



THE INTERNATIONAL MOUNTAINEERING AND CLIMBING FEDERATION
UNION INTERNATIONALE DES ASSOCIATIONS D'ALPINISME

Office: Monbijoustrasse 61 • Postfach
CH-3000 Berne 23 • SWITZERLAND
Tel.: +41 (0)31 3701828 • Fax: +41 (0)31 3701838
e-mail: office@uiaa.ch

OFFICIAL STANDARDS OF THE UIAA MEDICAL COMMISSION

VOL: 22a

Drug use and Misuse in Mountain- eering

Intended for mountaineers and medical lay persons
(version for professionals see Vol.22b, in preparation)

**D. Hillebrandt, T. Küpper, E. Donegani, U. Hefti, J. Milledge, V.
Schöffl, N. Dikic, J. Arnold, G. Dubowitz**

2014

Preamble

It is not the UIAA Medcom's intention to judge. We simply welcome openness and honesty but also want to protect mountaineers from possible harm. We do believe that, wherever possible, the use of drugs specifically taken with the intention to enhance performance should be avoided in the mountains.

Content

1	Introduction	3
2	Drugs	4
2.1	Acetazolamide (Diamox)	5
2.2	Alcohol.....	5
2.3	Ammonium Chloride.....	6
2.4	Amphetamines and other stimulants.....	6
2.5	Anabolic Drugs.....	6
2.6	Anti-epileptic drugs/Anti-migraine drugs	6
2.7	Aspirin	7
2.8	Beta blockers	7
2.9	Coca	7
2.10	Dexamethasone	7
2.11	Erythropoietin (E.P.O.), blood doping and haemodilution.....	8
2.12	Ginkgo Biloba	8
2.13	Ibuprofen	8
2.14	Inhaled Steroids	9
2.15	Low molecular weight Heparins	9
2.16	Nifedipine	9
2.17	Dietary Nitrate (Beetroot Juice).....	9
2.18	Opiates	9
2.19	Oxygen	10
2.20	Progesterone.....	10
2.21	Phosphodiesterase type-5 inhibitors eg sildenafil (Viagra), tadalafil (Cialis).	11
2.22	Psychotropic Drugs	11
2.23	Rhodiola crenulata	11
2.24	Salmeterol	11
2.25	Sleep Medication.....	11
2.26	Theophylline.....	12
3	References.....	13
4	Members of UIAA MedCom (in alphabetical order).....	16
5	History of this recommendation paper.....	16

1 Introduction

Since man has ascended mountains most people have looked for the easiest way to achieve their desired summit. As the “sport” of mountaineering has evolved and developed some people have striven for more challenging lines, more extreme altitude or more technically difficult climbs but it has to be appreciated that mountaineering “rules” are artificial and imposed by humans. Different specialised aspects of mountaineering have evolved. Some people enjoy solo ascents of challenging lines on Himalayan giants, others ski mountaineering, trekking, mountain running, frozen waterfalls, sport climbing or bouldering in wooded meadows. Some of these disciplines are formally competitive and need rules to maintain integrity. In this specialised field we leave the World Anti Doping Agency (WADA) to devise enforceable doping regulations and tests. A regularly updated list of their regulated substances can be found on their website (1).

Non WADA regulated individuals have to determine their own personal standards for enjoyment, challenge and acceptable risk on whatever route they choose. No system of drug testing could ever, or should ever, be policed for recreational climbers. Sponsored climbers or those who climb for status need to carefully consider both the medical and ethical implications if using drugs to aid performance. In some countries (e.g. Switzerland and Germany) administrative systems for mountaineering or medication control dictate a specific stance, but for most people any “rules” would be unenforceable and have to be a personal decision. The underlying principle must be honesty with oneself and honesty with one’s peers. This applies to the use of physical aids such as fixed ropes, bolts or top rope practice of a climb, It applies to transport aid such as porters, aircraft or boats on an approach or descent. It also applies to pharmacological aids. Just as one would be expected to declare points of aid (bolt or peg) on a rock climb so one should be prepared to declare the use of pharmacological aids. This has been accepted for years with Habler and Messner being singled out for praise for the first ascent of Everest without artificial oxygen. This in no way detracted from the first ascent by Hillary and Tensing who chose to use well designed oxygen apparatus based on the current cutting edge technology, and a bit of improvisation. At this time others were acknowledging the use of performance enhancing drugs in the mountains. Hermann Buhl on Nanga Parbat in 1953 used Pervitin (methamphetamine) on the ascent after a fight with his own ethical conscience (2). In doing this he was following the practice of amphetamine use by military personnel of several countries in the Second World War and which is still continued by some countries to this day.

Different cultures and different generations have different attitudes. This diversity and lack of informed information frequently comes to a head on Everest where one is dealing with the most extreme altitude combined with climbers with many differing motivating factors. To quote Dr Luanne Freer who has offered a base camp medical service on Everest since 2003 “We estimate that during our informal survey on Everest spring 2012, at least two thirds of climbers we contacted were prescribed several performance enhancing drugs (PEDs) and had intent to use them not for rescue, but to increase their chances of summit success. When a commercial guide of a large expedition asked our staff to counsel their team on use of PEDs for summit day, we were alarmed to find a tent full of anxious climbers with pockets full of prescription drugs (prescribed by their personal physicians and filled at home pharmacies) and with no understanding or instructions on when and how to use them. Who are the health care providers writing these prescriptions? We have a duty to provide education and specific instructions about how and when these potentially dangerous drugs should be used. We have treated several climbers over the years, who without good advice, ingested every single drug in their arsenal and lost their chances to summit because of symptoms related to polypharmacy. No matter where we sit on either side of this issue, it is our duty as health care prescribers to provide very clear instructions to our patients about how, when, why to use any drug we prescribe. If we aren't certain what doses or prescribing regimen are best for performance enhancement, then we shouldn't prescribe them for that purpose (or we should educate ourselves before doing so.) Let's encourage our colleagues to do the same.”

The generation of British climbers attempting major new routes on Himalayan peaks in the late 1970s and 80s strove to avoid any drug use on the mountain, including oxygen (3). It was however admitted that some might have considered using drugs had they been aware of their existence!

It is not the UIAA Medcom's intention to judge. We simply welcome openness and honesty but also want to protect mountaineers from possible harm. We believe that, wherever possible, the use of potentially performance enhancing drugs should be avoided in the mountains. Having said that we are aware of the many sides of the debate which were outlined in the editorial and following invited com-

mentaries and subsequent letters in Wilderness and Environmental Medicine (4) and also in the article by Devon O'Neil on "Climbing's Little Helper" (5).

As physicians who love the mountains we are aware of the desire for rapid ascent but are also increasingly aware of the potential for harm, especially when poorly proven potentially potent drugs are used at altitude (6). The more drugs that are used by mountaineers the greater the chance for pharmacological interactions with consequent dangerous side effects. The first identified attempt to look at the pros and cons of specific drug use at altitude was published in July 2000 (7) and a paper was presented on the subject at the Congress of the International Society of Mountain Medicine in Barcelona by Berghold in 2002 which provided the original idea for this paper (8). We are aware that some commercial expedition and trekking companies positively encourage the use of drugs by their clients. Ultimately this has to be to increase profits in preference to encouraging slow, sensible acclimatisation. We suggest clients think carefully before accepting this practice. We accept that there may be time when the use of drugs can be appropriate but this should be tailored to the individual patient or specific circumstances, such as a strong previous history of altitude illness or a rescue party going high in an emergency. For the business man or scientist going to altitude to work mountaineering ethics may not be relevant. Furthermore, one could have an eternal debate on the philosophical and ethical aspects of drug use on religious pilgrimages to high altitude shrines and festivals.

Whatever the ultimate personal decision it is preferable that any advice should come from an experienced mountain medicine doctor who will also be able to advise on sensible ascent profiles and management of acute problems in the field. The impression gained at Everest Base Camp is that many climbers are prescribed drugs by doctors with no mountain medicine experience. The dilemma for prescribing physicians is well illustrated in the case study outlined by Bärtsch and Swenson in the New England Journal of Medicine (9). Anonymous internet advice and drug supply via the internet or from a dubious unregulated pharmacy should be avoided and can be very dangerous.

Physicians advising youngsters should consider asking their parents how they feel about the principle of encouraging children to use drugs to aid sport performance or recreation which is in direct contradiction of the ethical principles of the international Olympic movement.

In this paper we will look at the pharmaceutical agents that are or have been used in the mountains of the world. We will look at the pros and cons, side effects and benefits, possible interactions, risks, and at the research evidence currently available for each drug. We hope to update this every few years as evidence changes. Each mountaineer, climber or trekker must make his own personal decisions whether acting as a professional or recreational mountaineer or as a commercial expedition client. In the final analysis be honest with yourself and with the international mountain community.

2 Drugs

Some authorities differentiate between drugs that enhance performance and those that change performance. An example of the former would be acetazolamide and an example of the latter would be cannabis. Some people also differentiate between conventional medical drugs, dietary supplements and herbal medication. In this advice paper we will not differentiate but it must be accepted that evidence from reputable peer reviewed journals may be absent in some cases. We accept that many of these drugs have a very valuable role to play in the treatment of potentially life threatening altitude and other illness and in this situation we have no hesitation in supporting their use often buying vital time for descent.

Interestingly, in the 2010 guidelines on the prevention and treatment of acute altitude illness published by the USA based Wilderness Medical Society (10) every section on prevention initially stresses slow ascent and every section on treatment initially stresses descent. Many readers seem to miss these vital points and skip straight onto the pharmacological sections in their rush to read the paper. They then rush to the pharmacy as part of their rush to "conquer" their mountain.

It should be noted that most research into drugs used at altitude is done at 5000m or below. There are very few research studies of quality done above this height. We have no way of knowing if the side effect profile of the same drugs used at higher altitude will be the same. Extrapolation of any scientific data is unsound and potentially dangerous.

The limited data available on drug use in mountaineers shows that the use of acetazolamide in Nepal rose from 1% in 1986 to 12% in 1998 to 25% in 2010 (11 & 12).

In a pilot study 38.9% of trekkers in the Khumbu used drugs “for acclimatization” (13). An older study from 1993 reported that a total of 9.8% of recreational mountaineers in the European Alps tested positive for amphetamine, with 2.7% positive at altitude of 2,500 to 3,300m and 7.1% positive above 3,300m (14). Since tests were not performed for other drugs the total percentage of mountaineers who used drugs to increase performance may have been significantly higher. According to observations undertaken trekking or mountaineering at the Bafaru Bivouac (4,860m) on Mt. Kilimanjaro 46.7% of those studied took acetazolamide, 40.0% dexamethasone, 4.5% coca leaves, and only 8.8% were “clean”. In most cases this use was based on peer advice and pressure rather than any medical indication. Despite this drug consumption 80.0% suffered from AMS, 2.2% (n=1) from HAPE and 2.2% (n=1) from high altitude cerebral oedema (HACE) (15). Data from other groups shows a similar increasing pattern.

In one study 28% of rock climbers reported climbing under the influence of drugs or alcohol and these climbers documented more injuries ($p < 0.008$) compared to those who climbed “clean”. Males admitted more illicit substance use ($p > 0.001$) compared to women. (16). Some climbing athletes have had positive drug tests by WADA.

2.1 Acetazolamide (Diamox)

To quote from one of the most respected high altitude medical textbooks “Acetazolamide remains the mainstay of pharmacologic prophylaxis against AMS” (17). Despite it being used for many years nobody is exactly sure how this mild diuretic carbonic anhydrase inhibitor works in AMS prevention. Its current primary medical use is for the treatment of refractory glaucoma. This group of drugs were first investigated for AMS prevention in 1965 (18). There are many theories about its mechanism of action and it certainly has a multifactorial effect on acclimatisation (19). Initially it was used in the same doses required in some cases of glaucoma but over the years studies have shown that lower doses work just as well such that a dose of 125mg twice a day, ideally started 24 hours prior to ascent, is now recommended (20).

Despite a large amount of evidence for its use in AMS it is not licensed for this so in some countries some doctors are reluctant to prescribe it. It is off patent so it is never likely to be economic for it to become licensed. In some countries it is freely available in pharmacies. In the past it was thought it might mask the symptoms of AMS making the user more at risk of HAPE or HACE but it is now thought that it “kick starts” the acclimatisation process (21).

PROS: It works and for most people has negligible side effects compared with some other drugs in this article.

CONS: It is a diuretic so users may become slightly dehydrated especially when undertaking unaccustomed exercise and the use of a pee bottle may become essential to avoid trips outside on a cold night at altitude. Its use should be avoided in patients who have decreased renal function at sea level. It can cause tingling of fingers and toes in some susceptible subjects and can make fizzy drinks taste flat. It is sulphonamide related so anybody who has a sulphonamide allergy or sensitivity should avoid its use although this is rare. Medical research on its action has only been undertaken to a maximum altitude of 5895m (22) so its use above this altitude is based on the assumption that it may continue to work at higher altitudes. The scientific jury is out on its use at extreme altitude.

INTERACTIONS: If taken with corticosteroids or theophyllines it can lower the blood potassium level (hypokalaemia). The commonly used diabetes drug metformin causes a degree of lactic acidosis as does acetazolamide. Used together this effect is increased which might, in some cases, cause major problems.

ETHICS: This is a personal decision. It is currently WADA banned due to its diuretic action rather than its acclimatisation effect.

2.2 Alcohol

Alcohol is used, abused and enjoyed by mountaineers throughout the world.

PROS: It can be a very social drink and in the form of whisky is one of the few ways that the true spirit of the mountains can be obtained in a bottle.

CONS: In even slight overdose it can mimic AMS or HACE. It also reduces reflex times, can interfere with physical balance and also impairs the ability to assess and manage risk. Its slow degradation in the body (0.12% per hour) means that these effects will persist if undertaking an early Alpine start to climb.

2.3 Ammonium Chloride

Included only for historical interest but based on some good theoretical science on acclimatisation in the early 1930s. It alters the acidity of the blood.

Raymond Greene based his pressure chamber research and his work on the 1933 Everest expedition on observations he made on Kamet in 1931 and Ruttledge made on Nanda Devi in 1932. He even predicted the use of high altitude laboratories for future research (23).

2.4 Amphetamines and other stimulants

Stimulant drug use has a long history: Anecdotal accounts suggest that many ascents of 8000m-peaks in the 50's were done with the use of drugs, mostly amphetamines.

In the UK in 1978 the Climbers Club journal published Jim Perrin's account of a solo ascent of the steep Coronation Street rock climb in the Cheddar Gorge using a combination of speed (amphetamine) and Cocaine. The article "Street Illegal" became a cult short story and a collector's piece.

CONS: There is a very real risk of overexertion if using these stimulants resulting in exhaustion, hypothermia, collapse and death.

Since the early Everest attempts some climbers have praised the use of Caffeine. Houston's account of the grief reaction of the British team members on Nanda Devi in 1936 when the tea container was dropped and lost may reflect on this drug dependency. The use of caffeine was discussed by Peter Hackett when he stressed that "Importantly, habitual caffeine users should not discontinue caffeine because of travel to altitude; the symptoms of withdrawal are very similar to AMS and can be misdiagnosed as AMS". He also postulated that its effects on ventilation, cerebral circulation and as a psychostimulant may be beneficial and merit further study (24).

2.5 Anabolic Drugs

Anabolic drugs may have been used in the preparation for expeditions and hard rock climbs. The main area of their use is in sport climbing where much training is done in Gyms and fitness centres (25) where they are easily available and primarily used for muscle regeneration after severe training.

CONS: Their multiple side effects include depression, hallucinations, aggression and hypertension. These side effects may be even more pronounced at altitude and may interfere with the diagnosis of HACE. Physicians, guides and coaches should be aware of this potential problem.

2.6 Anti-epileptic drugs/Anti-migraine drugs

Gabapentin which is normally used as a drug to control epilepsy, neuropathic pain and as an unlicensed drug for migraine control (26). It has also been studied for treatment of the altitude headache associated with AMS (27). The paper only looked at 24 subjects at 3500m and its action may only have been on High Altitude headache. One look at the drug's side effect profile would put most climbers off considering its use.

CONS: Possible drowsiness, dizziness, vertigo, nausea, vomiting, cough, flatulence and more. Not been studied for prevention.

Sumatripan is a 5HT1 receptor agonist which is used to treat migraine. It has been studied for the prevention of AMS (28 & 29). The second study was of 102 subjects at only 3500m and again potential side effects are more pronounced than low dose acetazolamide. Further work has not been undertaken.

2.7 Aspirin

Aspirin is a COX-inhibitor with non-steroidal anti-inflammatory action which has been studied for the control of high altitude headache in doses of 320mg four hourly (30). It is likely that its primary effect may simply be on headache control rather than true prevention of AMS.

CONS: Although easily available without prescription in many pharmacies around the world the adverse effects of Aspirin should not be underestimated. Its antiplatelet effect increases the risk of internal bleeding from the stomach and gut, brain, retina and respiratory system. It can cause indigestion and affect kidney function.

Some mountaineers use Aspirin on the grounds it reduces clotting of the thicker blood at altitude possibly helping to prevent a potential stroke, venous or pulmonary thrombosis. This possible benefit is very small (if at all) and has to be weighed up against the risk of gastrointestinal haemorrhage which would be further increased if combined with dexamethasone.

2.8 Beta blockers

Betablockers such as propranolol and atenolol have been used to reduce the physical symptoms of stress and anxiety and for this reason they might be considered by sports climbers. They have certainly been used in competitive events such as rifle target shooting and darts in the past. They may also be used for pre existing blood pressure control in patients going to high altitude (31).

CONS: Beta blockers reduce the maximum pulse rate and therefore maximal workload, can cause lethargy and decrease the circulation to the extremities potentially putting the person more at risk of frostbite.

2.9 Coca

Despite the popularity of Coca in South America to prevent AMS either as chewed leaves or as the infusion "mate de coca" there is no evidence of it working in any clinical trials (32).

2.10 Dexamethasone

This steroid drug is being increasingly used at altitude and this reflects the layperson's desire for a medical fix for the natural process of acclimatisation without an appreciation of the medical risk/benefit ratio.

Unlike acetazolamide it does not improve acclimatisation or affect ventilation but minimises the symptoms of altitude headache, one component of AMS. It is a very valuable drug for the treatment of HACE and can be used to buy time whilst preparing for descent in the treatment of life threatening altitude illness. It has been studied for prevention of AMS and if used for this the patient has already used the one potentially lifesaving drug should they later develop HACE.

PROS: At a dose of about 8mg daily in divided doses it has been shown to reduce the symptoms of AMS. THIS DOSE SHOULD NOT BE TAKEN FOR MORE THAN ABOUT 7 DAYS (33 & 34).

CONS: As with any powerful potentially lifesaving medication it comes with marked side effects and dangers. Since it does not actually facilitate acclimatisation the patient must be monitored carefully for symptoms of AMS or HACE especially if it is stopped abruptly when at altitude. This drug should not be used in children or pregnant women (except for life saving emergency treatment). Side effects include an Addisonian crisis if stopped abruptly after more than a few days, Cushing's syndrome if high doses are taken for a long time, mood changes, depression, hyperglycaemia, peptic ulcer, gastric haemorrhage and indigestion to name but a few (6). Corticosteroid induced euphoria can decrease the ability to assess and manage risk in the mountains.

Although recommended as the second line pharmacological agent for AMS prevention by the U.S.A based Wilderness Medicine Society (35) it should be noted that they recognise the potential risks and

state that slow sensible acclimatisation should be the first line of preventative behaviour and acetazolamide the first line drug if medication is still really required.

INTERACTIONS: The gastrointestinal side effects can be exacerbated if mixed with NSAID drugs including Aspirin or ibuprofen.

ETHICS: For recreational mountaineering the use of corticosteroids has to be a personal decision but the risk/benefit equation is very different from acetazolamide since the potential side effects, interactions and problems are much greater.

2.11 Erythropoietin (E.P.O.), blood doping and haemodilution

Drugs such as recombinant EPO, continuous erythropoiesis activator factor, novel erythropoietin stimulating protein (NESP) aim to increase the formation of oxygen carrying red blood cells (erythropoiesis) at altitude and have been used by competitive athletes to increase low altitude performance.

There is no doubt that blood doping by autotransfusion of stored blood taken from an athlete and then transfused prior to competition does increase sea level performance (36). Just as EPO is used to try to increase the oxygen carrying capacity of the blood by increasing the number of red blood cells and therefore thickening the blood this comes with the risk of blood clots causing strokes or pulmonary emboli.

No research has been done at altitude but logically they might further increase the natural thickening of blood at altitude therefore increasing the risk of clots causing stroke or pulmonary emboli (clots on the lung). Both are potentially fatal conditions.

Diluting the blood is designed to make it thinner so making it easier to flow through the blood vessels and possibly carrying more oxygen faster. It has not been shown to work at high altitude and may result in less oxygen being carried (37).

The fact that EPO, autotransfusion and haemodilution “treatments”, which have contradictory effects, have all been tried illustrates that this is based on dubious theory rather than medical evidence. In reality increased thickness (viscosity) of the blood results in reduced cardiac output and increase viscosity results in less oxygen carrying capacity in the blood. All have associated risks. It is possibly best to rely on sophisticated natural changes in the blood which occur with acclimatisation and have evolved over millions of years.

2.12 Ginkgo Biloba

This plant falls into the antioxidant radical scavenger class but in many countries is sold as a herbal medication without the strict formulation regulations of the established national and international pharmaceutical bodies. It is therefore difficult to assess its true efficiency and is subject to conflicting evidence (38, 39, 40, 41 & 42).

2.13 Ibuprofen

In 2012 two papers were published looking at the possible use of ibuprofen in the prevention of AMS based on the hypothesis that its antiprostaglandin anti-inflammatory properties may be relevant (43 & 44). The jury is still very much out after these two papers and Ken Zafren gives a good summary of the evidence and pitfalls in an editorial in the Wilderness and Environmental Medicine (45).

It is also known that ibuprofen is used to mask soft tissue pain in endurance mountain marathon runners and in sport climbers.

PROS: weak evidence in the above papers.

CONS: Real risk of gastrointestinal bleeds associated with this group of drugs which may be increased at altitude with the associated physiological stress of acclimatisation. In a dehydrated individual the known risk of renal failure is greatly increased.

2.14 Inhaled Steroids

Word has got round the mountaineering community that inhaled steroids such as beclomethasone reduce the symptoms of high altitude cough. This is unproven. Due to the uncritical acceptance by lay mountaineers of this perceived benefit a recent attempt to study this possible effect of inhaled steroids at Everest Base Camp struggled to enrol sufficient subjects who were willing to use a placebo as one critical arm of the study (46).

CONS: Not expected to ameliorate AMS. Unresearched. Can predispose to oral infections.

2.15 Low molecular weight Heparins

There is no evidence that these anticoagulants prevent AMS, HAPE or HACE. Some people have advocated their use to minimise the real risk of cerebrovascular events (strokes) at altitude. They require self injection and being heat labile require special arrangements for transport and storage (47). Like Aspirin they increase risks of bleeding and are potentially dangerous.

2.16 Nifedipine

Nifedipine is the drug of choice to buy time for the vital descent in the management of HAPE. Used like this it can be a life saver. It does not treat or prevent AMS. It has been shown to aid in the prevention of HAPE in susceptible individuals who, more importantly, must adopt a gradual ascent profile (48).

CONS: As with any powerful potentially lifesaving drugs nifedipine has side effects. If used for prevention it cannot be used for treatment. If the patient is taking any other drug from the same calcium channel blocker class it should be avoided due to a combined effect on lowering blood pressure. The long list of recognised side effects in some people include dizziness, flushing, peripheral oedema (potentially dangerous in tight boots predisposing to frostbite), insomnia, drowsiness and depression (49).

INTERACTIONS: Marked hypotension if used in very dehydrated people or if combined with a phosphodiesterase type-5 inhibitor (eg sildenafil "Viagra" or tadalafil "Cialis"). At altitude only slow release nifedipine preparations should be used.

2.17 Dietary Nitrate (Beetroot Juice)

Excessive inorganic nitrate within our diet has long been associated with several harmful side effects, yet hard evidence is far from conclusive. In contrast, recent scientific literature increasingly acknowledges the beneficial role of nitrate supplementation (e.g. concentrated beetroot juice) with respect to health and exercise. The exact underlying mechanisms remain unclear, however a strong hypothetical justification is presented for the effective use of beetroot juice to improve performance at altitude, where the conversion of dietary nitrate to its biologically active derivative, nitric oxide, may be enhanced. (50, 51, 52, 53, 54).

PROS: Well constructed double blind, placebo controlled studies have shown very promising results thus far, including increased exercise tolerance and reduced oxygen consumption during exercise and rest.

CONS: I) Individuals are cautioned against inorganic and organic nitrate confusion. II) Despite exciting initial findings, altitude and dose specific evidence still requires greater clarity. III) Side effects of chronic supplementation have yet to be examined, with specific sub-populations expected to present sensitivity and potential hypotensive concerns with overconsumption. IV) No apparent protection from AMS symptoms

2.18 Opiates

These narcotic drugs include codeine, dihydrocodeine, tramadol, fentanyl, morphine and are used in some sports to mask pain. This may have some advantage in extreme rock climbing but, ignoring obvious ethical implications, brings risks, especially at altitude.

To some degree all can depress breathing, cause drowsiness, reduce reaction times and risk appreciation, induce constipation and are potentially addictive.

2.19 Oxygen

ETHICS: The ethics of oxygen use have been extensively debated since the 1920s and will continue to be debated for many years to come. There is no doubt that oxygen is a drug, available only on prescription in many countries and that it increases performance at altitude. Some would say that any drug or artificial aid which increases performance is not acceptable for climbing and every mountaineer will express great respect for the very few climbers who have summited Mount Everest or other 8000m peaks without using artificial oxygen. On Mount Everest this is just over 60 out of a total of over 5000 ascents!

With this background it is not surprising that the oxygen section of this paper caused more debate within the UIAA Medcom members than any other section. In this area there is direct conflict between our ethics as doctors to help people maintain optimum health whereas our ethics as mountaineers accept a degree of personal risk and tend to want to minimise the use of artificial aids.

For altitudes below 5000m given time most people can acclimatise naturally so they can climb peaks of over 6000m from a high camp without using artificial oxygen. It is only well above 7000m where the pros and cons debate is truly relevant.

PROS: Artificial oxygen provides the human body with the one drug it really needs at extreme altitude! There are no interactions. Anybody doubting its effectiveness should read Edmund Hillary's account of the use of the first reliable system for the summit push on the first ascent of Everest (55). Despite the oxygen and supply system weighing 30 pounds its benefit was obvious when the mask was removed. Climbers now use lightweight cylinders and a much more sophisticated and reliable delivery system.

One study looked at the death rate in mountaineers attempting Everest without oxygen(56) another study looked at the death rates on both Everest and K2 (57). Both showed that the death rates in those not using oxygen were much higher. Do these alone justify the use of oxygen?

Two studies show that the brains of mountaineers operating at extreme altitude demonstrate changes on MRI scans but do not look at functional changes (58 & 59). One paper looked for evidence of neurological impairment in acclimatised individuals climbing to 7500m and showed no deterioration (60).

CONS: Cost, weight, bulk, cylinder supplies, reliability (now much improved), potentially major problems if supply runs out or delivery system suddenly fails. Due to their weight many climbers seem reluctant to carry used cylinders down the mountain resulting in unsightly littering. In the event of an extreme altitude rescue being attempted both the casualty and the rescuers will require extensive oxygen supplies.

PHYSIOLOGY: Oxygen does not affect performance at sea level, because neither the amount of available oxygen nor its partial pressure is the limiting factor for maximal performance. This changes dramatically with decreasing inspiratory oxygen partial pressure (p_iO_2) at extreme altitude, where the oxygen flow from the atmosphere to the mitochondria is limited by decreased p_iO_2 or capillary-mitochondrial ΔpO_2 , respectively. As a consequence, the ascent rate as an indicator of performance decreases significantly.

CONCLUSION: Again it is for the individual climber to make their own choice. There is little doubt that the use of oxygen at extreme altitude reduces the risks of death. It does not improve performance at low altitude.

2.20 Progesterone

On the theory that some women acclimatised better at different stages of their menstrual cycle a 1999 study looked at men at altitude in Peru taking the female hormone Progesterone in the interests of science. This hormone is known to be a mild respiratory stimulant. This was a small study but no statistical difference was seen between those taking the active drug and those taking placebo (61).

PROS: The paper's author does not remember any long term side effects (62)

CONS: The drug does not work!

2.21 Phosphodiesterase type-5 inhibitors eg sildenafil (Viagra), tadalafil (Cialis).

This is another group of drugs that lay mountaineers have latched onto for potential mountaineering performance enhancement at altitude. These drug's effects on inhibiting the effect on hypoxic pulmonary resistance at altitude is well documented (63). There is little published evidence on the therapeutic effect at altitude but one study does suggest that they may reduce the incidence of HAPE (64). These drugs have been adopted by doctors as an additional treatment for HAPE but based mainly on studies of individual cases and small scale studies rather than hard evidence (65).

CONS: Currently limited evidence. Potential for side effects such as headache.

2.22 Psychotropic Drugs

Some climbers believe that these substances may be of advantage on some "risky" climbs because of their euphoric properties. Mescaline and tetrahydrocannabinol (THC) has been used for several extreme big-wall climbs. Their use in Yosemite is documented by Steve Roper (66). Route names like "Mescalito" clearly indicate the circumstances of the first ascent.

CONS: All these drugs increase reaction time and reduce the risk management capability. Therefore they may be extremely dangerous if used when mountaineering. There are no data available about the degree of use in the climbing community.

2.23 Rhodiola crenulata

Extract of this plant is widely used in Tibet and the Himalaya to prevent AMS. It is a proven ACE inhibitor and alpha-amylase inhibitor. A double blind placebo controlled crossover study of 102 adults showed no evidence that it had any effect on AMS (67).

2.24 Salmeterol

The inhaled long acting beta2 agonist, salmeterol, was investigated for the prevention of HAPE (68). On the strength of this the WMS guidelines now suggest that it may help in the management of HAPE in combination with other therapy such as DESCENT and nifedipine. It is used in high doses which are close to the toxic level (125 micrograms twice a day).

With this poor evidence some lay mountaineers have assumed that it may also increase performance. There is no evidence for this and at high doses at altitude they may suffer important side effects such as tremor, tachycardia and dangerous heart rhythms, nausea, dizziness.

A case study on one climber using a drug combination of salmeterol with sildenafil and acetazolamide for secondary prevention of HAPE during his second attempt to summit on Everest is based entirely on theoretical research and despite being unreliable may have influenced the behaviour of other climbers who have taken it out of context (69).

2.25 Sleep Medication

Poor sleep is a commonly reported feature of travel to high altitude. The main concern when considering the use of sleep medications at high altitude is whether the sleep disruption is an environmental effect (discomfort or unfamiliarity with the setting) or a physiological one related to poor acclimatization or an over-active respiratory response to high altitude leading to intermittent or "periodic breathing" (70). With this in mind it is important to realise that most traditional sleep medications if used at altitude will worsen AMS if it is present. There is no evidence to support that sleep medications such as benzodiazepines worsen hypoxia in otherwise well acclimatized individuals even above 5000m (71). Equally there are no studies which document the exact effect of sedative sleep medications on people

with known AMS. Acetazolamide has been clearly shown to have a beneficial effect on sleep disturbances at altitude especially those related to poor acclimatization. However it comes at a slight cost as depending on individual susceptibility the diuretic effect of acetazolamide (meaning the individual needs to urinate more in the night) may disturb sleep just as much as the sleep disorder it is treating. Subjective reports suggest the quality of the sleep produced and the general feeling of well being is improved approximately equally with benzodiazepines and acetazolamide although no studies have effectively compared one to the other in a robust (double blind cross over) study with a large cohort.

If sleep disturbance is present and is due to acute mountain sickness or poor acclimatization, the first line of action should be to prevent or treat that underlying cause (eg by slow ascent or descent) and sleep medications are NOT recommended. However, if there are no other factors present and the individual is extremely well acclimatized, with no other signs or symptoms of AMS it is not unreasonable to consider sleep medications. This would be equivalent to considering the same intervention at sea level, it is neither recommended, appropriate nor acceptable to all individuals (at sea level or altitude) and each case should be considered on its individual merit. There is a great deal of literature on the dangers of sleep deprivation on judgment and safe decision making and in some of these circumstances judicious use of sleep medication might be considered as a safe pathway to enable descent. Using them to ensure safe ascent is an ethical decision.

Advantages: Acetazolamide, clearly defined physiological role in improving AMS and sleep at altitude. It is therefore a safer first line assuming the sleep disturbance is physiological and not environmental

Advantages: Low dose of benzodiazepines (such as 10mg Temazepam) treats both physiological (periodic breathing) and environmental causes and that sleep quality and sleep structure have been shown to be improved. Many authorities prefer to use benzodiazepines with short half lives such as Zopidem or Zopiclone.

Disadvantages: Acetazolamide are all of those included in the section above on its use in AMS, as well as small increase in need to urinate at night (which might be detrimental to sleep process). In addition it may not help with environmental causes and so only treats "half the picture".

With benzodiazepines, if AMS is not clearly excluded, there is a theoretical risk of worsening AMS and hypoxia especially if a higher dose of Temazepam is use (greater than 15mg) . However to date there are few if any studies describing the exact effects of high doses of benzodiazepine at altitude, but common sense and experience suggest higher doses are inadvisable at altitude and in any doses where AMS is clearly documented.

2.26 Theophylline

The theophylline group of drugs are known to be respiratory stimulants that work by increasing adenosine concentration in the breathing centre of the brain and have been shown to increase athletic performance at sea level (72) and to slightly reduce AMS symptoms at altitude (73 & 74). It has also been seen to improve sleep at altitude (75 & 76). Interestingly caffeine is a chemical relative of this group of drugs.

CONS: They have narrow therapeutic index meaning that anything that effects the blood level such as dehydration, alcohol, smoking, drug interactions or even viral illness could lead to potentially dangerous toxicity. A low dose of 250mg slow release was studied and showed no such adverse effects.

INTERACTIONS: This group of drugs have multiple interactions with other drugs and have a narrow therapeutic range. This means that with acetazolamide they can decrease the potassium level in the blood to potentially dangerous levels and if combined with Azithromycin, which is often used to treat traveller's Diarrhoea, it can easily reach toxic levels. .

3 References

- 1) World Anti-Doping Program: http://www.wada-ama.org/Documents/World_Anti-Doping_Program/WADP-Prohibited-list
- 2) Nagat Parbat Pilgrimage by Herman Buhl. Chapter "Above 26,000 ft".
- 3) Dick Renshaw, personal communication 2013.
- 4) Wagner DR. Medical and Sporting Ethics of High Altitude Mountaineering: The Use of Drugs and Supplemental Oxygen (editorial). *WEM* 23(3): 205-211 (2012)
- 5) Outside: <http://www.outsideonline.com/fitness/Climbings-little-helper.html>
- 6) Subedi et al. Complications of Steroid Use on Mount Everest. *W&EM* 21, 245-348. 2010
- 7) L Dumont, C Mardirossoff and M Tramer. Efficacy and harm of pharmacological prevention in acute mountain sickness; quantitative systematic review. *BMJ* Vol 321 p 267-72.
- 8) Health & Height. Proceedings of the 5th World Congress on Mountain Medicine and High Altitude Physiology 2002. Pub 2003 University of Barcelona. Drug abuse in the Mountains by Dr Franz Berghold pp 99-106.
- 9) Bartsch P and Swenson ER "Acute High-Altitude Illness" *N Engl J Med* 13; 368: 2294-302. 2013.
- 10) Luks AM, McIntosh SE, Grissom CK et al "Wilderness Medical Society consensus guidelines for the prevention and treatment of acute altitude illness" *W&EM* Vol21, issue 2 P146-155. June 2010.
- 11) Gaillard S, Dellasanta P, Loutan L, and Kayser B. Awareness, prevalence, medication use, and risk factors of acute mountain sickness in tourists trekking around the Annapurnas in Nepal: A 12-year follow-up *High Alt Med Biol* 5:410–419 2004
- 12) Kilner T and Mukerji S. 2010. Acute mountain sickness prophylaxis: Knowledge, attitudes, & behaviours in the Everest region of Nepal. *Travel Med Infect Dis* 8:395–400.
- 13) Kupper T et al. RIMAT1 study, unpublished data to be used for RIMAT2, in preparation.
- 14) Roggla G, Roggla M et al. Amphetamine doping in leisure-time mountain climbing at a medium altitude in the Alps. *Schweiz Z Sportmed* Vol 41, Issue 3 p 103-105 1993)
- 15) Kupper T, Ebel K, Gieseler U. *Modern Mountain and Altitude Medicine*. Gentner, Stuttgart, 2010
- 16) *J Trauma*. 2006 Dec;61(6):1517-25. "Injury patterns and safety practices of rock climbers" Gerdes EM, Hafner JW, Aldag JC
- 17) West JB, Schoene RB, Luks Am, Milledge JS "High Altitude Medicine and Physiology" CRC Press, 5th Edition 2013.
- 18) Cain SM, Dunn JE. "Increase of arterial oxygen tension at altitude by carbonic anhydrase inhibition" *J Appl Physiol*. 1965 Sep;20(5):882-4.
- 19) Swenson ER, Teppema LJ "Prevention of acute mountain sickness by acetazolamide: as yet an unfinished story" *J Appl Physiol* 102, 1305-7 2007.
- 20) Basnyat B, Gertsch JH, Holck PS et al "Acetazolamide 125mg bd is not significantly different from 375mg bd in the prevention of acute mountain sickness: the prophylactic acetazolamide dosage comparison for efficiency (PACE) trial." *HAM&B* 7, 17-27. 2006.
- 21) Leaf D E, Goldfab D S, Mechanisms of action of acetazolamide in the prophylaxis and treatment of acute altitude sickness. *Journal of Applied Physiology* Vol 102. No 4. 1313-1322 April 2007.
- 22) Greene MK, Kerr AM, McIntosh IB, and Prescott RJ. (1981). Acetazolamide in prevention of acute mountain sickness: A double-blind controlled cross-over study. *Br Med J (Clin Res Ed)* 283:811–813.
- 23) R Greene "Some Medical Aspects" chapter in "Everest 1933" by Hugh Rutledge published Hodder and Stoughton 1934.
- 24) Hackett P H. "Caffeine at High Altitude: Java at Base Camp" *HAM&B* Vol11 No1 2010.

- 25) Boos, C, et al., Medikamentenmißbrauch beim Freizeitsportler im Fitnessbereich. Dt Ärztebl, 1998. 95(16): p. B774-B781.
- 26) British National Formulary (BNF) 65 2013 4.7.3
- 27) Jafarian S et al. "Low dose gabapentin in treatment of high-altitude headache" *Cephalalgia* 2007;27:1274-1277.
- 28) Jafarian S et al. "Sumatripan for the prevention of acute mountain sickness" *Ann Neurol.* 2007;62:273-277.
- 29) Burtschler M et al "Ibuprofen verses sumatripan for high altitude headache" *Lancet* 346, 254-255. 1995.
- 30) Burtschler M et al. "Aspirin for the prophylaxis against headache at high altitudes: randomised, double blind, placebo controlled trial" *BMJ* Vol 316, 1057-1058.
- 31) Donegani, E; Hillebrandt, D; Windsor, J; Gieseler, U; Rodway, G; Schoffl, V; Kupper, T; "Pre existing Cardiovascular conditions and high altitude. Consensus statement of the medical commission UIAA. *Travel Med Inf Dis (TMAID)* Vol: 12 Issue 3 Pp: 237-252. May- June 2014.
- 32) Conway R. Evansl, Weeraman D. "Assesing travellers' knowledge and use of Coca for altitude illness" *Wilderness Environ Med.* 2012 Dec;23(4):373-4. doi: 10.1016/j.wem.2012.06.005. Epub 2012 Oct 4.
- 33) Johnson TS et al. "Prevention of Acute Mountain Sickness by Dexamethasone" *N Eng J Med* 310. 683-6. 1984.
- 34) Ellsworth AJ. "Acetazolamide or dexamethasone use verses placebo for acute mountain sickness prophylaxis" *Am J Med* 83. 1024-30. 1991.
- 35) Luks AM et al "Wilderness Medical Society Consensus guidelines for the prevention and treatment of ACUTE Altitude Illness" *W&EM* Vol 21 Issue 2 P145-155 June 2010.
- 36) Jelkman W, Lundby C, "Blood doping and its detection". *Blood* 118, 2395-404.
- 37) Young AJ et al. "Effects of erythrocyte infusion on VO₂ max at high altitude". *J Appl Physiol* 81, 252-9.
- 38) Leadbetter G et al. "Ginkgo biloba does- and does not-prevent acute mountain sickness". *W&EMJ* 20; 66-71 2009.
- 39) Dumont L et al. Efficacy and harm of pharmacological prevention of acute mountain sickness: quantitative systematic review. *BMJ* 321: 107-114 (2000)
- 40) Gertsch JH et al. Ginko biloba for the prevention of severe acute mountain sickness (AMS) starting one day before rapid ascent. *High Alt Med Biol* 3(1): 29-37 (2002)
- 41) Basnyat B. High altitude illness. *Lancet* 361(9373): 1967-74 (2003).
- 42) Bartsch P et al. Acute mountain sickness: controversies and advances *High Alt Med Biol* 5(2): 110-124 (2004).
- 43) Lipman GS et al "PAINS group. Ibuprofen prevents altitude illness: a randomised controlled trial for prevention of altitude illness with non-steroidal anti-inflammatories *Ann Emerg Med.* 2012;59:484-490
- 44) Gertsch JH et al "Altitude sickness in climbers and efficiency of NSAIDs in trail (ASCENT): Randomised, controlled trial of ibuprofen verses placebo for prevention of altitude illness" *W&EM* 23.307-315 (2012).
- 45) Zafren K. *W&EM* 23. 297-299 (2012).
- 46) Basnyat B personal communication. Nepal 28.8.13.
- 47) Kupper T et al. Drugs and drug administration in extreme climates. *J Travel Med* 13(1): 35-47 (2006)
- 48) Bartsch P et al. "Prevention of high-altitude pulmonary edema by nifedipine" *N Engl J Med* 1991; 325 1284-1289.
- 49) British National Formulary BNF No 65. 2013: 2.6.2.

- 50) Weitzberg et al. "Dietary nitrate- a slow train coming" J Physiol 2011; 589.22. 5333-5334.
- 51) Vanhatalo et al. Dietary nitrate reduces muscle metabolic perturbation and improves exercise tolerance in hypoxia. J Physiol 589.22 (2011) pp 5517–5528.
- 53) Masschelein et al. Dietary nitrate improves muscle but not cerebral oxygenation during exercise in hypoxia. J Appl Physiol 113:736-745, 2012.
- 54) Muggeridge et al. A single dose of beetroot dose enhances cycling performance in simulated altitude. Medicine and Science in Sports and Exercise in print June 2013.
- 55) Ascent of Everest by John Hunt 1953 and multiple reprints.
- 56) Pollard A & Clarke C deaths during mountaineering at extreme altitude. Lancet Vol 331, Issue 8597. p 1277. 1988.
- 57) Huey R B and Eguskitza X. Supplemental Oxygen and Mountaineer Death Rates on Everest and K2 JAMA Vol 284 No2 181, 2000.
- 58) Garrido E, Castelló A, Ventura JL, Capdevila A, Rodríguez FA. Cortical atrophy and other brain magnetic resonance imaging (MRI) changes after extremely high-altitude climbs without oxygen. Int J Sports Med. 1993;14(4):232-4
- 59) Fayed N, Modrego PJ, Morales H "Evidence of brain damage after high-altitude climbing by means of magnetic resonance imaging. Am J Med. 2006;119(2):168.e1-6.
- 60) Tobias M M et al "Cognitive performance high-altitude climbers: a comparative study of saccadic eye movements and neuropsychological tests". European Journal of Applied Physiology DOI 10.1007/s00421-013-2635-6.
- 61) Hillenbrand P, et al "A randomised controlled trial of progesterone in preventing altitude sickness. Proceedings of the 11th Hypoxia symposium. Jasper 1999.
- 62) Hillenbrand P. Personal communication 28.8.13.
- 63) West JB, Schoene RB, Luks AM, Milledge JS "High Altitude Medicine and Physiology" 5th Edition. CRC Press 2013. section 12.6 cardiovascular Responses with multiple references.
- 64) Maggorini M. et al "Both Tadalafil and dexamethasone may reduce the incidence of high-altitude pulmonary edema: a randomised trial".
- 65) Meta-Analysis of Clinical Efficacy of Sildenafil, a Phosphodiesterase Type-5 Inhibitor on High Altitude Hypoxia and Its Complications by Yu Xu, Yuliang Liu et al. HAM&B Vol:15 No:1 2014 P46-51.
- 66) Roper S. "Camp 4, recollections of a Yosemite Rockclimber" Chapter 10 "Bringing down the curtain" p217-218.
- 67) Te-Fa Chiu et al. "Rhodiola crenulata extract for prevention of acute mountain sickness: Complimentary and A 2013, 13.298.
- 68) Sartori c et al. "Salmeterol for the prevention of high-altitude pulmonary edema" NEJM 346;1631-36. 2002.
- 69) Dunin-Bell O and Boyle S. "Secondary Prevention of HAPE in a Mount Everest Summitter" High Altitude Medicine & Biology. Fall 2009, 10(3): 293-296.
- 70) Kupper T et al. Cheyne stokes breathing at high altitude: a helpful response or a troublemaker? Sleep Breath 12(2): 123-127 (2008)
- 71) Dubowitz G. Effect of temazepam on oxygen saturation and sleep quality at high altitude: randomized placebo controlled crossover trial. BMJ 316(7131): 587-589 (1998)
- 72) Pigozzi F et al "Oral theophylline supplementation and high-intensity intermittent exercise". J Sports Med Phys Fitness, 43(4): p 535-8. 2003.
- 73) Fischer R et al. "Theophylline improves acute mountain sickness". Eur Respir J. 15; 123-7. 2000.
- 74) Kupper T et al. "Prevention of acute mountain sickness with Theophylline" Proceedings of the 11th Hypoxia symposium. Jasper. 1999.
- 75) Kupper T et al. "Low dose theophylline improves ventilation at night and prevents symptoms of acute altitude sickness at high altitude" J trav Med 15(5);307-314 2008.

76) Fischer r et al. "Theophylline and acetazolamide reduce sleep disordered breathing at high altitude" Eur Resp J 23(1); 47-52 2004).

4 Members of UIAA MedCom (in alphabetical order)

A. Akca (Turkey), G. Agazzi (Italy), C. Angelini (Italy), B. Basnyat (Nepal), J. Bogg (Sweden), A.R. Chioconni (Argentina), E. v. Delft (South Africa), N. Dikic (Serbia), W. Domej (Austria), P. Dobbelaar (Netherlands), E. Donegani (Italy), Y. El-Sheikh (Canada), S. Ferrandis (Spain), U. Gieseler (Germany), A. Gurtoo (India), U. Hefti (Switzerland), D. Hillebrandt (U.K.), J. Holmgren (Sweden), V. Ismayil (Azerbaijan), A. Koukoutsis (Greece), A. Kokrin (Russia), B. Komoni (Kosovo), P. Konczakowski (Poland), J. Kubalova (Czech Republic), T. Kuepper (Germany), E. Mashkovsky (Russia), K. Matsubayashi (Japan), J. McCall (Canada), H. Meijer (Netherlands), M. Michailov (Bulgaria), J. Milledge (U.K.), D. Moens (Belgium), A. Morrison (U.K.), H. Mosaedian (Iran), R. Naeije (Belgium), M. Nakashima (Japan), S. Omori (Japan), P. Peters (Luxembourg), G. Rodway (USA), G.G. Roi (Italy), I. Rotman (Czech Republic), V. Schoeffl (Germany), J. Shahbazi (Iran), J.C. Skaiaa (Norway), H. Stave (Norway), J. Venables (New Zealand), S.-H. Wang (Taiwan), J. Windsor (U.K.)

Guest authors:

G. Dubowitz, (San Francisco, California, USA) and J Arnold (UK.)

5 History of this recommendation paper

This advice paper was first conceived by the UIAA Medical Commission in 2008 but differing national, cultural, medical and mountaineering attitudes resulted in repeated delays in reaching a consensus. The concept of a factual and non judgmental paper was accepted by all members at the annual Medcom meeting in Sweden in 2011. Work continued at the meeting in Canada in 2012 and Poland in 2013 with E mail discussions between. At the 2014 meeting in Bolzano in Italy it was decided to produce this paper for lay readers and a more detailed and technical paper for medical professionals which is planned to initially be published in peer reviewed medical journal. This version was approved at Bolzano in May 2014 with minor amendments.