger tidal volumes and result in improved compliances.
- (2) TIDAL VOLUME (V_t): 10 to 15 cc/kg (Oakes, 1994).
- (a) Large V_ts improve ventilation/perfusion and gas exchange, and prevent atelectasis; may decrease venous return.
- (3) FRACTION OF INSPIRED OXYGEN (FiO₂): 100% initially; reduce in 5%- to 10%-increments, maintaining PaO₂ of 60 to 100 mmHg.
- (4) PEAK INSPIRATORY PRESSURE: <35 cmH₂O.
- b. OBSTRUCTIVE AIRWAY DISEASE
- (1) RESPIRATORY RATE: 8 to 20 breaths/minute (Oakes, 1994).
- (a) Manipulate with tidal volume to achieve desired minute volume (PaCO₂).
- (b) Slower rates allow for larger tidal volumes and result in improved compliances.
- (2) TIDAL VOLUME (V_t): 10 to 15 cc/kg (Oakes, 1994).
- (a) Large V_ts may decrease venous return; smaller volumes with PEEP may be utilized.
- (3) FRACTION OF INSPIRED OXYGEN (FiO₂): 100% initially; reduce in 5%- to 10%-increments, maintaining PaO₂ of 50 to 60 mmHg.
- (4) PEAK INSPIRATORY PRESSURE: <35 cmH₂O.
- c. INITIAL PEDIATRIC SETTINGS
- (1) RESPIRATORY RATE: 12 to 25 breaths/minute (infants: 20 to 40 breaths/minute) (Oakes, 1996).
- (a) If intermittent mandatory mode or assist mode is used, set rate just below patient's spontaneous rate.
- (2) TIDAL VOLUME (V_t): 10 to 15 cc/kg (infants: 7 to 10 cc/kg) (Oakes, 1996).
- (3) FRACTION OF INSPIRED OXYGEN (FiO₂): 100% (infants: Keep oxygen saturation >90%) (Oakes, 1996).
- (4) PEAK INSPIRATORY PRESSURE: 25 to 35 cmH₂O (infants: 15 to 30 cmH₂O) (Oakes, 1996).
- d. OVERVIEW
- (1) INDICATIONS:
- (a) VENTILATORY FAILURE: PaCO₂ >55mmHg (or acute increase from patient's baseline); pH <7.25; deadspace ratio (VD/V_t%) >60% (Oakes, 1994).
- (b) OXYGENATION: PaO₂ <50 mmHg on room air; <70 mmHg on 40% O₂; <200 mmHg on 100% O₂ (Oakes, 1994).
- (c) PaCO₂ CONTROL: Hyperventilation therapy for head trauma and abnormal ventilatory drive (Oakes, 1994).
- (d) CHILDREN: May modify the following based on pathophysiology of disease state (initiate early in atelectatic states; avoid as long as possible in obstructive states) (Oakes, 1996):
- Ongoing CPR
 - Significant episodes of apnea
 - PaO₂ <60 mmHg on 80% FiO₂ and CPAP 6 to 8 cmH₂O OR
 - PaO₂ <60 mmHg on 40% FiO₂ if weight <1250 grams
 - PaCO₂ >55 to 64 mmHg with pH <7.1 if body weight <1500 grams
 - Cardiovascular collapse
 - Patient unresponsive to external stimuli
- (2) GOALS:
- (a) Physiologic objectives are to improve oxygenation or ventilation while decreasing the work of breathing; prevent further lung injury through successful

manipulation of pressure-volume relations in attempt to prevent and reverse atelectasis; promote lung and airway healing while avoiding ventilator-induced complications (Tobin, 1994).

- (b) In specific settings, additional goals are to permit sedation or neuromuscular blockade; decrease systemic or myocardial oxygen consumption; reduce intracranial pressure; stabilize the chest wall (Slutsky, 1993).

e. PHASE VARIABLES

(1) GENERAL: A phase variable is a physical quality (pressure, volume, flow, or time) that is adjusted, measured, or used to manipulate (start trigger, sustain limit, and end cycle) a phase of the ventilatory cycle (Oakes, 1994).

(2) TRIGGER VARIABLE:

- (a) Most commonly time and pressure; volume and flow changes caused by inspiratory effort of patient are used less commonly.
- (b) Patient effort required to trigger inspiration is dependent on the ventilator's sensitivity, which is adjusted by changing the preset value of the trigger variable.

(3) CYCLE VARIABLE:

- (a) VOLUME CYCLED: Most commonly used ventilator; once a preset volume of gas is delivered (regardless of pressure required to deliver it), ventilator stops inspiration and allows passive expiration.
- (b) PRESSURE CYCLED: Used mainly for short-term use; once a preset pressure is reached, ventilator stops inspiration and allows passive expiration.
- (c) FLOW CYCLED: Inspiration ends because a preset flow is attained.
- (d) TIME CYCLED: Inspiration ends because a preset time interval has elapsed.

(4) LIMIT VARIABLE:

- (a) PRESSURE LIMITED: Peak pressure reaches a preset value before inspiration ends.
- (b) VOLUME LIMITED: Peak volume reaches a preset value before inspiration ends.
- (c) FLOW LIMITED: Peak flow reaches a preset value before inspiration ends.

f. VENTILATOR SETTINGS

(1) TIDAL VOLUME (Vt): Volume of gas delivered by the ventilator.

- (a) VOLUME-TARGETED VENTILATOR: Variables considered when selecting Vt include lung/thorax compliance, system resistance, compressible volume loss, oxygenation, ventilation, and barotrauma (Kacmarek, 1987). Airway pressures must be monitored regularly to prevent barotrauma.
- (b) PRESSURE-TARGETED VENTILATOR: Vt delivered depends on target pressure selected, system impedance, and the spontaneous ventilatory pattern of the patient. Disadvantage is that Vt varies with airway resistance and lung compliance, which may result in inadequate alveolar ventilation.

(2) RESPIRATORY RATE: Mode of ventilation, Vt delivered, dead space to tidal volume ratio, metabolic rate, desired PaCO₂ level, and rate of spontaneous ventilation determine the ventilator rate setting (Kacmarek, 1987).

(3) PEAK INSPIRATORY FLOW: The single most common variable set inappropriately. Fast flowrates may increase airway pressures; slow flowrates may prolong inspiratory and expiratory times. Flow delivery must be set to exceed patient's spontaneous demand; preferred range is 40 to 100 L/m.

- (a) VOLUME-TARGETED VENTILATOR: Level of spontaneous inspiratory effort is the primary factor in selection of peak inspiratory flow rate; patient effort, work of breathing, and synchrony of patient and ventilator depends on selection of peak inspiratory flow (Marini, 1986).

(b) PRESSURE-TARGETED VENTILATOR: Interaction of the set

- pressure, respiratory resistance, and patient effort determines peak inspiratory flow.
- (4) INSPIRATORY TIME/I:E RATIO: Determination of inspiratory time (Ti) and I:E ratio is generally based on hemodynamic response to ventilation, oxygenation status, and level of spontaneous breathing.
 - (a) SPONTANEOUSLY BREATHING PATIENTS: Normally require a Ti between 0.8 and 1.2 seconds and an I:E of about 1:2 to 1:1.5 to ensure synchrony between gas delivery and patient inspiratory effort (Kacmarek, 1992).
 - (b) CONTROLLED VENTILATION: Ti and I:E ratios may be extended in effort to increase mean airway pressure and improve oxygenation. Factors that may limit increases include patient discomfort, need for sedation, development of auto-PEEP, and hemodynamic instability (Marini, 1992).
 - (5) SENSITIVITY: Determines patient effort required to trigger the ventilator; preferred range is -0.5 to 1.5 cmH2O. Triggering on flow is more sensitive than triggering on pressure and decreases the work of breathing.
 - (6) FRACTION OF INSPIRED OXYGEN (FiO2): Desired PaO2, level of PEEP, mean airway pressure, and hemodynamic status of patient determine setting. FiO2 should be set at the lowest acceptable level, although the possibility of oxygen-induced lung injury must be balanced with the potentially adverse effects of airway and alveolar pressures on lung tissue.
 - (7) PEEP: Optimal level depends on desired physiologic response and specific clinical setting.
- g. STANDARD VENTILATOR MODES
- (1) OVERVIEW
 - (a) Mode is determined by patient's condition and ventilatory needs. Basic modes include continuous mandatory ventilation (control), assist-control ventilation (ACV), (synchronous) intermittent mandatory ventilation (SIMV or IMV), and pressure support ventilation (PSV).
 - (b) Adjuncts to mechanical ventilation include use of positive end-expiratory pressure (PEEP) and continuous positive airway pressure (CPAP), which help to prevent alveolar collapse.
 - (c) Acute respiratory failure with asthma and chronic obstructive pulmonary disease (COPD) is associated with significant expiratory obstruction and hyperinflation. Both groups of patients benefit from ventilatory modes that maximize expiratory time, thereby reducing end-expiratory volume, extrinsic PEEP, and potential for hemodynamic compromise (Slutsky, 1993).
- h. VENTILATION, CONTROL
- (1) INTRODUCTION: Volume delivered and frequency of delivered breaths are preset. This mode is flow limited, volume cycled, and may be volume limited (Chatburn, 1995).
 - (2) INDICATIONS: Appropriate only for patients who are apneic secondary to conditions such as respiratory muscle paralysis, sedation, drug overdose, or brain damage (Tobin, 1990); quickly leads to respiratory muscle atrophy (Tobin, 1994a).
- i. VENTILATION, ASSIST/CONTROL
- (1) INTRODUCTION:
 - (a) Volume delivered is preset and is triggered by patient-initiated breaths or by the backup (preset) rate if no patient breath occurs within a preselected time. Also may be flow triggered between time-triggered breaths, depending on the presence of spontaneous breathing efforts and the sensitivity setting on the ASSIST component (Chatburn, 1995).
 - (b) Work of breathing during volume-targeted A/C depends on sensitivity, flow rates, and respiratory drive of patient, which is dependent on many variables, including fever, anemia, hypoxia, pain, hypovolemia, and level of consciousness.

- (2) INDICATIONS: Used in patients with normal respiratory drives but weak respiratory muscles. Combines controlled ventilation with the possibility of a synchronous breathing pattern of patient and ventilator. Ventilatory support is provided for every breath.
 - (3) COMPLICATIONS: Risks include excessive patient work if peak flow or sensitivity is inadequate; may be poorly tolerated in awake, nonsedated patients; may be associated with respiratory alkalosis; may possibly worsen air trapping in patients with COPD; tidal volume may vary with changes in lung impedences, patient ventilatory drive, or patient-ventilator dyssynchrony.
- j. VENTILATION, INTERMITTENT MANDATORY
- (1) INTRODUCTION:
 - (a) Both a ventilatory mode and a weaning mode. Intermittent mechanical breaths at a preset rate and volume are delivered while allowing spontaneous breaths between and independent of the IMV breaths.
 - (b) Mandatory breaths are flow controlled, pressure triggered, or time triggered; spontaneous breaths are pressure controlled, pressure triggered, and either pressure or flow cycled (Chatburn, 1995).
 - (2) INDICATIONS: May be of benefit to patients with respiratory alkalemia; may reduce mean airway pressure (Kirby, 1975); may promote more uniform intrapulmonary gas distribution (Downs, 1983); forestalls muscle atrophy and dyssynchrony; minimizes need for sedation and muscle paralysis (Petty, 1981).
- k. VENTILATION, PRESSURE-SUPPORT
- (1) INTRODUCTION:
 - (a) Ventilatory cycle is initiated by the patient and each spontaneous breath is augmented with a fixed amount of positive pressure. Patient determines respiratory rate.
 - (b) At the start of inspiration, pressure rises rapidly to a plateau and is maintained throughout the inspiration phase. Inspiratory duration is dependent on patient effort; airway pressurization always stops before reaching zero flow.
 - (2) INDICATIONS: Primarily designed to assist spontaneous breathing, although it is used during periods of stable ventilatory support and weaning. Respiratory rate, inspiratory time, and flow rate are controlled by the patient; tidal volume is determined by the level of PSV, patient effort, and pulmonary mechanics (Tobin, 1994).
- l. CONTINUOUS POSITIVE AIRWAY PRESSURE
- (1) INTRODUCTION:
 - (a) Provides continuous positive airway pressure by the ventilator throughout the ventilatory cycle in spontaneously breathing patients.
 - (b) Improves oxygenation if decreased lung volume is a contributing factor in hypoxemia. Reduces work of breathing in patients with dynamic hyperinflation (phenomenon in which there is airflow limitation resulting from inadequate expiration time) and auto-PEEP (positive alveolar pressure at end expiration); however, excessive CPAP levels may induce these phenomena (Fessler, 1995).
 - (2) INDICATIONS: Utilized in spontaneously breathing patients who can ventilate adequately but cannot oxygenate effectively because of decreased functional residual capacity; increases lung volume and oxygenation by elevating end-expiratory pressure to that above atmospheric pressure (Katz, 1985).
- m. POSITIVE END-EXPIRATORY PRESSURE
- (1) INTRODUCTION:
 - (a) Positive pressure applied to the expiration circuit prevents alveolar collapse that may occur between breaths. Serves to correct shunting and ventilation-perfusion mismatch resulting in increased functional residual capacity of the lung (Welsh, 1992; Bone, 1995).

- (b) Administering PEEP equal to intrinsic positive end-expiratory PEEP ("auto-PEEP") results in almost total resolution of intrinsic PEEP (Munoz, 1993).
- (c) Optimum PEEP may be evaluated by increasing PEEP by increments of 3 to 5 cmH₂O (starting at 0 cm) every 20 to 30 minutes. Assess blood pressure, arterial blood gases, cardiac output, and oxygen delivery calculations with each change. Best PEEP is the lowest level that allows a decrease in FiO₂ without compromising oxygen delivery (Welsh, 1992).
- (2) INDICATIONS: Used to improve arterial oxygenation in severely hypoxemic patients, or in an effort to decrease the FiO₂ to avoid oxygen toxicity. Major indication is PaO₂ <60 mmHg with an FiO₂ >50% in a patient with diffuse pulmonary injury and infiltrates (Tobin, 1990).
- (3) COMPLICATIONS:
 - (a) DECREASED CARDIAC OUTPUT: Most frequent complication, occurring commonly if PEEP exceeds 15 cmH₂O, if cardiovascular reflexes are impaired, if there is coexistent hypovolemia, or if A/C ventilation is being used; occurs secondary to decreased venous return.
 - (b) BAROTRAUMA: Relationship to PEEP is unclear; potential may increase with PEEP levels >18 cmH₂O; generally benign but can result in tension pneumothorax (Welsh, 1992).
 - (c) INCREASED INTRACRANIAL PRESSURE: Occurs only with high levels of PEEP (Tobin, 1990).
 - (d) DECREASED RENAL AND PORTAL BLOOD FLOW: Related to decreased cardiac output (Tobin, 1994).
- n. VENTILATION, HIGH-FREQUENCY
 - (1) Includes a variety of nonconventional modes of positive pressure ventilation utilizing low tidal volumes and increased ventilatory frequencies that serve to minimize the adverse effects of increased peak and mean airway pressures, thereby increasing functional residual capacity (Meliones, 1994).
 - (2) Dangers associated with HFV require that clinicians be very familiar with technique. Risks include hemodynamic compromise and barotrauma associated with outflow obstruction; air trapping due to high flow rates; severe necrotizing tracheobronchitis due to inadequate humidification (Meliones, 1994).
 - (3) High-frequency jet ventilation (HFJV) is one of the most commonly used technologies and utilizes a high-pressure air-oxygen gas to generate inspiratory gas flow; expiration is passive. Mean airway pressure (Paw) and peak airway pressure (PIP) are less than those generated during conventional PPV (Meliones, 1994).
 - (4) Requires a separate ETT and additional ventilator. Advantages include reduced airway pressures, improved hemodynamics, and less risk of barotrauma. Consider in patients with high airway pressures or those who are unusually sensitive to airway pressures (Meliones, 1994).
 - (a) NEONATES: Failure to respond to conventional therapy despite high PIPs is an indication for HFJV; consider HFJV when patient requires a Paw >= 15 to 20 mmHg or if a significant airleak is present.
 - (b) CHILDREN: Primarily indicated in postoperative congenital heart disease, ARDS, or perioperatively for thoracic surgery patients. In postoperative cardiac patients, HFJV is initiated when the Paw is >= 15 mmHg when pulmonary artery hypertension and/or right ventricular dysfunction is present (Meliones, 1991).
 - (c) ADULTS: Consider HFJV when Paw is >20 to 25 mmHg or when airleak is present; may be beneficial in patients during or after thoracic surgery or in patients with ARDS (Howland, 1987; Brimiouille, 1990).
 - (5) High-frequency oscillatory ventilation (HFOV) alternates positive and negative pressures in the airway (Fredberg, 1987); both inspiration and expiration are active. Disadvantages include increased

- Paw, air-trapping if high airway resistance is present, and because of the rigid nature of the HFOV circuit, patient position is relatively fixed.
- (6) Advantages include the ability of the clinician to manipulate oxygenation and ventilation independently, and the ability to apply HFOV without special ETT or additional ventilator. Consider in patients with impaired oxygenation or in whom barotrauma has occurred.
 - (a) NEONATES: Indicated for infantile respiratory distress syndrome (IRDS), barotrauma, refractory pulmonary artery hypertension, airleak, and diaphragmatic hernia.
 - (b) CHILDREN: Primarily indicated in patients with ARDS who have decreased oxygenation despite high levels of support or those who develop significant barotrauma.
 - (c) ADULTS: Possibly beneficial in ARDS; surgically induced airway injury; postsurgical patients at high risk for pneumonitis or aspiration (Freitag, 1989).
 - o. COMPLICATIONS OF MECHANICAL VENTILATION
 - (1) BAROTRAUMA:
 - (a) Occurs most often in patients with adult respiratory distress syndrome, especially those with severe disease requiring high peak inspiratory pressure or high (>18 cmH₂O) levels of positive end-expiratory pressure.
 - (b) Susceptibility may vary with disease process; prolonged ventilation may cause many forms of barotrauma to occur more frequently (Slutsky, 1993), the most disastrous of which is tension pneumothorax.
 - (c) Preventatory measures include permissive hypercapnia (Pesenti, 1990; Hickling, 1990; Reynolds, 1993; Gentilello, 1995); pressure-controlled ventilation (Nahum, 1992); and pressure-limited, volume-cycled ventilation (Marcy, 1991; Dries, 1995).
 - (d) TREATMENT: Emergency needle thoracentesis may be life-saving in tension pneumothorax; chest tube with water-sealed drainage may be required for a small pleural leak.
 - (2) OXYGEN TOXICITY: Prolonged use of oxygen at high concentrations (>50% over several days) can lead to irreversible pulmonary fibrosis (Bone, 1995).
 - (3) HEMODYNAMIC ALTERATIONS: Increases in intrathoracic pressure adversely affect cardiac output secondary to decrease in venous return (Slutsky, 1993).
 - (4) BREATHING EFFORT AND PATIENT-VENTILATOR ASYNCHRONY: Factors that increase work of breathing include endotracheal tube resistance, excessive triggering threshold or response delay, insufficient ventilator flow capacity to meet peak patient demands, and development of dynamic hyperinflation, which gives rise to auto-PEEP (Slutsky, 1993).
 - (5) AUTO-PEEP:
 - (a) DEFINITION: The difference between alveolar pressure and external airway pressure at end expiration. Management differs depending on the cause of auto-PEEP; may occur during mechanical ventilation when ventilated breaths occur prior to complete exhalation of the previous breath (Slutsky, 1993).
 - (b) RISK FACTORS: Common in obstructive lung disease, (particularly during acute exacerbations) when ventilator settings are set inappropriately for physiologic state. Variables that may contribute to the development of auto-PEEP include interruption in expiratory flow, respiratory rate, minute volume, size of endotracheal tube, and characteristics of the ventilatory circuit (Munoz, 1993; Fessler, 1995).
 - (c) MEASUREMENT: Can be measured by transiently decreasing ventilator rate and momentarily occluding the exhalation port at the usual time of inspiration, which results in equilibration of pressure; a manometer attached to the proximal airway will then reflect alveolar pressure.
 - (d) COMPLICATIONS: Similar to those of applied PEEP:

- severe hypotension and decreased cardiac output; barotrauma; erroneous pulmonary artery catheter measurements (high pulmonary-capillary wedge pressure) leading to misguided and inappropriate fluid therapy or diuresis (Welsh, 1992).
- (e) TREATMENT: Must reduce ventilator rates (sometimes to 1-2 breaths/minute) immediately to correct problem.
- C. BED REST
1. AMS: Rest alone may reduce symptoms. Oxygen and bed rest may preclude the need for descent if the patient improves (Hackett, 1992; Yaron, 1994; Bartsch, 1992).
2. HAPE:
- a. Absolute bed rest is important because physical exercise will aggravate it by increasing pulmonary artery pressure and reducing oxygen saturation (Hackett, 1992; Yaron, 1994).
- b. Once HAPE is resolved, patients are at further risk if they ascend higher on that particular excursion to high altitude and may have demonstrated an underlying susceptibility.
- D. MONITORING, CARDIAC
1. INDICATIONS:
- a. Respiratory and/or potential cardiac problems.
- b. Severe mental obtundation or coma.
- E. HYPERVENTILATION
1. Voluntary hyperventilation every 10 to 15 minutes is helpful in AMS.
- F. INTRAVENOUS LINE
1. INDICATIONS:
- a. Respiratory distress for administration of drugs if immediate improvement does not occur with conservative therapy.
- b. Severe mental obtundation.
- c. Unnecessary in patients with uncomplicated AMS.
- G. MONITORING, PULMONARY ARTERY PRESSURE
1. CONTROVERSY: Use is controversial; uncertainty regarding its safety and efficacy in contributing to improved patient outcomes (Connors, 1996; Dalen, 1996; Robin, 1987; Matthay, 1988; Sibbald, 1988; Spodick, 1989, 1989a; Shoemaker, 1990; Fink, 1997; Reinhart, 1997; Ginosar, 1997).
- a. Majority of critical care clinicians believe that information provided by the PAC is helpful in guiding therapy and improving outcome in selected critically ill patients. Provides hemodynamic information that cannot be supplied by clinical diagnosis alone, while allowing diagnostic classification of patients with cardiovascular dysfunction and other diseases (Chernow, 1997; Am Soc Anesthesiologists Task Force, 1993; Eur Soc Intensive Care Med, 1991).
- b. Results of an observational prospective cohort study in over 5700 critically ill patients in five US teaching hospitals indicate that, independent of severity of illness, placement of a PAC during first 24 h of stay in an ICU is associated with significant increased risk of death, as well as increased cost of care and length of hospitalization and ICU stays (Connors, 1996).
- c. However, both the Pulmonary Artery Catheter Consensus Conference (1997), organized by the Society of Critical Care Medicine, and a panel convened by The American College of Chest Physicians and the American Thoracic Society (Chernow, 1997) have concluded there currently is NO basis for a moratorium on PAC use. The decision to insert a PAC should continue to be based on specific clinical circumstances and a weighing of risks vs benefits of PAC by the physician providing care.
- d. The Pulmonary Artery Consensus Conference (1997) found that PAC may have value in very select settings; however, other methods of monitoring adequacy of resuscitation in critically ill patients (eg, echocardiography, tissue tonometry) may be better and less invasive adjuncts to conventional clinical tools (Fink, 1997).
- e. Prospective, randomized, controlled trials are indicated

- to definitively determine utility of PAC for various indications (Pulmonary Artery Consensus Conference, 1997; Chernow, 1997; Reinhart, 1997; Fink, 1997).
2. INDICATIONS IN REFRACTORY HEART FAILURE: May be useful in patients with severe or progressive HF. No proof of benefit in improving outcomes; research needed to determine whether such patients managed with PAC have better outcomes than those managed by less invasive means (Pulmonary Artery Consensus Conference, 1997).
 3. FINDINGS:
 - a. Elevated pulmonary artery pressure and pulmonary vascular resistance.
 - b. Normal or low pulmonary capillary wedge pressure.
 - c. Decreased cardiac output.
 - d. Decreased systemic blood pressure.
 - e. Normal or slightly elevated right-sided pressures (Hackett, 1992; Yaron, 1994).
 4. CARDIOGENIC PULMONARY EDEMA: Produces elevated pulmonary capillary wedge pressure (normal = 5-10 mmHg, with a range of 3-15 mmHg). Pressures may range from 18 mmHg to >30 mmHg. At 30 mmHg, frank intra-alveolar fluid accumulation usually occurs.

H. OXYGEN, HYPERBARIC

1. GAMOW BAG(R)

- a. Portable, one-person hyperbaric bags (Gamow Bag(R)) are available that pressurize victims of high altitude illness to 2 psi, equivalent to a descent of 5000 feet when operated at 14,000-foot altitude (King, 1990; Taber, 1990; Kasic, 1991).
- b. As effective as oxygen or descent and is safe in persons with AMS, HAPE, or HACE. Ventilation or CO₂ scrubbers prevent CO₂ accumulation. Length of treatment depends on severity of illness and can range from a few to many hours (King, 1990; Taber, 1990; Kasic, 1991; Bartsch, 1992).
- c. Long-term benefit (>12 h) of pressurization is controversial. Some studies have shown such benefit (Taber, 1990; King, 1990; Robertson, 1991), while others suggest the effect may be short-lived, possibly as short as 1 h (Bartsch, 1993; Kayser, 1993). There is no beneficial effect of single treatment session (Bartsch, 1992).
- d. Should be considered as additional treatment for symptomatic relief in severe cases if patient is unresponsive to or unable to tolerate medicine, prompt evacuation is not possible, and positive-pressure bag is available for use by experienced personnel (King, 1990).

6.3 PHARMACOLOGIC TREATMENT

A. OXYGEN

1. INDICATIONS:

- a. AMS: Treatment of choice in severe cases (Hackett, 1992; Yaron, 1994; Pigman, 1990; Bartsch, 1990; Callen, 1989).
- b. HAPE: Adequate treatment when combined with bed rest. Oxygen is both life-saving and curative (Marticorena, 1979; Rabold, 1989).
- c. HACE: May be temporarily life-saving but should not be regarded as a substitute for descent (Hackett, 1992; Yaron, 1994).

2. RECOMMENDATION:

- a. AMS: Administer oxygen by mask or nasal cannula at a flow rate that will alleviate hypoxemia as measured by pulse oximetry or produce good clinical response. If supplies of O₂ are limited, use low-flow (1 to 2 L/min) to maximize length of treatment.
- b. HAPE: Severe cases require 24 hours or more of O₂ for resolution if descent is not accomplished. During evacuation, oxygen should be given by face mask at 6 to 8 liters/minute for first 30 minutes, then decreased to 2 to 4 liters/minute for 12 to 48 hours to conserve oxygen. In the hospital setting, a 100% nonrebreather should be used (Rabold, 1989).
- c. HACE: Give oxygen at rate of 2 to 4 liters/minute (Hackett, 1992).

B. CARBON DIOXIDE

1. AMS: Use is controversial. Uncontrolled studies have suggested that use of CO₂-enriched air (3% CO₂) may be alternative treatment of AMS (Harvey, 1988). However, results of a controlled study did not support its usefulness; only significant effect was increased ventilation resulting in slight rise in PaO₂ (Bartsch, 1990).

C. INTRAVENOUS FLUID

1. CRYSTALLOIDS

a. INDICATIONS:

- (1) Initial fluid choices in HAPE and HACE. Should be administered to maintain normal vital signs and urine output of at least 30 mL/hr. Pulmonary capillary wedge pressure should be followed to ascertain appropriate fluid therapy, and a net positive fluid balance should be avoided.
- (2) Use of colloid solutions (eg, albumin) should be considered if venous pressure does not rise after crystalloid infusion or if hypoalbuminemia exists.

b. CAUTION:

- (1) A dilemma is encountered in the fluid resuscitation of the patient with HAPE or HACE. Too much fluid may expand intravascular volume and improve cardiac output, thus indirectly improving tissue oxygenation by getting the oxygen to the tissues. However, this may cause an increase in pulmonary fluid and thus worsen hypoxemia. In addition, any increase in capillary hydrostatic pressure in the presence of an increase in permeability may result in an increase in lung water.
- (2) Although possibly improving alveolar capillary oxygen exchange, too little fluid may reduce cardiac output (Robin, 1972). This effect may be more disastrous if PEEP is instituted.
- (3) In the hypovolemic patient, restoration to normal intravascular volume once the damage to the alveolar/capillary membrane is accomplished may precipitate worsening pulmonary edema. However, crystalloid resuscitation has been shown not to worsen pulmonary edema (Tranbaugh, 1982).
- (4) A delicate compromise needs to be reached utilizing all modalities available: Swan-Ganz measurements, tissue oxygenation and consumption as manifested by PVO₂, and clinical examination.

D. CARBONIC ANHYDRASE INHIBITORS

1. ACETAZOLAMIDE

a. INDICATIONS (Treatment):

- (1) Mild to moderate AMS; relieves symptoms, improves arterial oxygenation, and prevents further impairment of gas exchange (Grissom, 1992; Hackett, 1992; Pigman, 1990; Bradwell, 1986).
- (2) Not recommended for established HAPE and HACE; should not be a substitute for descent, rest, and oxygenation once symptoms develop.
- (3) Not effective in all individuals and should not be substituted for acclimatization and slow ascent.

b. RECOMMENDATION (Mild to moderate AMS): 250 milligrams orally every eight hours (children >6 years: 5 milligrams/kilogram/day orally in three divided doses) for 48 hours (Pigman, 1990).

c. AVAILABLE FORMS: Diamox(R) (time-release capsules, tablets).

d. DOSING IN SPECIAL SITUATIONS: Increase dose interval in renal failure; dose adjustment not required in liver disease.

e. PRECAUTIONS: Sulfa drug. Contraindicated in hypokalemia, hyponatremia, severe renal insufficiency and hyperchloremic acidosis; long-term use contraindicated in chronic non-congestive angle closure glaucoma; caution in pulmonary obstruction or emphysema; may antagonize effects of lithium and methenamine; may increase quinidine toxicity.

f. MAJOR ADVERSE REACTIONS: Paresthesias; drowsiness; nausea and vomiting; thrombocytopenia; aplastic anemia;

- metabolic acidosis; renal calculi; myopia.
- g. MONITORING PARAMETERS: Serum electrolytes.
- E. ANALGESICS
1. ASPIRIN
 - a. INDICATIONS: May be used to relieve headache (Hackett, 1992; Yaron, 1994).
 - b. RECOMMENDATION: 650 milligrams orally every four to six hours as needed (children: 10 to 15 milligrams/kilogram orally every four to six hours; maximum, 650 milligrams/dose).
 - c. AVAILABLE FORMS: Ecotrin(R); Bufferin(R); many generic preparations.
 - d. DOSING IN SPECIAL SITUATIONS: Dose reductions not required in impaired renal function; avoid in severe hepatic insufficiency.
 - e. MAJOR ADVERSE REACTIONS: Increased bleeding time and potential bleeding episodes; hypersensitivity reaction (urticaria or anaphylaxis); hepatotoxicity with high doses; overdose toxicity (tinnitus); adverse reactions with prolonged use.
 - f. PRECAUTIONS: Contraindicated in bleeding disorders, in last month of pregnancy, hypersensitivity to aspirin; caution in asthma, nasal polyps, ulcers, and in patients receiving anticoagulants; many drug interactions. Contraindicated in viral illness (eg, influenzae and chickenpox) in children due to possible association with Reye's syndrome.
 2. IBUPROFEN
 - a. INDICATIONS: Treatment of high altitude headache (Broome, 1994).
 - b. RECOMMENDATION: 400 milligrams orally every four to six hours PRN; maximum, 2.4 grams/day.
 - c. AVAILABLE FORMS: Motrin(R) (tablets); Nuprin(R) (tablets, caplet); Medipren(R) (tablets); or equivalent NSAID.
 - d. DOSING IN SPECIAL SITUATIONS: Increase dosage interval in renal failure.
 - e. MAJOR ADVERSE REACTIONS: Tinnitus; hearing loss; GI bleeding; cholestatic jaundice; anaphylaxis.
 - f. PRECAUTIONS: Contraindicated in patients with hypersensitivity to aspirin or other NSAIDs; caution in active peptic ulcer disease, renal insufficiency, hepatic dysfunction, and patients with compromised cardiac function (edema); potentiates effects of warfarin; concomitant antacid administration may reduce absorption.
 3. CODEINE
 - a. INDICATIONS: May be used to relieve headache unaffected by aspirin (Hackett, 1992; Yaron, 1994). Must be administered with caution as any increase in sedation may potentiate alveolar hypoventilation and worsen cerebral edema (Sutton, 1979).
 - b. RECOMMENDATION: 30 to 60 milligrams orally as needed (children: 3 milligrams/kilogram/day orally in divided doses).
 - c. AVAILABLE FORMS: Generic tablets and injection; numerous combination products.
 - d. DOSAGE IN SPECIAL SITUATIONS: Dose reductions are not required in renal insufficiency; dose reductions required in hepatic disease.
 - e. MAJOR ADVERSE REACTIONS: Respiratory depression; hypotension; addiction with prolonged use.
 - f. PRECAUTIONS: Contraindicated in patients with respiratory depression or coma; use with caution in the presence of convulsions, shock, asthma or COPD; additive CNS depression with other depressant drugs.
- F. STEROIDS
1. DEXAMETHASONE
 - a. INDICATIONS (Treatment):
 - (1) AMS: Patients with neurologic deterioration, eg, ataxia, change in level of consciousness, severe headache and/or vomiting, particularly when descent is impossible or to facilitate cooperation in evacuation efforts (Ferrazini, 1987; Levine, 1989; Hackett, 1992;

Montgomery, 1989a; Johnson, 1984).

(2) HACE: Although no studies have demonstrated effect of dexamethasone on HACE, severe AMS includes symptoms of cerebral edema, and dexamethasone has shown improvement of symptoms with severe AMS.

(3) HAPE: No proven value (Hackett, 1992; Yaron, 1994).

b. RECOMMENDATION:

(1) AMS: 4 milligrams orally or intramuscularly every six hours (Levine, 1989).

(2) HACE: 10 milligrams intravenously initially, then 4 milligrams every six hours (children: 0.25 to 0.5 milligrams/kilogram/dose intravenously every six hours).

c. AVAILABLE FORMS: Decadron(R) (tablets, injection); Dexone(R) (tablets); Hexadrol(R) (tablets, solution).

d. DOSING IN SPECIAL SITUATIONS: Dosage adjustments may be required in patients with cirrhosis because of possible enhanced steroid effects.

e. MAJOR ADVERSE REACTIONS: Peptic ulceration may occur with high doses; fluid retention may precipitate CHF in susceptible patients.

f. PRECAUTIONS: Contraindicated in the presence of systemic fungal infections; adrenal suppression may occur with administration of high doses for prolonged periods; large doses may induce hypokalemia, which is accentuated by concomitant therapy with diuretics.

G. ANTIEMETICS

1. PROCHLORPERAZINE

a. INDICATIONS: Treatment of nausea and vomiting; also increases ventilatory response to hypoxia (Olson, 1982; Hackett, 1992).

b. RECOMMENDATION:

(1) ORAL: 5 to 10 milligrams orally every six to eight hours (children >2 years: 0.4 milligrams/kilogram/day orally in three to four divided doses).

(2) RECTAL: 25 milligrams per rectum every 12 hours (children: 0.4 milligrams/kilogram/day as needed in three to four divided doses).

(3) INTRAMUSCULAR: 5 to 20 milligrams intramuscularly; maximum 40 milligrams/day (children: 0.2 milligram/kilogram/day intramuscularly in three to four divided doses).

c. AVAILABLE FORMS: Compazine(R) (capsules, syrup, tablets, injection, suppository).

d. DOSING IN SPECIAL SITUATIONS: Reduce dose in severe liver disease; dose reduction not required in renal insufficiency.

e. MAJOR ADVERSE REACTIONS: Extrapyramidal reactions (dystonias that may mimic tetanus); hepatotoxicity; blood dyscrasias (granulocytopenia, thrombocytopenia); adverse reactions with prolonged use.

f. PRECAUTIONS: Contraindicated in children under 2 years, in severe hypotension, and in patients with bone marrow depression; use with caution in glaucoma, hepatic dysfunction, and prostatic hypertrophy.

g. MONITORING PARAMETERS: Monitor for dystonic reactions.

H. VASODILATORS

1. OVERVIEW

a. HAPE is characterized by marked pulmonary vasoconstriction. Pulmonary vasodilators exert a beneficial effect on hemodynamics and oxygenation in these patients (Hackett, 1992a; Oelz, 1989, 1992).

2. NIFEDIPINE

a. INDICATIONS: Potential emergency treatment of HAPE when descent or evacuation is impossible and supplemental oxygen is not available (Oelz, 1989, 1992; Jamieson, 1992).

b. RECOMMENDATION: 10 milligrams sublingually plus 20 milligrams orally of slow-release nifedipine. If systolic BP does not decrease 10 mmHg or more within 10 minutes, repeat sublingual dose after 15 minutes. Subsequently, give 20 milligrams of slow-release nifedipine every six hours for entire time at altitude (Oelz, 1989).

- c. AVAILABLE FORMS: Procardia(R) (capsules); Procardia XL(R) (sustained-release tablets).
 - d. MAJOR ADVERSE REACTIONS: Hypotension (during initial treatment, more frequent in patients receiving beta-blockers); increased frequency or severity of angina upon initiation; CHF (in patients receiving beta-blockers); palpitations; dizziness; headache.
 - e. PRECAUTIONS: Caution if clinical history or EKG suggests recent angina or ischemia and in patients receiving beta-blocking agents; may exacerbate withdrawal syndrome or beta-blockers if initiated after withdrawal (taper beta-blocking agents before starting nifedipine). Caution in patients with hepatic impairment and in patients with tight aortic stenosis (increased risk of CHF). Increased risk of hypotension has been reported when patients are volume-depleted or are receiving diuretics or other antihypertensive drugs.
 - f. EFFICACY: Results in clinical improvement, better oxygenation, reduction of alveolar arterial oxygen gradient and pulmonary artery pressure, and progressive clearing of alveolar edema (Oelz, 1989, 1992; Jamieson, 1992).
3. PHENTOLAMINE
- a. Marked pulmonary vasoconstriction in HAPE may involve increased alpha adrenergic activity. A short-acting alpha blocker, eg, phentolamine, is particularly effective (Hackett, 1992a).
- I. MORPHINE SULFATE
1. INDICATIONS (HAPE): Effective in decreasing dyspnea, reducing pulmonary blood volume, and improving oxygenation, but depression of ventilatory drive may worsen alveolar hypoxia, pulmonary hypertension, and oxygen delivery. May be helpful when descent is not possible and oxygen is not available (Hackett, 1992; Yaron, 1994). Little actual experience with its use in HAPE.
 2. RECOMMENDATION: 2 to 10 milligrams intravenously (children: 0.1 to 0.2 milligram/kilogram intravenously slowly); may be repeated every 10 to 15 minutes PRN; observe for hypotension and respiratory depression.
 3. AVAILABLE FORMS: Many generic preparations (injection).
 4. DOSING IN SPECIAL SITUATIONS: Reduce dose in hepatic insufficiency; dosing adjustment not required in renal failure.
 5. MAJOR ADVERSE REACTIONS: Respiratory depression; hypotension; bradycardia; hallucinations; anaphylaxis when given IV; nausea and vomiting; constipation; urinary retention.
 6. PRECAUTIONS: Contraindicated in patients with respiratory depression, coma, or allergy to morphine; caution in the presence of convulsions, shock, asthma, or COPD; CNS depression accentuated with other depressant-type drugs, including phenothiazines.
 7. MONITORING PARAMETERS: Respiratory depression is common, especially in patients with chronic pulmonary disease. It is maximal 10 minutes after an intravenous dose and may cause acute respiratory failure or apnea. Therefore, the patient must be observed for hypotension and respiratory depression following administration of the initial dose of morphine.
 8. MECHANISM OF ACTION:
 - a. Vasodilation via histamine release;
 - b. Arteriolar dilatation via central suppression of adrenergic tone;
 - c. Decrease in myocardial oxygen consumption;
 - d. Decrease in left ventricular end-diastolic pressure;
 - e. Relief of anxiety.
- J. DIGOXIN
1. Has no proven value in the treatment of HAPE (Hackett, 1992; Yaron, 1994).
- K. DIURETICS
1. FUROSEMIDE
 - a. INDICATIONS: Correction of fluid retention and volume overload.

- (1) AMS: Excellent results reported in treating moderate to severe AMS; use in field when monitoring of dehydrated patients is difficult and is not recommended (Hackett, 1992; Yaron, 1994).
- (2) HACE:
 - (a) No data supporting role of diuretics in treating HACE; in field environments, patients may become overly dehydrated, weak, and unable to descend; however, a degree of dehydration in a medically supervised setting, if carefully observed for hypovolemia, is acceptable (Hackett, 1992; Yaron, 1994).
 - (b) Dehydrated patients with neurologic signs who are not responding to oxygen and descent may benefit from mild diuresis (Houston, 1975).
- (3) HAPE: Role of diuretics has been questioned on the grounds that these patients are already dehydrated, and diuretics may potentiate dehydration, hypotension, and severe weakness which could interfere with rescue attempts and descent (Hackett, 1992; Yaron, 1994). Caution in dehydrated patient on mechanical ventilator secondary to hypotension.
 - b. RECOMMENDATION: 20 to 40 milligrams intravenously every 12 hours until improved (children: 1 to 2 milligrams/kilogram/dose intravenously).
 - c. AVAILABLE FORMS: Lasix(R) (injection).
 - d. DOSING IN SPECIAL SITUATIONS: Higher doses may be required in renal failure to induce effective diuresis; no specific dosing adjustment is required in hepatic insufficiency.
 - e. MAJOR ADVERSE REACTIONS: Ototoxicity can occur in patients with renal failure; electrolyte depletion may occur with large doses; acute hypotensive episodes may occur with rapid diuresis.
 - f. PRECAUTIONS: Contraindicated in anuria; the drug should be used with caution in the presence of increasing renal insufficiency and/or oliguria during treatment of severe renal disease; may precipitate hepatic encephalopathy in liver disease; excessive hypokalemia may occur during concomitant therapy with corticosteroids, amphotericin B and other diuretics.
 - g. MONITORING PARAMETERS: Periodic determination of serum electrolytes; serum uric acid and glucose levels.
- L. TRANSFUSION, BLOOD
 1. Necessary treatment modality only if the patient's hemoglobin concentration is so low that it interferes with the transport of oxygen to the tissue (Hackett, 1992; Yaron, 1994).
- M. SEDATIVES/HYPNOTICS
 1. Sedatives may worsen sleep oxygenation, potentiate cerebral edema (Sutton, 1979), and contribute to HAPE (Hackett, 1992).
- N. NALOXONE
 1. A single case report showed that naloxone was apparently successful in ameliorating the clinical and laboratory abnormalities of HAPE (Bar-Or, 1982); however, this requires further study and is not recommended.
- O. PROPHYLAXIS, HIGH ALTITUDE ILLNESS
 1. ACCLIMITIZATION
 - a. AMS is almost universally experienced during acclimitization to extreme altitude but noticeable symptoms of AMS also develop in travelers to intermediate altitudes (2000 to 3000 m), particularly in persons arriving from altitudes <900 m (Montgomery, 1989; Pigman, 1990; Houston, 1990).
 - b. Stopping the ascent and waiting for the body to better acclimatize may be adequate for mild cases of AMS; 24 to 48 hours may be required. Gradual ascent of no more than 300 m/day above 3000 meters is recommended (Pigman, 1991; Houston, 1990).
 - c. Drinking additional water, avoiding salt and alcohol, and being only moderately active also helpful (Houston, 1990).
 - d. The term "acclimatization" probably should not be used for extreme altitudes >8000 m, since the body steadily

- deteriorates at such altitudes (West, 1993).
2. ACETAZOLAMIDE
 - a. INDICATIONS: Drug of choice to help prevent or minimize AMS symptoms (Sutton, 1979; Bradwell, 1981; Milles, 1987; McIntosh, 1986; Pigman, 1991; Med Lett, 1992).
 - b. RECOMMENDATION: 250 milligrams orally twice daily, or 1 sustained-action (500-milligram) capsule orally every 24 hours (children 6 to 12 years: 5 milligrams/kilogram/day orally in two divided doses), beginning 2 to 3 days before ascent and continuing for first 3 days at altitude (Pigman, 1991; Barkin, 1994).
 - c. AVAILABLE FORMS: Diamox(R) (time-release capsules, tablets).
 - d. DOSING IN SPECIAL SITUATIONS: Increase dose interval in renal failure; dose adjustment not required in liver disease.
 - e. PRECAUTIONS: Sulfa drug. Contraindicated in hypokalemia, hyponatremia, severe renal insufficiency and hyperchloremic acidosis; long-term use contraindicated in chronic non-congestive angle closure glaucoma; caution in pulmonary obstruction or emphysema; may antagonize effects of lithium and methenamine; may increase quinidine toxicity.
 - f. MAJOR ADVERSE REACTIONS: Paresthesias; drowsiness; nausea and vomiting; thrombocytopenia; aplastic anemia; metabolic acidosis; renal calculi; myopia.
 - g. MONITORING PARAMETERS: Serum electrolytes.
 3. DEXAMETHAXONE
 - a. INDICATIONS: Helps prevent or minimize AMS in persons ascending >2700 m but is not indicated routinely. May be considered for persons without contraindications who are intolerant of acetazolamide, for whom acetazolamide is ineffective, or who must make forced, rapid ascent to high altitude for short period of time with guaranteed retreat route (Pigman, 1991; Montgomery, 1989a; Rock, 1989; Ellsworth, 1991).
 - b. RECOMMENDATION: 4 milligrams orally every six hours for six doses beginning at time of exposure (Montgomery, 1989a).
 - c. AVAILABLE FORMS: Decadron(R) (tablets); Dexone(R) (tablets); Hexadrol(R) (tablets).
 - d. DOSING IN SPECIAL SITUATIONS: Dosage adjustments may be required in patients with cirrhosis because of possible enhanced steroid effects.
 - e. MAJOR ADVERSE REACTIONS: Peptic ulceration may occur with high doses; fluid retention may precipitate CHF in susceptible patients.
 - f. PRECAUTIONS: Contraindicated in the presence of systemic fungal infections; adrenal suppression may occur with administration of high doses for prolonged periods; large doses may induce hypokalemia, which is accentuated by concomitant therapy with diuretics.
 - g. EFFICACY: Significantly decreases incidence of AMS and severity of symptoms (Montgomery, 1989a); positively influences cognitive performance and mood states at altitude but has no residual effect on personality (Jobe, 1991).
 4. NIFEDIPINE
 - a. INDICATIONS:
 - (1) Prevention of HAPE in susceptible persons. Not indicated routinely because of potentially harmful side effects (eg, hypotension, dizziness) and lack of evidence regarding long-term safety and efficacy at altitude. May be considered for persons at risk for HAPE who go to altitudes where supplemental oxygen is not available and rapid descent is not possible (Reeves, 1991; Bartsch, 1991; Oelz, 1992).
 - (2) Not recommended for prevention of AMS (Hohenhaus, 1994).
 - b. RECOMMENDATION: 20 milligrams orally of slow-release nifedipine every eight hours (Bartsch, 1991).
 - c. AVAILABLE FORMS: Procardia(R) (capsules); Procardia XL(R) (sustained-release tablets).
 - d. MAJOR ADVERSE REACTIONS: Hypotension (during initial

- treatment, more frequent in patients receiving beta-blockers); increased frequency or severity of angina upon initiation; CHF (in patients receiving beta-blockers); palpitations; dizziness; headache.
- e. PRECAUTIONS: Caution if clinical history or EKG suggests recent angina or ischemia and in patients receiving beta-blocking agents; may exacerbate withdrawal syndrome or beta-blockers if initiated after withdrawal (taper beta-blocking agents before starting nifedipine). Caution in patients with hepatic impairment and in patients with tight aortic stenosis (increased risk of CHF). Increased risk of hypotension has been reported when patients are volume-depleted or are receiving diuretics or other antihypertensive drugs.

7.0 DISPOSITION

7.1 ADMISSION CRITERIA

- A. All patients with moderate to severe HAPE or HACE require hospitalization if still symptomatic after descent.

7.2 HOME CRITERIA

- A. All emergency department patients must be screened, stabilized, and discharged in accordance with the COBRA (antidumping) law. For the full-text of this document, SEE CLINICAL REVIEW, COBRA STATUTE.
- B. AMS and mild HAPE and HACE can be managed on an outpatient basis.

7.3 CONSULT CRITERIA

- A. Uncomplicated AMS does not require subspecialty consultation.
- B. All patients suspected of having HAPE should be admitted under the care of a primary care physician, with pulmonary and/or cardiology consultation readily available.
- C. All patients suspected of having moderate to severe HACE should be admitted under the care of a primary care physician, with neurologic and/or neurosurgical consultation available.
- D. All patients suspected of having high altitude retinal hemorrhage should have ophthalmologic consultation.

7.4 TRANSFER CRITERIA

- A. All emergency department patients must be screened, stabilized, and transferred in accordance with the COBRA (antidumping) law. For the full-text of this document, SEE CLINICAL REVIEW, COBRA STATUTE.
- B. Patients with uncomplicated AMS need not be transported, other than to descend to a lower altitude for the relief of severe symptoms. Descent can be readily accomplished by foot, stretcher, or automobile. Native altitude residents require only oxygen.
- C. For patients with HAPE or HACE, start evacuation by foot. If symptoms are severe, evacuation by litter will be necessary because the effort of climbing down may increase the severity of the edema (Hackett, 1992; Yaron, 1994).
- D. In field conditions, high flow O₂ by plastic mask can be concomitantly administered to patients with HAPE or HACE (Hackett, 1992; Yaron, 1994). Portable, one-person hyperbaric bags may be used to pressurize victims to 2 psi (King, 1989; Taber 1989).
- E. A life-line should be established and EKG monitoring done in nonambulatory patients.
- F. Patients with uncomplicated retinal hemorrhage require no special transport.

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