ALTITUDE ILLNESS: AMS, HACE and HAPE
Notes for doctors and trek/expedition leaders (Reviewed by Dr Ross Anderson Feb. 2013)

As you ascend to altitudes above 2000m, your body has to acclimatize to the decreasing amount of oxygen available. The three main acclimatization mechanisms are:
- Deeper breathing and an increased respiratory rate (from 8 to 12 breaths/min at rest at sea level to around 20 breaths/min at 6000m). This starts immediately on arrival at altitude
- Producing more urine. This starts within hours and takes a day or two. If this mechanism is not efficient, the characteristic puffiness of early AMS appears in the face, hands and feet (water retention)
- An increase in the number of red cells in the blood. This only begins after a week at high altitude

If the ascent is too fast and/or the height gain too much, these mechanisms do not have time to work, and symptoms and signs of altitude illness (also called high altitude illness or altitude sickness) will appear.
Altitude illness becomes common above 2500m and presents in the following ways:
- AMS (Acute Mountain Sickness): common but not life-threatening if dealt with correctly
- HACE (High Altitude Cerebral Edema): less common but life-threatening
- HAPE (High Altitude Pulmonary Edema): less common but life-threatening

Depending on the altitude gain and speed of ascent, the incidence AMS ranges from 20 to 80%. HAPE is roughly twice as common as HACE and together they occur in approximately 1 to 2% of people going to high altitude. These three forms of altitude illness can vary from mild to severe, and may develop rapidly (over hours) or slowly (over days). HACE and HAPE can occur individually or together.
People often refuse to admit they have altitude illness and blame their symptoms on cold, heat, infection, alcohol, insomnia, exercise, unfitness or migraine, and risk death by continuing to ascend. Warning: do not ascend with symptoms or signs of altitude illness, as this has led to many deaths from HAPE/HACE.

RISK OF DEVELOPING ALTITUDE ILLNESS
In any group there will be ‘fast’ and ‘slow’ acclimatizers needing different ascent rates. While a flexible schedule is always preferred, the fact is that many trekkers are on tight schedules (often, but not always, members of commercial groups) leading to a higher incidence of altitude illness. Slow acclimatizers in these tight schedule situations are at extra risk, and prompt diagnosis and treatment becomes even more important. However, even if a trekker has a flexible schedule, they may still feel pressurized to ascend with symptoms (by pride, peer pressure, rivalry, not wanting to appear weak, etc). Interestingly, fit and impatient young people can be more at risk of altitude illness than unfit and patient older ones!

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<tr>
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<th>Flexible schedule</th>
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<tr>
<td>FAST ACCLIMATIZERS</td>
<td>LOW RISK</td>
<td>MEDIUM RISK</td>
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<td>SLOW ACCLIMATIZERS</td>
<td>MEDIUM RISK</td>
<td>HIGH RISK</td>
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AMS (ACUTE MOUNTAIN SICKNESS)

AMS varies from mild to severe and the main symptoms are due to the accumulation of fluid in and around the brain. Typically, symptoms appear within 12 hours of the ascent. If the victim now rests at the same altitude, symptoms usually disappear quickly over several hours (but for ‘slow acclimatizers’ this can take up to 3 days!) and they are now acclimatized to this altitude. AMS may reappear as they ascend higher still, as acclimatization to the new altitude has to take place all over again.

Symptoms & signs
A diagnosis of AMS is made when there has been a height gain in the last few days, AND:
- The victim has a headache (typically throbbing, often worse when bending over or lying down)
- PLUS there is one or more of the following symptoms:
  - Fatigue and weakness
  - Loss of appetite, or nausea, or vomiting
  - Dizziness, light headedness
  - Poor sleep, disturbed sleep, frequent waking, periodic breathing
In AMS, the victim’s level of consciousness is normal. The Lake Louise Score can be helpful as a guide to quantify your diagnosis of AMS and assess progression.
Note: AMS and HACE are two extremes of the same condition and it can help to think of AMS as ‘mild HACE’.
Note: the only early signs of altitude illness in a young child (under 7 years old) may be an increased fussiness, crying, loss of interest and/or loss of appetite.

HACE (HIGH ALTITUDE CEREBRAL EDEMA)

HACE is the accumulation of fluid in and around the brain. The important symptoms and signs are: severe headache, loss of physical coordination and a declining level of consciousness. Typically, symptoms and signs of AMS become worse and HACE develops (but HACE may come on so quickly that the AMS stage is not noticed). Also, HACE may develop in the later stages of HAPE.

Symptoms & signs
A diagnosis of HACE is made when there has been a height gain in the last few days, AND:
- The victim has a severe headache (not relieved by ibuprofen, paracetamol or aspirin)
- There is a loss of physical coordination (ataxia):
  - Clumsiness: the victim has difficulty (and often asks for help) with simple tasks such as tying their shoelaces or packing their bag. When examined they fail to do, or have difficulty doing (or refuse to do) the finger-nose test
  - Staggering, falling over. When examined they fail to do, or have difficulty doing (or refuse to do) the heel-to-toe walking test or the standing test
- Their level of consciousness is declining:
  - Early on, this presents as loss of mental abilities such as memory or mental arithmetic. When asked, the victim cannot do or have difficulty doing (or refuse to do) simple mental tests
  - Later on, they become confused, drowsy, semiconscious, unconscious (and will die if not treated urgently)
- Other symptoms and signs that may appear:
  - Nausea and/or vomiting, which may be severe and persistent
- Changes in behaviour (uncooperative, aggressive or apathetic, "Leave me alone", etc)
- Hallucinations, blurred or double vision, seeing haloes around objects, fits or localized stroke signs may all occur but are less common

**TESTS FOR HACE**

Failure or difficulty doing any one of these tests means the victim has HACE. If the victim refuses to cooperate, assume they are suffering from HACE. If in doubt about the victim's performance of the tests, compare with a healthy person. Be prepared to repeat these tests to monitor progress.

- **Finger-nose test.** With eyes closed, the victim repeatedly and rapidly alternates between touching the tip of their nose with an index finger, then extending this arm to point into the distance (useful test if the victim is in a sleeping bag or cannot stand up).
- **Heel-to-toe walking test.** The victim is asked to take 10 very small steps in a straight line, placing the heel of one foot in front of the toes of the other foot as they go. Reasonably flat ground is necessary and the victim should not be helped, but be prepared to catch the victim if they fall over! Excessive wobbling is difficulty (to do the test), falling over is failure.
- **Standing test.** The victim stands, feet together and arms folded across their chest, and then closes their eyes (the victim should not be helped, but be prepared to catch the victim if they fall over! Excessive wobbling is difficulty (to do the test), falling over is failure.

- **Mental tests** are used to assess level of consciousness. You must take into consideration pre-existing verbal/arithmetic skills and culture; it is a decline in ability over time that is significant. Examples of tests include: “Spell your name backwards”, “Take 3 from 50 and keep taking 3 from the result”, or ask their birth date, about recent news events, etc.

**HAPE (HIGH ALTITUDE PULMONARY EDEMA)**

HAPE is the accumulation of fluid in the lungs. The important sign is breathlessness. HAPE may appear on its own without any preceding symptoms of AMS (this happens in about 50% of cases) or it may develop at the same time as AMS or HACE. Severe cases of HAPE may result in the development of HACE in the later stages.

HAPE may develop very rapidly (in 1 to 2 hours) or very gradually over days. It often develops during or after the second night at a new altitude. HAPE can develop while descending from a higher altitude. It is the commonest cause of death due to altitude illness. HAPE is more likely to occur in people with colds or chest infections. It is easily mistaken for a chest infection/pneumonia. If you have the slightest doubt, treat for both.

**Symptoms & signs**

- Reduced physical performance (tiredness, fatigue) and a dry cough are often the earliest signs of HAPE
- Breathlessness:
  - Early stages: more breathless than usual with exercise, takes a little longer to get breath back after exercise
  - Later stages: marked breathlessness during exercise, takes longer to get breath back after exercise. This finally progresses to breathlessness at rest
  - At any stage, the victim may become breathless while lying flat and prefer to sleep propped up
• Breathing rate at rest increases as HAPE progresses. (At sea level, resting breathing rate is 8 to 12 breaths/min at rest. At 6000m, normal acclimatized resting breathing rate is approximately 20 breaths/min)
• A dry cough
• As HAPE gets worse, the cough may start to bring up white frothy sputum. Later still, this frothy sputum may become bloodstained (pink or rust coloured): this is a serious sign
• 'Wet' sounds (fine crackles) may be heard in the lungs when the victim breathes in deeply (place your ear on the bare skin of the victim’s back below the shoulder blades; compare with a healthy person)
  Note: wet sounds may be difficult to hear (or absent), even in severe HAPE
• As HAPE gets worse, lips, tongue or nails may become blue due to lack of oxygen in the blood
• There may be: fever (up to 38.5ºC), a sense of inner cold, or pains in the chest or even upper belly
• As HAPE worsens, the victim becomes confused, drowsy, semiconscious, unconscious (and will die if not treated urgently)

WHAT ELSE COULD IT BE?

If the illness comes on after 4 days at a new altitude and/or does not respond to descent, oxygen, dexamethasone and/or nifedipine, reconsider your diagnosis:
・.. HACE may be difficult to distinguish from: migraine, meningitis, diabetic coma, CO poisoning
・.. HAPE may be difficult to distinguish from: pneumonia, asthma, pulmonary embolus (a blood clot from a DVT), heart attack, hyperventilation (panic attack)
・.. Hypothermia, dehydration or low blood sugar (due to not eating) share similar symptoms to altitude illness

Unless absolutely sure, treat as HACE or HAPE (or both) PLUS your alternative diagnosis.
 Note: the basic treatment of all of these problems is roughly the same: re-warm, re-hydrate, 're-sugar', re-oxygenate and descend.

TREATMENT OF ALTITUDE ILLNESS

If someone is ill at altitude after a recent height gain, carry out a full secondary survey (especially level of consciousness and breathing rate), a 'Lake Louise Score' and the tests/examination for HACE and HAPE.
Because the victims of altitude illness often fail to take care of themselves, they are likely to develop hypothermia, dehydration and/or low blood sugar (due to not eating). There comes a point when it is vital that the leader/doctor/companion starts making decisions for the victim (e.g. ordering immediate descent), even if the victim disagrees.

General treatment of altitude illness
• Descent is the treatment for altitude illness. Prompt descent will begin to reverse the symptoms. Descend immediately if symptoms are severe, even if it means at night or in bad weather. Resting at the same altitude is only acceptable if the victim has mild AMS and is improving with treatment
• Oxygen: give oxygen, either as bottled oxygen or in a hyperbaric bag if the symptoms are severe and descent is not immediately possible (e.g. dangerous terrain or weather, not enough helpers to carry an unconscious victim, waiting for a helicopter) or the victim is too ill to move
• **Rest** is recommended even for mild symptoms. With more serious illness, if at all possible avoid even the slightest exertion, as just walking a few steps may make symptoms worse or reappear; carry the victim or, as a minimum, assist them to walk and carry their rucksack
• Keep the victim warm and hydrated, give occasional sugary drinks
• Prop the victim up in a semi-reclining position, as lying flat can make them feel worse
• If at any stage the victim has difficulty breathing, is turning blue or lapsing into unconsciousness, assist them with mouth-to-mouth (rescue) breathing before they stop breathing altogether

### Specific treatment of altitude illness

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<th></th>
<th><strong>mild AMS (Lake Louise Score 5 or less)</strong></th>
<th><strong>moderate to severe AMS (Lake Louise Score 6 or more)</strong></th>
<th><strong>if HACE is present</strong></th>
<th><strong>if HAPE is present</strong></th>
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<tbody>
<tr>
<td><strong>Descent?</strong></td>
<td>Rest at the same (or lower) altitude until symptoms clear (this will take a few hours to a few days)</td>
<td>If you have no oxygen, or symptoms do not disappear rapidly, or if symptoms get worse despite oxygen, descend at least 500 to 1000m</td>
<td>Descend immediately. Descend as low as possible, aim for 1000m or more</td>
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<tr>
<td><strong>Painkiller for Headache (Paracetamol/Ibuprofen)</strong></td>
<td>If necessary</td>
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<tr>
<td><strong>Antivomiting Medication</strong></td>
<td>If necessary</td>
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<td><strong>Acetazolamide (Diamox™)</strong></td>
<td>Consider 125 to 250 mg 12-hourly for the rest of the time at altitude if an unavoidable ascent is due the following morning, or if symptoms are still present at bedtime, or for ‘slow acclimatizers’ on tight schedules</td>
<td>250 mg 12-hourly for the rest of the time at altitude</td>
<td>250 mg 8-hourly for the rest of the time at altitude</td>
<td>250 mg 8-hourly for the rest of the time at altitude</td>
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<tr>
<td><strong>Dexamethasone 논</strong></td>
<td>Consider (8 mg at once then 4 mg 6-hourly) for severe symptoms</td>
<td>8 mg at once - IM or by mouth - then 4 mg 6-hourly</td>
<td>Only if symptoms of HACE are present</td>
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<tr>
<td><strong>Nefidipine 닫</strong></td>
<td>Consider only if symptoms of HAPE are present</td>
<td>MR or LA tablets (20 to 30 mg 12-hourly, for at least 3 days)</td>
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<td><strong>Oxygen: 1) Bottled, OR 2) Hyperbaric Bag</strong></td>
<td>Consider 1) 2 L/min or more, OR 2) until symptoms clear and then for an additional 30 minutes</td>
<td>1) 2 L/min or more, OR 2) until symptoms clear and then for an additional 30 minutes</td>
<td>1) 2 to 4 L/min or more until improving, OR 2) 4 hours or more</td>
<td>1) 6 to 8 L/min, OR 2) 6 to 8 hours or more (if you have a pulse-oximeter, aim for a PO2 of 90%)</td>
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<tr>
<td><strong>Other Treatment</strong></td>
<td>Use an asthma reliever spray 2 puffs 4-hourly using a spacer</td>
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논 Dexamethasone is an effective and rapid treatment (especially if given IM). However, once it is started the victim should descend and stay down for at least 3 days because dexamethasone does mask the symptoms and signs of AMS/HACE (unlike acetazolamide). Only stop the dexamethasone after at least 3 days of treatment and once staying below 2500m. Tail off the dose slowly by giving the last 3 doses 12-hourly.

닫 Nifedipine can have the serious side effect of dropping the victim's blood pressure; this is more likely when they are dehydrated and cold (treat as for shock if this occurs). Re-warming and rehydrating the victim, and avoiding standing up suddenly, reduces this risk. The modified release (MR) or long acting (LA) preparations of the drug are safer in this respect than the fast-acting preparation.

닫 Sildenafil (Viagra™) is presently under investigation as a treatment for HAPE, as an alternative to, or given in conjunction with, nifedipine.
Hyperbaric bags (PAC™, Certec™, Gamow™) are equivalent to a bottled oxygen flow rate of 2 to 4 L of oxygen/min. Although you cannot ‘turn up the flow rate’ like you can with a bottled oxygen, they never ‘run out’.

- If both bottled oxygen and hyperbaric bag are available, give a short treatment with high flow oxygen from the bottle while preparing to put the victim in the hyperbaric bag
- While treating a victim in a hyperbaric bag, short breaks may be taken (e.g. for examination, while descending, or for toilet purposes)
- While in the hyperbaric bag, the victim will often breathe better (especially with severe HAPE) with the bag at a 15° angle, head up
- If the victim is semiconscious/unconscious, place them in the safe airway position (lateral position) in the hyperbaric bag, and keep a continuous watch on their condition and breathing. If either deteriorates, remove the victim immediately

**GOING BACK UP AGAIN?**

- Anyone seriously ill with HACE or HAPE needing oxygen, treatment in a hyperbaric bag or dexamethasone or nifedipine, should descend immediately after treatment. As, even if they feel completely recovered, symptoms may rapidly re-appear with even mild exertion or further ascent
- Cautious re-ascent may be considered once symptom-free for 4 weeks (ideally seek the advice of a doctor qualified in mountain medicine). Long haul jet flights should be avoided while symptomatic, unless oxygen is available
- If re-ascent is unavoidable (e.g. driving out of Tibet over high passes), give:
  - Acetazolamide 250 mg 12-hourly
  - If the original problem was HACE, add dexamethasone (4 mg 12-hourly)
  - If the problem was HAPE, add modified release nifedipine (20 mg 12-hourly)
  - Give oxygen while crossing passes
- If symptoms of AMS disappear and the person is feeling well (and has been off dexamethasone for at least 3 days), they may try re-ascending slowly while continuing to take acetazolamide. Otherwise, continue descending

**PREVENTION**

**In general**

- Above 2000m, altitude illness (AMS, HACE and HAPE) is a possibility, and above 2500m it becomes common. Keep an eye on each other and use the Lake Louise Score to detect symptoms and signs of altitude illness (including periodic breathing).
- As a rough guide, above 2500m the maximum daily height gain between sleeping altitudes should not exceed 300m (slow acclimatizers) to 500m (fast acclimatizers), with a rest day every third day (or after every 1000m of ascent). Over 5000m, the daily height gain for the slow and fast acclimatizers is halved to 150m and 250 meters per day, respectively
- If you must fly or drive rapidly to 2500m or higher, spend a minimum of two nights at your arrival altitude (or lower if possible) or until symptoms disappear, before ascending further. If ascending rapidly to 3000m or higher, consider using acetazolamide (Diamox™)
- Avoid overexertion and breathlessness while acclimatizing, especially if experiencing symptoms of AMS
- Dehydration does not cause altitude illness, but it is an unnecessary complication. Drink enough liquid to keep your urine pale and plentiful. An increased urine output after an ascent is a good sign, while a decrease in urine output indicates that altitude illness (or dehydration) is developing
- Some medications can have adverse effects at altitude (see below)
- Avoid alcohol, excess caffeine, salt and protein (your diet should be 70% carbohydrate above 3500m)

Note: altitude illness, dehydration, hypothermia and hypoglycaemia (due to not eating) are all very common in mountain environments. If you suspect any one of these problems, look for them all.

**MEDICATIONS AT ALTITUDE**

- At altitude (above 2500m) some medications such as sedatives, strong painkillers, some antihistamines and most sleeping tablets (except zopiclone and zolpidem) may depress breathing. This may make altitude illness more likely or more severe, especially at night. If you have to use any of these medications, consider giving acetazolamide (Diamox) 125 to 250 mg 12-hourly to stimulate breathing, and check the person frequently
- Oral contraceptives (“the pill”) slightly increase the blood’s tendency to clot, so they should be avoided for long stays above 5000m
- Aspirin and NSAIDs (non-steroidal anti-inflammatory drugs, e.g. ibuprofen) may cause bleeding in the eye (retina) at high altitude (over 5000m) especially if coughing is present

Note: see also handout *Notes on Acetazolamide (Diamox™)*