

Medicine at high altitude

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ABSTRACT – Medicine at high altitude provides important insights into the acute and chronic effects of hypoxia. Acute mountain sickness (AMS) is a common syndrome occurring after acute ascent to over 2,500 m and is caused by increased capillary permeability. A number of factors have been identified that increase the risk of AMS, in particular exercise. Avoiding rapid ascent, undue exercise and the use of acetazolamide are useful preventative measures but severe symptoms may require oxygen, dexamethasone and descent. Acute mountain sickness is usually self-limiting but may progress into the serious syndromes of pulmonary and cerebral oedema. Acclimatisation and adaptation are important for workers and residents at high altitude and the improvement seen in maximum exercise has been incorporated into some training schedules for endurance athletes. Chronic and subacute high-altitude diseases largely result from polycythemia and pulmonary hypertension.

KEY WORDS: acclimatisation, acute mountain sickness, high altitude, hypoxia

Introduction

*You are one person in one place, another in another. At the Alta Vista, I became as one incapable of arithmetic...*¹

High-altitude mountaineering medicine is important for anyone drawn to such areas of the world

especially trekkers,² climbers, miners, military personnel and astronomers³ and more recently high altitude has become of considerable interest for endurance sports training.⁴ Why sleep high, train low and sleep low, work high? Why do domestic cattle get brisket disease at altitude but yaks are protected? These are two of the fascinating lessons learnt from studies at high altitude. Convincing colleagues that study leave is justified for conferences and research in the Alps, Andes, Himalayas or Rockies can be difficult and some remain sceptical even when shown the resulting Beau's lines in the nails,⁵ when told of the terrors of long nights disturbed with periodic breathing⁶ and of the ignominy of descent when ill.⁷ Hypobaric chambers can provide some of the answers but simulating long periods of exposure in cramped conditions is difficult and unpleasant. The medical problems of altitude largely stem from hypoxia (Fig 1) but in such environments there are also risks of dehydration, accidental injury, cold injury, weight loss and psychological stress. Many visitors still suffer unnecessarily from the effects of acute exposure to high altitude, largely through ignorance, poor advice or poor leadership. The recently established Diploma in Mountain Medicine in the UK will help correct some of these problems.⁹

The history of high-altitude physiology and medicine has been skilfully assembled by John West.¹⁰ Modern high-altitude physiology dates from Paul Bert,¹¹ Claude Bernard's successor in the Chair of Physiology at the Sorbonne, who proved that the harmful effects of high altitude were caused by low partial pressure of oxygen. We now know that the alternative explanation based on the suggested primary role of hypocapnoea¹² is of secondary importance. Both gases are relevant and have contrasting effects, best illustrated by the hypoxic vasodilatation and hypocapnoeic vasoconstriction of the cerebral arteries and the opposite effects on the pulmonary arteries. Much of the pathology of acute altitude-related illnesses is due to increased capillary permeability¹³ and therefore there is considerable interest in the role of key factors such as arterial and capillary pressures and flow, vascular permeability factors such as vascular endothelial growth factor (VEGF), oxygen sensing mechanisms and the responses of hypoxia inducible factors (HIF), HIF-1 alpha and HIF-1 beta. The pathology of chronic altitude illnesses is due to long-term adaptation to hypoxia, highlighting the

WIDER HORIZONS IN MEDICINE

The annual Advanced Medicine conference held at the Royal College of Physicians has been a continuing success. After the 25th conference in 1989 the manuscripts were published in a volume entitled *Horizons in medicine*. This is now a classic publication, indeed a reviewer recently commented that:

Any physician who has this series on his or her bookshelf, and has read each volume, can truly claim to be keeping up to date.

Humphrey Hodgson, *Clinical Medicine*

This familiar title has been adapted for a new Journal series concerned with contributions to clinical medicine in spheres beyond the conventional. The series illustrates the remarkable breadth of opportunities that still exist for those with enterprise, enthusiasm and flare.

This series opens with a contribution from Alex Wright concerning the challenges and rewards of mountaineering medicine. While it may be romantic in concept, he shows that it is more commonly exciting, demanding, challenging and extremely tough. Individuals are encouraged to submit their own contributions to the Journal for consideration.

role of hypoxia in respiration, angiogenesis, erythropoietin production and muscle metabolism.

Acute altitude illness

Clinical features and epidemiology

Acute mountain sickness (AMS) has been well reviewed with useful bibliographies and website addresses.^{14,15} Symptoms of headache, anorexia, nausea, vomiting, fatigue, dizziness and sleep disturbance commonly occur 6–12 hours after acute ascent to more than 2,500 m. Symptoms are avoided in commercial aircraft, maintained at a pressure of 2,000–3,000 m, but the altitude of the Alta Vista hut on Tenerife (3,500 m) is sufficient to cause significant symptoms, as reported by Barcroft¹ while he was studying oxyhaemoglobin dissociation curves. Individual susceptibility to AMS varies considerably with a prevalence rate ranging from 10–50% depending on the altitude achieved and the rate of ascent. In our experience AMS occurs with moderate symptoms in about a third of a group, mild symptoms in another third and none in the remainder. It probably occurs more commonly in the young and in the obese but it is unrelated to physical fitness, smoking, heart disease or hypertension. Useful guidelines have been published on the particular problems that women may suffer at high altitude¹⁶ but the risk of

Key Points

Acute mountain sickness (AMS) is a common syndrome occurring after acute ascent to over 2,500 m

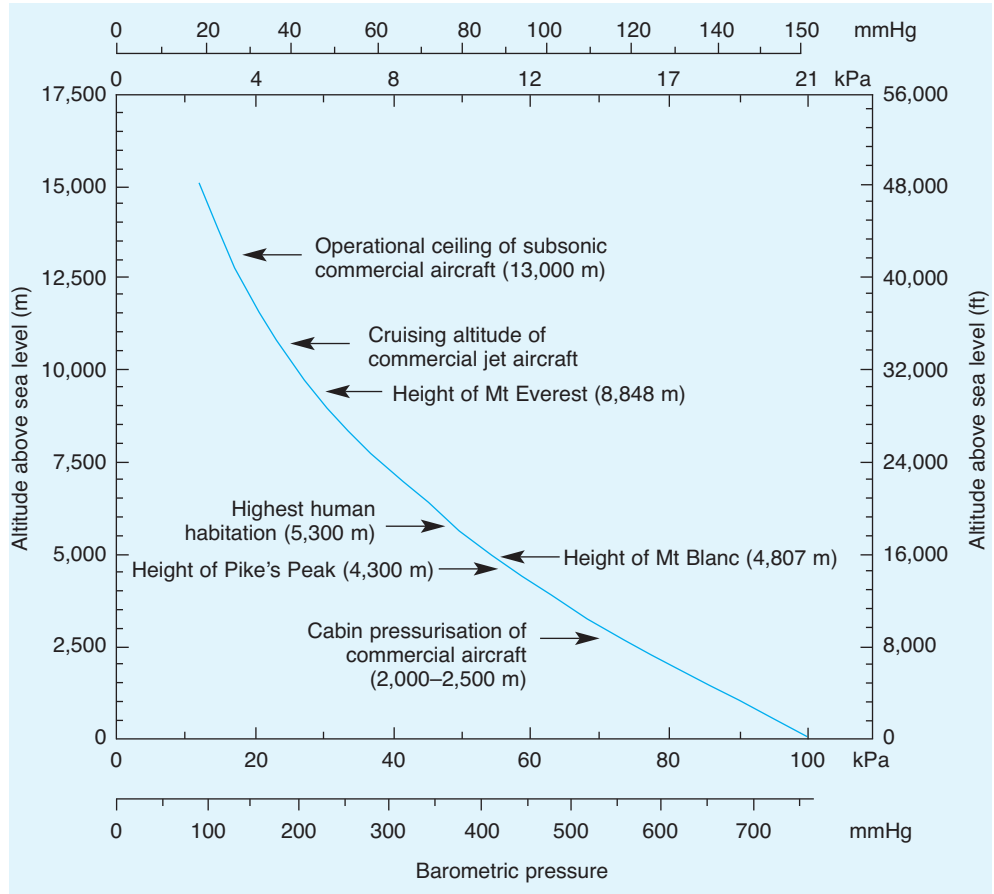
AMS is usually self-limiting but requires careful management including adequate preventative measures

Acute pulmonary and cerebral oedema are serious and potentially fatal syndromes

Acclimatisation and adaptation to high altitude are important for those working and living at altitude but may result in chronic and subacute high-altitude disease

AMS is the same for both sexes. A number of factors may exacerbate the hypoxia including exercise, sleep disturbance (especially combined with obesity), low ventilatory drive, respiratory infections and other lung disease, arterio-venous shunting and pulmonary oedema. Symptoms of AMS usually settle after two or three days acclimatisation, but this relatively benign form of AMS may progress rapidly to one of two potentially fatal forms of altitude illness – high-altitude pulmonary oedema (HAPE) and high-altitude cerebral oedema (HACE).

Fig 1. Altitude and partial pressure of oxygen. Reproduced with kind permission of Oxford University Press.⁸



Pathogenesis of AMS (Fig 2)

It is likely that there is a genetic predisposition to AMS but angiotensin-converting enzyme genotype is not associated with AMS even though it is related to successful high-altitude performance.¹⁷ Vascular endothelial growth factor is a possible cause of AMS but plasma levels do not correlate with symptoms scores. Low concentrations of the scavenger VEGF receptor SFlt-1, however, which binds circulating VEGF, may predispose some subjects to AMS.¹⁸ We have been particularly interested in the effect of exercise at altitude (Fig 3) and have shown that falling cerebral oxygenation and oxygen delivery may limit exercise at altitude and contribute to the problems of AMS and HACE.¹⁹ The rise in cerebral blood flow occurring on acute ascent does not appear to relate directly to AMS²⁰ (Fig 4), and intracranial pressure changes are also not the immediate cause of uncomplicated AMS.²¹

Management of AMS

Prophylaxis. Once above 3,000 m, the best preventive measure is limitation of the daily rate of ascent to 300–600 m and to have a rest day for every 1,000 m gained. Advising on drug prophylaxis is made easier if there is known previous exposure to high altitude as AMS tends to recur in similar conditions. Susceptible individuals should be offered acetazolamide²² and the dose should be at least 125 mg twice daily, starting one day before ascent.²³ Dexamethasone is also effective²⁴ but with more potential side effects.

Acute symptoms. For mild symptoms analgesics, anti-emetics, plenty of fluid and a rest before further ascent should be sufficient. For severe symptoms, such as vomiting and confusion, or if symptoms worsen, descent should be arranged. If immediate descent is impractical consider oxygen therapy, a compression bag or dexamethasone with or without acetazolamide²⁵ if not already taken.

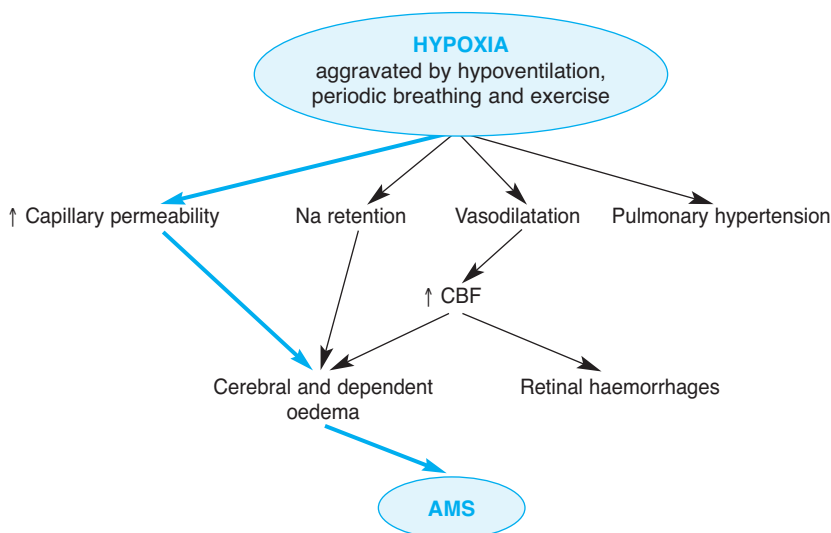


Fig 2. Pathogenesis of acute mountain sickness (AMS). CBF = cerebral blood flow.

High-altitude cerebral oedema²⁶

Symptoms of AMS may not necessarily precede HACE and indeed it may appear in well acclimatised climbers, as surveys show that HACE occurs in approximately 0.5–1% of subjects above 4,000 m. This serious altitude illness may develop secondarily to high-altitude pulmonary oedema but, unlike HAPE, no pre-existing physiological abnormalities have been identified as risk factors. HACE is thought to be due to vasogenic oedema. Symptoms include confusion, hallucinations, disorientation, ataxia, focal neurological signs, seizures and can lead to coma and death. Urgent treatment is required and descent essential as soon as is practical. Dexamethasone 8 mg followed by 4 mg six-hourly and oxygen, if available, should be started immediately. Prevention of HACE is the same as for AMS but at extreme altitude, where the onset may be abrupt, some climbers use dexamethasone prophylactically for summit days.

High-altitude pulmonary oedema^{27,28}

This serious altitude illness occurs in approximately 2% of subjects above 4,000 m. Symptoms include dyspnoea on exertion progressing into dyspnoea at rest, cough, signs of pulmonary oedema, and it can lead to coma and death. HAPE is related to, and to some extent can be predicted by, the pulmonary artery response to either hypoxia or exercise or both combined and indeed exercise is an important contributing factor. HAPE is not related to hypoxic ventilatory drive or other pulmonary function tests. The hypoxic rise in human pulmonary artery pressure is not seen in all animals.²⁹ For example, yaks appear to be adapted to altitude by augmented endogenous nitric oxide production. Higher nitric oxide levels have also been found in high-altitude natives.³⁰ HAPE requires urgent treatment and descent is essential once treatment has been started. Oxygen is helpful if available, and nifedipine 10 mg stat followed by 20 mg sustained-release may relieve symptoms. Phosphodiesterase type-5 inhibitors may also be used to reduce pulmonary artery pressure.

Chronic and subacute high-altitude disease³¹

Chronic hypoxia in high-altitude residents often results in pulmonary hypertension and polycythemia which are accompanied by headache, fatigue, dizziness, dyspnoea, sleep disturbances and bone and muscle pain. Cerebral thrombosis may occur and pulmonary hypertension may result in right heart failure. Increasing haemoglobin concentrations allows greater oxygen extraction which is maximal at arterial oxygen saturation of 87% and haemoglobin concentration of 17.5g/dl. Syndromes of subacute mountain sickness have been described³² consisting of severe hypoxic pulmonary hypertension and heart failure.

Acclimatisation

Acclimatisation to altitude usually refers to the 'beneficial' changes in response to hypoxia. Some changes are rapid, such as ventilation and acid-base balance over 1–20 days, and others, such as haemoglobin concentrations, occur over six weeks. 'Sleep high–train low' for endurance sports⁴ is based on the finding of an approximate 3% improvement in VO_{2max} after residing at altitude, though the increase is quite variable and may be less in elite athletes. Those that respond also show a greater erythropoietin response. At least 12 hours a day for more than three weeks at an altitude of 2,000–2,500 m is required for optimum effect. Higher altitudes may be associated with a decrease in performance.

Unanswered questions

We still do not know what makes some subjects susceptible to AMS or to HACE and so we are unable to predict the risks of high altitude. The exact mechanism linking hypoxia to increased capillary permeability requires further study which may lead to more effective treatments. The variability of acclimatisation and effects of altitude on athletic performance, the many roles of erythropoietin, the male predominance of Monge disease sufferers and how native Tibetan, Ladakhi, Aymara and Quechua people have adapted to living at high altitude also require further study.

Conclusions

No one can deny there is a certain romance in mountain medicine, especially when sitting comfortably at sea level, recounting epic travel adventures, admiring glorious mountain pictures and possibly even in reading this article. The reality is a special form of medicine in a tough, hostile environment, often remote and isolated, where human physiology may be strained to the limit and where serious illness, trauma and fatalities may occur.³³ Acute and chronic syndromes are important clinical entities deserving further research and their study provides important insights into the fundamental challenges of hypoxia.

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Fig 3. Pugh's portable exercise cycle at Gorak Shep (Everest) 5,076 m.



Fig 4. Author having cerebral blood flow measured at 5,430 m.

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