# The Newsletter of the International Society for Mountain Medicine

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## *International Society for Mountain Medicine*

The International Society for Mountain Medicine, founded in 1985, has the following goals: to bring together physicians, scientists and allied professionals interested in mountain medicine; to encourage research on all aspects of mountains, mountain peoples and mountaineers; to organize and co-organize international scientific meetings and publish a newsletter to spread scientific and practical information about mountain medicine around the world.

## FROM THE EDITOR

In this edition of the ISMM Newsletter we review two recent mountain medical events: Jim Milledge reports on Hypoxia '99 and discusses the broad range of interesting presentations that were brought together at that meeting (further information about the Hypoxia series appears in the announcements section of the News, page 18); and Annabel Nickol presents a summary of the activities of last year's British Medical Kangchenjunga expedition which ran a large number of field studies. But this edition begins with a state of the art review of weight loss at altitude by Matthias Tschöp and Katherine Morrison that draws attention to the possible role of hormones and cytokines in this altitude-related phenomenon. This month's case discussion highlights our lack of understanding of neurological syndromes occurring at altitude and the correspondence section provides some criticisms of recent articles which reassures the Editor that this publication is closely read.

Events on Mount Everest over the past few weeks have led to renewed interest and comment on Himalayan climbing in the media. There has been yet more loss of life on those high slopes alongside a succession of successful ascents, but all this has been overshadowed by the probable discovery of the body of George Mallory on the North side of Everest. Those of us who are involved in, and represent mountain medicine must consider carefully whether we are in a position as a body or as individuals accompanying expeditions to prevent these tragedies. With this in mind, I draw your attention to the 1997 UIAA voluntary code of practice for high altitude guided commercial expeditions. This code is directed at very high altitude expeditions with mountaineering objectives and has been adopted by the many companies offering commercial expeditions to high altitude.

The code recommends that:

"3. A doctor in the party is very desirable but at the very least advance arrangements must be made for medical help. Advance arrangements must also be made for evacuation assistance in case of emergency.

"4. The minimum safety equipment available must be walkie-talkie radios, a satellite phone, medical oxygen and recommended first aid supplies.

"5. Advertising must give a true picture of all the difficulties and dangers involved, and avoid promising the impossible. Biographical information about the team should be included"

There remains no such code of practice for low altitude expeditions and commercial treks.

AJP

## FROM THE PRESIDENT

While you can read an excellent and comprehensive summary of the 11th Hyploxia Symposium 1999, held at Jasper, in this issue, preparations for the next highlight to which I would like to draw your attention are under way. It is the **4th World Congress on Mountain Medicine and High Altitude Physiology** held in the north of Chile, in Arica from October 1-6, 2000. I am sure that this congress will be equally interesting and attractive as our previous international conferences regarding both, scientific and social aspects. Dr. Claus Behn, Professor of Physiology at Santiago, Chile, leads the organising committee of this conference that is held in conjunction with the Physiological Society of Chile, the Chilean Society of Sports Medicine and the ISMM. Medical problems of acute, intermittent and chronic exposure to high altitude and the physiology of acute, intermittent and chronic hypoxia will be addressed at the clinical and molecular level in state of the art lectures and reports from latest research. The organisers are very pleased that this world congress is supported by the major mining companies and the Ministry of Mining of Chile. Many of you may have received first announcements which were sent out recently. Soon more information can be obtained on the internet through a link in our web site. I ask you all to mark the date of this event in your diary and I draw the attention of all young investigators (under the age of 35 years) to the **Scientific Prize 2000 of ISMM** that will be awarded at this conference. More information about this prize can be obtained in the 'announcements' section of this news letter.

Peter Bärtsch, President ISMM

# *THINNER IN THIN AIR: IS WEIGHT LOSS AT HIGH ALTITUDE HORMONALLY MEDIATED?*

**Introduction**

Loss of weight and appetite occur frequently at altitudes above 5000 m, but little is known of the pathophysiology of weight loss and changes in body composition at extreme altitude. Weight loss at high altitude appears to result from a marked difference between energy intake and energy expenditure. Proper acclimatisation to altitude and high caloric intake with a wide variety of nutrients can help to minimise but cannot completely prevent significant weight loss at high altitude (1). The effect high altitude has on metabolic systems related to weight maintenance is not fully understood. The effects of altitude are being reexamined in light of new information into the physiological controls of weight. This article will briefly review what is known about weight loss at high altitude, and will examine further newer information on the endocrinology of energy homeostasis, and the effects of high altitude exposure on this balance.

**Weight loss at high altitude**

Numerous studies have sought to further clarify the anthropometric changes that occur at high altitude, and the reasons for them. The degree of weight loss varies depending on altitude achieved, and length of stay there, and has been as extreme as 8.9% of body weight at outset after a 62 day expedition to 8047m (2). In most studies, the majority of the weight loss is attributable to fat loss (3, 4, 5, 6, 14, 7, 9) although decreases in muscle mass, accompanied by a negative nitrogen balance also occur (4, 10). One study has suggested however, that although under 5000 m 70% of the weight loss is fat loss, over 5000m only 27.4% of weight loss is secondary to loss of fat (3). Effects were not consistent over all groups, as Sherpas who showed half as much body fat as the mountaineers, maintained their weight during residence above 5,400m.

Decreased caloric intake (4, 12) and a negative energy balance (7, 8) have been noted at high altitude, and these were considered the major contributors to weight loss (11). However, efforts to overcome this with a wider variation in food stuffs does not fully prevent weight loss (6). Malabsorption of fat has also been noted, but is not confirmed in all studies (13, 14).

An interesting study, to determine whether hypoxia due to decompression causes weight loss was conducted by the US Army Research Institute of Environmental Medicine. Six men, provided with a palatable ad libitum diet, were studied during progressive decompression to 240 Torr over 40 days in a hypobaric chamber where hypoxia was the major environmental variable. Caloric intake ($p<0.001$). Over the 40 days of the study the subjects lost 7.4 +/- 2.2 (SD) kg and 1.6% (2.5 kg) of the total body weight as fat. Computerized tomographic scans indicated that most of the weight loss was derived from fat-free weight. This study concluded that hypoxia can be sufficient cause for the weight loss and decreased food consumption reported by mountain expeditions at high altitude (10).

Efforts to eliminate weight loss at high altitude have included increasing energy intake, as described above. Researchers have also attempted to ameliorate the effects of altitude with acetazolamide (Az). Bradwell et al., in a placebo-controlled trial, examined exercise performance and muscle mass in 21 acclimatised subjects at an altitude of 4846m. Although weight loss was less and exercise performance was better in the Az treated group (n=11), altitude effects were not completely prevented (15)

It appears, therefore, that hypoxia during high mountain expeditions induces weight loss by hypophagia, and possibly malabsorption and increased metabolic rate.

**Weight loss and hormonal changes at high altitude**

The factors mediating these changes are not clearly understood. Hundreds of clinical and experimental studies have shown various changes in endocrine parameters at high altitude.

Because of their effect on energy homeostasis, thyroid hormones have been considered a possible contributor to weight loss. At high altitude TSH secretion from the pituitary gland appeared to be enhanced, and total and free thyroxine were found to be elevated, but peripheral conversion from T4 to the active form of thyroid hormone, T3 was impaired. Correlation of these changes with marked weight loss was not found (16), leaving their importance in the weight loss phenomenon in question.

Another important system for the regulation of body composition is the somatotropic axis including growth hormone (GH), growth-hormone-releasing hormone (GHRH), insulin-like growth factor-I (IGF-I) and IGF-binding proteins. Increased hGH response to administration of the GH releasing stimulant GHRH, in healthy volunteers at high altitude has been demonstrated (17), but levels of the effector protein IGF-I remained unchanged. An increase in several IGF-binding proteins (IGFBP-1, 2, 3, 4, 5) at altitude has also been recently reported, but the relation of these to weight loss remains unclear. (18).

The first work examining the role of the gonadotropic axis, including LH, FSH, estrogens and androgens, in weight loss at high altitude was

1977. They showed that weight loss in castrated rats at simulated altitude of 6000 m is not reversible by administration of testosterone or estradiol (19). In most of the studies analysing the function of the gonadotropic axis during hypoxia, no significant changes in LH, FSH, testosterone or estradiol-levels with hypoxia were found compared to normoxic conditions in men (20).
Studies on the effects of hypoxic conditions at high altitude on the CRH-ACTH-Cortisol axis have demonstrated increases in serum cortisol levels with a concomitant loss of the typical diurnal rhythm of ACTH and Cortisol secretion (21). This increase seems to be suppressible by administration of exogenous corticosteroids (22), and it's relationship to weight changes is unknown.
Changes in endocrine function at high altitude are described frequently, but results and conclusions are often quite contradictory. An endocrine link between the changes induced by hypoxia, and energy homeostasis or weight loss is still missing.
It is not possible to conclude from the literature to date, that a hypoxia induced impairment of the traditional endocrine system (the hypothalamic-pituitary-peripheral glands -axes) can explain the phenomenon of weight loss at high altitude.

**Leptin and Energy Homeostasis**

Under physiological conditions, weight remains relatively stable, indicating that energy balance may be controlled by a feedback loop, which maintains constancy of total body energy stores. It has been proposed that signals reflecting nutritional state are sensed by the hypothalamus, which, in turn, modulates food intake and energy expenditure. The demonstration that hypothalamic lesions cause hyperphagia, decreased energy expenditure, and obesity have led to the homeostatic models of body weight regulation. Until recently, the key players in this system had not been identified. The discovery of leptin, and other neuropeptides has shed considerable light on what was once a black box.
The leptin story begins with the ob/ob mouse, a mouse strain discovered in the Jackson Laboratories. A recessive gene mutation in the ob/ob mouse produces a phenotype characterised by the behavioural trait of hyperphagia and the morphological trait of obesity, resulting in sterile adult mice with 50% body fat content. Similar phenotypic features are seen in db/db mice, but they also suffer from diabetes. Coleman, from the Jackson Laboratories (23) conducted the famous parabiosis (interindividual cross-circulation) studies in which the ob/ob mice, once exposed to the circulation from db/db mice decreased their food intake and body weight. In contrast, their db/db pairmates, although exposed to the circulation of ob/ob mice, continued to increase their food intake and weight. Coleman concluded, that ob/ob mice fail to produce a circulating factor important in appetite control, that their brains can respond to, whereas db/db-mice make the circulating factor in abundance, but their brains are unable to respond to

Zhang et al reported in 1994 that they had identified the gene responsible for obesity in these mice, and it encoded a 146 amino-acid protein (plus a 21 amino acid secretory signal sequence). This protein was initially called the obese gene product (24). Because the ob-protein caused a reduction in food intake (as well as an increase in metabolic energy expenditure) it has subsequently been called leptin from the Greek "leptos" for "thin". It is now known that leptin is secreted by adipocytes and, in lesser amounts, also by the placenta and stomach. The finding that intrathecal or peripheral administration of recombinant leptin to diet-induced-obese mice led to impressive weight loss initiated a "leptinomania" in biomedical research, and in the media. In addition to it's role in energy homeostasis, leptin also signals nutritional status to several other physiological systems and modulates their function. This broader role includes effects, at least in rodent models, on pubertal development, fertility, hematopoesis, immune function and angiogenesis.
The initial hypothesis that human obesity is also explained by leptin deficiency has been proven wrong. In general, obese individuals have higher leptin levels, and leptin levels correlate closely with body mass and body fat mass indices. This is not to suggest that leptin deficiency never results in obesity in man. In fact, O´Rahilly et al in 1997 described two young cousins with a genetic leptin deficiency, marked hyperphagia and extreme obesity. Although a rare cause of obesity, these patients have confirmed the essential role of leptin regulation of energy homeostasis in humans (25).
The etiology of obesity in the majority of individuals is likely secondary to environmental features leading to a positive energy balance in conjunction with a biological disposition that favours weight gain but defends against weight loss. This picture is consistent with the concept of leptin resistance as opposed to deficiency.
The effects of leptin in reducing food intake, and increasing metabolic energy expenditure are likely to be the basis for drug development aimed at the treatment of obesity in the coming years.
(26, 27, 28, 29, 30, 31, 32)

**Leptin - a player at high altitude?**

As loss of appetite is one of the most frequent symptoms of acute mountain sickness (AMS) (33), as weight loss occurs frequently above 5000 m and, as leptin is a key mediator in the neuroendocrine regulation of energy homeostasis and appetite (35), we investigated the effect of hypobaric hypoxia at high altitude on serum leptin levels in men, using a highly sensitive and specific method for leptin quantification (34, 36). This research was done in collaboration with P. Bärtsch (Heidelberg) and J. Biollaz (Lausanne). We measured mean serum leptin levels in 20 male mountaineers (age: 19-42 years, Capanna Margherita, Switzerland) after active ascent to 4559 m and documented changes in appetite with the

leptin concentration increased from 1.22±0.19 ng/ml (9:00 a.m. at 120 m, all values mean±SEM) to 2.06±0.34 ng/ml (9:00 a.m at 4559 m, 22 hours after ascent p=0.0003). The mean pO2 at altitude was 43.2 mmHg. This effect on leptin was not reversible after 1 hour of treatment with 33% oxygen-enriched air and appeared to be more pronounced in subjects with loss of appetite (78% increase, n=11), than in those without loss of appetite (52% increase, n=9).

However, physical strain during the active ascent and single measurements of leptin, which is secreted in a pulsatile manner by adipocytes (ca. 32 peaks/24 hours), may have been confounding factors in this study. Therefore, in a second study, serum leptin levels were measured in 18 volunteers (age: 20-41 years) at 490 m (after 1, 4, 12 and 20 hours) and at 4559 m (1, 4, 12, 20 and 32 hours after transportation to 4559 m by helicopter). Appetite was assessed as above, and the diagnosis of Acute Mountain Sickness (AMS) was defined as a functional Lake Louise Score > 1 (5). Twelve of the 18 individuals studied developed loss of appetite, and 10 developed AMS. In individuals with loss of appetite, mean serum leptin levels increased from 3.19±0.89 ng/ml (6°° a.m.at 490 m) to 4.89±1.18 ng/ml (6°° a.m. at 4559 m, p=0.02), but no significant increase was found in individuals without loss of appetite (2.17 ng/ml vs. 2.55 ng/ml, p=0.35). An increase in integrated serum leptin levels (mean area under the curve) from 53.8±13.8 ng/ml*h to 66.3±16.2 ng/ml*h was also found in individuals with loss of appetite (1-20 hours, p=0.008), but not in those without loss of appetite (38.7±6.4 ng/ml*h (490 m) vs. 40.8±13.2 ng/ml*h (4559 m), p=0.35).

The 10 individuals who developed AMS, also had a significant increase in their leptin level at 4559m compared to at 490 m (p=0.028). Effects due to change in plasma volume have been excluded. Individuals with loss of appetite tended to have higher leptin levels at baseline than those without loss of appetite (p=0.1), but mean body mass indices were not significantly different between the analysed subgroups. Non-parametric testing (Mann-Whitney test and Wilcoxon test) were used for the statistical analysis.

In summary, in two independent studies, leptin levels increased at high altitude and this increase was found to be associated with loss of appetite. Thus, leptin may be a player in the altered neuroendocrine regulation of energy homeostasis at high altitude, leading to loss of appetite, increased energy expenditure and weight loss.

A further link between hypoxia and increased leptin secretion has recently been shown by Mise and coworkers (38). They demonstrated that leptin is also a placentally derived hormone in humans and suggested its significance in human pregnancy. They demonstrated that serum leptin levels were higher in women with pre-eclampsia (PE), a condition associated with placental hypoxia, than in gestational age- and body mass index-matched pregnant women ($p<0.0001$), and the extent of the severity. After delivery, leptin levels returned to those expected for their body mass indices. In addition, leptin mRNA levels were higher in placentas from women with PE than in those from normal women. In vitro studies confirmed that cells cultured under hypoxic conditions had higher leptin levels than those cultured under standard conditions ($p < 0.01$) (38).

Our findings showing increases in leptin at high altitude in individuals with loss of appetite and AMS, in conjunction with the finding that hypoxia alone can trigger anorexia and weight loss, and that leptin levels increase under hypoxic conditions in another biological system, are all consistent with the hypothesis that the hypoxia which occurs at altitude results in an increase in leptin. This increase may result in loss of appetite, anorexia and increases in metabolic rate leading to weight loss.

**More players in the endocrine regulation of energy homeostasis**

It seems unlikely, however, that leptin alone causes these changes. Under certain conditions various cytokines, for example, are also able to induce anorexia (Plata-Salaman, 1998). We have shown significant increases in circulating interleukin-6, interleukin-1-receptor-antagonist and C-reactive protein in 10 healthy individuals after 2 days at 4559 m. Increased cytokines were also demonstrated in a study of 12 male subjects at an altitude of 3458 m (Jungfraujoch, Switzerland) and were associated with clinical symptoms (39, 40).

Furthermore, there is some evidence that leptin interacts with neuropeptide-Y (NPY), one of the brains most potent neurochemicals involved in appetite. Leptin, NPY and other agents (Melanocorticotropic hormone (MCH), Galanin, Orexin A and B, Peptid YY, Noradrenaline, "Cocaine and amphetamine regulated transcript peptide" (CART), Cholecystokinin, Corticotropin releasing hormone, a-Melanocyte Stimulating Hormone, Insulin, Phospholipase-1, Bombesin, Urocortin, Serotonin) are involved in a peripheral central circuit which links an adipose tissue signal with central appetite mechanisms and metabolic activity. Within the interaction between excitatory and inhibitory processes there is ample room for the operation of a large number of mediating orexic or anorexic neuromodulating substances (41). There exists an expanding family of hypothalamic modulators of food intake, which includes NPY, and it is likely that leptin modulates the activity of some or all of these factors and that they modulate leptin activity in return. A detailed understanding of the functional relationships between leptin and other neuropeptides and neurotransmitters is necessary to clearly delineate the mechanisms regulating food intake and body weight.

The mystery of weight loss at high altitude has not been solved. However, recent research has begun to reveal new roles for endocrinological investigation in high altitude research. Further studies leading to a more complete understanding of the neuroendocrine regulation of body

weight loss have been identified and characterised, therapeutic agents that can prevent uncontrollable weight loss in mountaineers during high altitude expeditions are conceivable.

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# HYPOXIA SYMPOSIUM 1999

**Introduction.**

The 11th Hypoxia Symposium was held at the Jasper Park Lodge in the Canadian Rockies from Feb 27th to March 5th. The change of venue from Lake Louise was dictated mainly by the rising cost of the Chateau. Jasper is rather more challenging to reach as one of the British members demonstrated. When driving on his own, he spun off the snowy road between Lake Louise and Jasper in the early hours of Monday morning desperately trying to get posters and slides to his colleagues for presentation later that day! The views may not be quite so dramatic but the conference facilities are better, the skiing was great and the record number of registrants endorses the decision of the organizers to change the venue. It was also the first symposium organized by Rob Roach and Peter Hackett after taking over from Charlie Houston, Geoff Coates and the late John Sutton. They, with help from Bengt Kayser, and Toshio Kobayashi, are to be congratulated on running a very successful symposium. Sharon Studd did a great job in backroom support. I particularly welcomed the format of the proceedings and the splendid name badges which were in large enough type for even the most presbyopic to read at a safe distance. She even had the conference time table on the back of the label, a great idea.

There were 232 registrants from 24 countries. USA were by far the largest contingent (104) followed by UK (26), Germany (17), and Japan (16) and it was good to see many from less developed countries such as Bolivia, Kyrgystan, and Poland. In some cases delegates were enabled to come through financial support from Medical Expeditions Ltd., UK and the U.S. Army Medical research and Materiel Command.

**Scientific Program, Day 1**

The first day opened with a talk from Drummond Rennie who reminisced through his own climbing and research career and that of Herbert Hultgren. Herb, known to many for his early work on high altitude pulmonary edema (HAPE), died in 1997 just after completing his book, "High Altitude Medicine". This Hypoxia Symposium was dedicated to him.

The rest of the day was devoted to "A day in Mountain Medicine". Brownie Schoene discussed the pulmonary patient at altitude; apart from asthmatics who usually do well, they do badly. Susan Niermeyer talked about the pregnant altitude visitor; AMS may be less common but danger of pre-term labour and danger of trauma late in pregnancy suggests cautious advice in this area. John West discussed the problems posed by the requirement to staff new mines at altitudes around 5000 m in Chile with labour from the coast. Men enrichment of the air in sleeping quarters as being beneficial and practical. Peter Hackett gave a talk based partly on his recent paper in JAMA on MRI scans in high altitude cerebral edema (HACE). This together with talks in the session on Monday on Frontiers in Neuroscience gave us a lot to think about in this area. There seems to be a growing consensus that HACE is a development or a more severe form of AMS, the mechanism being one of cerebral edema. It is suggested that hypoxia causes an increase in permeability of the blood brain barrier with its "tight endothelial junctions". There was also discussion of why some are susceptible. Perhaps they have little room for expansion of brain within the skull - tight brains. But while CSF was shown to decrease in volume at altitude (a paper on Tuesday by Milton Icenogle) and the brain to swell (a poster by Steve Muza on Wednesday both using MRI), there was no correlation of these changes with AMS scores.

After the ski break we had a number of papers on HAPE and possible mechanisms. Simon Gibbs gave us evidence of high tone in the pulmonary arteries of subjects susceptible to HAPE, rather than the suggestion that they might have small lungs, and that this, with patchy vasoconstriction (as originally proposed by Hultgren), might be the mechanism of edema formation, though inflammation might add to the problem at a later stage. Marco Maggiorini also concluded, from a study of HAPE susceptible subjects, that there was an initial increase in pulmonary capillary pressure before any increase in permeability (measured by labeled transferin) or in various cytokines. Urs Scherrer, using a rat model where peri-natal exposure to hypoxia induced an exaggerated pulmonary pressor response, showed that such a response by itself was insufficient to produce HAPE. He suggested that it needed also a defect in transepithelial sodium transport such as he had found in HAPE susceptible subjects. This is thought to be due to a defect in the amiloride sensitive Na channel. His group had two posters on this subject one using transgenic mice, the other looking at the nasal PD in HAPE susceptible subjects and controls. The HAPE susceptible subjects had 30% lower PD and smaller decreases in PD with amiloride than controls suggesting a defect in amiloride sensitive Na channels in their epithelium. Another poster from Peter Bartsch's group also found altered ion transport in the mononuclear leukocytes of HAPE susceptible subjects. A study of incidence of HAPE in a cohort of 262 unselected subjects climbing to the Margarita Hut (4559 m) was reported by George Cremona. Using rather subtle changes in the chest X-ray as the criterion of HAPE they found an incidence of 15%. Many of these cases would be sub-clinical but does confirm, what many of us

altitude, especially after exercise, sub-clinical HAPE is not uncommon.

There followed three papers in a session called, "Hot topics in Mountain Medicine". Gerrit Van Hall told us that there was no Lactate Paradox in very healthy subjects fully acclimatized to 5200 m. They produced very respectable lactate levels after exercise. Why these results were at variance with most of the literature was not apparent. Thomas Kuepper reported a placebo controlled double blind trial of Theophylline (450 mg) in preventing AMS. There was a significant beneficial effect especially on sleep and there were no side effects. Finally Ian Clark made a case that the symptoms of AMS can be attributed to induction, by hypoxia, of inducible nitric oxide synthase analogous to the situation in cerebral malaria.

**Science Day 2**

Monday morning was devoted to neuroscience with contributions from scientists coming to Hypoxia from a primary interest in neurology. John Krasney, who chaired this session, indicated that a consensus had now developed, that the symptoms of AMS as well as HACE were due to cerebral edema, as mentioned above. This in turn might be either vasogenic or cytotoxic. The two next speakers, Lester Drews and Lothar Schilling explored these possibilities. Lester gave us a splendid up-date on the blood-brain barrier and the characteristics of the tight junctions in this endothelium. Lothar reviewed the various mediators which might induce cerebral edema, including bradykinin, arachidonic acid, free radicals and, as Ian Clark had told us the day before, nitric oxide. Insights from research in migraine and in stroke were given by Michael Moskowitz and Konstantin Hossman. These were fascinating talks but their relevance to altitude and AMS was not as clear as it might have been. However it had been a good morning of cross fertilization; what "Hypoxia" is all about.

At four o'clock we had the first of two poster session, some 67 posters to get round and digest. A new innovation was the "3X3" presentations, three minutes, three slides and 3 minutes questions, of the best 10 posters. This seemed a good compromise between practice I have come across, presenting all posters with 2 minutes each or no presentation at all. I can only mention a few posters; apologies to the many who's good work is left unsung. Katrina Riboni and colleagues address the long running question of AMS incidence and the menstrual cycle. They found no difference in AMS scores between the mid luteal and mid follicular phases of the cycle in subjects during 12 hour chamber exposures. The question was asked, "What about the pre-menstrual phase?". Answer, "We don't know". This session had a further eleven posters on women or gender differences at altitude, many by Lorna Moore and friends. There have been anecdotal reports of the efficacy of garlic in all sorts of conditions including AMS. A poster by Sue Hopkins investigated its efficacy in subjects mg/kg/day for two days) and then their pulmonary artery pressure estimated by Doppler echocardiography on air or 12.5% oxygen. The normoxic pressure was lower and the response to hypoxia less on garlic than control! The Birmingham group were present in force and had a number of posters including one showing that breathing 3% $CO_2$ improved oxygenation at altitude in healthy subjects as did $O_2$ . A mixture of the two was even more effective. Such a mixture might be useful in refractory cases of HAPE or HACE.

**Science, Day 3**

On Tuesday we had a session on Lactate and Hypoxia with the latest views of George Brooks, and George Heisgenhauser. Brooks pointed out some time ago that, just to measure the venous lactate and assume that exercising muscles turn over to anaerobic metabolism when exercise gets hard, is too simplistic. Lactate is produced elsewhere as well and is actually being used as a substrate by working muscles. Their use of lactate increases from 13% at rest to 40% on exercise. So exercising muscles are both using and releasing lactate. Having previously talked about lactate being shuttled from cell to cell, on this occasion he discussed an intracellular shuttle of lactate between cytosol and mitochondria. The second George focused our attention on the conversion of pyruvate to lactate by pyruvate dehydrogenase (PDH). The reason lactate goes up in hard exercise is not oxygen lack but because pyruvate production exceeds the catalytic activity of PDH and since the equilibrium constant of lactate dehydrogenase markedly favours lactate, small increases in pyruvate result in large increases in lactate concentrations.

Peter Hochachka discussed the importance of intra cellular motion or streaming which promotes substrate-enzyme interaction thus increasing the flux of a metabolic pathway with very little change of chemical concentrations. There followed a very good session on Hypoxia and Regulation of vascular growth in which Kurt Stenmark, John Kingdom and Hans Hoppeler took us into the world of molecular cellular physiology where many new advances are taking place.

In the afternoon we had a session of fifteen minute papers called, "Hot topics in Hypoxia" amongst others we hear of a study from Operation Everest III (Comex '97) by Paul Robach on the effect of replacing plasma volume, normally reduced on ascent to altitude. The effect was to improve, significantly, $VO_2max$. Urs Scherrer presented a study on ten healthy young adults identified from neonatal intensive care unit records as having had hypoxic episodes in infancy. They were found to have normal pulmonary artery pressure at low altitude (by Doppler u/s) but had higher pressures than controls at altitude (4,559 m). Their response to NO was also greater. But despite such high pressures none of them had HAPE suggesting that HAPE susceptibility is more than just a brisk

**Science, Day 4**

On the last day there was a session on extreme altitude in which John West first reviewed results from the summit of Everest of both barometric pressure and physiological; the latter, from both actual Everest summit and simulated in chamber studies. Recent results appear to confirm the validity of the one reading of barometric pressure made in 1981 by Chris Pizzo, of 253 Torr. Long term chamber studies supported the proposition that the alveolar $PO_2$ is defended at about 35 Torr. This being the case the $P_ACO_2$ cannot be higher than about 8 Torr in the steady state if R=1.0. If R is less than 1 it will be even lower.

Jean-Paul Richalet gave us a brisk over-view of Operation Everest III (Comex) of which he was the leader. Eight male subjects, having pre-acclimatized in the Valot Hut on Mt. Blanc, spent 30 days in the chamber eventually reaching the equivalent pressure of Everest summit on a number of occasions. There were 14 teams working on as many projects (or more) so only a few can be mentioned. Altitude cough was documented and was a problem despite comfortable temperature and humidity. Blood volume and left atrial diameters were reduced. They were able to get some results up to four days post exposure. Hb was back to normal at four days (altitude training enthusiasts please note) but PA pressure was still elevated, as was HVR and ventilation. Maximum heart rate was blunted at altitude but returned to normal rates quickly on return to normal pressure. A disturbing feature was that there were three cases of transient ischaemic attacks, fortunately with no long term effects. Ben Levine gave us an erudite paper on cerebral autoregulation at altitude. The conclusion was that altitude impairs this function probably because of the hypoxic vasodilatation.

Annabel Nicol and David Collier told us briefly about the science done on the recent "Medical Expeditions" trip to Kangchenjunga. 65 members plus a climbing team of 7 were involved in about 20 projects on themes including Respiratory, Cardiovascular, Sensory and Humoral. Data was collected in London and on the trek out. Observations were repeated at the Northern Base Camp (5100 m) soon after arrival and in some cases after a further period of acclimatization at this altitude or above. Finally we had a debate on the limiting factors to exercise at high altitude between Peter Wagner and Loring Rowell moderated by Jack Reeves. The debate turned on the role of cardiac output and if it is important in limiting exercise. The result, inconclusive.

The second poster session, with again the best ten selected for presentation, ended the formal part of the meeting. Again there were far more posters than I, at least, could digest, some 89 in this session. Perhaps we need three poster sessions or to limit the numbers of posters, though I hope not. The facilities for viewing were much superior to those at Lake Louise.

Prediction of AMS was studied by Markus Hoefer who used a 10 minute period of breathing 10% $O_2$ and noting the change in ventilation as a measure of HVR. He found this correlated with subsequent AMS scores. The change in heart rate during this time was an even better predictor. Most workers have not found a correlation of HVR with AMS but the use of a longer period of hypoxia may account for the difference. Peter Bartsch had a poster on the latest episode in the sumatriptan for altitude headache story. In a placebo controlled trial the results were not very clear since many in the placebo group improved. However it was considered that sumatriptan did confer some benefit at least in male subjects. Another poster from this group, the results of a questionnaire in 926 mountaineers, confirmed the common impression that migraine sufferers were more likely to have a history of AMS but since they tended to take a slower ascent plan, they did not actually have higher AMS scores than migraine free mountaineers. A poster by Hillenbrand and the Birmingham group failed to show a significant protective effect of progesterone for AMS in a group of 20 subjects. Andrea Ponchia had a poster giving further evidence of the low risk of moderate altitude (up to 2900 m) for asymptomatic patients with myocardial ischaemia. A poster that attracted considerable attention was by Bill Hayward who found that human sexual intercourse, at moderate altitude (1650 m), did not increase cerebral blood flow (using transcrainial Doppler) despite a rise in heart rate of 51 bpm at orgasm.! So that's all right.

**Evenings Entertainments**

As relaxation after the hard day's work the organizers laid on some very good evening talks. Scot Parazynski gave us a wonderfully illustrated talk about "Life in Space, Life on Earth" about space flights, space walks and views of Earth from space. Charlie Houston gave us a splendid personal view of his long and distinguished climbing and altitude research life. John Severinghaus delivered a moving tribute to Niels Lassen with whom he had worked on cerebral blood flow and who has contributed so much to our understanding in that area of physiology and Oswald Oelz gave us a typically idiosyncratic and self depreciating account of his "High Adventures". On the final night a banquet was followed by a party at which undiscovered talent, singing and dancing were displayed by a number of delegates. I am happy to report that the 11th Hypoxia Symposium was as successful as any previous one and there is every sign that the outlook for the next millennium is good.

Jim Milledge Chorleywood
March 1999

**A Venture Undertaken with "Medical Expeditions"**

In September of 1998 "Medical Expeditions" embarked upon its second major Himalayan venture, this time to Kangchenjunga, the third highest mountain in the world, situated in the far east of Nepal. It forms part of a majestic chain of mountains which straddle the border with Sikkim and can be seen across the tea plantations from Darjeeling. Medical Expeditions is a charitable organization made up of enthusiasts of high altitude medicine and mountains. This latest enterprise was borne of the success and ongoing enthusiasm which just didn't die down following our first research expedition to Everest in 1994. Our research team on Kangch was large with over 20 personnel in the field and many more contributing in some vital way back home. The research program included a well-balanced blend of work following on from Everest, and entirely new ideas. Our trekkers and climbers acted as volunteers for the research lured by the wonderful descriptions of the trek, promising to take us over two weeks from the beautiful lush green rice paddy fields around Basantipur, through bamboo and rain forest up into the foothills, and finally to the high glaciers and mountains. One of strengths of the expedition was the large numbers of trekkers involved, who came out in small staggered groups to Pang Pema base camp, situated at 5000m. This added a most welcome diversity of skills to the party. The commitment of the trekkers to the research was borne out by the fact that over 90% of them attended sea level pre-expedition data collecting week ends, collected daily simple data measurements whilst on the trek and took part in many of the studies taking place at base camp. During the expedition a small climbing team led by Chris Comerie attempted Kangch by the Boardman-Tasker route, successfully climbing to above the North Col, and another party climbed a new route on Ramtang, a 6700m peak. Below is a brief resume of the projects undertaken.

RESPIRATORY

**Airway Defense** *(Peter Barry, Andrew Pollard, Sarah Bakewell, Kate Wilson, Roger McMorrow, David Williams and Nigel Hart)*

Debilitating dry cough is an all but too familiar problem at high altitude, and previous work by this group has shown cough threshold, as determined by inhalation of varying concentrations of citric acid, to be reduced at high altitude. Twice daily inhaled serevent or nedocromil sodium was found to diminish altitude related lowering of cough threshold compared to placebo, although this change was not significant, suggesting that they may have a role in prophylaxis of high altitude cough. Nasal muco-ciliary clearance has also been shown to be reduced on ascent to high altitude, as demonstrated by measuring the time taken for saccharin placed in the nostril to be and although the usual decline in muco-ciliary clearance with altitude was reduced, this trend did not reach significance. It has been speculated that normal subjects exposed to cold and hypoxia may develop increased bronchial reactivity, and that these airway changes may be involved in some way in hypoxic cough. Bronchial reactivity was investigated using varying concentrations of inhaled histamine. These results are still awaited.

**Inspiratory Muscle Training** (*Lee Romer, Rick and Gill Havely and Alison McConnell*)

Ventilation is significantly increased on ascent to high altitude, and marked dyspnoea is often noticed. The effect of inspiratory muscle training using a "POWERbreathe" was investigated. Subjects were randomized either to the intervention group (30 inspiratory efforts of 50% max inspiratory muscle strength, twice daily from 8 weeks prior to departure and for the duration of the trek) or control group (no respiratory muscle training). On ascent to high altitude the control group was found to have a significant reduction in both inspiratory and expiratory muscle strength, and in inspiratory muscle endurance. In contrast the experimental group demonstrated a small increase in inspiratory muscle strength at altitude compared to pre-training. They suffered from a smaller decline in inspiratory muscle endurance than the control group, but still demonstrated the same decrease in expiratory muscle strength as the control group. Base line and transitional dyspnoea indices were carried out for both groups. The level of dyspnoea experienced by the trained group was marginally less than that of the control group. The functional significance of these observations is not yet clear.

**Ventilatory Control** (*David Collier, Annabel Nickol, Henriette van Ruiten, Jim Milledge, David Williams and Chris Wolff*)

Peripheral chemoreceptors are known to detect and respond rapidly to second by second oscillations in arterial $CO_2$ generated by the ventilatory cycle, and so are candidates for an important role in ventilatory acclimatization. Peripheral chemoreceptor function was studied in volunteers exercising gently on a bicycle ergometer by measuring the ventilatory response to small inhaled pulses of $CO_2$ given either early in every breath (thought to augment arterial $CO_2$ oscillations), or late in every breath (thought to dampen $CO_2$ oscillations). At sea level under normoxic conditions a ventilatory response to the timing of $CO_2$ pulses was observed, with ventilation being significantly greater with early than late pulses. This response was completely abolished by hypoxia (equivalent to the $PiO_2$ at Pang Pema base camp) at sea level. At base camp pre-acclimatisation (days 0-3) ventilation was greater with early pulses, although this difference was not significant, but after a period of acclimatisation there was a highly significant ventilatory response to the timing of $CO_2$ pulses. This work shows that

acute hypoxia but then gradually restored and even heightened during acclimatisation. This response may be important in ventilatory acclimatisation during the first **few** week**s** at high altitude.

CARDIOVASCULAR

**Systemic Circulation** *(David Collier, Richard Weller, Mukul Agarwal, Nigel Benjamin, and Pablo Forte)*

Systemic blood pressure has previously been shown to be elevated at high altitude. Blood pressure measurements of all participants of the expedition were made at sea level, and then daily during the trek and sojourn at high altitude. A new technique was used to measure total body nitric oxide turn over, involving an infusion of 15N labeled L-arginine and subsequent determination of 36 hour urinary 15N excretion. Recent work has shown that large differences in NO turn over between patients with essential hypertension and matched controls exists. Nitric oxide may also play a role in altitude related hypertension.

**Peripheral Circulation** *(Henriette van Ruiten and H Daanen)*

When the extremities are exposed to an extreme cold environment there is an initial vaso-constriction followed by vaso-dilatation, so called "cold induced vasodilatation" or CIVD. This opening and closing of blood vessels is seen as an important protective mechanism against the occurrence of local cold injuries. CIVD in the finger exposed to water at $0^{o}C$ has previously been found to be reduced during initial exposure to high altitude. It was not certain whether this is due to the effect of hypoxia or lowered core body temperature. This study confirmed the presence of CIVD, and also showed that core temperature was actually higher at altitude, suggesting that it is hypoxia per se which is responsible for this phenomenon. In subjects who were well acclimatised to 5000m and had spent time at extreme altitude, CIVD increased again towards normal sea level values demonstrating the restoration of a protective mechanism against cold injury.

**Electrical Impedance in the Thorax** (*Nick Mason, Mukul Agarwal, Jim Milledge, A Wilson, David Williams and B Brown*)

Pulmonary impedance measurements were made in subjects at sea level, on initial arrival at base camp, and in a limited number of subjects before and during oxygen therapy. This may enable changes in lung water to be estimated.

**Systemic and Pulmonary Circulation** (*Nick Cruden, D Newby, David Webb*)

Endothelin-1 is a potent vasoconstrictor peptide, which is secreted by endothelium both basely and in response to various stimuli including hypoxia. Levels are thought to be elevated at high altitude, and may be implicated in the development of pulmonary hypertension and possibly HAPE. increased production, in which case big endothelin-1 levels will also be elevated, or to reduced clearance. Both endothelin-1 and big endothelin-1 levels were measured in subjects at sea level and during sojourn at high altitude.

METABOLIC

**The role of Female Hormones in Acclimatisation** *(Debby Miller and Liz Bowen)*

The role of progesterone, a respiratory stimulant, and pre-menstrual changes in body water distribution in susceptibility to Acute Mountain Sickness (AMS) have yet to be clearly defined. All trekkers and climbers completed twice-daily AMS scores, and recorded daily oxygen saturations. Resting end-tidal $CO_2$ measurements were made both at sea level and on initial arrival at 5000m. Menstrual and contraceptive histories were taken, and the day of peak Luteinizing Hormone was determined using urinary dipsticks to indicate the day of ovulation. This data will be compared in men, and women at different phases of their menstrual cycle, taking the oral contraceptive pill or on depo-provera.

**Appetite and Anthropometrics** *(Matthias Tschoep)*

Leptin has been described as an "obese gene" product which was discovered in 1994. It is thought to be important in the regulation of body weight and energy balance, acting as a signal to the brain and several other peripheral organs and endocrine sub-systems regarding energy stores of the body. It is speculated that changes in leptin levels may occur at high altitude since weight loss at extreme altitude and changes in appetite are known to occur, and furthermore impairment of reproductive function and reduced growth and adult height are known to occur in high altitude populations. A highly sensitive immunoassay using monoclonal antibodies and biotin-streptavidin technology has recently been developed. This has enabled leptin to be measured in conditions where levels are known to be very low such as in anorexia nervosa or in cachectic individuals. Leptin levels were determined both at sea level and during sojourn at high altitude, and may play a role in the pathophysiology of hypoxia induced endocrine disorders.

***Appetite and anthropometrics*** *(Sandra Green, David Collier, Mike Richards and Damian Bailey)*

Daily questionnaires and visual analogue scores were completed regarding appetite and satiety during the trek. Weights and detailed anthropometrics were recorded at staggered intervals prior to and during the expedition. In addition electrical impedance allowed the estimation of body fat composition.

SENSORY AND NEUROLOGICAL

**Sensory Function** *(Jim Milledge, Martin Rosenberg, David Collier and Gwilym Rivett)*

It is widely known that many aspects of cognitive

affected by high altitude. Several aspects of these changes were studied. Perception of horizontal and vertical was investigated by asking subjects to rotate an electronically controlled arm until it was exactly horizontal or vertical. This was carried out in a darkened environment 20 times, and the mean error from the true positions determined for each subject. There was found to be a small but highly significant increase in error at high altitude. Postural body sway was measured using a pressure sensitive plate under four conditions: eyes closed, eyes open with central fixation on a single light emitting diode (LED), eyes open with attention to peripheral vision (four LEDs on at the periphery of vision), and with attention to both central and peripheral vision (all five LEDs on). 28 subjects were studied and shown to have increases in sway at altitude, which was highly significant under all conditions except using peripheral vision alone. It is uncertain whether these changes can be attributed to changes in the vestibular apparatus or more central higher centers.

**Movement Perception** *(Diana Depla and Mark Howarth)*
Reduced perception of movement in the peripheral visual field is know to occur at high altitude. This phenomenon was studied on arrival at high altitude and after a period of acclimatisation, with and without supplementary oxygen in both cases. Preliminary results suggest that short term oxygen therapy works very effectively at restoring peripheral vision loss secondary to hypoxia.

**Motor function** (*Eli Silber*)
There is known to be a deterioration in fine motor function at altitude, however, little is known about the effects of age and acclimatisation. Nine-hole pegboard tests were performed on 46 subjects at sea level and at base camp. The results show that there is a deterioration in fine motor co-ordination at altitude, and that those over 50 appear particularly susceptible. Difference between those tested within 24 hours of arrival at base camp and after this period suggest that acclimatisation is important in optimizing fine motor function.

**Headache** *(Eli Silbert, Andrew Pollard and David Murdoch*)
A detailed questionnaire was carried out to fully characterize features of headache at high altitude, and to assess whether any individuals are at particular risk of developing high altitude headaches, eg: those known to suffer from migraine. Results of this study are still being collated. A further study investigated the role of acupuncture at specific points in the skin in prophylaxis of headache at high altitude. *(Paul Richards)* Lack of randomization of matched subjects with similar ascent profiles to intervention or control groups make the results of this study difficult to interpret... (there was only one investigator!)

**Autonomic Function** (Mark Howarth and Diana Depla)
Autonomic function was studied in the eye by performing pupillometry both at sea level and high altitude, pre and post acclimatisation. A topical agent was given which is known to interfere with the autonomic function of the eye, and pupillometry performed before and half an hour after this. It is hypothesized that the parasympathetic system is down regulated at high altitude. This study may help to throw light on this hypothesis, and to determine whether this effect in the eye is mediated centrally or at the motor end plate.

INFECTION AND IMMUNITY
Increased incidence of gastro-intestinal and respiratory infections is common amongst trekking parties ascending to high altitude. This is likely to be due mainly to exposure to new unfamiliar pathogens, but may be contributed to by hypoxia induced changes in immune function.
*(Damian Bailey and Mike Richards)*
A number of biochemical processes which are thought to be affected by high altitude and are important in maintaining effective immunity were studied. These included changes in glutamine concentrations, changes in free radical induced cell damage and anti-oxidant status. These results will be correlated against acute mountain sickness scores and infective episodes, which were documented on a twice daily basis.
*(Lance Jennings, Warren and Leonie Dellow, David Murdoch and David Collier)*
A further large-scale epidemiological study investigated the incidence and pathological aetiology of both clinical and sub-clinical respiratory tract infections. Daily respiratory symptoms were recorded. Attempts to identify pathogens involved were made by taking serum samples for respiratory titres, respiratory secretions and nasal and throat swabs pre and post expedition and at specific points in the trek. This study will provide interesting data not only on the types of respiratory pathogens acquired in this part of Nepal by western trekkers, but also on the spread of infection as trekkers in well defined groups meet and separate from other parties.

CLOSED CIRCUIT OXYGEN DELIVERY SYSTEM
*(Ullrich Steiner, R Fischer, K Voll and R Huber)*
A new closed circuit breathing system was trialed in both normal volunteers and patients with suspected HACE or HAPE at Pang Pema base camp. It comprises a tight fitting facemask, breathing bag, $CO_2$ absorber and carbon fiber oxygen cylinder. It was found to function reasonably well and to have the advantage of being lighter than conventional systems at 4.5kg.

Annabel Nickol, UK

*Medical Expeditions obtained a number of small*

*substantial number of projects were funded by a grant from Liverpool University. Research leaders of the expedition can be contacted for further information:*

*David Collier (djcollier@mds.qmw.ac.uk), Annabel Nickol (annabel.nickol@virgin.net) and Jim Milledge (jmilledge@cix.co.uk).*

## JULY CASE DISCUSSION

***The subject of this case is a fit 42 year old Mountain Rescue team leader and experienced high altitude mountaineer.***
***In 1992 he reached 8000m on Mount Everest with no problems and has no history of altitude-related problems. Of note, he is under investigation for hypertension (BP180/100), but has not been commenced on treatment.***
***In October 1998 following 2 rest days at base camp (BC, 4545m) on Ama Dablam he set off unloaded for ABC (5000m) with the intention of picking up personal kit and continuing on to Camp 1.***
***Soon after leaving BC he noted that his peripheral vision was closing in and experienced a feeling of "other worldliness". Physically he felt strong but felt the need to tell another member of the team to keep an eye on him.***
***His peripheral vision became worse and he noticed that the colours of clothing etc were becoming increasingly intense. On arrival at ABC he was unable to remember the names of his teammates and became increasingly confused. He did not exhibit slurred speech or weakness and his gait was not ataxic. He was then helped back down to BC where he quickly recovered, leaving him feeling tired but otherwise well. He went on to reach Camp 1 the following day and summitted 4 days later with no further problems.***
(Case Supplied by Louise Woolrich FRCS)

**Charles Clarke, UK**
I am not quite sure of the timescale of this illness, but I am assuming it was all over in hours/a day. Generally, I would not worry too much about it, and remember, if one says it is 'likely to be.....vascular', there are potentially important issues - driving, job etc. The positive visual phenomena sound migrainous. The subsequent symptoms described would also do for basilar migraine. In 1997 near Sepu Kangri, I climbed a 5600m pass from 4600m one morning. On the way down, I had on odd shimmery whole field visual disturbance, and couldn't see edges, which lasted several hours. I felt a bit odd. I thought it was a migraine - I do get a very occasional one - and on return to base camp in the late afternoon, I certainly was a bit odd, jumbled, getting words wrong, and not my usual sparky self over the dinner table. This all lasted several more hours. It was all followed by a trivial headache in the evening.
I feel sure this was a basilar migraine. I have had no problems this year. I think migraine/migraine-a tendency to focus on the serious, the vascular or possible brain oedema, quite naturally.

**Buddha Basnyat, Nepal**
What you describe here in this 42 year old gentleman who had this experience of confusion in the vicinity of 5000 m is not an uncommon event and as you note here is outside the setting of AMS as we know
it. I believe what he had is " Transient Global Amnesia " a well known adult neurological disease entity characterisied by short lived confusion with intact motor functions. This is sometimes brought on by a highly emotional experience (perhaps the scenery was magnificent and moving). It could be a form of a transient ischaemia attack (TIA). TIAs are well described at these altitudes in trekkers and climbers. This is by all accounts a benign illness and does not presage a
stroke.

**Ken Zafren, USA**
This case concerns a 42 year old experienced high altitude mountaineer with neurologic symptoms occurring just above Ama Dablam base camp. The history implies that this man was well-acclimatized. It would be useful to know if he had a history of migraine headaches. This does not sound like HACE since he had no headache and was not ataxic. I think that the top two diagnostic possibilities are migraine equivalent and TIA. It is probably impossible to sort these out in this case. I would favor TIA as the diagnosis. Reports of TIA at altitude seem to be increasingly common. The risk of recurrence with repeated exposure to altitude has never been studied, as far as I know.

**Gerald Dubowitz, USA**
The combination of hypertension and subsequent déjà vu with visual changes at altitude bring up the possibilities of epilepsy, temporal lobe hypoxia or transient ischaemia with or without embolic phenomena.
Judging by his excellent recovery, my money would be put on a migrainous type event here. It is very hard to establish whether this is the same as the transient ischaemia (described on expeditions ranging from Makalu in the 1960's through to Everest in 1994). I believe they are all variations on a similar theme. This could be a transient neurological event that may mimic migraine (tunnel vision, photopsia and déjà vu) or one which mimics transient ischaemic events (e.g transient dysarthria, hemiplegia and confusion).
It would be fair to say that we still have no real

the individuals get better and nothing can be found back at sea level. Interestingly some go on to do well on their next sojourn at altitude and some get re-entrant events when they return to similar altitudes.

**David Syme, UK**
As a GP I just wonder about something simple like migraine. There does seem to be an association between migraine and Hypertension. Certainly patients of mine have had fewer symptoms when their hypertension was treated.
I personally would have serious doubts about leaving a BP of 180/100 untreated in a man of 42and would have wanted to complete the investigations before leaving. Perhaps this illustrates again the risks that mountaineers take with their health to undertake activities that are optional rather than essential.

**David Hillebrandt, UK**
A good G.P. type morning consultation involving differential diagnosis. Pity our surgery is not at 5000m ! Well of course one must consider low pO2 and HACE but what about migraine?

**Brownie Schoene, USA**
Migraine vs TIA as a result of his pernicious and probably real hypertension. The hypertension needs to be worked up and treated. His blood pressure should have been checked during the incident. Catecholamines are high upon first arrival at altitude and then down again such that he may have had even more accentuated hypertension upon arrival. Symptoms are certainly compatible with migraine as well which may well be provoked by altitude.

**Gustavo Zubieta Sr, Bolivia**
This symptomatology is tricky. There is insufficient clinical information, except that he has arterial hypertension. That suggests that his blood pressure is probably going up and down, influenced by many factors. We can only speculate in this case, since the symptoms disappear on arrival to the low lands, we believe that he had a vascular spasm localized in the peripheral or central area which controls the vision (painless). The symptoms have some similarities with migraine, a painful affection that is recurrent, where the etiopathogenesis, until now is unclear. Besides, he should have controlled his hypertension, at any altitude.

**Jim Milledge, UK**
The 42 year old Mountain Rescue team leader would seem to have suffered an unusual form of transient ischaemic attack. He demonstrated a good recovery from it by summiting Ama Dablam shortly after the episode.

**Jim Litch, Nepal**
As in many case reports, we are missing important details and information. Given the information presented I have the following comments.
The very sudden onset of the neurologic symptoms during ascent without prodromal mild symptoms argues very strongly against high altitude cerebral edema. (2) His initial symptoms of narrowing of peripheral vision and a feeling of "other worldliness" are very suspicious for hyperventilation. The individual was exerting fully at the time. We are not given specific information on the duration of these specific symptoms. Was there a component of anxiety present? Is there a history of anxiety disorder? (3) The worsening confusion, and inability to recognize teammates, without other focal neurologic signs present, makes me suspicious of Transient Global Amnesia. Transient global amnesia may be precipitated by cerebral vasoconstriction. Could hyperventilation have promoted this episode? (4) Both hyperventilation syndrome and transient global amnesia at high altitude are related to a recent gain in altitude in unacclimatized individuals, and not necessarily associated with altitude illness.

Litch JA, Bishop RA. Transient global amnesia at high altitude. NEJM 1999;340(18):1444

## *CORRESPONDENCE*

Editor,
I was appalled by the advice some of the experts gave on employing a Sherpa with a history of HACE who required helicopter evacuation. He is now being offered a job that would require him to go far higher as a “compensation”.
The debate over whether an attack of HACE is a risk factor for further HACE is interesting (or would be if there was a consensus which there would not appear to be). But we are talking about a man’s life, probably a man with a wife and young family, no social security, and possibly an insurance company with some awkward questions to ask. An expedition leader who takes this man to problems with his conscience if anything goes wrong and so is an expedition doctor who does not at least try to veto it.
Fortunately you have a GP on your panel who was able to give some balance. This is probably a good illustration of the principle that expedition doctors are best recruited from the ranks of informed GPs rather than of specialists!

*Mark Howarth, UK*

Editor,
I have a comment regarding the article in the last newsletter about People with pre-existing conditions

Anecdotally we see more tourists with epilepsy which occurred in the mountains than in Kathmandu valley and many of these patients have a history of epilepsy in the past which seems to have re appeared at high altitude in the Himalayas after a quiescent period of years. As I say this is anecdotal, but what would be interesting would be to study willing volunteers with a past history of epilepsy and do EEGs in a hypobaric chamber setting and my hypothesis would be that these people who have a past history of epilepsy would be more likely to have an abnormal EEG than a controlled population. In Nepal we do not have a hypobaric chamber and so this would be an intriguing project for an enthusiastic neurologist or a neurophysiologist from the Western hemisphere who has access to a hypobaric chamber.

*Buddha Basnyat, Nepal*

Editor,
In the last issue of the International Society for Mountain Medicine Newsletter Drs. Zubieta presented an interesting case of Monge's disease with a previous review about Bernardo Guarachi, the famous Bolivian Andinist. Commenting about its activities in the Andes mountains range they referred to the Aconcagua as placed in the Republic of Chile.
Argentina has had many border conflicts with Chile. An extensive mountain frontier separates both nations and curiously Aconcagua is in the region of the Central Andes placed between the Altiplano and the Patagonian Andes, which has *never* been the object of a quarrel because both parts adopted the "Divortium aquarum" criterion to delimit the frontier. This is the region where the dividing waters runs west of the high tops, and the Aconcagua is situated there. For the above reasons there have been no doubts concerning Aconcagua's location inside the Argentine territory.
I thank you beforehand for taking the necessary steps to make the corresponding corrections in order to avoid such a kind of error in the future, which may lead to disbelief regarding authors and editor's scientific quality. I would like to let you know that the mentioned Newsletter has a vital place among the people interested in the mountain medicine and its development in the more distant planet sites.

*José Carlos Pesce M.D.*
*Chief of the Mountain Medicine Department.*
*APTUS Sport Medicine Institute*
*Buenos Aires*
*República Argentina*

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# FORTHCOMING MEETINGS

***World Congress III on Wilderness Medicine***
***Whistler, British Columbia (Canada) August 7-12, 1999***

Details from: Dian Simpkins, Wilderness Medical Society 3595 East Fountain Blvd., Suite A-1, Colorado Springs, CO 80910 USA. Sponsored by the Wilderness Medical Society, ISMM and International Society for Trave; Medicine.
Phone 1.719.572.9255,
Fax 1.719.572.1514
***e-mail: dian@wms.org***

***Wilderness Emergency Medical Technician (EMT)/Command Physician, Aberdovey, Wales. November 8th-13th 1999***

The first course in the UK will be held at Aberdovey, Wales, 8-13 Nov 99. If anyone is interested,please contact the organiser, Dr Jel Coward at jel@wildmedic.org or Jon Pote, at potes@enterprise.net

***THE THIRD UKRAINIAN CONGRESS OF PATHOPHYSIOLOGISTS* with international participation, *Honoring Academician Nikolay Gorev (1900 - 1992)***
***Odessa, 24-27 May, 2000***

*The Congress is organized by*:
Ministry of Public Health of the Ukraine, Ukrainian National Academy of Sciences, Ukrainian Pathophysiological Society, Odessa Medical University.

ADDRESS of the Organizing Committee:
Bogomoletz Institute of Physiology
of the Ukrainian Academy of Sciences
Bogomoletz St.,4 Kiev 252024, UKRAINE
Phone : (380-44) 293-6151, 256-2492, 256-2489, 256-2479
Fax : (380-44) 293-1678, 293-3431
E-mail: sereb@mail.kar.net

***4th World Congress on Mountain Medicine and High Altitude Physiology, Arica, Chile 1st-6th October 2000***

Details from:
Claus Behn, Physiology and Biophysics, ICBM, Faculty of Medicine, University of Chile, Independencia 1027, Santiago, Chile Phone: 56-2-678-6215; Fax 56-2-777-6916; email
cbehn@machi.med.uchile.cl

# MOUNTAIN MEDICINE COURSE ADDRESSES

If you run a course and would like information included in ISMM News or if you have been on a course and would like to make comments about it please contact:

Dr. med.Patrick Peters
Mastbruchstr. 133
D-33104 Paderborn
Germany
Phone: +49 5254 809150
Fax: +49 5254 809156
E-mail: peters.patrick@t-online.de

**Address list of course organisers**

**Austria**
- Special winter course 18 - 24 April. Special trekking/expedition medicine course 25 April - 1 May. Basic mountain medicine course 6 - 12 June. Special summer course 11 - 17 July . Österreichische Gesellschaft für Alpin- und Höhenmedizin (ÖGAHM), Secretary: Univ.-Doz. Franz Berghold, Postfach, A-5710 Kaprun 130, Austria, Phone: +43 6547 8227 Fax: +43 6547 7772

**France**
- ARPE, Association pour la recherche en physiologie de l'environnement, UFR de Médecine, 74 rue Marcel Cachin, F-93012 Bobigny cedex, France, Phone: +33 1 48387757 Fax: +33 1 48387777
- Prof. Pierre Girardet, Département d' anesthésie-réanimation 2, Centre Hospitalier Universitaire de Grenoble, Hôpital Albert Michallon, BP 217, F-38043 Grenoble cédex 09, France, Phone: +33 76765426 Fax: +33 76765183
- Prof. Ch. Virenque, CESU de Toulouse, Hôpital Purpan, F-31059 Toulouse cédex, France, Phone. +33 61772490, Fax: +33 61777451

**Germany**
- High altitude medicine intensive course for doctors 20-26th March and June 26th-July 2nd. Prof. Dr.med. P. Bärtsch, Universität Heidelberg, Medizinische Klinik und Poliklinik, Abteilung für Sport- und Leistungsmedizin, Gebäude 4100, Hospitalstrasse 3, D-69115 Heidelberg, Phone: +49 6221 568101, Fax: +49 6221 565972

**Italy**
- Dr. Carlo Vettorato, Soccorso Alpino Valdostano, Ospedale di osta, Via Ginevra 3, I-Aosta, Italy, Phone: +39 165 304660- Prof. Dr.med. C. Angelini, Universita' degli studi di Padova, via Giustiniani, I-35128 Padova, Italy, Phone: +39 49 8213610, Fax: +39 49 8751770

**Netherlands**
- Dr.med. Franken Marco, Groen van Prinsterlaan 27NL-2271 EM Voorburg, Netherlands
- Dr.med. Heleen Meijer, Brouwersgraacht115f, NL-1015 GD Amsterdam, Netherlands, Phone: + 20 6391302, Fax.: + 20 6391302

**Spain**
- Theoretical and practical courses on mountain medicine, Universitat Autonoma de Barcelona. Postgrade Program. Director: dr. A. Ricart de Mesones. Institut d'Estudis de Medicina de Muntanya Dr. Castello Roca. Muntaner, 231. E-08012 Barcelona. E-mail: ricart.demesones@bcn.servicom.es Secretary: RCT. Aulestia Pijoan, 12, baixos. E-08012 Barcelona. Phone: 34 93 4156938 fax: 34 93 4156904 E-mail rct@ssc.es

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- Dr.med. Bruno Durrer, President of the MedCom UIAA, Arztpraxis, CH-3822 Lauterbrunnen, Switzerland, Phone: +41 36 553838, Fax: +41 36 553852

**United Kingdom**

- *Mountain and High Altitude Medicine.*

Dr. Andrew J. Pollard, Department of Paediatrics, 7th Floor QEQM Wing, St.Mary's Hospital, South Wharf Road, London W2 1NY, United Kingdom, Fax ++ 44 171 886 6284, Phone: +44 181 478 1222

email: ajpollard@csi.com

Outdoor Medicine Course 23rd-27thFebruary. Dr. David Syme, Loch Tay Cottage, Killij, Perthshire, Scotland, United Kingdom, HL 21 8 UH; e-mail: dsyme@kilmed.demon.co.uk

# ANNOUNCEMENTS

### *ISMM Prize 2000*

A prize of 1500 Swiss Francs (approximately 1000 US$) will be awarded to a young investigator for research for research devoted to all aspects of acute, intermittent and chronic exposure to high altitude that has been published or accepted for publication in a scientific journal between July 1, 1998 and March 1st, 2000.

The applicant must have done the work by himself and be the first author of the publication, i.e. she/he must have played the major role in planning and conducting the project as well as in analyzing and interpreting the data. The applicant must be born after March 31st 1965.

The jury consists of the president and the vice-presidents of ISMM, the editors of the ISMM Newsletter and the presidents of the Medical Commissions of UIAA and IKAR.

The winner will be announced by the end of June 2000. The prize will be awarded at the Arica Meeting, to be held in Chile June 2000. She/he will have free registration at the meeting and the travel expenses up to 1500 SFr will be paid by the ISMM.

Applicants can obtain an application form from the President of the Society (address on the front page of the Newsletter). A completed application form together with 10 copies of their publication, a curriculum vitae and birth certificate (copy) and a statement describing their principal role in the submitted work by the department chair should then be sent to the president of ISMM (address on front page). Papers received after March 31st 2000 cannot be considered for the ISMM prize.

### *Meeting for the Constitution of the "Italian Society of Mountain' Medicine*

On Saturday 3 and Sunday 4 July 1999 will be organized in Arabba (Dolomites) (BZ Italy) a Meeting in order to found the "Italian Society of Mountain's Medicine".The Constitutive Group is represented by G.C. Agazzi,A. Cogo,O. Pecchio,and A. Ponchia ,Italians Medical Doctors.The Meeting will begin at 14,30 ( Saturday July 3th. 1999).Will participate Carlos Monge, from Peru,Peter Bartsch,the President of the "International Society of Mountain's Medicine",Franz Berghold,as delegate of the "U.I.A.A.",A. Cogo and Basnyat Buddha from Nepal.The Prof. Cerretelli will be the Chairman of the Meeting.The Secretary' Office is the following : "Key Congress and Communications" S.r.l. tel (049) 659330-fax (049) 8763081

E-mail keycong @protec.it

### *Hypoxia Symposia:*

The complete proceedings of the ten Hypoxia Symposia (1981-1997) are available on one CD. Email: studd@fhs.mcmaster.ca Sharron Studd, Division of Continuing education, McMaster University, 1200 Main St West, Hamilton, Ontario L8N 3Z5, Canada.

### *Bibliography of High Altitude Medicine and Physiology*

Bibliography of High Altitude Medicine and Physiology The 1999 edition of the Bibliography of High Altitude Medicine and Physiology is now available. The Bibliography is based on citations hand selected from the libraries of Drs. Hackett, Roach, Houston and Richalet. The new version has been updated to contain over 6000 references germane to the broad field of high altitude medicine and physiology. And in 1999, the bibliography contains many citations with abstracts. One CD contains the bibliography in several formats, plus demonstration versions of some of the most popular bibliography management software programs. The included programs include demos of EndNote, Reference Manager and Procite. The Bibliography is provided in native format for each of those databases, and in text format. All databases and demo programs are for the PC, except for EndNote where a MacIntosh version is also provided. The cost is $75 US, plus shipping and handling ($5 North America, $10 International). The Bibliography may be ordered by writing to Dr. Rob Roach, BHAMP, Box 343, Montezuma, NM 87731, USA. Email: rroach@hypoxia.net. US orders by check or money order. International orders, please inquire.

# ISMM WEBSITE

The homepage has moved to
**http://www.medicine.mc.duke.edu/ismm/**

The site contains useful links to other relevant sites. The site has been transferred to Duke University, North Carolina, USA.

# SUBMISSION OF ARTICLES

Articles covering all aspects of mountain medicine from the academic science of high altitude physiology to the practical management of altitude illness and from treatment issues in hypothermia to practical medicine in mountain rescue will be considered for publication in the newsletter. Articles submitted for publication must be in English and will be subject to editorial review by appropriate members of the editorial and advisory boards. To reduce administrative costs, submissions to cope with other electronic formats also. Non-electronic submissions by fax or mail will also be considered from individuals who do not have access to a suitable computer. PLEASE DO NOT USE ANY AUTOMATIC REFERENCING SOFTWARE SUCH AS ENDNOTE OR REFERENCE MANAGER.

Articles covering the following areas should be submitted to the editor at the address on the front cover:

***3) Case Histories which will be discussed by email by an international expert panel.***
***4) Management guidelines for debate.***
***5) Biographies, historical reviews and obituaries.***
***6) Book reviews of English language books on any aspect of mountain medicine.***
***7) Reports on international and local mountain medicine meetings and conferences.***
***8) Information about national societies, courses, future meetings and books of interest to ISMM members.***

References for inclusion in the section on latest references should be sent to Bengt Kayser (kayser@cmu.unige.ch)
AP

## *MEMBERSHIP SUBSCRIPTIONS*

Subscriptions are due on the 1st January each year. A single reminder will be sent to members who forget to pay on time and if fees are still not received by the membership secretary, membership of the society will cease. Where members have difficulty in paying their subscriptions, they may apply in writing to the President of the society for complimentary membership.

Please ensure that you complete the entire back page of the newsletter each January when you renew your subscription, so that we can be sure that we have your correct address. The coordination of newsletter production, is a complicated international process. Please let us know if you experience any problems.

**INTERNATIONAL SOCIETY FOR MOUNTAIN MEDICINE**
**APPLICATION FOR MEMBERSHIP and MEMBERSHIP RENEWAL FORM**

There are several ways by which you can pay your membership fees: **1.** By credit card: please use the form below or **2.** Send a ***Euro***check (in Swiss Francs) in favour of the ISMM directly to the Membership Secretary **3.** Give your bank the order to transfer the appropriate equivalent amount to our account: nr.CO-257.980.0, United Bank of Switzerland (UBS), CH-1211 Geneva 4, Switzerland. **4.** *Swiss* members can pay by postal check to PC 12-172-9 and mention the ISMM account number CO-257.980.0 at UBS. Renewal of membership is due on the 1st January each year. If fees are not received on time, membership will cease, after a single reminder.

**USE FOR NEW APPLICATION & FOR MEMBERSHIP RENEWAL ON 1st JANUARY EACH YEAR**

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***Send to: Dr.Bruno DURRER, Membership Secretary of the ISMM, Arztpraxis CH 3822 Lauterbrunnen, SWITZERLAND, Fax:++41 33 856 26 27, email: B.Durrer@popnet.ch***