

High Altitude Illness

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Introduction

The aims of this article are to outline the physiology of high altitude, the treatment of altitude illness and to describe the opportunities for further education in mountain medicine. This article updates a previous J R Army Med Corps article [1] drawing upon recently published consensus guidelines to update the therapeutics of the altitude-related illnesses.

Human difficulty with the rarefied air at high altitudes has been recognised since ancient times. Writing attributable to Aristotle (384-322 BC) describes travel on Mount Olympus in Macedonia: “Also, because the rarity of the air which was there did not fill them with breath, they were not able to survive there unless they applied moist sponges to their noses” [2]. International frontiers frequently follow geographic feature such as mountain ranges. This means that conflicts may well arise in high altitude areas (the European Alps of France and Italy in the Second World War, the Himalaya regions of India and Pakistan, and more recently the highlands of Afghanistan) with major implications for the conduct of military operations. Levels of high altitude may be defined as follows:

- High Altitude 2500-3500m
- Very High Altitude 3500-5800m
- Extremely High Altitude beyond 5800m

Physiology of altitude

Sudden exposure of an un-acclimatised individual to an altitude above 6000m will result in loss of consciousness within 10 minutes; that mountaineers can remain conscious at these altitudes and reach the summit of Mount Everest (8848m) without the use of supplementary oxygen bears witness to the remarkable adaptive changes that take place with acclimatisation to hypobaric hypoxia at extreme altitude. Acclimatisation is the process whereby people adjust to altitude hypoxia. The body makes a series of adjustments, which increase the delivery of available oxygen to cells, and increases the efficiency by which that oxygen is used. The most important component of acclimatisation is an increased rate and depth of breathing and this occurs relatively rapidly. Changes in bicarbonate concentration, haematocrit and haemoglobin occur over days to months.

Hyperventilation

Immediately on exposure to hypoxia the peripheral chemoreceptors in the carotid bodies stimulate the respiratory centres in the brainstem to increase ventilation. This hyperventilation causes a respiratory alkalosis, which initially limits the increase in ventilation by reducing the respiratory drive from the respiratory

chemoreceptor. Over the next few days however, the cerebrospinal fluid pH is normalised by a mechanism which is, as yet, not fully understood. The brake to ventilation is removed allowing further hyperventilation and ongoing defence of arterial PO₂.

Renal function and fluid balance

Rapidly after arrival at altitudes above 3500-4000m plasma volume is reduced by about 5% and this deficit would appear to persist for up to four months. Total body water is also reduced by around 5% probably due to a combination of decreased water intake, changes in thirst regulation, increased insensible losses and an inappropriately unchanged urine output. Sodium and potassium balance seems to be unchanged. Acute Mountain Sickness (AMS) is associated with an anti-diuresis and fluid retention which is partly responsible for the characteristic sign of peripheral oedema seen in this condition.

Haematological changes

The rapid reduction in plasma volume results in an increase in haemoglobin concentration whilst at the same time hypoxia stimulates renal and hepatic erythropoietin production resulting in erythropoiesis and increase in red cell mass.

Cardiovascular changes

It is possible to think of the purpose of acclimatisation as maintaining as near normal an oxygen delivery to the tissues as possible; central to this is the cardiovascular system. Acute exposure to high altitude results in an increase in heart rate and cardiac output both at rest and for a given amount of work compared to sea level. With acclimatisation heart rate and cardiac output return towards their sea level values at rest up to altitudes of approximately 4500m. Above this altitude resting heart rate tends to be higher than resting at sea-level rate. During exercise, for a given level of work, heart rate still remains elevated compared to sea level although cardiac output returns to sea level values. Thus stroke volume must be reduced despite myocardial contractility being well preserved. In general the normal heart tolerates even severe hypoxia very well. Cardiac arrhythmias are rare at altitude and even at extreme altitude the ECG shows only the changes of pulmonary hypertension. The increase in haemoglobin concentration which occurs as a result of plasma volume contraction and increased erythropoiesis has the effect of increasing the arterial oxygen content of the blood. Thus a well-acclimatised individual at altitudes up to 5500m will have a similar arterial oxygen content and therefore oxygen delivery at sea level.

Oxygen Consumption and Exercise

Maximal work, or oxygen consumption (VO₂max), decreases in increasing altitude. Up to 6000m a mountaineer functions at 50-75% of their VO₂max, but as altitude increases so the effort required

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for even simple physical tasks moves closer towards VO_2 max. On the summit of Mount Everest the VO_2 max is around 1.2 litres per minute, a work rate corresponding to walking slowly on the flat.

Acute Mountain Sickness

Acute Mountain Sickness (AMS) is defined by the Lake Louise consensus criteria [3] as the presence of a headache and at least one of the following symptoms after a recent increase in altitude: loss of appetite, nausea, vomiting, fatigue, weakness, dizziness, light-headedness or sleep disturbance. Typically the sleep disturbances include difficulty in onset of sleep, frequent waking and periodic breathing. Headache is throbbing, worse at night and early in the morning. Classically the AMS sufferer has a headache, is off their food and has difficulty sleeping. Rapid ascents to altitudes above 2500m will frequently cause AMS. There are no pathognomic clinical signs in AMS, but symptoms appear 6-12 hours after ascent, and usually resolve within three days if further ascent does not occur.

Treatment

AMS is a mild altitude illness and is more of a nuisance in that it delays progression towards the object of the exercise. The major concern in identifying AMS is that it may lead to life threatening high altitude cerebral oedema (HACE) or high altitude pulmonary oedema (HAPE). Principles of treatment (Figure 1):

- Stop further ascent
- Descend if there is no improvement or if the condition worsens. 500-1000m of descent is usually sufficient to rapidly reverse the symptoms of AMS.
- Descend immediately if there are symptoms or signs of cerebral or pulmonary oedema.

When symptoms are mild, rest alone is often sufficient for symptoms to resolve. Aspirin, ibuprofen or paracetamol may relieve headache and antiemetics may be useful for symptomatic relief.

If symptoms are severe then the subject must descend to a lower altitude. If descent is not practical (due to position or clinical situation) then the following treatments may be beneficial: oxygen given by Hudson type mask at 1-2 litres per minute or simulated descent in a portable hyperbaric chamber (PHC) will relieve symptoms when descent is impossible due to weather or terrain constraints. Drug therapy may improve symptoms, allowing a patient to walk out rather than be carried. Oral acetazolamide 250mg twice daily [4] and dexamethasone (4mg four times daily, orally or intramuscularly) are both appropriate, (paediatric dose 2.5 mg/kg 12hrly [5]). The patient with AMS should never be left alone as the condition may progress to HACE or HAPE, and descent should be to an altitude lower than that where the symptoms began.

High Altitude Cerebral Oedema

High Altitude Cerebral Oedema (HACE) is rare but life threatening occurring in 1-2% of those who ascend rapidly to 4500m [6]. HACE and AMS are thought to be opposite ends of the same disease spectrum, and AMS usually precedes HACE. It is unusual below 3500m but has occurred as low as 2500m. When death occurs it is due to brainstem herniation.

Signs and symptoms

HACE is characterised by ataxia and altered consciousness. The classic HACE victim progresses from AMS to become confused,

disorientated, irrational and ataxic. The victim then begins to hallucinate. Lethargy progresses to coma, and death follows rapidly if emergency treatment is not commenced. Even when treated successfully it should be noted that ataxia may persist for some days afterwards before the person returns entirely to normal and cases with residual neurological deficit have been reported. These may be cases of 'non HACE neurological problems of altitude'.

High altitude pulmonary oedema (HAPE) may occur concurrently with HACE, and should be treated if present.

Treatment

Descent is imperative. Although exhaustion, dehydration, hypothermia, alcohol hangover or migraine may mimic AMS and HACE, any suspicion of HACE mandates immediate descent [7]. Heel-toe walking in a straight line is a simple tool to gauge ataxia. The Sharpened Romberg Test has also been shown to reliably demonstrate ataxia in the field as part of a clinical examination [8]. Dexamethasone should be given intramuscularly, intravenously, or orally if the patient is not vomiting. The initial dose is 8mg followed by 4mg six-hourly [9] (paediatric dose 0.15 mg/kg/dose 6 hourly [5]). This will provide symptomatic relief in order to facilitate descent; it does not treat the underlying cause of the condition (hypoxia). When descent cannot proceed immediately either due to weather, terrain or other safety constraints, or due to the condition of the patient, then oxygen and drugs must be administered regularly and prolonged hyperbaric treatment must continue. Once the patient has been successfully treated and evacuated to a lower altitude, review by a medical practitioner as early as possible is mandatory.

High Altitude Pulmonary Oedema

High Altitude Pulmonary Oedema (HAPE) is usually provoked by very rapid ascent to high altitude. In one study, 10% of climbers ascending very rapidly (e.g. by helicopter) to 4500m developed HAPE [10]. With usual ascent profiles only 1-2% of climbers would be expected to develop HAPE in ascending to the same altitude. It is concerning that climbers at extreme high altitude on occasion develop HAPE, the common situation being that they have acclimatised to 5500m, but then develop HAPE during rapid ascent to 7000m or more.

Signs and symptoms

The hallmark of HAPE is disproportionate dyspnoea. HAPE may be preceded by AMS, but may occur in isolation. Exertional dyspnoea and reduced exercise tolerance occur, which are worse than that expected for the altitude or worse than that of the victim's expedition peers. This progresses to disproportionate dyspnoea and tachypnoea, at rest, worse at night. Early symptoms of HAPE include an annoying dry cough, which may be indistinguishable from the usual cough experienced at high altitude. As the condition progresses, the cough becomes bubbly and wet with sputum which may be bloodstained. Tachycardia and tachypnoea occur at rest and it is possible to hear crackles in the lung fields with a stethoscope. There may be a mild fever (commonly less than 38.5°C), and for this reason it may be difficult to differentiate HAPE from pulmonary oedema. The measurement of arterial oxygen saturation (SpO_2) in itself will not confirm a diagnosis of HAPE, but SpO_2 can be used to mark the progression of the condition once treatment has commenced [11]. A fingertip probe such as the Nonin Onyx TM (Nonin Medical Inc., 13700 1st Avenue North, Plymouth, Minnesota, USA) is compact and ideal.

Treatment

Oxygen must be given immediately if available, and descent commenced [12]. Ideally, oxygen should be titrated until SpO₂ reaches 90%, but care must be taken in conserving oxygen supplies for the expected duration of treatment, prior to evacuation [13]. If available, Continuous Positive Airway Pressure (CPAP) should be used as an adjunct to supplemental oxygen therapy. Exertion and cold exacerbate HAPE through an increased sympathetic drive causing further pulmonary vasoconstriction. The patient should ideally be carried in a sitting position and kept warm. Nifedipine should be given by mouth in the dosage of 60mg slow release preparation daily in divided doses: 30mg SR twice daily, or 20mg SR three times daily [14].

There are currently no trials that have confirmed the proposed benefit of phosphodiesterase inhibitors in HAPE treatment. However there is strong rationale for their use as they cause pulmonary dilatation and decrease pulmonary artery pressure. Tadalafil 10mg twice daily or sildenafil 50mg three times daily are appropriate doses where the use of these drugs has been recorded in the treatment of HAPE [15]. Salmeterol has also been employed in the treatment of HAPE [15]. It should be administered by inhalation in the dose of 125 micrograms twice daily. However, it is not to be used as monotherapy and should only be used in conjunction with oral medication.

Dexamethasone should be added to the regime when HACE co-exists with HAPE, in the same treatment dose as for stand-

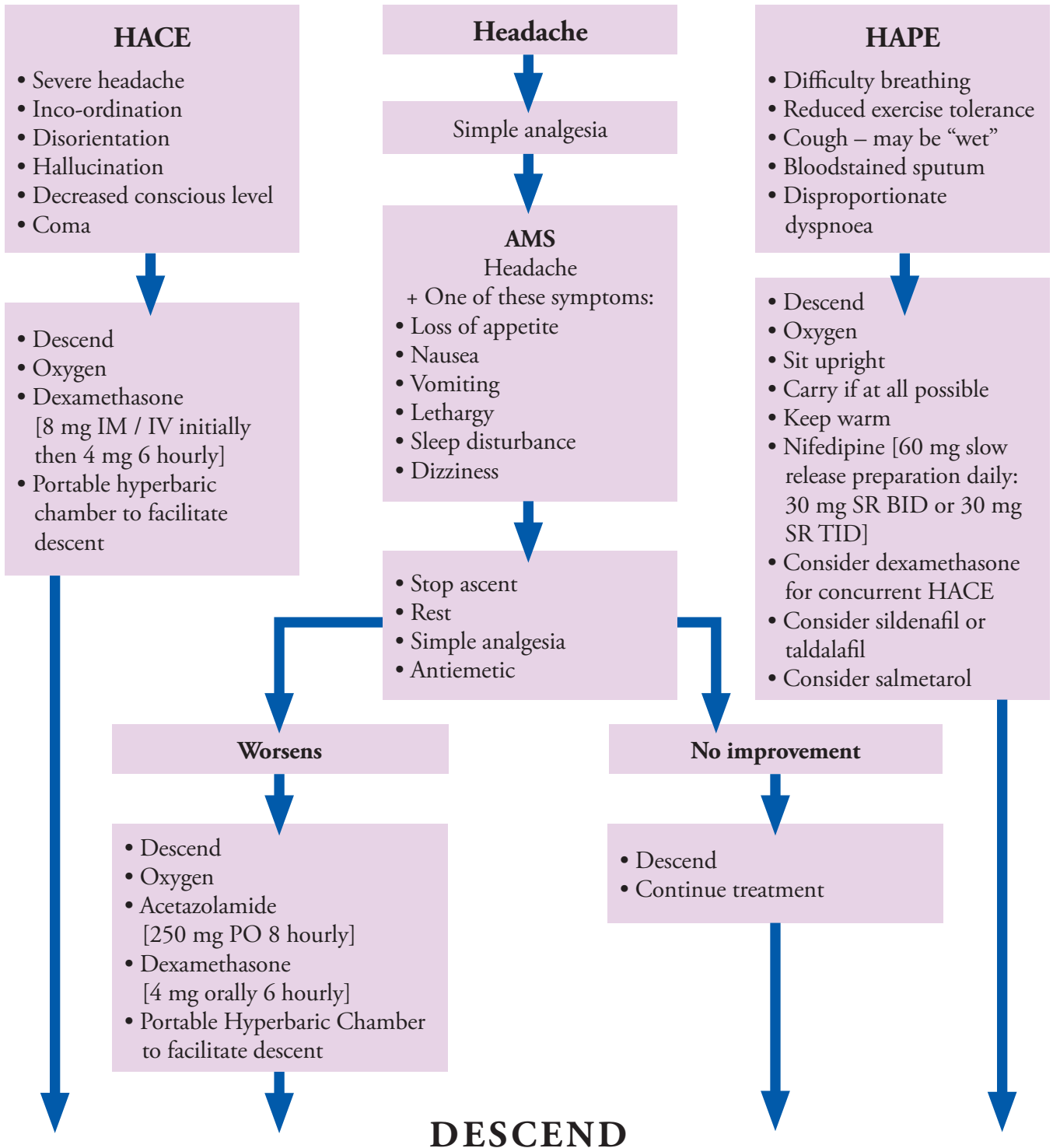


Figure 1. Universal Altitude Illness Treatment Algorithm

alone HACE. Note that when these two conditions co-exist, nifedipine may induce hypotension, which in turn may reduce cerebral perfusion and cause further abnormal neurological function. If immediate evacuation is impossible, then similar considerations as HACE should be observed. HAPE is considered in more detail elsewhere in this journal [16]

Hyperbaric Therapy and the Portable Hyperbaric Chamber

Portable hyperbaric chambers have been in use since the late 1980s [17]. Currently there are three models available: the Gamow bag, the CERTEC bag, and the Portable Altitude Chamber (PAC). The apparatus consists of a conical or cylindrical fabric bag that is capable of being pressurised by a hand or foot driven pump. The patient is placed inside the bag lying flat. Each kit is lightweight and robust and weighs around 7kg in total. The patient is zipped within the bag and pump strokes are made continuously to maintain the internal pressure at between 105 and 165 mmHg depending upon the model of bag. The air around the patient is thus pressurised. In this way the PHC stimulates descent. Used correctly at 6000m, the apparent altitude within the bag can be reduced to between 3500m and 3000m. Because of this, dramatic improvement can be produced in a patient with AMS, HACE or HAPE. Care must be taken if the patient is vomiting and, therefore, at risk in an enclosed bag. Instruction must be given in ear decompression by valsalva manoeuvre. It can be useful for the patient to take an altimeter into the chamber with them and to hold it up to the window to indicate the virtual descent that has been achieved. Patient with HAPE may not tolerate the supine position and so the whole bag may need to be inclined to alleviate their distress. This can be improvised in the field using articles of camp equipment. One to two hours treatment is required to cause sufficient clinical improvement for a patient to be able to descend more easily. The benefit is short-lived outside of the bag, and will last no longer than 10 hours. When descent is not possible the hyperbaric therapy should be repeated at intervals of no less than five hours [12]. Irrespective of the benefit from hyperbaric therapy, any patient who has been sick enough to require this form of treatment must descend as soon as practicable to an altitude below that which symptoms began, and re-ascent must only take place after consultation with a medical practitioner familiar with altitude medicine.

Prevention of altitude illness

The key to the prevention of altitude illness is to allow acclimatisation to proceed. The adoption of a safe ascent profile is essential. Some people acclimatise rapidly, while others develop acute mountain sickness and require longer period of time to acclimatise. If someone has been a slow acclimatiser on the journey, then it should be expected that the same pattern would repeat on subsequent trips. It is therefore important to allow party members to acclimatise at their own pace. Successful acclimatisation has occurred when the symptoms of AMS disappear and sleep becomes more settled. Further ascent to a higher altitude will require further acclimatisation, and on descent to lower altitude the beneficial effects will last no longer than eight days. Rapid ascent to high altitudes should be avoided. If absolutely necessary, exercise should be kept to an absolute minimum on subsequent days after arrival at altitude. The optimum is a graded ascent. Above 3000m, sleeping

altitude should be sited at an elevation no more than 500m above that of the previous night. A rest day should be taken after every third or fourth day. Further ascent should not proceed in individuals who are experiencing symptoms of AMS. These individuals must be supervised by a companion, and not left alone. Descent must be considered as life threatening altitude illness (HACE, HAPE) may supervene.

Risk	Description
Low	Individuals with no prior history of altitude illness and ascending to \leq 2800m Individuals taking \geq 2 days to arrive 2500-3000m, with subsequent increases in sleeping elevation $<$ 500m per day
Moderate	Individuals with no prior history of AMS and ascending to 2500-2800m in 1 day No history of AMS and ascending to $>$ 2800m in 1 day All individuals ascending $>$ 500m per day (increase in sleeping elevation) above 3000m
High	History of AMS and ascending to \geq 2800m in 1 day All individuals with a prior history of HAPE or HACE All individuals ascending to $>$ 3500m in 1 day All individuals ascending $>$ 500m per day (increase in sleeping elevation) above $>$ 3500m Very rapid ascents (e.g. commercial expeditions to Kilimanjaro)

Table 1: Risk categories for acute mountain sickness [18]

Chemoprophylaxis

Table 1 serves as a tool for assessing the need for chemoprophylaxis. In low risk situations chemoprophylaxis is not necessary as individuals should acclimatise through adopting a gradual ascent profile. The use of prophylactic medication should be considered when a moderate or high risk exists, and these situations can be summarised as follows:

- When the ascent profile is likely to provoke altitude illness through forced rapid ascent, e.g. flying or driving to high altitude due to time of logistical constraints, or when a rescue mission is initiated and personnel have to move rapidly to high altitude.
- In those personnel who have a proven susceptibility to AMS or HAPE through previous exposure to high altitude.
- During military operations where personnel may be air-lifted to altitudes of 3500m or more, and be expected to undertake immediate physical activity.

Acetazolamide is the preferred agent. The standard regime is 125mg twice daily [18] (paediatric dose 2.5mg/kg twice daily [5]), commencing 24 hours prior to ascent. Other regimes are quoted, but maximal efficacy will be achieved with this regime. Dexamethasone may be used as an alternative, or given in conjunction with acetazolamide in the dose of 4mg twice daily, or 2mg four times daily [18]. Maximum use should not exceed 10 days to prevent glucocorticoid toxicity or adrenal suppression.

Dexamethasone should not be used prophylactically in children, due to side effects unique to this age group and the availability of safer alternatives.

When chemoprophylaxis is employed, acetazolamide should be started the day before ascent, and dexamethasone on the day of ascent. When individuals will remain at elevation for many days, prophylaxis should be discontinued two to three days after reaching target altitude. When the itinerary involves ascent to a projected high point, followed by descent, then prophylaxis should be discontinued once descent has commenced [18].

HAPE prophylaxis

Drug prophylaxis should only be considered for individuals with a proven susceptibility to HAPE. Nifedipine is the preferred option in such cases. It should be commenced on the day prior to ascent and continued until descent is initiated, or maintained for five days if a particular target altitude has been reached [18].

In those individuals who develop HAPE, further ascent or re-ascent should only be commenced once their symptoms have resolved, they maintain stable oxygenation at rest and with mild exercise whilst off supplemental oxygen therapy and vasodilators. One case report describes the use of a combination of salmeterol, acetazolamide and sildenafil as chemoprophylaxis in a successful ascent of Mt Everest in a climber who had suffered an episode of HAPE on that mountain some three weeks previously during a previous attempt on the summit [19].

Activity at Extreme Altitude

Adults can fully acclimatise to about 5000m-5800m. Above this there is a trade off between adjustments to altitude and deterioration due to prolonged hypoxia. Above 8000m, no acclimatisation occurs at all and a prolonged stay at that altitude is incompatible with life. Despite being fully acclimatised, prolonged exposure to heights above 7000m in excess of 3-4 days should be avoided as the physical and psychological stress becomes greatly exacerbated. Typical features include progressive weight loss, worsening appetite, poor sleep and increasing apathy. Minor ailments such as a viral sore throat or chest infection, that would simply be inconvenient at lower elevations, become more significant at extreme altitude and contribute to the overall malaise of the individual. For those expeditions going to extreme altitude, the base camp should be sited at or below 5000m when possible, so that proper recovery can take place, between sorties to higher elevations.

Altitude Medicine

In both Mountain Medicine and Military Medicine the environment frequently dictates the management of the patient. This requires a doctor who is capable of working without immediate support from colleagues and who can adapt protocols to the conditions and terrain encountered.

To work in an extreme environment the first essential is to be confident in that environment. The best training for mountain medicine is to be familiar with the mountain environment in all its guises. One needs to build up experience in all aspects of the sport in summer and winter, by day and night, at all altitudes from sea cliffs to high mountains, on foot and on skis.

Most expedition medical problems, are, in fact, minor and involve a large psychological element and, therefore, experience in general practice is extremely useful. Emergency Medicine and Critical Care are disciplines that will develop confidence

and practice in managing traumatic injury and life threatening illness, as well as minor injuries and ailments. Pre-Hospital Care experience makes one aware of environmental risks [20].

Professional organisations relevant to mountain medicine are: The British Association for Immediate Care (BASICS – <http://www.basics.org.uk>), the British Travel Health Association (BTHA – <http://www.btha.org>), The International Society for Mountain Medicine (ISMM – <http://www.ismm.org>) with its journal 'High Altitude Medicine and Biology', and the USA based Wilderness Medicine Society (WMS – <http://www.wms.org.uk>) with its journal 'Wilderness and Environmental Medicine'.

The Diploma of Mountain Medicine is coordinated at an international level by the Union Internationale des Associations d'Alpinisme Medical Commission (UIAA Medcom). Currently about 2000 doctors hold this worldwide, and in the UK it is administered by Medical Expeditions (<http://www.medex.org.uk>) [21]. It is no coincidence that 50% of the syllabus involves mountain skills [22] but there is input via national universities with rigorous and robust academic assessment as well as mountain skill assessment [23, 24]. The UIAA diploma is currently offered in France, Spain, Switzerland, Italy, Austria, Germany and the Netherlands [25]. In the USA the WMS runs relevant courses and some universities are setting up programmes [26].

It is neither possible, nor desirable, to have doctors available in all remote areas so high quality training is needed for lay mountaineers [27]. These climbers need to understand the principles of altitude and remote area medicine and to be competent to administer life saving medication to buy time for descent.

Further Reading

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Conflict of Interest

All authors are faculty of the UK UIAA/IKAR/ISMM Diploma of Mountain Medicine. DH and PR undertake part time work as medical advisors to a Commercial Expedition Company (Jagged Globe).