**A Guide to Acute Mountain Sickness (AMS)**
**(Altitude Sickness)**

*Annapurna Circuit, Nepal, 2012*

**Disclaimer**

**This is an educational aide memoir and does not represent any medical advice. For that you need to see a qualified medical practitioner, ideally familiar with high altitude trekking and climbing. In particular, if using medication to assist in mitigating AMS please see your GP well in advance of your trip.**

**Version 2.2**

## Document Control

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## Know Your Enemy

Acute Mountain Sickness (AMS) is potentially fatal. Yet few who venture into its realm take the time to study and understand it. A survey of 65 trekkers in Nepal, who trekked the same Annapurna Circuit that Blue Steel Dash completed in 2012[1] revealed as much. The trekkers were asked questions designed to test their abilities to recognize and identify treatment for common symptoms of AMS. The trekkers had varied understandings of altitude sickness. 78% of them had heard of altitude sickness, but 75% were not aware of ever having experienced it themselves. The trekkers were asked a series of questions to test their awareness of AMS, the maximum score being 20. The average score was 10.9, a number skewed upwards by a number of trek leaders and guides who had high scores. That is, most trekkers gained a 'FAIL' score on a subject they should know everything about.

On the other hand a US Navy study[2] revealed approximately 95% of participants in a survey of Marines and sailors training at a mountain warfare centre reported knowledge of AMS, a factor which the researchers felt was a contributing factor to the relatively low incidence of AMS. Other research suggests awareness of AMS and its symptoms contributes to a lower incidence.[3] Makes sense really, doesn't it? There simply is no excuse for not knowing about something that can kill you. Hence this little bit of reading homework. So strap on, here we go.

### Oxygen + Pressure

Our body is designed to function using some key ingredients as fuel – beer, jelly snakes, deep fried foods and oxygen. While you might think snakes are critical to survival it's oxygen we are mainly interested in here. The atmosphere contains about 21% oxygen at sea level. And it's mainly at that level that we all live. And your body has gotten used to functioning with a certain amount of oxygen in its system – in our case the oxygen found at sea level. But more importantly it has gotten used to functioning with a combination of oxygen available under a certain amount of pressure. As we ascend above sea level the percentage of oxygen in the air stays the same (up to about 39,000'/12,000m) but the pressure lessens (and on some flights so does the beer) until we reach a point where the body is not able to take up enough oxygen to keep us alive. In fact, even while the percentage of oxygen remains the same, barometric pressure decreases exponentially as altitude is gained. Even though it is not entirely accurate it is convenient for us to express it this way: at an altitude as low as say, 8,000'/2438m there is 25% less oxygen available than at sea level. The combined drop in pressure, together with a reduced number of oxygen molecules means our cells are not getting the number of oxygen 'fuel cells' they need in order to function .

The following table shows how quickly we run out of oxygen. A gym session or jog in your first week in Nairobi or Kabul leaves you fatigued until your body adjusts to even just a 3% decrease in oxygen. We will explore in more detail below why pressure is the main factor in thinking about acclimatization and AMS. In the meantime the reduced capacity to take up oxygen due to reduced pressure is called *hypobaric hypoxia*.

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[1] Glazer, James L ; Craig, Edgar; Siegel, Matthew S . "Awareness of Altitude Sickness Among a Sample of Trekkers in Nepal" Wilderness & Environmental Medicine 16.3 (Fall 2005): 132-8

[2] High Altitude Headache and Acute Mountain Sickness at Moderate Elevations in a Military Population During Battalion-Level Training Exercises, Norris, Jacob N, MSC USN; Viirre, Erik, MD, PhD; Aralis, Hilary, MPH ; Sracic, Michael K, MC USN; Thomas, Darren, MC USN; et al. Military Medicine 177.8 (Aug 2012): 917-23.

[3] Vardy J, Vardy J, Judge K: Can knowledge protect against acute mountain sickness? Journal of Public Health 2005; 27(4): 366-70.

Table 1[4]

| Altitude (feet) | Altitude (m) | Pressure kPa | Oxygen % | Category | Example |
|---|---|---|---|---|---|
| Sea Level | Sea Level | 101.325 | 20.9 | Low | Sydney |
| 1000 | 305 | | 20.1 | Low | |
| 2000 | 610 | | 19.4 | Low | |
| 3000 | 914 | 91 | 18.6 | Medium | Katoomba (1030m/90kPa) |
| 4000 | 1219 | | 17.9 | Medium | |
| 5000 | 1524 | 85 | 17.2 | Medium | Nairobi |
| 6000 | 1829 | 82 | 16.6 | Medium | Kabul |
| 7000 | 2134 | 79 | 16.0 | Medium | Mount Kosciuszko<br>Kokoda Track (Mt Bellamy) |
| 8000 | 2438 | | 15.4 | High | |
| 9000 | 2743 | 74 | 14.8 | High | Head of Tasman Glacier |
| 10000 | 3048 | | 14.2 | High | |
| 11000 | 3353 | | 13.7 | High | Highest Ethiopian residents. Cusco, Peru |
| 12000 | 3658 | 66 | 13.2 | High | Mt Cook. Highest Andes residents |
| 13000 | 3962 | | 12.7 | Very High | |
| 14000 | 4267 | | 12.2 | Very High | |
| 15000 | 4572 | | 11.7 | Very High | |
| 16000 | 4877 | | 11.3 | Very High | Highest Tibetan residents – at Chantong |
| 17000 | 5128 | | 10.9 | Very High | |
| 18000 | 5486 | 53 | 10.5 | Extreme | Thorung La |
| 19000 | 5791 | 51 | 10.1 | Extreme | Kilimanjaro |
| 20000 | 6096 | | 9.7 | Extreme | |
| 21000 | 6401 | | 9.3 | Extreme | |
| 22000 | 6706 | 45 | 9.0 | Extreme | Ama Damlam  Aconcagua (6900) |
| 23000 | 7010 | | 8.6 | Extreme | |
| 24000 | 7315 | | 8.3 | Extreme | |
| 25000 | 7620 | | 8.0 | Extreme | |
| 26000 | 7925 | | 7.7 | Death Zone | |
| 27000 | 8230 | | 7.4 | Death Zone | Cho Oyu |
| 28000 | 8534 | | 7.1 | Death Zone | K2 |
| 29000 | 8839 | | 6.8 | Death Zone | Everest |

Before you have a panic attack about this table, bear in mind that Blue Steel Dash walked into Thorung La strong and without any AMS symptoms. You will hear this a lot – good strategies, planning and discipline help prevent AMS.  The table helpfully shows that at Kilimanjaro you have about 50% less oxygen available to you than at sea level. That is pretty close to what the group dealt with as it crossed Thorung La in Nepal.

[4] There is a handy calculator at http://www.altitude.org/air_pressure.php that allows you to look at oxygen and barometric pressure.


*18,000' mark, Thorung La, Nepal. Nil AMS symptoms – just happy trekkers.*

As Table 1 shows, up to a certain altitude humans can adapt to low oxygen levels and live there all their lives. That maximum height is about 15,000'/4,572m. Humans can survive at higher altitudes – Everest is 29,028'/8,848m but being exposed to oxygen depleted atmosphere above 15,000'/4,572m for long periods of time poses the problem of diminishing returns – body and muscle mass is significantly reduced.[5] But the ability to live at altitude, as many in the Andes, the Himalayas and the mountains of Ethiopia do, is not just a matter of acclimatization. Evidence is emerging that shows there is a genetic predisposition that allows some to survive at altitude and others not.[6]

## Atmospheric Pressure and Oxygen

Here is a weird thing. Even at 30,000' the percentage of oxygen in the air actually remains the same – roughly 21%. What has changed is the number of molecules present but, more importantly the pressure has dropped. It is the drop in pressure that makes the uptake of oxygen a problem for us. Without that pressure even the oxygen that is in the air is not accessible to us without some acclimatization. (But as we note elsewhere, eventually we get to a point, about 7000m, where not even pressure helps).

- At sea level, the standard barometric pressure is 101.325 kPa (760 mmHg). This means that there is 100% of the oxygen available at sea level.

- At 1000m, the standard barometric pressure is 90 kPa (679 mmHg). This means that there is 89% of the oxygen available at sea level. Believe it or not that is about the height of Katoomba. Drive to the Blue Mountains and you are already running short of oxygen.

[5] Muscle Structural Modifications in Hypoxia H. Hoppeler, D. Desplanches International Journal of Sports Medicine 1992; 13: S166-S168

[6] 'The cerebral effects of ascent to high altitudes' Wilson, Mark H ; Newman, Stanton ; Imray, Chris H. The Lancet Neurology 8.2 (Feb 2009): 175-91.

- At 5000m, the standard barometric pressure is 56 kPa (420 mmHg). This means that there is 55% of the oxygen available at sea level.

And at 5791m (Kilimanjaro), the standard barometric pressure is 51 kPa (379 mmHg). This means that there is 50% of the oxygen available at sea level. Which reflects the table above. Remember, the real driver behind oxygen access is atmospheric pressure.

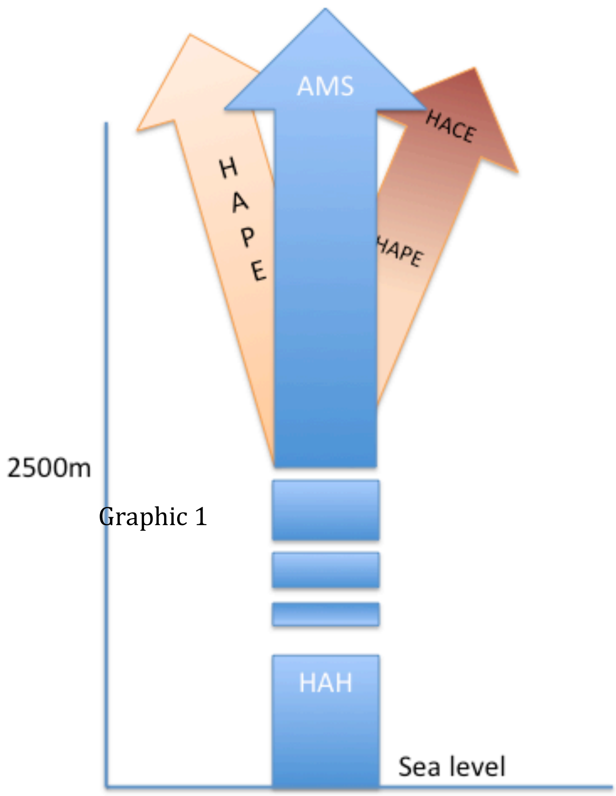
## So What?

So what has this got to do with AMS? Simple really. If we travel too quickly and too energetically from our sea level saturation to a height to which our bodies have not adapted to the lower pressure and fewer oxygen molecules available, we can cripple ourselves. That hypobaric hypoxia enemy is what we are up against and the brain, "exquisitely sensitive to hypoxia is the first organ to be compromised." And it is not just the rate of ascent that matters. An overly energetic approach to the climb has been shown to contribute to AMS. A 'steady as she goes' or 'cruise' approach is best. If we are in any doubt about this point two separate studies carried out at 17,257'/5260m showed increased brain artery pressure and velocity 'at exercise', underscoring and reinforcing what mountaineers and high altitude physicians have said all along – exercise at altitude increases the risk of AMS. Rather, get fit first, adopt a steady as she goes approach to your energy output and avoid overexerting yourself.[7]

So, just to repeat, How much disabling? Well, in a worst case AMS can be fatal. Which is why we take it seriously.

## Some Terminology Helps – HAH, AMS, HAPE and HACE

To help us understand AMS a little better we need to establish some terminology. AMS usually addresses all the symptoms of illness at altitude. But to throw everything in a single basket may mask our understanding of the extreme manifestations of AMS.



Graphic 1

At low altitudes you may experience High Altitude Headaches (HAH) that may or may not go away with over-the-counter medicines. They will go away in a short period if a constant altitude is maintained as your body adjusts. HAH is a precursor to AMS which can first be evident in the altitude band of 8,000'/2438m – 15,000'/4578m. Be aware that HAH can be difficult to differentiate between hydration headaches. However they should rapidly resolve

[7] Studies cited in 'The cerebral effects of ascent to high altitudes' Wilson, Mark H ; Newman, Stanton ; Imray, Chris H. The Lancet Neurology 8.2 (Feb 2009): 175-91.

with panadol, hydration, and oxygen will remove them in ten to fifteen minutes. If not, you may have a more serious issue on your hands.

The core affliction, AMS, manifests itself through headache, nausea, anorexia, dizziness, fatigue, and vomiting and disturbed sleep. Mild AMS usually requires no more than cessation of ascent, rest, ensuring of good hydration and use of simple analgesics. Paracetamol, aspirin, ibuprofen and codeine are all effective.[8]

A rare but potentially lethal form of AMS can occur above 14,763'/4,500m. Its called high altitude cerebral edema, or HACE. 1-2% of climbers get HACE. The symptoms are discussed below but are usually, but not always preceded by AMS symptoms.

The other form of AMS to which we need to be alert is high altitude pulmonary edema or HAPE. This usually occurs when a person arrives at altitude quickly – say, by aircraft in Nepal or in the Andes, by car. For those trekkers who travelled to Thorung La you will recall the town of Muktinath where there is a shrine sacred to Hindus and Buddhist alike. Many Hindus fly in from India and arrive at the shrine the next day. While only at 12,000'/3657m rapid travel invites not just AMS consequences on these pilgrims but instances of HAPE as well. HAPE is also quite rare but climbers and trekkers die by simply not being aware of the symptoms and not reacting quickly enough.

As a general rule we can represent AMS as we have in Graphic 1, though don't be rigid about this – HACE and HAPE can occur at low altitude for some people and before you are aware of any specific AMS symptoms. Unfortunately the scientific and medical community agree to disagree about defining how all the forms of AMS fit together and speculate whether or not one leads to the other.[9] Just be aware of the symptoms for all forms of AMS and watch yourself and your buddies. We examine HAPE and HACE in more detail below. But for the moment we will talk about how AMS occurs and in that discussion we refer to all forms of AMS.

## How Does it Happen?

Despite being aware of AMS for many years there is no sound scientific understanding of how AMS comes about. We are very familiar with the symptoms and the treatment. And we know it happens because of the body's inability to rapidly adjust to lower levels of oxygen. And we know how to respond to the symptoms and how to treat someone suffering from AMS. We explore in more detail below what happens when the body acclimatizes. That is some science that we do have a good grip on.

### Who Can Get It?

You. But not you. Which is one way of saying there is no way of knowing who might get it and who might not. Some are afflicted by it to a greater degree than others. However anyone who is not acclimatized to a particular altitude is likely to experience AMS symptoms. AMS can impact different people in different

[8] 'High Altitude Sickness' Richards, Paul. Practice Nurse 27.6 (Mar 26, 2004): 49.
[9] For example 'The cerebral effects of ascent to high altitudes 'Wilson, Mark H ; Newman, Stanton ; Imray, Chris H. The Lancet Neurology 8.2 (Feb 2009): 175-91.

ways. Edmund Hillary, first to the top of Everest and very familiar with AMS mused how he struggled with AMS when he ascended by foot but felt few symptoms when he flew to a high landing strip – and you don't get a quicker ascent than that. Some have no symptoms at all. From Lima one can ascend to 18,000'/5486m in a single day by car. Some unacclimatised folk make that transition with no effect. Others are violently ill. For tourists flying directly to 9,842'/3700m to start their holidays in Nepal the incidence of AMS can be as high as 84%.[10] There is no evidence to suggest AMS is different for young or old. Teenagers are just as susceptible to it as the elderly. Menstruation, smoking, hypertension, coronary artery disease, diabetes, pregnancy or mild chronic obstructive pulmonary disease (in other words, clagged lungs, mainly due to smoking) do not appear to predispose a person to AMS.[11] There is emerging evidence to suggest that obese people can be more prone to it than those carrying normal weight.[12] However the one principle does apply – if you ascend too quickly you should expect to suffer AMS.

Another way to answer this question is to look at where AMS occurs. This table[13] tells its own story or two about AMS.

| Altitude | AMS Incidence % | Site |
|---|---|---|
| **1900-2940** | 25 | Colorado |
| **2000-2800** | 12 | Colorado |
| **2850** | 9 | Swiss Alps |
| **3050** | 13 | Swiss Alps |
| **3650** | 34 | Swiss Alps |
| **4243** | 43 | Pheriche Nepal |
| **4394** | 67-77 | Mt Rainier, USA |
| **4550** | 38 | Tuo-Tuo Nepal |
| **4559** | 53 | Swiss Alps |
| **5400** | 63 | Thorung La |
| **5949** | 40 | Indian Himalaya |
| **6195** | 30 | MtMcKinley, Alaska |

Table 2

The high incidence of AMS in Colorado at slightly lower altitudes might be attributed to the number of people coming to ski at levels to which they are not acclimatised. But even the military report AMS at heights up to 8,250'/2,500m.[14] The US Marines studied the incidence of AMS at these relatively low levels and found 14.6% of their staff suffered symptoms of AMS.

But the really big numbers of AMS come from those high altitude trekking and climbing areas that are easily accessible to someone with average fitness and a good pair of boots. Combine that with lack of awareness of AMS, failure to acclimmatise and you have a recipe for potential death. One of the largest numbers in this table is Thorung La. Thorung La is not a technical climb but it is very high. The good news for Blue Steel

[10] High Altitude Sickness Richards, Paul. Practice Nurse 27.6 (Mar 26, 2004): 49.

[11] High Altitude Sickness Richards, Paul. Practice Nurse 27.6 (Mar 26, 2004): 49.

[12] High-altitude cerebral effects: risks and mechanisms/Authors' reply Strapazzon, Giacomo; Semplicini, Andrea; Burtscher, Martin; Wilson, Mark; Imray, Chris. The Lancet Neurology 8.7 (Jul 2009): 604; author reply 605.

[13] Pollard and Murdoch, The High Altitude Medicine Handbook, p 8

[14] High Altitude Headache and Acute Mountain Sickness at Moderate Elevations in a Military Population During Battalion-Level Training Exercises Norris, Jacob N, MSC USN; Viirre, Erik, MD, PhD; Aralis, Hilary, MPH ; Sracic, Michael K, MC USN; Thomas, Darren, MC USN; et al. Military Medicine 177.8 (Aug 2012): 917-23.

Dash is that Thorung La was safely crossed with zero incidence of AMS by the Blue Steel Dash team in 2012 following a properly managed and disciplined ascent in which the team stuck to its acclimatisation plan.

**Doing it Right?**

Under an overly dramatic headline "Former Newcastle Knights players cheat death at Mount Everest base camp" the press reported how a group of former NRL players suffered the effects of AMS on a trek to Everest Base Camp. "All of a sudden, six blokes just went down. We were lucky we had a doctor on the trip with us [orthopaedic surgeon Steve Rimmer] who won [the trip] in one of the auctions. We had blokes on the oxygen tanks, they were vomiting, they were going wobbly with their speech." It's impossible to know exactly what has happened based on press reporting only but we would argue these symptoms are only going to occur when an acclimatisation plan is not put in place or adhered to.

http://www.smh.com.au/rugby-league/newcastle-knights/former-newcastle-knights-players-cheat-death-at-mount-everest-base-camp-20171025-gz854s.html 29 Oct 2017

The most benign judgment we can make of our fellow trekkers is that they simply were not aware of the issues at altitude. After all we fly at great heights without any effect don't we? We do indeed but that is what being pressurized as all about. An aircraft has a false atmosphere created in it so your body thinks it is travelling at say 8,000'/2,500m instead of 35,000'/10,670m. And you are getting some extra oxygen pumped in there as well.

## At what Altitude does AMS Occur?

Good question. As we noted above, the US Navy recorded AMS at altitudes as low as 6,561'/2,000-8,200'/2,500m and some ski fields are now training their staff to look out for skiers who suffer AMS at low altitude. But as a general rule 9,842'/3000m is a good rule of thumb. Above 10,000'/3048m we need to be alert to AMS symptoms but also we need to seriously manage our acclimatization planning. In Nepal some of our team started feeling mild symptoms at this height. Others are able to fly to 9,842'/3000m and then spend a week climbing at that altitude without displaying any symptoms.

False Starts A recurring theme in many case studies of AMS is the rapid initial ascent to the 'kick off point" of a climb. In the first half of the 20th Century when expeditions were being directed at Everest the trek to base camp could take months. In that time the climbers had ample time to acclimatize. These days we can fly to high altitude airfields and start our trek with a geographical head start. But it is a head start with a potentially fatal handicap – a plane ride offers no acclimatization. If engaging a company to take you to height look at their acclimatization plan. The trip to Ama Dablam starts in Kathmandu with a slow trek to the base of the mountain instead of flying in. Similarly the kick off point for Kilimanjaro is quite low.

On the other hand those of us who walked the Salkantay Track in Peru experienced the impact of sudden high altitude starts when we arrived in Cusco. Cusco is at 3400m and we had flown in from sea level an hour earlier. Many of us were 'green' but some were down for the count for a full day and a couple of nights, even with all the best precautions taken. If a high altitude start is required then the sensible strategy to counter AMS is to stay at that jump off point for as long as you possibly can, staying hydrated the whole time.

## Do I have AMS or am I just Knackered?

An excellent question and one that you should always be asking yourself as you ascend. Early onset of AMS is very difficult to diagnose as the symptoms can be very similar to those experienced by someone who is fatigued. What are the symptoms?

- Fatigue
- Aching of Head
- Nausea
- Dizziness
- Anorexia
- Vomiting
- Disturbed sleep

"FANDAVD"

You can see that the AMS symptoms can be confused with exhaustion, dehydration, hypothermia, migraine, hangover or a viral infection. It is one good reason that high altitude climbers save their alcohol for the parties back home. Given the potential to confuse symptoms, err on the side of caution and assume AMS, especially if sleep is disrupted and the headache is not resolve with water and painkillers.

The headache will not be anything different to a usual headache. Though it may throb more than a usual headache and can be worse at night and first thing in the morning. A disturbed stomach and gut is very common and nausea and anorexia is very common.

Disturbed sleep is probably the most common symptom and many of us have experienced that. It's hard to drop off to sleep, and when you do you only find yourself waking through the night. Periodic breathing can occur as well – that pause in breathing for up to ten seconds that can wake you with a start. Acetazolomide (Diamox, discussed below) can go some way to reducing sleep disturbance.[15] And you might just feel like not doing a damn thing – apathy and carelessness and an inability to do simple things like tie up bootlaces can be a symptom. No excuses for any of that at sea level ya hear!

You may hear one side or the other of your chest 'crackling" as you breath. If that is the case you are heading from mild AMS into the territory of pulmonary oedema and need to descend immediately. (We talk some more about things pulmonary below).

## So what is Actually is Going on?

[15] 'The cerebral effects of ascent to high altitudes 'Wilson, Mark H ; Newman, Stanton ; Imray, Chris H. The Lancet Neurology 8.2 (Feb 2009): 175-91.

The best way to get a grip on AMS is to get an understanding of how the body gets its oxygen and what happens when the body detects a reduced oxygen uptake.[16] Understanding some basic biology of our own bodies is the best way to get informed about AMS, as well as how the medication for AMS works. The body reacts to the lack of oxygen in a number of complementary ways. The key reaction and responses are laid out in the table below.

| | |
|---|---|
| Hyper-ventilation | Sounds obvious. We start breathing deeper and harder. The key biological mechanism is the need to expel more $CO_2$ given there is now an imbalance of $CO_2$ and $O_2$ in the blood stream as we ascend. Less $O_2$ outside, more $CO_2$ inside – the end result is the body triggers a breathing response to get things back in balance. Kind of cool really. |
| HPV | The pulmonary arteries constrict when oxygen levels drop, redirecting blood flow to alveoli (lung wall components) with a higher oxygen content. This process is known as Hypoxic Pulmonary Vasoconstriction (HPV). |
| Arterial Pressure | Arterial chemoreceptors detect the lack of oxygen in the air and trigger two main responses. First, the body increases arterial pressure as we noted above, and secondly it redistributes its blood flow.[17] Blood is redirected to organs with high metabolic requirements and so the body makes better use of the oxygen that is delivered. In addition a vasoconstrictor response occurs in skeletal muscle and the bowel, thereby maintaining arterial pressure. It is the body's equivalent of the pressure suit or g-suit fighter pilots wear to counter blood loss from the brain and heart under high g-loads. There is little response in cerebral vessels and vasodilatation occurs in coronary vessels so that blood flow is maintained in these organs.[18] That is, in the brain and the heart. Remember this when we get to discuss HAPE and HACE below. |
| Hematocrit | There is an increase in red blood cells as a percentage of our blood, along with an associated reduction in plasma volume. Our red cell count is about 45% of the volume of blood, the rest being made up of white blood cells and plasma, which coincidentally carries about 3% of your oxygen (but in a dissolved and therefore inefficient form). That is, 45% at sea level. (It's this percentage that is called *hematocrit*). This percentage lifts at altitude but as you might imagine it takes some time for this percentage to increase. The body obviously produces these extra cells to help capture as much oxygen through the lung wall as possible and to expel as much $CO_2$ as quickly as possible. |
| Sheer numbers of red blood cells | Naturally an increase in the percentage of red blood cells implies an increase in the overall number of red blood cells. That is, the body triggers an increased production of red blood cells from your bone marrow. |

Table 3

Our blood comprises white blood cells, plasma, and red blood cells. And a few other things. But it's the red blood cells we are interested in. The main job of the red blood cells is to take oxygen from our lungs to the cells in the organs and tissues that need it. Which is everything actually, except the cornea which gets its oxygen from the air.

[16] A very technical explanation can be found here Effect of Altitude on the Heart and the Lungs Peter Bärtsch, MD; J. Simon R. Gibbs, MD, FRCP Circulation. 2007; 116: 2191-2202

[17] Circulatory Adjustments to Hypoxia Donald D. Heistad,M.D.,and Francoism.Abboud,M.D., Circulation. 1980; 61: 463-470

[18] Circulatory Adjustments to Hypoxia Donald D. Heistad,M.D.,and Francoism.Abboud,M.D., Circulation. 1980; 61: 463-470

Each red blood cell contains a molecule called hemoglobin which is specifically designed to hold oxygen and carry it to the cells that need it. About 33% of each red blood cell is hemoglobin. Each hemoglobin molecule contains four iron atoms and each iron atom is able to bind with one oxygen molecule (which actually has two atoms (hence O2) so eight oxygen atoms bind to each hemoglobin molecule. In the lungs the oxygen easily binds with the hemoglobin where there is plenty of oxygen and then easily releases in the capillaries in the organ and muscle tissue where there is a dearth of oxygen.

On the return trip after delivering oxygen to the organs and tissue the red blood cells help remove CO2 from the body. It is carried back to the lungs where we exhale it as we breathe. Red blood cells contain an enzyme called carbonic anhydrase which helps the reaction of CO2 and water to occur 5000 times faster. Carbonic acid is formed which then separates into hydrogen and bicarbonate ions. Why do I need to know this? It helps us understand how Diamox works.

When we ascend to altitude there are less oxygen molecules in the air with which to fuel our organs and tissue. The body had multiple sensors which detect this reduced oxygen and, as we saw in Table 3 they trigger various responses to help compensate. Our acclimatization plan (see below) is a timetable that is designed to allow these responses to take effect – climb too quickly and the body does not have enough time to adjust.

The body takes time to make all these adjustments. It is a process that can take days or months. The body can make these adjustments up to about 7000m. Above 8000m the body simply refuses to acclimatise at all – hence the rather apt reference to 'being in the death zone' when climbing at these heights.

This graphic[19] gives a really nice summary of the way the body reacts to a lack of oxygen (Acute hypoxia) and a potential consequence – pulmonary hypertension. That is, the lungs being put under pressure.

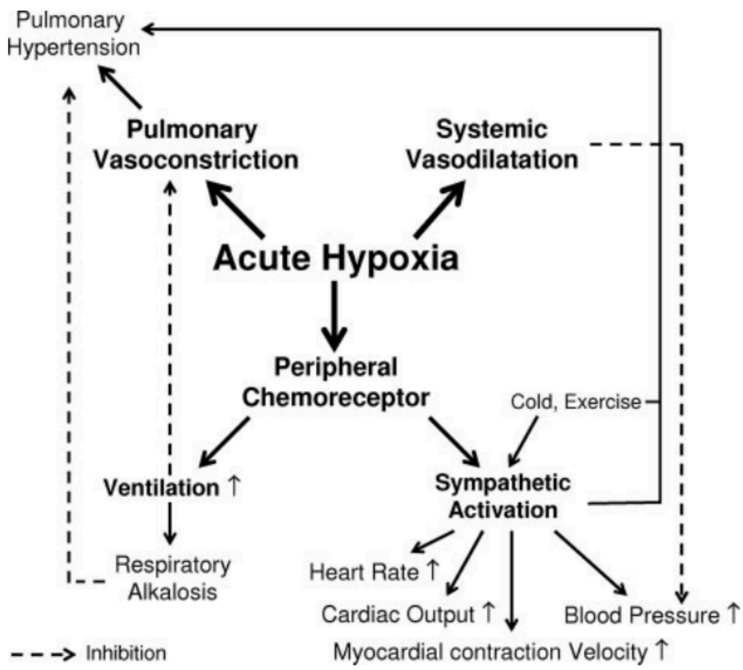
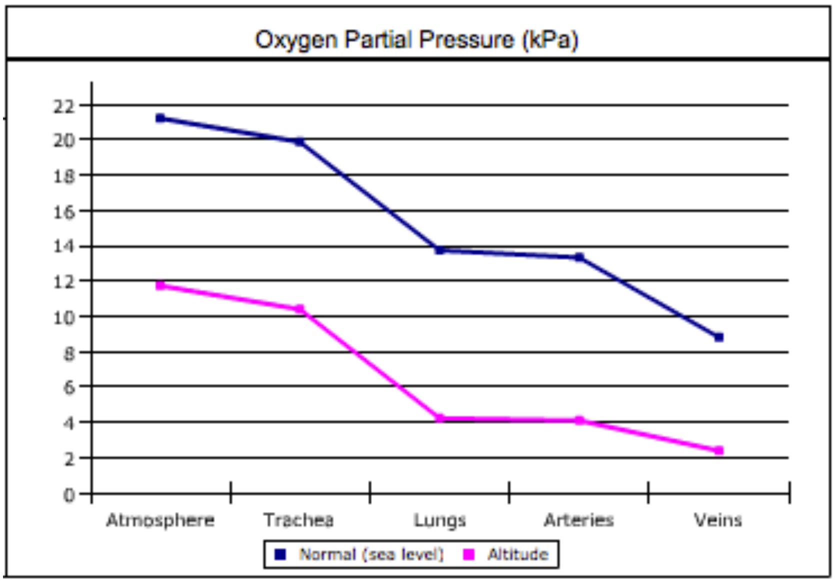



**Figure 1.** Effects of hypoxia on systemic and pulmonary circulation.

[19] From Bärtsch P, Gibbs J. Circulation 2007;116:2191-2202

## Understanding the Impact of Pressure on this Biology

Okay now we mess the biology up by introducing some physics. We keep talking about pressure. Here is where it kicks in.




Gases dissolve, diffuse, and react according to their partial pressures, and not according to their concentrations in gas mixtures or liquids. As we noted above, as we climb higher the barometric pressure drops and therefore the partial pressure of oxygen drops, and therefore our ability to take up oxygen falls away as well. Partial pressure is the hypothetical pressure of any gas if it alone occupied the volume of the mixture at the same temperature. Still with us? No. That's OK. We're still back to the basic principle that as we ascend, barometric pressure drops and the ability of the body to take up oxygen reduces. However, up to a certain altitude the body is able to adapt to that drop in partial pressure and still deliver oxygen to organs and muscle tissue.

Here is why pressure is important. The transfer of oxygen through the lung wall to the red blood cells is a passive process – the oxygen simply moves down a pressure gradient. It's a pressure gradient in the capillaries that also underlies the transfer of the oxygen atom to the muscle tissue. As the pressure gradient weakens less oxygen is able to move through the lung wall. In addition, the ability of the hemoglobin to bind oxygen to its iron atoms weakens as the partial pressure drops. Hence pressure, rather than concentration of oxygen, is really the main issue relating to AMS.

This graphic might help understand what is going on. This shows the difference between oxygen partial pressure at sea level (blue line) and what is available at 5000m (pink line). Apart from anything else you can see how the gradient between various parts of the body has flattened, making it more difficult for that oxygen to make its passive transfer, not only through the lung wall but from the red blood cell to the muscle cells that need it for fuel.

An analogy that might help is that of a marble (oxygen molecule) rolling towards a piece of tissue (lung wall). If the slope down which the marble rolls is steep enough it will pass through the tissue. If the slope lessens the marble does not make it through. (That's not exactly how pressure gradients work but you get the idea).

## High Altitude Cerebral Edema (HACE)

We introduced HACE and HAPE earlier. They are forms of AMS and are dangerous, potentially fatal dangerous. So pay attention. The good news is that very few people suffer these forms of AMS and usually only those who have ascended rapidly. Flying to high altitude then getting out and climbing without subscribing to any acclimatization plan is a common reason for people suffering HACE or HAPE. Sadly it occurs on Kilimanjaro, probably because trekkers attempt to simply haul straight to the top.

Having said all that, it is HACE and HAPE for which we all should be very alert. Predicting who might, or might not suffer HACE or HAPE is impossible. So we watch for the signs of both of them.

HACE stands for High Altitude Cerebral Edema. If we were going to be perfectionists we would spell it oedema but that would mess the acronym now wouldn't it? Cerebral relates to 'the brain' as I am sure you already know. Now that you are aware of the body's response to a lack of oxygen, and in particular that blood pressure is increased and oxygenated blood pushed to the organs that need it the most you will understand that your brain tissue is not only the prime recipient of that extra oxygen but it is also now under pressure. Under extra pressure the brain accumulates fluid, the brain swells and soon you are not functioning properly.

Someone who shows signs of HACE has probably already displayed signs of AMS. In fact AMS and HACE might be considered either ends of the altitude spectrum though the distinction between the two is increasingly blurred. Although HACE can occur as low as 8,202'/2,500m it is more likely to occur above 11,482'/3500m.[20] Because this low-oxygen injury affects the brain and thought process, a person with high-altitude cerebral edema may not understand that symptoms have become more severe until a traveling companion notices unusual behavior.[21] Watching out for each other is so very critical when climbing at altitude.

### HACE Symptoms

Often/commonly but not always preceded by AMS

- Ataxia
- Hallucinations
- Disorientation
- Behaviour Change
- Confusion
- Decreased levels of consciousness
- Coma

Someone with HACE becomes confused, irrational, unusually quiet or noisy, clumsy and unsteady on their feet and can hallucinate – the "third climber" effect. They eventually become sleepy and lethargic before slipping into a coma. It's a process that can take as little as 12 hours from first signs to coma. One of the fist signs is ataxia – being uncoordinated – and heel-toe walking is a good way to test for it. First signs to appear

[20] Pollard and Murdoch, The High Altitude Medicine Handbook p 14
[21] Altitude Sickness Harvard Health Publications. Health Topics A - Z. (Jan 2013)

are often the last to go so ataxia will probably persist even when the person is successfully on the mend. Anyone with ataxia at altitude should be assumed to be suffering HACE. If in doubt **assume** HACE.

## Treatment for HACE

There is only one treatment for HACE – descend immediately. Acetazolomide has no effect on HACE. However dexamethasone can be administered (in our case orally) 8mg initially followed by 4mg every six hours. If you have access to oxygen administer oxygen straight away. And if there is recourse to a portable hyperbaric chamber then use it. But these measures need to be part of a descent plan and actually descending!

**Our Experience with HACE**

Kilimanjaro, Tanzania

December 2014. On arrival at Kibo Huts one of our team suddenly collapsed, vomited and otherwise was in bad shape. A headache which had started just a little earlier was now overwhelming. Our guides insisted a nights sleep would cure the problem but it was obvious this was serious. The person was confused and disoriented and was unable to walk. All classic symptoms of HACE. Unhappily the guides felt all would be well but we insisted the member be taken off the mountain immediately, the guides only reluctantly agreeing when we insisted the whole party would leave the mountain rather than summit if the guides did not comply. The guides eventually agreed and escorted the person down the mountain. This proved a serious case of HACE which was not completely remedied even after a number of days in hospital and the impact continues to linger three years later. **Lesson**: know the AMS symptoms and insist on the safety of your own party. You cannot abrogate your life and health to someone else. Be prepared to take immediate action to save a life. Don't wait for someone else to make that decision for you.

Salkantay Track, Peru

July 2016. Only a few hundred metres from the summit (15,000'/4600m) of Salkantay Pass we came on a father and daughter who had never heard of AMS, and were unaware altitude could kill them. The daughter was disoriented, seriously distressed, and her ataxia was extreme. Once again we saw extreme symptoms of HACE. Despite our warnings the father pressed to the summit. Once there we urged him to get his very ill daughter down the other side. When we saw them a few hundred metres lower eating a meal the daughter appeared hale, hearty and displayed no symptoms of HACE. **Lessons**: (1) they got away with it but 'pressonitis' not only kills fighter pilots but trekkers and climbers who ignore the symptoms in order to just get to the top. No summit is worth your life. (2) only a short descent will ease the symptoms, in this case extremely markedly.

## High Altitude Pulmonary Edema. H A P E

*Pulmonary* refers to the lungs. It's hardly surprising that this organ might get stressed out. It is a tough and flexible piece of organ tissue but, for all that, the lungs are doing a massive amount of work and are central to the whole oxygenation process. But the alveoli (points through which gaseous exchange happens) between the blood and the air can and do rip and rupture, as do blood vessels, thanks to that increased pressure we referred to above – the body's response to lower amounts of O2. That is exacerbated by the lower barometric pressure which makes for a large pressure differential between blood vessels and the surrounding tissue. Short story - fluid builds up in the lungs and that is never a good thing.

Feral goat lungs – inflation demonstration

If there is good news about HAPE, it is that it is quite rare. But it is also potentially fatal so we keep an eye out for it in the same way we watch out for HACE.

While the factors that control susceptibility to HACE are poorly understood[22] it is also most common when climbers rapidly ascend at ridiculous rates of ascent, or overly exert themselves. Remember the 'steady as she goes' advice. Symptoms of high-altitude pulmonary edema commonly appear at night and can worsen during exertion.

HAPE usually but not always (that's the problem with HACE and HAPE – nothing is 'typical') is preceded by AMS. The first signs of HAPE are significantly reduced fitness – strength is reduced when walking uphill and recovery speeds become drawn out. This is followed by breathlessness even when resting, especially at night. An irritating cough will accompany this which will start dry but becomes wet, sputum filled and often blood stained. Note that a dry cough will almost always happen in the drier air at altitude and should not be confused as a HAPE symptom.

Signs and symptoms for HAPE are subtle to start with. At rest a heart beat of 100 beats per minute of above is a possible indicator. As is rapid breathing at rest. Rapid breathing is anything over 20 breaths a minute. There is usually fever and the lung will crackle as the condition worsens. There can be shortness of breath. Dry cough and blood stained sputum.

[22] The cerebral effects of ascent to high altitudes Wilson, Mark H ; Newman, Stanton ; Imray, Chris H. The Lancet Neurology 8.2 (Feb 2009): 175-91.

- Chest tightness or fullness
- Extreme fatigue
- Inability to catch your breath, even when resting
- Blue or gray lips and fingernails
- Coughing, which may produce pink frothy fluid
- Fever (temperature is above normal but is less than 38.3° Celcius)
- Noises when breathing, such as rattling or gurgling sounds

## Treatment

No ifs and buts – descend. Any other treatment without descending is pointless. Exertion should be kept to a minimum so the climber may need assistance. Oxygen can make a significant and dramatic difference. Because cold raises pressure in the arteries of the lungs keep the climber warm.

Nifedipine, 10mg sublingually (a capsule broken and held under the tongue), followed by 20mg (slow release preparation) by mouth four times daily, has been shown to help relieve symptoms and is the most useful.[23]

The use of acetazolamide to help manage AMS may help prevent the advent of HAPE.

[23] Pollard and Murdoch, p 19

## So What Can I do About AMS?

The symptoms of AMS will disappear 24-36 hours after appearing if you do not continue to ascend. If the symptoms persist then the only option is to descend to a lower altitude which will cause the symptoms to rapidly disappear.  But there are some good preventative measures which help ensure you don't experience AMS or only experience mild symptoms. It's a package of measures that include hydration, sleep, avoiding over exertion, drugs, slow ascent and an acclimatization plan that includes a "climb high/sleep low" strategy.


## Hydration

Simple really. Keep the fluids up. Not so simple in practice as many of you know. You need to drink but there is every chance you won't actually feel thirsty.  And Diamox can make what you are drinking taste odd.  One way to solve the problem of not feeling thirsty is to drink sports drinks. Drinking water alone triggers the 'no longer thirsty' message in your brain and so you will stop drinking even when you are dehydrated.[24] So having water in your Camelbak is well and good, but having a couple of litres of water mixed up with a sports drink powder is the way to go too. The US Navy study that explored the incidence of low altitude AMS found those who were hydrated were less likely to suffer from AMS.[25]

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[24] The Australian Institute of Sport has an excellent study on this phenomenon at http://www.ausport.gov.au/ais/nutrition/factsheets/hydration/fluid_-_who_needs_it

[25] High Altitude Headache and Acute Mountain Sickness at Moderate Elevations in a Military Population During Battalion-Level Training Exercises Norris, Jacob N, MSC USN; Viirre, Erik, MD, PhD; Aralis, Hilary, MPH ; Sracic, Michael K, MC USN; Thomas, Darren, MC USN; et al. Military Medicine 177.8  (Aug 2012): 917-23.

## Sleep

For reasons no one fully understands the acclimatization process is enhanced by sleep. The US Navy, cited above, affirm that in their study. So we aim to get as much sleep as we can. You will be fatigued at any rate and will find you are in bed early. A key point to note is that at altitude you should **NOT** use sleeping pills to help you sleep. Those things suppress your breathing and that is a potentially fatal step to take. So leave your valium at home please. The benefits of sleep are also the basis of our 'climb high/sleep low strategy discussed below. Another suppressant of your breathing at altitude is alcohol. Confusing the symptoms of AMS is one reason climbers don't drink while climbing. Shutting down your breathing reflex is a jolly fine reason as well. Leave the booze at home too.

## Drugs!

No, not those we found on the side of the track in Nepal – though that stuff may just help too. A number of chemicals have been shown to be beneficial in mitigating the effects of AMS and professional alpine groups ascending above 15,000'/4,572m will often insist on taking medicine as part of an acclimatization strategy. Our drug of choice is Acetazolamide (or Diamox). It is important to understand that Diamox does NOT remove the need to climb slowly and within safe rates of ascent. Some mountain rescue teams will use large doses to help manage rapid ascent (above 500m/day) but there is a reasonable argument that can be made that says Diamox is not needed for modest rates of ascent.[26] Where there might be any room for doubt about rates of ascent, and/or where we have climbers unsure about how they might respond to altitude then we climb with Diamox.

Diamox is also NOT used in very dry climates such as the Andes where humidity can be as low as 7-9%. This is because the relative humidity makes managing your hydration doubly difficult and Diamox only exacerbates the challenges of managing your water intake and retention. The doctors and guides on Aconcagua will insist you not take this drug at all.

Diamox is a drug that has been shown to be very effective in preventing the onset of AMS. It is not a substitute for good ascent discipline or a good acclimatization plan. But used in conjunction with these tools (discussed below) it is the difference between a successful trip and an uncomfortable trip.

You NEED to see your doctor and have them prescribe Diamox for you. In Australia you cannot buy Diamox without a prescription. The tablets come in various sizes. You need to purchase 250mg rather than 500mg. You should only have to pay about $20. It's on the PBS register if that helps.

[26] 'Efficacy and harm of pharmacological prevention of acute mountain sickness: Quantitative systematic review' Dumont, Lionel; Chahe Mardirosoff; Tramer, Martin R. British Medical Journal, International edition 321.7256 (Jul 29, 2000): 267-72.

## How Does Diamox Work?

Diamox forces our kidneys to excrete bicarbonate which makes the blood more acidic. In turn the body 'assumes' it has too much $CO_2$ in the blood and so breathes harder and deeper to expel this imaginary excess from the body. As we noted above, this hyperventilation increases the amount of oxygen in the blood. The hyperventilation results in reduced carbon dioxide (an acid) and a respiratory alkalosis. The normal physiological response to a respiratory alkalosis is for the kidneys to increase excretion of bicarbonate to compensate for the loss of carbon dioxide. This kidney response takes a few days. However acetazolamide in a sense accelerates this process by leading to a more rapid renal bicarbonate loss (metabolic acidosis).

### Diamox Side Effects

Acetazolamide has been in use since the 1930s and there are no known adverse affects to the drug, in part because it is used for such a short period of time. At least for those of us climbing. It has other medical uses as well. It is a sulphur drug. Allergies to sulphur drugs are rare[27] but if you are allergic to sulphur drugs talk to your doctor about an alternative to diamox. As a general rule it does not interact with other medicines but again check with your doctor first. In particular make sure any emergency antibiotics you get prescribed from your doctor don't interact with acetazolamide. Having said that, there are three things you are likely to notice when taking this drug.

- Excessive Urine. You will pee a lot more. Heaps more. More than seems normal, and as much as 3 litres in any 24 hour period. That amount tells you just how important hydration is. Excessive urination is known as *polyuria*.

- Pins and Needles. You may also get a sensation not unlike pins and needles. It's not an excessive or overly unpleasant sensation such as having insects crawling under your skin. But it can be a bit uncomfortable. It's known as *parasthesia*. (Insects or other beasties under your skin is known as *formication*). In the case of acetazolamide our experience has been that of tingling in the fingertips, something some of the Thorung La trekkers experienced, though some did initially confuse that sensation as an AMS symptom.

- Taste This may be the most distressing thing for some. A few in Nepal were not able to drink flavoured drinks such as Coke as their sensation of taste was so disrupted.

### Non Drugs – Water

It needs to be said again. Hydration is a key factor in helping prevent AMS. Make sure you have a good hydration plan and stick to it. There is no scope for macho, dry climbing tactics.

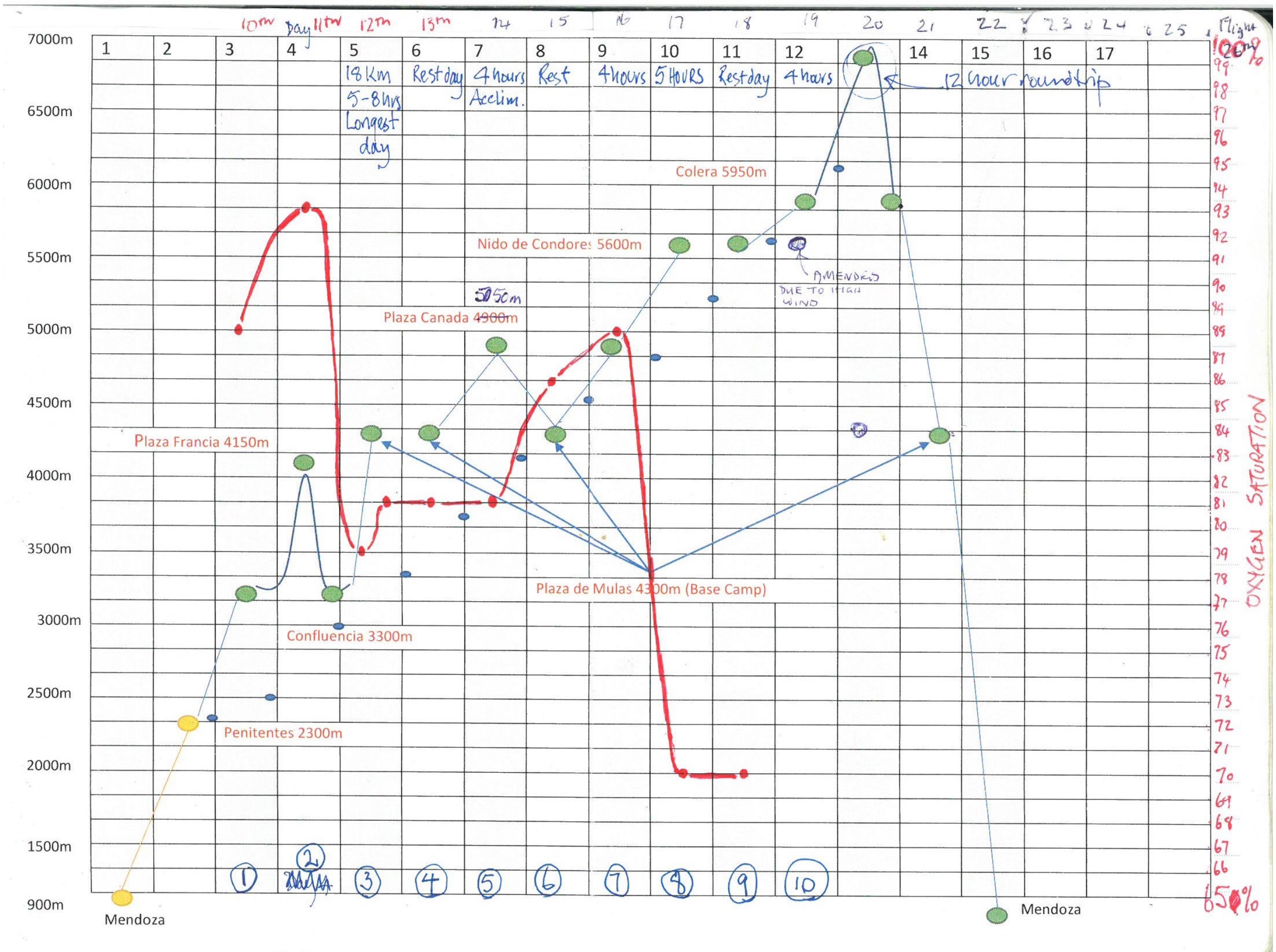
[27] High Altitude Sickness Richards, Paul. Practice Nurse 27.6 (Mar 26, 2004): 49.

## Effort - Fitness and Strength

Fitness plays a part in helping manage the onset of symptoms but will not save you. A mallee bull will die just as surely as a lard-arse if you ignore the symptoms and don't descend if AMS strikes you. In fact there is numerous evidence that suggests the very fit are more prone to AMS, given their inclination to ascend at a rapid rate. One of the fittest females on the planet came down with AMS. Former tennis champion Martina Navratilova was hospitalized for pulmonary edema-fluid build-up in the lungs-while climbing Mount Kilimanjaro.[28] Which is neither here nor there other than as a useful warning that fitness and strength does not preclude you from AMS.

## Oxygen Saturation

The government doctors at each camp on Aconcagua will check your physiology and your mental health and in particular measure and watch your oxygen saturation. Your results at one camp are transmitted to the doctor at the next camp so there is no fudging it! And if the doctors are not happy with your saturation they have the authority to pause your ascent until you are better acclimatized, or to stop your climb. This discipline is in stark contrast to the approach on Kilimanjaro which invites problems.




In this plot the oxygen saturation plotted against my ascent of Aconcagua can be seen in red, measured in percentage terms (right hand scale). This percentage reflects the amount of hemoglobin saturated

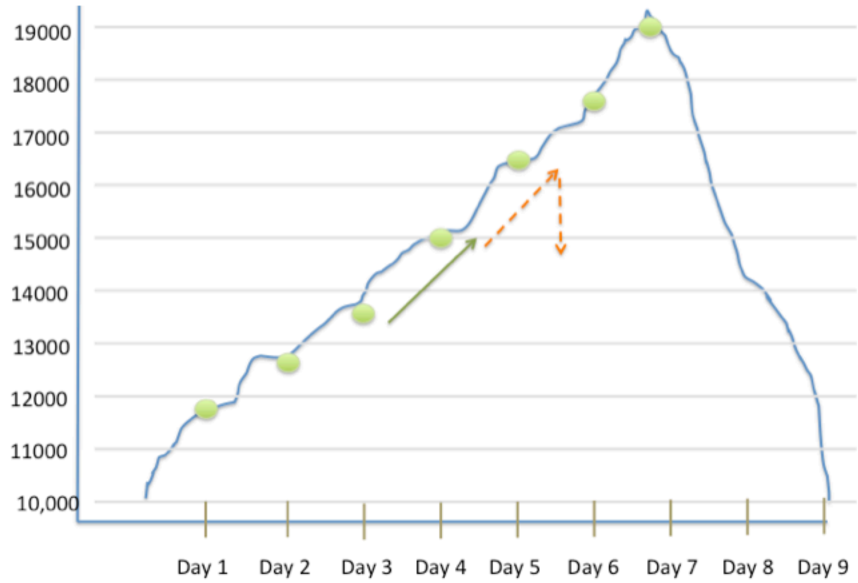
[28] www.VerticalNews.com 9 January 2011

with oxygen in the blood. You will recall from the notes above that hemoglobin is critical to oxygen being carried in our blood. The acclimatization plan and each camp is plotted in green.

The first reading was taken at 3300m and returned 88%, lifting to 93% when we reached 4100m. Thereafter the oxygen saturation continues to reflect the adjustment of my body to altitude. In particular you can see the adjustment upwards as we acclimatized at Plaza Canada. The ascent to Nido de Condores at 5600m saw my oxygen saturation drop to 70%. Unfortunately a two week storm blew us off the mountain at that point and measurements ceased – and ceased to be relevant as we descended. However the stabilisation at 70% reflects the earlier stabilisation on days three, four and five and I'm confident the ascent to the summit would not have been inhibited by oxygen uptake.

## Acclimatisation Plan

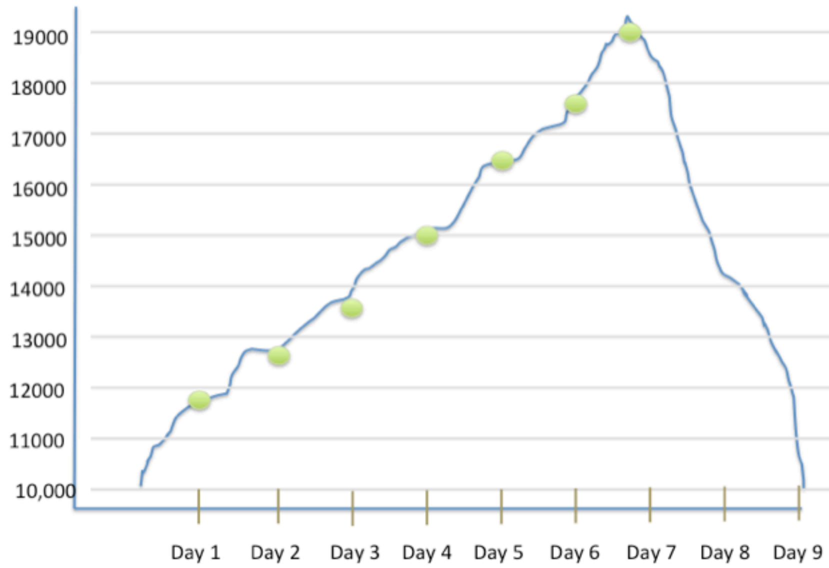
Quite simply the best defence against AMS is to ascend according to a rate that allows your body to adjust to the conditions you are putting it through. This is what we call our acclimatization plan. The plan includes three key variables: rate of ascent and the number of nights spent sleeping at altitude, supported by a program of 'climbing high and sleeping low. The acclimatization plan is the foundation of all safe high altitude climbing.




The rule of thumb is not to have a cumulative ascent any greater than 1000'/300m in any given day over 10,000'/3,000m. Some advice suggests as much as 1,500'/460m a day is safe. And every third day, stay one day and two nights at that altitude.

So the theoretical rate of ascent for a 19,000' peak looks something like this.

Each green dot represents our overnight stop. However the key factor to bear in mind here is that, within reason it is the cumulative height gained that is important. So when the Blue Steel Dash Team crossed Thorung La at 18,000' they climbed from 15,000, gained 3,000' at the pass then dropped to 12,000 at Muktinath on the other side for a net altitude accumulation of -3000'/-1000m. Climbing 3000'/1000m in the one day was hard work but as part of a good acclimatization plan it was managed well by everyone.

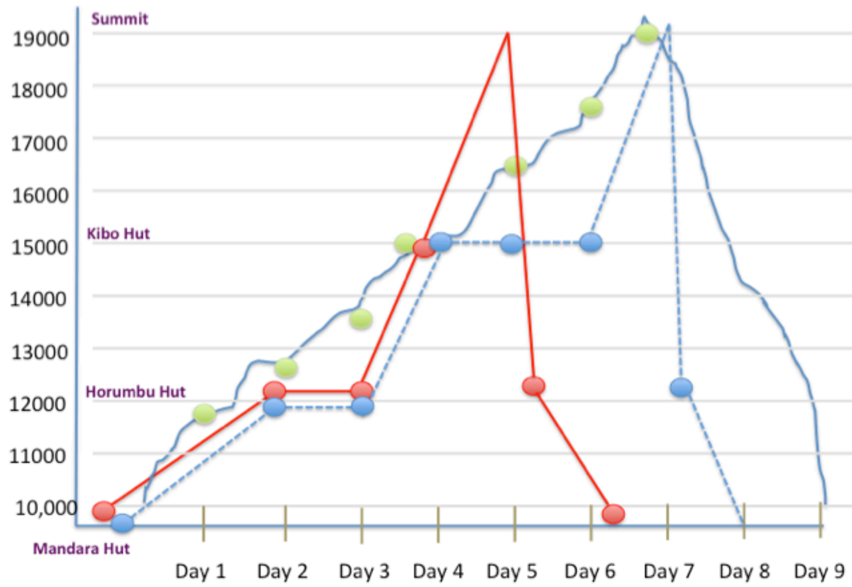



### Climb High/Sleep Low

In addition to the rate of ascent an acclimatization plan incorporates a 'climb high/sleep low strategy. At the end of each day we drop packs, take fluids and climb 1000'/300m then return to our camp site. As we noted above, we acclimatize better as we sleep.

We back all that up by sleeping multiple nights at the same altitude every second or third day.

This theory is better reflected in the real life planning for Kilimanjaro. In the graphic here the red dots show the "packaged" rate of ascent which many groups attempt on Kilimanjaro. That is one reason why only 4 out of 10 starters make it to the top. The green dots reflect the theoretical rate of ascent, while the blue dots reflect one plan for Blue Steel Dash. There are two options - to spend a third night at either 12,000'/3,658m or at 15,000/4,572m as part of our acclimatization plan. The dotted blue line brings us closer to the overall theoretical green dot rate of ascent.




In looking at this plan there are variables contributing to potential AMS which stand out. The rate of ascent initially proposed. The cumulative altitude gained in any given day. And the possible exertion required to achieve these huts each day. And finally, though the descent date is indeed very rapid and represents significant altitude drop, there is the matter of a 4,000'/1,220m ascent to the summit, 1000'/300m more than the effort at Thorung La.

# The Lake Louise Consensus on the Definition of Altitude Illness

The following definitions on the diagnosis of altitude illness were adopted at the 1991 International Hypoxia Symposium, held at Lake Louise in Alberta, Canada.

| | |
|---|---|
| **AMS** | In the setting of a recent gain in altitude, the presence of headache and at least one of the following symptoms:<br><br>- gastrointestinal (anorexia, nausea or vomiting)<br>- fatigue or weakness<br>- dizziness or lightheadedness<br>- difficulty sleeping |
| **HACE** | Can be considered "end stage" or severe AMS. In the setting of a recent gain in altitude, either:<br><br>- the presence of a change in mental status and/or ataxia in a person with AMS<br>- or, the presence of both mental status changes and ataxia in a person without AMS |
| **HAPE** | In the setting of a recent gain in altitude, the presence of the following:<br><br>**Symptoms:** at least two of:<br>- dyspnea at rest<br>- cough<br>- weakness or decreased exercise performance<br>- chest tightness or congestion<br>**Signs:** at least two of:<br>- crackles or wheezing in at least one lung field<br>- central cyanosis<br>- tachypnea<br>- tachycardia |

# AMS Worksheet

Name________________________________ Age _____ Sex____ Date ______________

Prev Hx AMS/HAPE/HACE? Meds: Ascent Profile: Treatment:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time | | | | | | | |
| Altitude | | | | | | | |
| | **SYMPTOMS** | | | | | | |
| HEADACHE | No headache 0 | | | | | | |
| | Mild headache 1 | | | | | | |
| | Moderate headache 2 | | | | | | |
| | Severe/incapacitating 3 | | | | | | |
| | | | | | | | |
| GI | No symptoms 0 | | | | | | |
| | Poor appetite or Nausea 1 | | | | | | |
| | Moderate nausea or vomiting 2 | | | | | | |
| | incapacitating 3 | | | | | | |
| | | | | | | | |
| FATIGUE | Not tired or weak 0 | | | | | | |
| | Mild fatigue/weakness 1 | | | | | | |
| | Moderate fatigue/weakness 2 | | | | | | |
| | Severe F/W, incapacitating 3 | | | | | | |
| | | | | | | | |
| DIZZY/LIGHTHEADED | Not dizzy 0 | | | | | | |
| | Mild dizziness 1 | | | | | | |
| | Moderate dizziness 2 | | | | | | |
| | Severe, incapacitating 3 | | | | | | |
| | | | | | | | |
| DISTURBED SLEEP | Slept well as usual 0 | | | | | | |
| | Did not sleep as well as usual 1 | | | | | | |
| | Woke many times, poor night's sleep 2 | | | | | | |
| | Could not sleep at all 3 | | | | | | |
| | **SYMPTOM SCORE** | | | | | | |
| CHANGE IN MENTAL STATUS | No change 0 | | | | | | |
| | Lethargy/lassitude 1 | | | | | | |
| | Disoriented/confused 2 | | | | | | |
| | Stupor/semiconsciousness 3 | | | | | | |
| | | | | | | | |
| ATAXIA | No ataxia 0 | | | | | | |
| | Maneuvers to maintain balance 1 | | | | | | |
| | Steps off line 2 | | | | | | |
| | Falls down 3 | | | | | | |
| | Can't stand 4 | | | | | | |
| PERIPHERAL EDEMA | No edema 0 | | | | | | |
| | One location 1 | | | | | | |
| | Two or more locations 2 | | | | | | |
| | **CLINICAL SCORE** | | | | | | |
| | **TOTAL SCORE** | | | | | | |

Serial evaluations several hours apart give a good measure of whether a patient is responding to treatment or deteriorating.