APEX 4 – Report to the Myre Sim Committee

Dr Matt Wilkes / October 2014

The Myre Sim Fund

The Myre Sim Fund kindly granted me £1000 pounds in support of my project to study the changes in the optic nerve sheath diameter (ONSD) at altitude. I gathered the data for the project during the APEX4 expedition to Chacaltaya, Bolivia from 30 May to 12 June 2014.

The APEX4 Expedition

The Altitude Physiology Expeditions (APEX) research group was founded in Edinburgh in 2000. Prior to APEX4, the group had mounted three previous research expeditions, each contributing peer-reviewed, published research to the field of altitude medicine. [1] [2] [3] [4] [5]

Preparation for APEX4 began in November 2013, led by a committee of Edinburgh medical students. They were supervised by APEX Founders, Drs Kenneth Baillie and Roger Thompson and by University of British Columbia researcher Dr Martin MacInnis. Patrons and supporters included the University of Edinburgh, altitude physiologist John West, President of the Medical Research Council Sir John Savill; Mountain Rescue Doctor Hamish MacInnes and mountaineers Sir Chris Bonnington, Doug Scott, Cameron McNeish and Chris Tiso.

Apart from my own project, there were a number of other scientific studies that took place on the expedition. These were: subclinical pulmonary oedema and gene expression, cardiac acclimatisation to hypoxia, acute mountain sickness and patent foramen ovale and hypercoagulability at altitude.

While the previous expeditions had generated plenty of worthwhile research, the challenges of mounting another expedition to Bolivia had grown considerably since

APEX3. In particular, the Bolivian press had picked up on an interview by an American former APEX investigator, discussing the potential military applications of altitude research. [6] [7] In response, the Bolivian government then strongly opposed any further foreign altitude research taking place in the country and put strong pressure on the Bolivian Academy of Sciences to do the same.

We lost access to our research building that we had used on previous expeditions and APEX 4 became subject to an ever-changing and baroque set of visa requirements. Indeed, it was only after actually arriving in La Paz that we knew for certain that we would be able to enter the country at all. A large quantity of our research equipment was impounded by customs on arrival, and it was only through days of effort by the British Embassy and the APEX Logistics Officer that it was eventually released.

Nonetheless, at 3am on 31 May 2014, twenty-eight student volunteers, three researchers and two expedition doctors (of which I was also one) arrived in La Paz. We based ourselves in a hostel and made preparations for the first day of testing. Strikes and blockades by discontented bus drivers hampered our efforts to obtain the oxygen and dry ice that we required, but hours spent in taxis and some very kind local assistance contributed to our eventual success in obtaining all of the necessary supplies. The first test day took place in the hostel in La Paz a little over 24 hours after arrival on 1 June. Though most of our kit was still impounded in customs, we had managed to secrete enough equipment in hand luggage for the day to be a success.

Forty-eight hours after arriving, we experienced our most severe case of altitude illness when one of the student volunteers developed HAPE. He knocked on our door at 2am, complaining of a cough productive of pink sputum, shortness of breath and a severe headache. The crepitations on his chest could be heard from across the room. We treated him with acetazolamide, dexamethasone and nifedipine and took him down to a clinic at the base of La Paz. Such a severe case of HAPE at 3,700m was a first for APEX and may have been due to an underlying atypical pneumonia. After stabilisation at the clinic, we evacuated him to Miraflores in Lima (79m) where he made a full recovery.

On our fourth full day in Bolivia, we ascended from La Paz to Chacaltaya (5,300m). As we had lost use of our previous research facility, we made our accommodation in the only other building there: Club Andino. Club Andino was a dilapidated old ski lodge. It had fallen from use since the glacier's snows had receded and what remained were the absolute bare bones of a building; however, what it lacked in facilities or waterproofing, it made up for with spectacular views of the stars and the 6,000m Huayna Potosi and Illimani peaks.

The view at Chacaltaya. In the foreground is an old hypobaric chamber, in the background the lights of La Paz 1300m below and the stars of the Milky Way (Photo: Author)

The first two nights at Chacaltaya were hard. The nature of the study meant that we were all likely to experience some degree of AMS and many did. The doctors stayed awake through the night, administering reassurance, simple analgesia and antiemetics (the only medicines allowed within the confines of the studies).

Twenty-four hours after arriving at Chacaltaya, we evacuated two of the students. One had a severe headache, unrelieved by analgesia. The other had intractable vomiting.

Though they were keen to stay in the studies, as doctors we felt it unethical that they remained at the laboratory with such symptoms. We gave them acetazolamide, dexamethasone and oxygen and prepared them for evacuation. After just minutes on oxygen, their misery subsided and they boarded the jeep down the mountain, accompanied by one of the expedition doctors.

However, the driver was worried. He had heard reports of violent robbers hijacking cars on the unlit road down to La Paz. Much to everyone's relief, the road proved straightforward. Though now excluded from the studies and on acetazolamide, both students were able to re-join us at Chacaltaya after another 48 hours of acclimatisation in La Paz.

In our eight days of research at our makeshift 5,300m laboratory in Club Andino, we experienced a number of challenges: acute mountain sickness, diarrhoeal illness, cabin fever, unwell and unwelcome tourists, lightning storms, power cuts, blockades, government obstruction and equipment failure; however, we still managed to complete almost all aspects of the studies as planned. Most importantly, all descended safely to continue their travels around South America.

The ONSD Study

High altitude is broadly considered as being above 2,500m. Above that, the environment becomes increasingly hostile.[8] The sun's rays are stronger, the winds are fiercer and the temperature falls lower; however, it is the reduction in partial pressure of oxygen (hypoxia) that often has the most profound effects on human beings. These effects and the body's subsequent attempts to adapt to the lack of oxygen (acclimatisation) are incompletely understood.

The pathological effects of an overly rapid ascent to high altitude can be manifest in a number of different ways. Cerebrally, the patient may suffer high altitude headache (HAH), sleep disturbance, acute mountain sickness (AMS) and high altitude cerebral oedema (HACE). In the lungs, the hypoxia can progress to high altitude pulmonary oedema (HAPE). Though all share the common precipitant of hypobaric hypoxia, the exact relationship between some of these clinical syndromes still requires further clarification.[1]

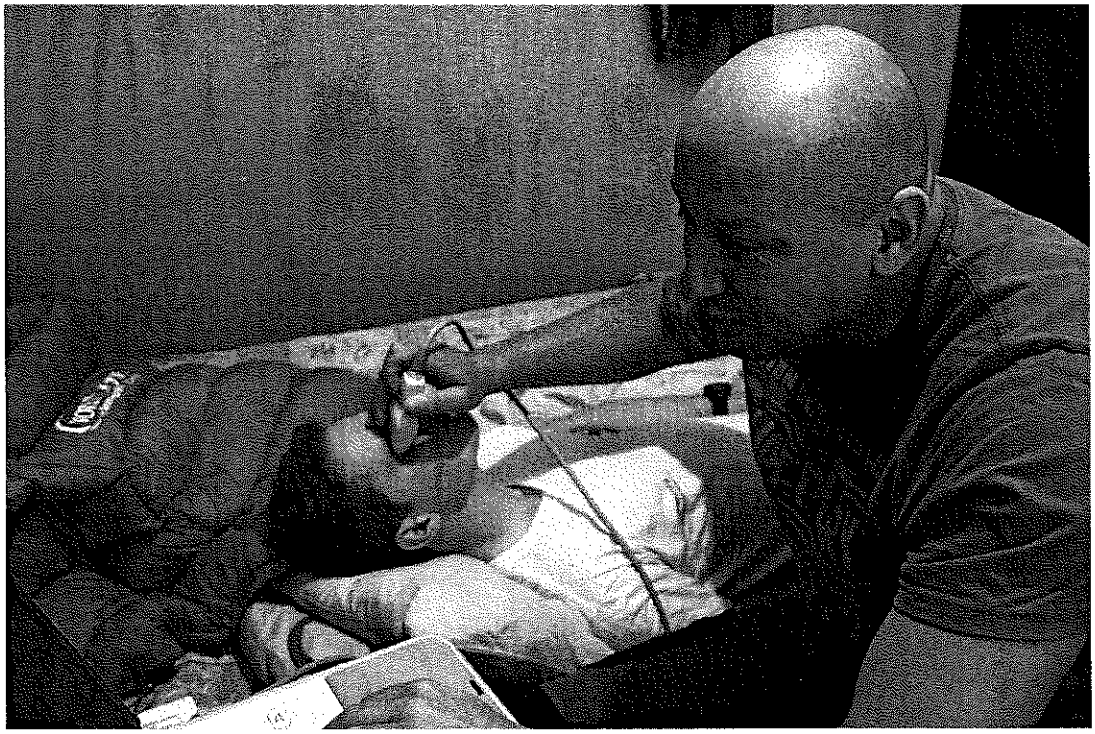
The pathophysiology of HAPE is now reasonably well delineated, however the process underlying the cerebral effects of altitude is more opaque.[8] One theory is that it may include a rise in intracranial pressure.[9] However, intracranial pressure has only been measured directly at altitude once, and then in a very small number of climbers.[10] Given the potential hazards of direct invasive intracranial pressure monitoring at altitude, a number of surrogate measures have been proposed of which optic nerve sheath diameter (ONSD) is one.

To measure ONSD using ultrasound, the subject sits semi-recumbent with their eyes closed.[11] Ultrasound gel is applied to the eye and the probe is gently placed on the temporal portion of the closed eyelid. The gaze and the probe may be aligned for axial views or deviated for lateral/coronal views. We imaged both views in our study.

Once the optic nerve is visualised as a hypoechoic structure behind the globe, its diameter is measured 3mm posterior to the optic disc along an axis perpendicular to the nerve.[11][12] 3mm is the chosen distance, as it is the anterior portion of the nerve

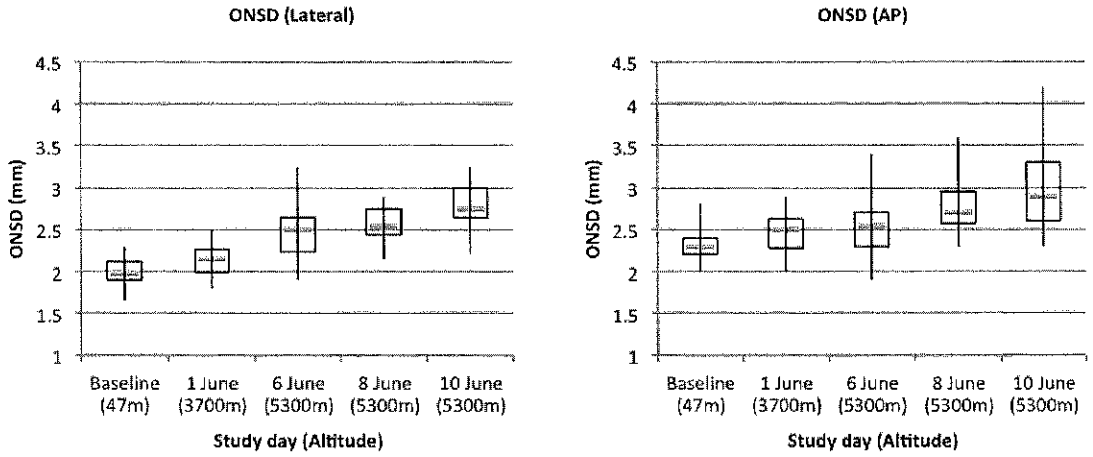
sheath that is most distensible. [13] Typically, multiple measures are recorded and the results averaged.

In individual studies, ultrasound ONSD has been shown to correlate well with both invasive and non-invasive measures of intracranial pressure, with low intra- and interobserver variabilities. [14] [15] [16]



Apex Ultrasonographer, Mr Wayne Pringle measuring ONSD (Photo: Eilidh Potter)

We were able to complete scans on our subjects at baseline and at five timepoints while on expedition, up to an altitude of 5300m. We compared changes in their ONSD with symptoms of acute mountain sickness, demonstrating that ONSD increased significantly with altitude (figure below). However we found ONSD to be uncorrelated with both symptoms of acute mountain sickness, and of headache alone.



The increase in ONSD with time spent at altitude (lateral and AP views of the nerve)

Five altitude ONSD studies had been published prior to APEX4. However, all bar one had significant methodological flaws. [17] [18] [19] [20] [21] Of the five, all found that ONSD increased at altitude but only two had found ONSD and AMS symptoms to be correlated. Our study, though it had its weaknesses, was adequately powered, took place above 5000m, controlled for altitude profile, exercise rates and medication use and used an improved imaging protocol for the nerve.

We concluded that ONSD increased significantly at altitude but was uncorrelated with symptoms of AMS. This provided evidence to support the argument that a rise in intracranial pressure is not part of the pathophysiology of AMS.

We intend to submit our results for publication later in the year and the project will form part of my dissertation for the MSc in Mountain Medicine (Leicester).

I am very grateful to the Myre Sim Fund committee for their support in this project.

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