# Lessons learned while undertaking high altitude medical research in the Himalayas

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**Abstract**

Undertaking medical research during military adventurous training expeditions presents a unique set of challenges to medical personnel, and for those considering doing so in the future the task may seem daunting. This article details some of the challenges faced whilst undertaking high altitude research on a recent Defence Medical Services (DMS) adventurous training expedition to the Dhaulagiri circuit in Nepal. By discussing what led to some of the problems encountered, how they were overcome, and in some instances how they could have been avoided in the first place, it is hoped that the article will act as a guide for others who plan on undertaking future research in a similar environment.

## Introduction

In February 2015, fifteen doctors from the United Kingdom (UK) Defence Medical Services (DMS) embarked on a three-week adventurous training expedition to the Dhaulagiri region of Western Nepal. The expedition's main aims were to teach junior doctors about high altitude medicine, thus increasing their capability as future expedition medical officers, and to reconnoitre the Dhaulagiri circuit before the much larger British Services Dhaulagiri Medical Research Expedition (BSDMRE) in 2016. The expedition also served as an opportunity to carry out primary high altitude research on participants and test the research protocols to be used on BSDMRE 2016. Problems with research equipment and adverse weather conditions combined to create several setbacks that threatened the success of the project and were only overcome by adapting the original research protocol and working closely with fellow team members and local staff. This article discusses some of the challenges faced, with special attention to research ethics, study design, equipment and the transportation of frozen samples.

## Study synopsis

An important physiological adaptation to high altitude is the reduction of total body water and circulating blood volume facilitated through marked changes in endocrine function and subsequent diuresis (1). Failure to adapt adequately has been shown to predispose people to developing high altitude illnesses (2). The role of cortisol, a stress hormone that causes fluid retention, remains unclear, with several studies reporting a rise in the hormone at high altitude (3,4), while others, including a recent DMS study by Woods et al (5), have reported no increase, or a fall, in cortisol levels.

Several studies have also reported that raised cortisol levels correspond with the severity of acute mountain sickness (AMS) (6,7), while paradoxically the administration of corticosteroids is effective for both prophylactic prevention of AMS (8) and treatment of AMS and high altitude cerebral oedema (HACE) (9).

The drop in cortisol at high altitude reported previously may be due to blunting of the adrenal response to adrenocorticotrophic hormone (ACTH), the pituitary hormone that stimulates cortisol production. This hypothesis was to be tested by performing short synacthen tests (SSTs) at 3600, 4200 and 4800m, and comparing the results to baseline testing performed at sea level prior to the expedition. The SST, most commonly used to diagnose adrenal insufficiency, involves the administration of a 250µg dose of a synthetic ACTH and measurement of the subsequent rise in blood cortisol levels. Participants' altitude sickness scores and basic observations were also to be recorded daily to see if the ability to adapt to high altitude was linked to adrenocortical function.

## Ethics

Ethical approval for the study was sought through the Ministry of Defence Research Ethics Committee (MoDREC). An initial application was submitted in August 2014 before being presented to the MoDREC in November 2014. The Committee recommended several changes to the application and an amended version was granted ethical approval in January 2015, one month prior to the expedition's departure. The process can be a lengthy one and researchers should allow at least six months for its completion.

One particular concern of the Committee was that expedition members would be coerced into consenting to be tested if they thought this had any bearing on their eligibility to go on the expedition. This was never the case, but to avoid any confusion particular care was taken to explain so in the participant information sheet and in person on the briefing day. An independent medical officer, not involved in any aspect of the research and therefore not biased, was also present throughout the expedition and could terminate a participant's involvement in the study at any time on medical grounds.

**Study design**

Performing research in the expedition setting brings with it a variety of unique challenges. However, many of these can be met through meticulous planning and appropriate study design. Study protocols must try and strike a balance between being robust enough to produce reliable and repeatable results, whilst recognising that adaptation and flexibility are often necessary in order to overcome the inevitable problems that the environment will pose during the trip.

The ability to adapt was tested during the expedition when, upon reaching Italian Base Camp (3600m) at the foot of Dhaulagiri I's west face, it was met with severe weather that saw four feet of snow fall in twenty-four hours, worsened by gale force winds and spindrift. Plans to perform SSTs on the first morning at 3600m were quickly abandoned as the team's priority shifted from the research effort to digging tents out of the snow. Instead, the decision was made to extend the stay at Italian Base Camp and wait for the weather to improve. When, one day later, there was a window of good weather it allowed the research to be undertaken with the participants better rested and in a more relaxed environment. Perhaps most importantly, it also made helicopter evacuation possible if necessary, in the very unlikely event of anything going wrong during the procedure. The fresh snowfall did mean the expedition was unable to continue further along the Dhaulagiri Circuit, as ascent to higher altitude was deemed too dangerous because of the high risk of avalanche. While this decision meant forgoing the planned SSTs at 4200 and 4800m, it ensured the safety of the group, which must remain the priority of team leaders above all else.

Creating a comfortable environment to undertake research in makes for a more pleasant experience for both researchers and participants. Temperatures at 3600m often dipped below freezing, and the willingness of participants to take warm layers off to have electrocardiograms and blood pressure measurements taken would have soon waned if not for a warm, dry tent to do it in. Creating such an environment is not just important to maintain team morale, it also prevents the introduction of confounding factors to the research. Cortisol's sensitivity to myriad factors, including body temperature (10) and acute psychological stress (11), meant this was of particular importance for the study. The tent used doubled as both the mess tent and the research area, and was supplied by the expedition company. Even at very high altitudes tents will warm up quickly when in direct sunlight, and bringing a portable heater is another way of warming the research environment, although this carries with it the risk of carbon monoxide poisoning if equipment is not well maintained.

**Research equipment**

One of the major challenges of performing research on any expedition is the transportation of research equipment, most of which is not designed for high altitudes. Most of the Dhaulagiri circuit is completely inaccessible by road, so the transport of equipment relies upon local porters and mules. The expedition used 120-litre plastic barrels lined with foam roll mats and with clip-on lids to store equipment. Upon reaching the trail, each barrel was strapped to the top of a porter's doko (a large woven bamboo basket) and carried between camps. Researchers should inform their expedition company of how much equipment they plan on bringing to ensure that extra porters can be recruited to carry it if necessary.

Many of the problems encountered were caused by a faulty petrol generator, which the expedition was heavily reliant on to power electrical research equipment. The generator first overloaded the electrical centrifuge during testing, three days before the first SSTs were due to be performed, and later ceased to function entirely. The expedition company quickly sourced a hand-powered centrifuge in Pokhara and a porter was dispatched with it to catch up with the rest of the team along the trail. The hand-powered centrifuge was capable of holding four blood bottles at a time and achieved reasonably good separation of plasma after ten minutes of continuous spinning. However, it did not pack red cells as tightly as its electrical counterpart and so yielded less plasma – a problem exacerbated at altitude by polycythaemia. Despite this lowered yield, and given the low cost of the unit, taking one as a reserve option for any study involving blood samples is certainly worthwhile. The problem might have been avoided entirely if more time had been available to test all of the research equipment upon arrival in Kathmandu, before leaving for the trail. Researchers should consider arriving a few days earlier than the rest of the group to allow time for testing equipment and getting it repaired or replaced if need be. Spare parts for equipment should also be taken, and at least one member of the expedition team or porter staff should be a competent mechanic with a good working knowledge of the generator.

**Maintaining the cold chain**

In theory, transporting blood samples back to the UK for laboratory analysis should be relatively simple. Once blood is collected it can be centrifuged and the serum pipetted into cryovials, which can then be frozen and preserved in a dry shipper, capable of maintaining liquid nitrogen temperatures for up to three weeks and able to be carried by a single porter along the trail. Since dry shippers do not contain free liquid nitrogen they are permitted on commercial flights without any need for airline approval and can be carried as hold luggage. Serum samples in which there is a minimum likelihood of pathogens being present, including those taken from healthy participants for research, are also exempt from the stringent shipping regulations placed on other biological specimens. Once the samples reach the laboratory in the UK they can be thawed before being tested. Communicating with laboratory staff prior to the arrival of samples that they need to be dealt with quickly and are not easily acquired again should help to ensure that the process runs smoothly.

The expedition's experience of maintaining the cold chain from blood sampling at 3600m back to the UK was somewhat less straightforward. Because of uncertainty about whether a UK-purchased dry shipper was compatible with liquid nitrogen filling systems in Nepal, the expedition dry shipper was purchased in Kathmandu. However, upon arrival, this proved to be too small for purpose and an alternative had to be sought. These problems were compounded by the delay in getting ethics committee approval (which delayed the purchase of equipment in the UK) and the short time in Kathmandu before departure for the trail. Unable to source a larger dry shipper in time, the choice was made to use a portable freezer brought from the UK. This had two major drawbacks: it ran on electrical power and the lowest temperature it was capable of maintaining was -20°C. Since a generator cannot be run whilst being carried, solar panels were used to power the freezer when moving between camps. This proved unreliable, failed to generate enough power to cool the freezer adequately and was dependent upon good weather. When the petrol generator eventually ceased to function, the expedition was left with no means of powering the freezer overnight; the only way to save the samples was by storing them in thermos flasks and dispatching two fit and willing team members to run them thirty miles to the nearest village with electricity before they thawed. Here they were stored in the chest-freezer of a local ice-cream shop until the porter with our expedition freezer caught up.

The experience demonstrates the necessity for either a liquid nitrogen dry shipper, or a dependable portable power supply (car batteries have previously been used), and the advantage of having as little reliance on electricity as possible. It also further supports the point made previously that research equipment should be sourced in the UK whenever possible, and adequate time should be left before any expedition for testing, repairing and if need be, replacing it.

**The relevance of high altitude medical research to the military**

Military personnel are regularly subjected to high altitude environments during adventurous training and in an operational capacity. In Afghanistan, for instance, coalition forces were regularly deployed to areas above 3000m altitude, often without adequate time to acclimatise due to operational constraints (12). AMS affects 9% of people at an altitude of 2800m and 53% of those ascending to 4600m, and can lead to the potentially fatal conditions of HACE and high altitude pulmonary oedema (HAPE) (13). In the military the development of these conditions does not only impact on the patient, it can also seriously affect force generation. Continued research into high altitude physiology is vital in order to keep improving the standard of care provided for personnel travelling to high altitude environments.

**Conclusion**

Undertaking high altitude medical research in the field presents unique challenges that researchers must overcome. Many of these challenges can be met through meticulous planning, appropriate study design and the correct equipment. However, regardless of how well-planned and executed research protocols are, the unpredictable nature of the environment is likely to create problems that researchers have not foreseen. The resourcefulness and adaptability of team members is essential in order to overcome these problems, as is maintaining solid lines of communication between team members and local staff.

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