

***HIGH ALTITUDE RESEARCH EXPEDITION: KANGCHENJUNGA
1998
A Venture Undertaken with "Medical Expeditions"***

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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 tasted. Nasal moistening using a saline spray four times a day was compared with a control group, 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 Havelly 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 CO₂ 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 CO₂ given either early in every breath (thought to augment arterial CO₂ oscillations), or late in every breath (thought to dampen CO₂ oscillations). At sea level under normoxic conditions a ventilatory response to the timing of CO₂ pulses was observed, with ventilation being significantly greater with early than late pulses. This response was completely abolished by hypoxia (equivalent to the P_iO₂ at Pang Pema base camp) at sea level. At base camp pre-acclimatization (days 0-3) ventilation was greater with early pulses, although this difference was not significant, but after a period of acclimatization there was a highly significant ventilatory response to the timing of CO₂ pulses. This work shows that sensitivity of the peripheral chemoreceptor to a dynamic signal is present at sea level, abolished by acute hypoxia but then gradually restored and even heightened during acclimatization. This response may be important in ventilatory acclimatization during the first few weeks 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 ^{15}N 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°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 basally 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. Elevated endothelin-1 levels may be secondary to 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 and other neurological function are adversely 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 known 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, CO₂ 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 grants to assist in funding this research. A substantial number of projects were funded by a grant from Liverpool University. Research leaders of the expedition can be contacted for further information:

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