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Acute Mountain Sickness

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Since times immemorial mountains have fascinated human beings tempting them to come, explore and conquer them. The magnitude of these explorations was limited but still one comes across many writings and its extent especially in Alps and Andes. In 20th Century with opening of these areas for economic activities, tourism and as battle ground in Indo-China war and Indi-Pak war at Siachin, the real extent of manifestations were noticed. Air travel has also compounded the problem by enabling unacclimatised travelers to reach high altitude. The exact incidence of Acute Mountain Sickness is unknown as mild symptoms are not reported and ignored as travel related exertion.

INTRODUCTION

It is estimated that about 150 million people reside permanently at an altitude of 2500 meters or above and about 50 million people enter these areas every year. These new entrants to high altitude areas comprise mainly tourists, trekkers, mountaineers, pilgrims, porters, workers, soldiers etc. The entry of these un-acclimatized individuals along with native highlanders who reenter high altitudes after moving down or ascending up further from native heights renders them liable to Acute Mountain Sickness (AMS) at high altitude (HA) ranging from Benign Acute Mountain Sickness to life threatening or fatal disorders like acute High Altitude Pulmonary Oedema (HAPO) or High Altitude Cerebral Oedema (HACO).

There is no consensus of the altitude at which high altitude illness can occur but 2500 meters altitude is taken as high altitude by most. Altitudes over 5400 meters are taken as extremely high altitudes as at this level permanent acclimatization is not possible. However, occasionally high altitudes illnesses are known to occur even at moderate altitudes of 2000 meters to 2700 meters.

As a person ascends from altitude of 2000 meters one becomes susceptible to high altitude illnesses. The probability of developing symptoms depends mainly on altitude reached, speed of ascent, physical activities carried out after attaining that altitude and other variables like age, sex, obesity, prior history, hydration status etc. At present however, there is no consensus yet of the, association of these variable with high altitude illnesses.

Arrival in high altitude results in certain physiological adjustments enabling the person to survive in that environment. If a person fails to acclimatise or loses the gained acclimatization he can develop acute high altitude illnesses. The factors contributing significantly in the process are the environmental factors, genetic factors and changes induced in cardiovascular, respiratory and oxygen transport/delivery systems.

ENVIRONMENTAL FACTORS

The environmental factors responsible are:

1. Decreased partial arterial pressure of oxygen (PaO_2). It falls further due to hypoventilation in sleep leading to tissue hypoxia.
2. Cold temperature, high wind velocities and resultant drop in humidity of air. All these lead to dehydration due to increased insensible loss of water from body.
3. Increased ionizing and non ionizing radiations.
4. Lowered bariatric pressure which is directly proportional to high altitude is a major factor responsible for acclimatization and development of acute mountain sickness.

PATHO PHYSIOLOGY OF HIGH ALTITUDE ILLNESSES

At HA due to hypobaric hypoxia ventilation increases resulting in reduced oxygen gradient from inspired air to alveoli. This response in seen within few hours of ascent and increases in next few days and is mediated by peripheral chemoreceptors in carotid and aortic bodies and results in increased respiratory rate and tidal volume. The resultant respiratory alkalosis is slowly compensated by renal excretion of bicarbonate. If an individual is unable to provide this chemoreceptor mediated ventilator response, acclimatization is impaired leading to high incidence of high altitude related disorder. At high altitude a small drop of oxygen tension results in significant drop in SaO_2. The difference in Arterial O_2 tension and alveolar O_2 tension is called A-a difference. This A-a difference is also reduced in high altitude. Thus due to hypoxia induced pulmonary vasoconstrictions there is increase in pulmonary artery pressure leading to more uniform perfusion of lungs and is seen in all acclimatized low-landers

However despite this hyperventilation and reduction in A-a gradient arterial oxygen tension is still lower than at sea level. It is compensated by increase in hemoglobin. This transient increase in low-landers depends on extent, rate and duration of ascent and returns to normal within 3 weeks of descent.

Initially this rise in hemoglobin is due to increase hemoconcentration due to diuresis resulting in decrease in plasma volume by 15-20% but after few days it is due to increase release of erythropoietin. The hyperventilation, reduction of A-a gradient and increase in haemoglobin and haematocrit help in bringing oxygen level in blood to near normal. However to decrease the affinity of hemoglobin with oxygen there is increase in partial pressure of oxygen at HA which reduces the affinity of hemoglobin to oxygen and shifts the hemoglobin oxygen dissociation curve to right. This shift to right favours offloading of oxygen from hemoglobin.

At HA in spite of tachycardia there is fall in cardiac output due to drop in stroke volume by about 20-25%. This drop in stroke volume is due to decrease in venous return and hypoxia induced myocardial depression. Plasma volume also normally decreases on ascent due to alkaline diuresis. This reduction in plasma volume is sustained along with subsequent increase in total blood volume.

The hypoxic ventilator response (HVR) is a basic response to hypoxia via the chemoreceptors and is foundation for successful acclimatization. A subnormal HVR would lead to alveolar hypoventilation, lower alveolar O_2 tension causing pulmonary vasoconstriction leading to cerebral vasodilatation due to high CO_2 in blood. The likely pathogenesis of benign AMS and HACO is different from other HA illnesses. The basic abnormality between Benign AMS and HACO is cerebral oedema, the common underlying unifying factor with HAPO is probably pulmonary arterial hypertension. The increase in pulmonary blood flow and pulmonary artery pressure leads to "stress failure" of the pulmonary capillaries leading to leakage of fluid in to interstitial and alveolar spaces resulting in pulmonary oedema. Exercise further increases the PA pressures and can therefore precipitate HAPO.

The key determinant of HA illness, risk and severity include both individual susceptibility factors and altitudinal factors (rapid rate & height) of ascent and total change in altitude.

Individual factors contributing to AMS include underlying disease like cardiac and pulmonary disease, pre existing blood disorders and other chronic medical diseases. Those with symptomatic cardiac or pulmonary diseases are more likely to develop AMS & should avoid high altitude.

CLINICAL FEATURES

Benign Acute Mountain Sickness

Of all types of mountain sicknesses Benign Acute Mountain Sickness is commonest. The exact incidence is not known but it usually develops within 6-96 hours of stay at altitude. The presentation of AMS commonly starts with headache which is frontal in location, throbbing in character and is bilateral. It increases in morning on waking up, on exertion and straining. It may be accompanied by lightheadedness, malaise, nausea, vomiting, sleep disturbance and shortness of breath. In many cases the headache can be the only symptom and it usually respond to analgesics but in few it becomes severer with progression of disease failing to respond to analgesic. It may be associated with decreased urinary output also.

The physical examination may not yield any characteristic findings. These symptoms will have a benign and self limiting course and will tend to disappear in a week. The relationship of AMS with history of ascent to higher altitude is characteristic. AMS may have to be differentiated from common viral illnesses, effects of alcohol and from a dangerous syndrome of HACO. Karinen et al noted that it was possible to predict and diagnose AMS at an early stage by measuring oxygen saturation by pulse oxymeter at rest and after moderate exercise. They concluded that lowering of SaO_2 predicts the impending AMS.

The Lake Louis Consensus group derived Lake Louis Scoring System is gold standard for AMS (Table1) which is based on clinical and subjective symptoms. A score 3 or more signifies AMS and a score >5 indicate severe mountain sickness.

High Altitude Pulmonary Oedema (HAPO)

Of all altitude related illnesses HAPO is commonest and in a large study it contributed about half of all high altitude related illnesses. It has been associated with altitude as low as 2500-3000 meters.

The first symptoms of HAPO occur within 1-3 days after arrival at altitude. In adults, these symptoms commonly occur after exercise and consist of cough, shortness of breath, chest tightness, and fatigue. In approximately half the cases, these symptoms are associated with the typical symptoms of AMS. Initially, the cough is nonproductive, but thin, clear, or yellowish sputum is later produced. In some cases, the sputum is tinged with blood. Fatigue may be the first symptom, occurring even before dyspnea develops and manifest as the inability of the affected individual to maintain the pace of the group. In a study of 417 cases by Rao et al the majority of cases occurred in those who ascended rapidly especially by air travel, and in those who re-entered HA. The onset of symptoms occurred within a week and in majority it occurred within first three days of arrival at HA. In about 50% of cases symptom appeared within 12 hours and occurrence was rare after one week. The onset was earlier among reinducted individuals when compared with fresh arrivals. Five patients in the study developed symptoms immediately on arrival at HA.

Physical findings in HAPO include cyanosis, temperature as high as 101°F (38.5°C, a higher fever creates suspicion of pneumonia), flat neck veins, and crackles over the mid chest. Heart and respiratory rates are increased. In a large study conducted on soldiers of Indian Army posted at HA, cough (96%), breathlessness ((94%), headache (94%), fever (65%), expectoration (60%), chest pain (59%), bodyaches (48%), haemoptysis (37%), vomiting (34%), dizziness (30%) and anorexia (25%) were main features noted. Majority of patients complained of disturbed sleep

Table 1: Lake Louise Score of Acute Mountain Sickness

A. Questionnaire	B. Clinical assessment
1. Headache	6. Change in mental status
0. No headache	0. No change in mental status
1. Mild headache	1. Lethargy/lassitude
2. Moderate headache	2. Disoriented/confused
3. Severe headache	3. Stupor/confused
2. Gastrointestinal Symptoms	4. Coma
0. No GI symptom	7. Ataxia (heel to toe walking)
1. Poor appetite or nausea	0. No ataxia
2. Moderate nausea and vomiting	1. Maneuvers to maintain balance
3. Severe nausea or vomiting, incapacitating	2. Steps offline
3. Fatigue and/or weakness	3. Falls down
0. Not tired or weak	4. Cannot stand
1. Mild fatigue/ weakness	8. Peripheral Oedema
2. Severe fatigue/ weakness incapacitating	0. No peripheral oedema
4. Dizziness/ Lightheadedness	1. Peripheral oedema at one location
0. Not dizzy	2. Peripheral oedema at two or more location
1. Mild dizziness	**C. Functional score**
2. Moderate dizziness	Overall if you had any symptoms how did they affect your activities?
3. Severe dizziness, incapacitating	0. Not at all
5. Difficulty sleeping	1. Mild reduction
0. Slept as well as usual	2. Moderate reduction
1. Did not sleep as well as usual	3. Severe reduction
2. Woke many times, poor sleep	
3. Could not sleep	

and decreased urinary output was also reported after onset of symptoms. Rao et al classified HAPO in to three grades of severity on clinical criteria (Table 2).

On examination, patient is sick looking with tachyponea and tachycardia. The presence of altered sensorium may indicate underlying cerebral oedema and presence of cyanosis also indicate severe disease. On auscultation of chest, the extent of crepitation will depend on severity of the disease. Fine crepitations at bases of lung are audible in early part and resolving disease. The presence of fine crepitations in the interscapular area has been reported as earliest auscultatory clinical finding of HAPO. Signs of pulmonary arterial hypertension can also be present with

Table 2: Severity of High Altitude Pulmonary Oedema

	Mild	Moderate	Severe
Pulse (bmp)	<120	120-140	>140
Cyanosis	-	±	±
Respiratory rate (/min)	<40	40-50	>50
Conscious	Yes	Yes	Yes/No
Crepitations	<1/2 lung field	>1/2 lung field	>1/2 lung field

loud pulmonary component of second heart sound.

Lake Louis Consensus on definition of altitude illness defines HAPO as (in the presence of recent gain in altitude) the presence of at least 2 of 4 symptoms (dyspnoea at rest, cough, weakness or decreased exercise performance, and chest tightness or congestion) and any 2 of 4 signs (crackles/wheezing in at least one lung field, central cyanosis, tachypnoea and tachycardia).

Investigations may reveal mild to moderate polymorphonuclear leucocytosis. It ranges from 7000-28000 and may not be related to severity of HAPO. The mean pH, PO_2 and oxygen saturation may be 7.4, 34 mm Hg and 63% respectively and respiratory alkalosis. The ECG shows sinus tachycardia, right axis deviation, right atrial enlargement and T wave inversion in right precordial leads. Echocardiography may show dilatation of right ventricle and pulmonary artery and diastolic dysfunction of left ventricle.

The diagnosis of HAPO is based on history, clinical features and is confirmed by performing X-ray chest. X-ray chest can reveal bilateral soft fluffy, non-homogenous shadows which can be asymmetric. The involvement of right side of lung is more common, and mid and lower zones are also more commonly involved than upper zone. Main pulmonary trunk and right pulmonary artery are prominent. Lichtenstein et al reported the utility of Ultrasound Comet Tail Sign (UCTS) for detection of interstitial pulmonary edema resembling a comet with tail. Performing ultrasonography of chest routinely at HA has been able to diagnose subclinical HAPO by UCTS and correlates inversely with oxygen saturation. It is a useful in diagnosis of HAPO in early stage.

High Altitude Cerebral Dedema (HACO)

It is least common but most dangerous high altitude illness and is also called malignant acute mountain sickness. HACO in isolation is not common but it occurs usually in combination with HAPO. It should be suspected in patients of AMS with altered sensorium. The onset of ataxia is earliest. Dimmunition of vision, dizziness, drowsiness progressing to confusion and coma are other features noted. Psychiatric symptoms like mood changes and hallucinations have been noted. Seizures, incontinence or retention of urine have also been reported. The onset of HACO in AMS can occur in 1-3 days in untreated cases and alteration in level of consciousness is most important sign. It may be associated with VI and

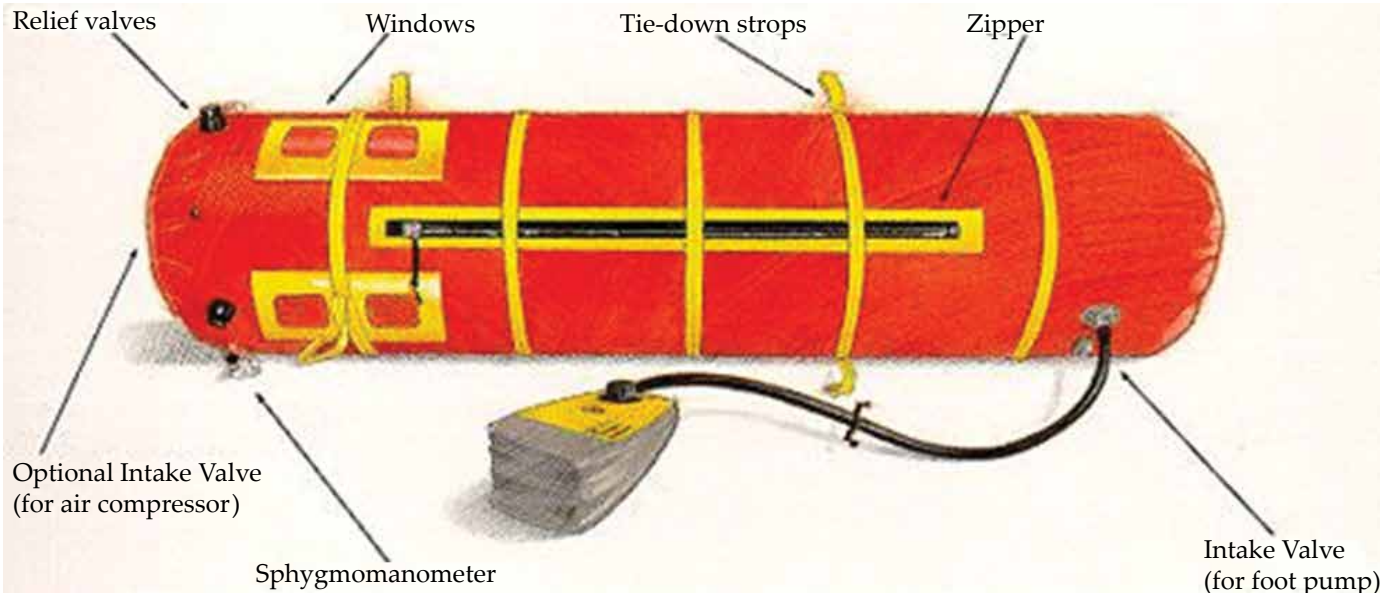

Fig. 1: Hyperbaric (Gamow) Bag

VII cranial nerve palsies, hemiparesis and changes in muscle tone. Ophthalmological examination can reveal venous engorgement, blurred margins of optic disc and papillioedema. The presence of papillioedema is specific to HACO.

HACO usually occur at isolated places often as an emergency where investigations are not available. The diagnosis is made on clinical picture and if available, x-ray chest may show co-existing HAPO.

TREATMENT

Benign Acute Mountain Sickness

In mild cases, rest, analgesics and cessation of ascent are sufficient and patient is asked to acclimatize at same altitude. Ibuprofen is helpful for HA headache, intramuscular prochlorperazine or promethazine orally are helpful for vomiting. However in severe cases or in those with progression of symptoms, descent is recommended and if not possible then hyperbaric bag should be used. Actazolamide 250 mg twice or thrice a day for 2-3 days is helpful; it is reported to be of use in insomnia also. Sedation and alcohol should be avoided. Low flow oxygen therapy at night is useful in treatment of mild AMS.

High Altitude Pulmonary Oedema

The evacuation of patient to lower altitude is the ideal treatment if it is not possible, oxygen therapy remains mainstay of treatment. In mild to moderate cases oxygen is delivered at high flow rate with face mask. It is continued till patient improves which is apparent within 1-2 hours of therapy and pulse rate is a sensitive indicator of response to therapy. The use of positive pressure masks have been shown to be beneficial also. Nifedipine (10 mg) orally every 4-6 hours or 20 mg sustain release every 12 hours reduces pulmonary artery pressure and is useful.

A portable lightweight, fabric hyperbaric bag called Gamow bag (American) or Certec bag (French) is available commercially for the emergency treatment of malignant HA illness (Figure 1). The patient is placed in the bag which is inflated with a foot pump. The pressure inside bag is raised above ambient atmospheric pressure which simulates descent. The exact descent simulated is directly related to the altitude of patient. At an altitude of 3000 m, the altitude simulated in bag is 1555 m whereas at 4500 m the altitude reached in bag is 2787 m. Hyperbaric chamber is also used for treatment of HAPO in which more than one patient can be placed and pressure inside is built up to sea level. In a study inhaled NO increased PaO_2 significantly and lead to faster clinical and radiological recovery. A combination of inhaled NO and O_2 was better than either alone. Ghofrani et al conducted a double blind randomized controlled trial which demonstrated the efficacy of oral sildenafil in reducing pulmonary artery systolic pressure at rest and during exercise at HA and it enhanced exercise capacity. Inhaled Beta-agonists have been found useful in prevention of HAPO by improving dynamics of oedema fluid removal from alveolar spaces, tightening of alveolar-capillary barrier and decreased vasoconstriction to hypoxia. The mortality due to HAPO was 2% in a series by Rao et al.

High Altitude Cerebral Oedema

High flow oxygen and rapid descent are indicated and if evacuation to lower altitude is not feasible, use of hyperbaric bag is life saving. Parenteral dexamethasone 8 mg stat followed by 4 mg every 6 hours is indicated. Other cerebral decongestants like parenteral mannitol, low dose furosemide and oral glycerol have been used even in the absence of evidence of their efficacy. Endotracheal intubation with ventilation is needed in patients in comma. Rao et al observed the mortality rate of 25% due to HACO even with adequate treatment.

High Altitude Retiopathy

The eye involvement is common at HA. Asymptomatic retinal hemorrhages can be seen in about one third cases and are related directly to altitude. The pathogenesis has been related to increased retinal flow that occurs with

Table 3: Summary of the Wilderness Altitude Illness Guidelines 2010

Prevention of AMS/ HAPO		Prevention of HACO	
Recommendation	**Grade**	**Recommendation**	**Grade**
Gradual ascent	1C	Gradual ascent	1B
Nifedipine 60 mg SR (Divided doses)	1A	Acetazolamide 125 mg BD	1A
Salmetrol 125 ug BD	2B	Dexamethasone	
Tadalafil 10 mg BD	1C	• 2mg 6h or 4 mg 12h	
Dexamethasone 16 mg (Divided doses)	1C	• Duration not more than 10 days	1A
Acetazolamide	2C	Ginko biloba	2C
		Cocoa leaves	NR
		Forced hydration	NR

Table 4: Acclimatisation Procedure

First stage

For > 2700 m up to 3600 m. Acclimatisation period up to 6 days

- 1st & 2nd day: Rest except short walk, not involving climb
- 3rd & 4th day: Walking at slow pace for 1 ½ -3 Km, avoid steep climbs
- 5th & 6th day: Can walk up to 5 Km and climb up to 300 m at slow pace

Second stage

For > 3600 m up to 4500 m. Acclimatisation period up to 4 days

- 1st & 2nd day: Slow walk of 1 ½ -3 Km, avoid steep climbs
- 3rd day: Slow walk and climb up to 300 m
- 34th day: Climb up to 300 m

Third stage

For > 4500 m. lasting for 4 days and is same as second stage

Reentry

For those who left HA for > 10 days, require acclimatization again

- Those who were away > 4 weeks, require full acclimatization
- Those who were away > 10 days but < 4 weeks, require acclimatization for 4 days at each step

- 1st & 2nd day: Rest except short walk
- 3rd day: Walking at slow pace for 1 -2 Km, avoid steep climbs

- 4th day: Walk 1-2 Km and climb up to 300 m

increased cerebral flow associated with acclimatization and are more commonly noted in fresh entrants. These usually disappear after descent. Hyperaemia of optic disc and venous congestion are very common. Papilloedema is usually associated with HACO.

PREVENTION OF ACUTE MOUNTAIN SICKNESS

The Wilderness Altitude Illness Guidelines 2010 described the prophylactic measures for prevention of AMS. Table 3 and Table 4 describes the acclimatization procedure for prevention of AMS.

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