TRAVEL MEDICINE

(8) ENVIRONMENTAL HAZARDS

By Larry Goodyer, PhD, MRPharmS

Travellers should be aware of the dangers associated with exposure to extreme environmental conditions. This article focuses on acclimatisation and the managment of problems associated with travelling in hot climates and to high altitudes

Until recently, the dangers of exposure to extremes in environmental conditions were mainly of concern to people undertaking scientific or military expeditions, those involved in special outdoor pursuits, such as mountaineering, and to expatriate workers. However, the "adventure holiday" is becoming increasingly popular and a wider range of travellers may be exposed to extremes of temperature and high altitudes.

This article outlines the appropriate advice that pharmacists can offer to travellers to reduce the physiological risks associated with exposure to such conditions.

Dr Goodyer is director of pharmacy practice research at King's college London, and superintendent of Nomad Travel Pharmacy

The drug management of altitude sickness will be examined as an area of particular interest to pharmacists. Travelling to cold environments and diving will also be briefly considered.

There are three broad themes that run through this review:

- The prevention of potential problems by careful preparation and by observing some simple rules concerning acclimatisation
- Avoiding situations that could overwhelm normal temperature control homeostatic mechanisms. (It is particularly important that those who might have impaired homeostatic mechanisms, such as the elderly, are aware of such problems)
- Management of conditions caused by environmental extremes

ACCLIMATISATION TO HOT CLIMATES

Those travelling from temperate to hot climates may be unaware of the dangers associated with exposure before acclimatisation has occurred and of the long-term risks associated with undertaking a great deal of physical activity. It sometimes helps to consider the various types of hot climate to devise strategies to minimise the risk.[1]

In hot, wet climates such as the tropics, particularly rain forests, there is little variation in day and night time temperatures, combined with high humidity. In hot, dry climates, such as deserts, the temperature can fall dramatically at night, and humidity is low.

The body possesses the ability to survive in these types of climate, however, the necessary thermoregulatory mechanisms can take some time to develop if travelling from temperate regions. When environmental temperature exceeds body temperature, the most effective means of heat loss is evaporation of sweat from the surface of the skin. It is failure of the sweating mechanism that causes most problems for travellers. After arriving at a destination with a high ambient temperature, the sweat glands adapt and start to increase their output. On continued exposure to high temperatures, the kidney will begin to retain more sodium, and hence more water.

The key point is that time is required for these adaptations to take place. Acclimatisation is crucial in hot, wet climates where evaporation of sweat is more difficult and, unlike desert conditions, there is no period of "rest" for the sweat mechanism at night. Factors associated with heat-induced illness, which are particularly important in the first week of exposure, are summarised in Table 1. It should be noted that full acclimatisation can take up to three weeks to occur.

Heat stroke and heat exhaustion Heat stroke and heat exhaustion are sometimes confused. They broadly describe a breakdown in the body's thermoregulatory mechanisms, either caused by these mechansims becoming overloaded or by poor acclimatisation.

Heat stroke Heat stroke, which is sometimes incorrectly referred to as sunstroke, is a dangerous condition in which the sweat and other thermoregulatory mechanisms suddenly stop functioning. Body temperature rapidly rises in excess of 40C and the subject will sweat very little and appear flushed. Sufferers may initially complain of headache and will later become confused. Delirium and convulsions will follow with death occuring in just a few hours if measures are not taken to cool the patient. The condition carries about a 25 per cent mortality.[2] A further danger to be aware of is that some of these symptoms could also represent cerebral malaria. The exact physiological cause of heat stroke has not been well defined, but will almost certainly be triggered by the factors listed in Table 1.

Heat exhaustion Heat exhaustion carries a lower mortality than heat stroke. However, some forms of heat exhaustion are associated with impairment of sweating and can progress to heat stroke if not treated. Heat exhaustion can be difficult to differentiate from heat stroke, but elevation in body temperature and central nervous system (CNS) disturbances tend to be less profound.

Heat exhaustion can simply be caused by water deficiency. Surprisingly large amounts of fluid (in excess of 10 litres per day) might need to be consumed in some hot conditions. If fluid intake is restricted in such circumstances, dehydration can result and insufficient sweat will be produced to cool the body. Initially the patient will be thirsty with dry lips and mouth. Urine output is reduced and there will be mild CNS disturbances, such as giddiness and neuropathy. With a slight rise in body temperature (to no greater than 40C), breathing becomes rapid and the patient appears cyanosed. Coma and death can follow if the patient is not rehydrated.

Salt deficiency is another cause of heat exhaustion, particularly in those undergoing strenuous activity where there is profuse sweating. The subject might have maintained fluid intake but not replaced the salt lost in their sweat. Signs of salt deficiency include lethargy and muscle or "heat" cramps. Another, rarer, form of heat exhaustion is called anhidrotic heat exhaustion, which can appear many months after living in a hot climate. In a similar way to heat stroke the sweat glands appear to malfunction, the problem being mainly in the trunk and upper arms.

Prevention and treatment of heat-induced illness Prevention of the problems outlined above is summarised in Table 1. Acclimatisation is particularly important.[3] While acclimatising to a warmer climate, the individual should take care not to undertake a high level of physical exertion. When acclimatised, the individual will respond much more efficiently to heat stress, with both an earlier onset of response and more profuse sweating. Apart from diuretics, which cause salt and water loss, other medication can affect sweating and heat regulation. For instance, phenothiazines can suppress sweating, and tricyclics can increase heat production.[2] Similarly, medicines with anticholinergic properties, including some antihistamines, can adversely affect sweating mechanisms.

It is also important to stress that travellers to warmer climates should have an adequate intake of water and realise that simply drinking enough to quench thirst might not be sufficient. Alcoholic beverages, in particular, should not be used as a source of fluid intake. An early danger sign of insufficient fluid intake is reduced urine output that is dark in colour.

Other problems experienced when undertaking heavier physical exercise can be avoided by ensuring a sufficiently high salt intake. Pharmacists are sometimes asked to supply salt tablets, but these should generally not be supplied for this purpose. Apart from causing gastrointestinal disturbances, the tablets themselves neither provide an adequate daily intake of salt nor disperse sufficiently in water. Instead, travellers should be advised to use extra salt on food. Alternatively, water can be pre-salted (about half a teaspoonful per litre[1]) and then can be used to make beverages.

Heat exhaustion must be treated with rehydration therapy. If the patient is not comatose, about half a litre of water should be given every 15 minutes until urine output returns to normal. Some authorities advise against using isotonic electrolyte solutions for treating heat exhaustion, because a high water intake is more important than salt intake.[3] In the case of salt-induced deficiency problems, the body's reserves must be made up relatively quickly. If given orally, about two teaspoonfuls of salt are needed per litre of water and about half a litre of this salted water should be given every hour for six hours.[1] Following heat exhaustion, it is advisable to keep in the cool for three days and only gradually return to strenuous activity. For anhidrotic heat exhaustion, such recuperation can last up to a month. In all cases, admission to

TABLE 1: FACTORS ASSOCIATED WITH HEAT-INDUCED ILLNESS AND PREVENTIVE MEASURES

Factor	Preventive measure
Recent arrival	Graded physical activity in the first few weeks of arrival. Avoid long periods of continuous exertion
Lack of fitness and obesity	If strenuous activity is to be undertaken, build up fitness before travel
Inappropriate clothing	Advance planning of clothing and equipment
Certain drugs (diuretics, sympathomimetics) and alcohol	Avoid
Salt loss	Replace in food and/or beverages
Any skin condition that reduces sweating	Extra vigilance recommended
Insufficient fluid intake	Good supply of clean water consumed even if not thirsty

hospital is recommended.

Any strategy to cool a patient with heat stroke should be used while transfer to hospital is made. This will involve shelter from the sun, removing all clothing and covering with a wet sheet or similar material. Fluid replacement is also essential, and will need to be given intravenously if the patient is unconscious.

HIGH ALTITUDES

Acute mountain sickness (AMS), which is associated with travelling to high altitudes, is of some interest to pharmacists. Acetozolamide, dexamethasone and nifedipine have all been used in both the treatment and prevention of this condition. AMS most commonly occurs at altitudes of greater than about 3,000m, although cases have been reported at as low as 2,000m. It has been reported to affect 50 per cent of trekkers at altitudes above 4,000m.[4] A more recent study[5] estimated a 25 per cent incidence at 2,000–3,000m and identified that people who were younger, less fit and with lung problems were more likely to develop symptoms.

A particularly important contributory factor to AMS is the speed of ascent to high altitudes. Thus, people travelling to high altitudes by road or rail, rather than walking and allowing the body to acclimatise, have a greater chance of encountering problems. Similarly, when flying straight to destinations that are over about 3,000m above sea level, as might be the case when travelling to some destinations in South America, travellers risk high altitude problems.[6]

Panel 1 summarises the range of symptoms associated with AMS. The condition most commonly manifests itself as mild or benign AMS, where the symptoms are troublesome but not life threatening. It is possible for the benign form to result in more serious complications affecting either the lungs (high altitude pulmonary oedema [HAPE]) or the central nervous system (high altitude cerebral oedema [HACE]), although both can exists together. More rarely HAPE and HACE can occur with little warning. There is a 4 per cent risk of AMS suffers experiencing such complications.[4]

Although AMS is a well recognised condition, the causes remain controversial. Symptoms are related to a range of physiological effects on the body, which are effected by a reduction in atmospheric pressure. Other factors, such as cold and physical exertion, also contribute. However, there is little evidence that physical fitness confers any protection.[7] Table 2 lists some of the physiological effects that might have a bearing on developing AMS. Increased capillary permeability, caused by chemical mediator release in response to hypoxia, probably contribute to HAPE and HACE. The resulting oedema is compounded by the fluid retention observed in subjects with AMS.[4] It is not known if cerebral oedema contributes to the CNS effects of AMS (eg, dizziness and headaches).

A suggested explanation of why some individuals seem to develop symptoms of AMS more readily than others is that their tolerence to any minor "brain swelling" at high altitudes may be determined by their craniospinal anatomy.[8] Ibuprofen is a safe and effective remedy to AMS-induced headache.[9]

Whatever the true cause of AMS, ways of preventing the problem are well recognised. A slow rate of ascent is important. For instance, experienced mountaineers who carefully plan their climbs are less susceptible to AMS than casual trekkers. Another maxim is to "climb high but sleep low", indicating that AMS can be avoided if one always returns to lower ground when resting during the night. This is probably an important reason why AMS is less common among alpine skiers: night time lodgings in the Alps tend to be on lower ground. It is always worthwhile advising travellers who are flying direct to the high Andes, for example, to take things easy for a few days.

One of the best predictors of problems from AMS is a previous history of the condition since it does tend to reccur in susceptible individuals.[3]

Treatment of AMS Immediate treatment of AMS is simple: go down to a lower altitude. Climbers developing the initial symptoms of benign AMS should be advised to rest and climb no further until the symptoms resolve. In the case of pulmonary or cerebral symptoms, a rapid descent can be life saving. Some climbers have reported that special inflatable hyperbaric chambers are of use, although these have been criticised for providing only short-term relief and potentially delaying descent.[10]

A range of drugs have been used for both the prevention and treatment of AMS (see Table 3). However, their exact mechanism of action in this situation is not well understood.

Acetazolamide Acetazolamide is used to treat and prevent benign AMS (unlicensed indication), although its true place in therapy is somewhat contentious. It must be remembered that, in itself, this form of AMS is not fatal and there is no evidence that acetazolamide prevents progression to a more serious form. Therefore, the benefits of taking acetazolamide should be weighed against the risk of adverse effects.

Acetazolamide is a carbonic anhydrase inhibitor and induces mild metabolic acidosis. Its mode of action in AMS might therefore be through stimulation of respiratory drive, hence improving partial pressure of oxygen. The most common adverse effect at the recommended dosage (see Table 4) is paraesthesia in the fingers and toes.

A few trials have shown that acetazolamide can be used as prophylaxis, but it is unclear what the most effective regimen might be, whether it should be taken in advance of travel and how long before. Some experts argue against it being used routinely in this way, except in cases where AMS is known to be particularly troublesome, or the rate of ascent is relatively fast.

A recent review of published data concerning the prophylactic use of pharmacological agents for preventing AMS concluded that a daily dose of acetazolamide 750mg was more efficacious than the widely used 500mg daily dose. In addition prophylaxis was not thought to be worthwhile if the rate of ascent was less than 500 metres per day.[11] However, this particular analysis was criticised[12] for not including the results of important trials, for comparing two doses which considered different rates of ascent and for having too strict an end point re-

PANEL 1: SIGNS AND SYMPTOMS OF ACUTE MOUNTAIN SICKNESS

Mild (benign)
Headache
Loss of appetite
Nausea and vomiting
Insomnia
Tight sensation in the chest
Poor performance
Dizziness

High altitude pulmonary oedema
Dyspnoea
Cough
White sputum
Cyanosis

High altitude cerebral oedema
Headache
Drowsiness
Loss of balance
Abnormal behavior
Loss of consciousness or coma
Nightmares

TABLE 2: SOME PHYSIOLOGICAL FACTORS WHICH CAN CONTRIBUTE TO AMS

Observation	Possible explanation
High alveolar CO_2	Poor respiratory response to hypoxia in some individuals
Development of pulmonary oedema	Changes in pulmonary perfusion Increased capillary permeability
Central nervous system dysfunction	Increased capillary permeability or oedema Formation of blood clots due to nitrogen bubbles CNS hypoxia
Fluid retention	Hormonal changes — possible role of atrial natriuretic peptide

garding the presence of AMS.

Acetazolamide has also been used to resolve symptoms associated with benign AMS. The issue here might be one of safety, since it is possible that, on gaining symptomatic relief, a subject might be tempted to continue the ascent, which could in turn precipitate a more serious form of the condition. If acetazolamide is to be taken in this way, it is still wise to take time to rest and to have a slower rate of ascent. The evidence base for acetazolamide's use in the treatment of AMS is not as strong as that for prophylaxis.[3] A small study has indicated that a single dose of 250mg could relieve symptoms in those with established AMS.[13]

Dexamethasone The principle use for dexamethasone is in the relief of HACE. It is important not to rely on this agent alone for a cure and, again, descent to a lower altitude is essential. Its principal effect is probably a reduction of cerebral oedema, which it does by reducing vascular permeability. It may also be effective prophylactically, but acetazolamide is usually used in preference.

Nifedipine Nifedipine's use in relieving HAPE in an emergency situation (unlicensed indication) has been demonstrated by studies.[14] However, to date, there is little evidence supporting its usefulness and the recommended regimen is largely empirical. Its mechanism of action is probably via pulmonary vasodilation. This relieves pulmonary hypertension, a physiological response to alveolar hypoxia known be present in HAPE.[15] Concomitant therapy for HAPE includes using oxygen, where available, for the treatment of hypoxia. For the treatment of oedema associated with HAPE and HACE, furosemide can also be used.

Local cures In the high Andes, travellers are likely to come across a number of local remedies for the prevention of AMS. AMS is known locally as *soroche*. Chief among these is an infusion of tea made from coca leaves. There is probably little cocaine in this infusion, but, anecdotally, travellers have claimed some symptomatic relief from mild AMS from drinking it. The use of a paste of coca leaves, held in the mouth, could well help to relieve the symptoms of AMS, although such practice is not to be advised to travellers. Even more worrying, I have come across instances where respiratory stimulants, such as nikethamide, are freely sold to travellers.

TABLE 3: DRUG MANAGEMENT OF ACUTE MOUNTAIN SICKNESS

Name	Regimen	Principle use
Acetazolamide	Prophylaxis: 500mg slow release *nocte* or 250mg *bd* commencing the day before reaching 3,000m (but see text) Treatment: 250mg *stat*	Prophylaxis and management of mild symptoms
Dexamethasone	8mg *stat* then 4mg every four hours	Management of cerebral complications
Nifedipine	10mg *stat* sublingual then 20mg slow release six-hourly while at altitude. Repeat sublingual dose every 15 minutes if blood pressure does not drop more than 10mmHg within 10 minutes	Management of pulmonary symptoms

COLD CLIMATES

It is not possible to acclimatise the body to cold environments. Appropriate clothing and equipment help to avoid potential problems, such as hypothermia and frostbite. These conditions mostly occur on expeditions to cold climates where prolonged exposure to extreme conditions is expected eg, polar regions. However, community pharmacists would not normally advise these travellers. By far the largest group of travellers in this category would be those undertaking skiing holidays, where suitable clothing and equipment are of the greatest importance.

DIVING

Travellers going on diving holidays should be aware of the physiological dangers associated with this sport, eg, decompression sickness. This would not usually be an area where pharmacists would be called on to give advice. However, all those who attempt this sport should be strongly advised to take a recognised diving course, either in the UK or at the destination. Travellers should be warned only to attend diving courses overseas that are certified by the Professional Association of Diving Instructors (PADI) or the National Association of Underwater Instructors (NAUI).

Certain medical problems, ranging from sinus to cardiac conditions, might make a person unfit for diving. A particularly important piece of advice to all divers is to avoid flying for a day or so after a dive to avoid decompression illness.

REFERENCES

1. Adam JM. Effects of climatic extremes. In: Dawood R, editor. Travellers' health: How to stay healthy abroad. Oxford: Oxford University Press; 1992. pp232–49.
2. Hett HA, Brechtelsbauer DA. Heat related illness. Postgrad Med 1998;103:107–20.
3. Beeley JM, Smith DJ, Oakley EHN. Environmental hazards and health. Br Med Bull 1993;49:305–26.
4. Hackett PH, Rennie D, Levine HD. The incidence, importance and prophylaxis of acute mountain sickness. Lancet 1976; 2:1149–54.
5. Honigman B, Thies MK, Koziol-McLain J, Roac R, Yip R, Houston C, et al. Acute mountain sickness in a general tourist population at moderate altitudes. Ann Int Med 1993;118: 587–92.
6. Dickinson J. High altitude. In: Dawood R, editor. Travellers' health: How to stay healthy abroad. Oxford: Oxford University Press; 1992. pp224–31.
7. Milledge JS, Beeley JM, Broome J, Luff N, Pelling M, Smith D. Acute mountain sickness susceptibility, fitness and hypoxic ventilatory response. Eur Resp J 1991;4:1000–3.
8. Hackett PH. The cerebral etiology of high-altitude cerebral edema and acute mountain sickness. Wilderness Environ Med 1999;10:97–109.
9. Broome JR. Stoneham MD, Beeley JM, Milledge JS, Hughes AS. High altitude headache: treatment with ibuprofen. Aviation Space Environ Med 1994;65:19–20.
10. Pollard AJ. Treatment of acute mountain sickness. BMJ 1995; 311:629.
11. Dumont L, Mardirosoff C, Tramer MR. Efficacy and harm of pharmacological prevention of acute mountain sickness: quantitative systematic review. BMJ 2000;321:267–72.
12. Hackett P. Pharmacological prevention of acute mountain sickness. BMJ 2001;322:48.
13. Grissom Ck, Roach RC, Sarnquist FH, Hackett PH. Acetazolamide in the treatment of acute mountain sickness:clinical efficacy and effect on gas exchange. Ann Int Med 1992; 116:461–5.
14. Oelz O, Maggiorini M, Ritter M, Noti C, Waber U, Vock P, et al. Prevention and treatment of high altitude pulmonary oedema by calcium channel blocker. Int J Sports Med 1992; 13 (Suppl 1): S65–8.
15. Oelz O, Maggiorini M, Ritter M,Waber U, Jenni R, Vock P et al. Nifedipine for high altitude pulmonary oedema. Lancet 1989;2:1241–4.