



THE UNIVERSITY of EDINBURGH  
Student Experience Grants



KETTLEproduce Ltd



# APEX6

## Expedition Report

### Altitude Physiology Expedition (APEX) 6

**Huayna Potosí, La Paz, Bolivia (4775m)**

25<sup>th</sup> June – 8<sup>th</sup> July 2022

**Key Aim:** To further our understanding of human physiology at high altitude whilst involving and exposing future generations in the hope they will go on to do the same







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*Section 7 was adapted from previous work by Dr Nina Rzechorzek, Dr Sophie Hattersley, Dr Alastair Woodhead, Dr Sarah Lewis, Dr Denisa Strončková and Dr Erin Bennett*

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# 1. Summary



The APEX 6 Team with Huayna Potosí in the background

## Why Did We do This?

Low oxygen levels (hypoxia) experienced at high altitude present a significant challenge to the human body. Hypoxia is often only experienced in critically ill patients at sea level and is thus difficult to study in a controlled way. **Altitude Physiology Expedition (APEX) 6** follows a series of high altitude research expeditions aiming to further our understanding of human physiology at high altitude whilst involving and exposing future generations in the hope they will go on to do the same. It is hoped that the findings of APEX 6 will go on to improve investigation and management of patients with critical illnesses.

## How Did We do This?

34 University of Edinburgh student volunteers, 2 expedition doctors and 4 student organisers travelled to Bolivia from 25th June-8th July 2022. 177 students applied to volunteer on the expedition. Acclimatisation took place in La Paz (3640m) from days 1 to 5 before ascent to Huayna Potosí base camp (4775m) for days 6 to 13. Venous and arterial blood samples were taken during the expedition in addition to non-invasive data collection methods. Baseline data collection took place before and after the expedition.

## What Did We Find?

Data collection is now complete, however, analysis and interpretation of results is ongoing. APEX 6 aims to present and publish results within the next 18 months.

## What is the Potential Impact?

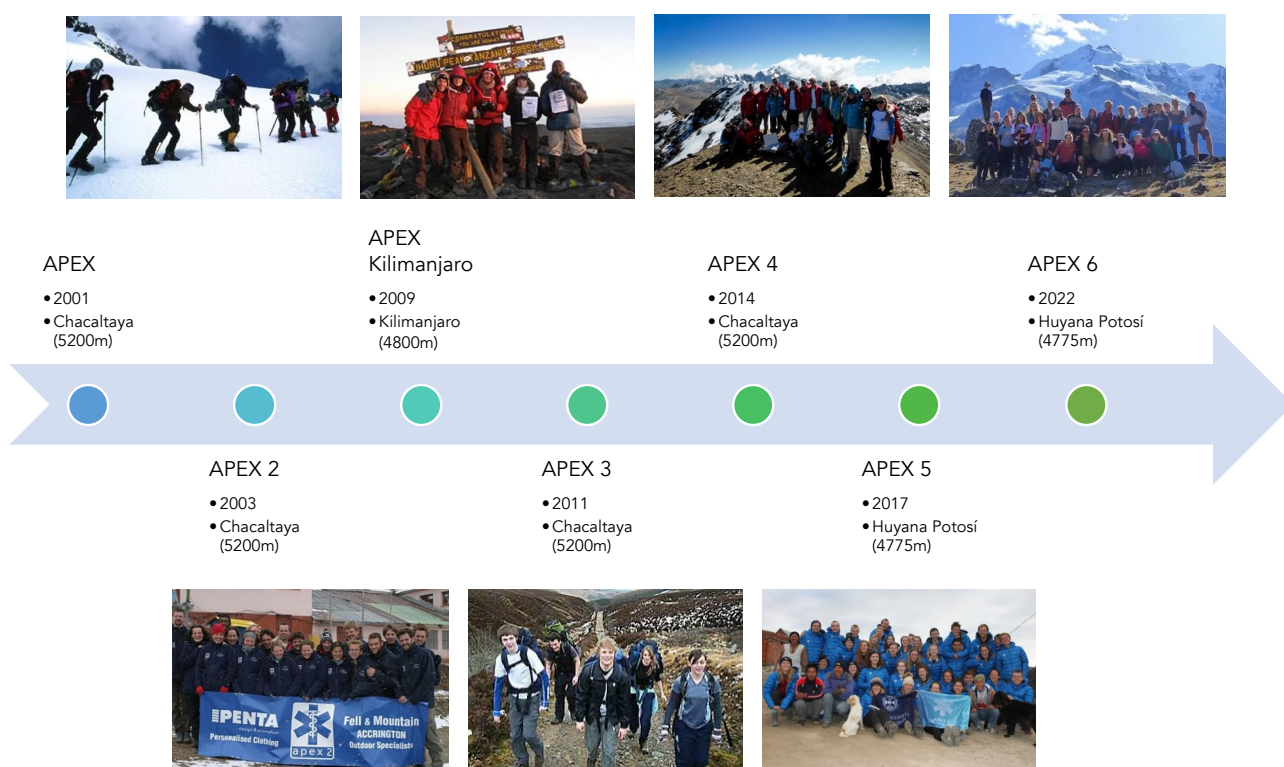
APEX 6 uniquely studied the following at high altitude: (1) a new method of measuring lung oxygenation using arterial blood gases, (2) dark adaptation of the eye and retinal function using portable devices, and (3) body clocks using wearable technology. APEX 6 further investigated neutrophil hypoxia and expression quantitative trait loci (eQTL), building upon findings from previous expeditions. Furthermore, the expedition enabled 34 new individuals to experience high altitude medicine and Bolivian culture who otherwise may not have. The future of APEX is secure, with a number of students inspired to lead the next expedition, APEX 7.



## 2. Introduction

### Background

Altitude Physiology EXpeditions (APEX) was founded by medical students at the University of Edinburgh in 2001 with the aim of investigating the effect of high altitude hypoxia (low oxygen levels) on the human body. Since then, there have been six expeditions, five to the Bolivian Cordillera Real and one to Mount Kilimanjaro. Each expedition has been independently conceived, organised, and led by students under the supervision of the APEX charity and associated researchers and clinicians. The expedition research is made possible thanks to the commitment of student volunteers, who may also choose to consent to take part in scientific research. It is often these volunteers who are inspired to go on and lead future expeditions and research projects.



**Figure 1:** Timeline of APEX Expeditions (2001-2022)

### APEX 6

Preparations for APEX 6 began in 2017 when several students, many of whom had been volunteers on APEX 5, met to begin planning a new expedition. Eventually, a team of six medical students emerged and commenced planning for a 2020 expedition under the guidance of the APEX charity. Initial focus turned to the research questions to be answered as well as expedition logistics. APEX 6 aimed to build upon some findings of previous APEX expeditions, as well as explore new areas of research including circadian rhythms, dark adaptation, menstruation, and lung oxygenation. Due to the significant impact of the SARS-CoV-2 (COVID-19) pandemic, the expedition was twice postponed, with four of the organising team stepping back and two new members brought on board. The expedition to Huayna Potosí, Bolivia eventually took place in Summer 2022, comprising four undergraduate organisers, two expedition doctors and 32 University of Edinburgh student volunteers. The expedition aimed to improve understanding of hypoxia on human physiology as well as inspire colleagues to engage in medical research and travel.



## 3. Expedition Members

### Organising Committee



Oliver Vick  
Isla Petrie  
Alastair Woodhead  
Suzanne Green

Expedition Leader  
Sponsorship and Events  
Research and Financing  
Volunteering and Comms.

### Expedition Doctors



Dr Ben Warrick  
Dr Katie Flower

Consultant Anaesthetist and Trust Trauma Lead  
Anaesthetics Registrar

### Previous Organising Committee



Sophie Hattersley  
Erin Bennett  
Sarah Lewis  
Denisa Strončeková

Expedition Leader (18-21)  
External Funding (18-21)  
Volunteering (18-20)  
Sponsorship (18-20)

### Logistical Support

Miriam Centellas  
Sonia Altamirano  
Nelly Gallardo  
Ivan Quispe  
Hugo Centellas  
Fredy Victor Blanco  
Cecilio Mamani Condori

Co-Owner, Bolivian Mountains  
Owner, Refugio Casa Blanca  
Head Cook, Bolivian Mountains  
Assistant Cook, Bolivian Mountains  
Bolivian Mountains  
Expedition Driver, Bolivian Mountains  
Expedition Driver, Bolivian Mountains



## Expedition Volunteers



Anna Prvulovich



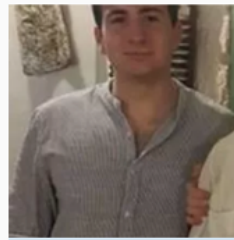
Hannah Appleton



Camille Maezelle



Madryn Riewer



Martin Rosenzweig



Cameron Norton



Alex Thomson



Ella McElnea



Colette Revadillo



Theodora Kontaxi



Gus Bartlett



Renée de Maat



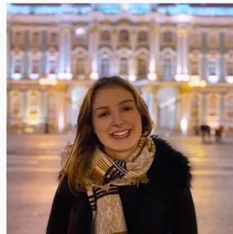
Wiktorja Karbow...



Gemma Woodh...



Ella Crowther



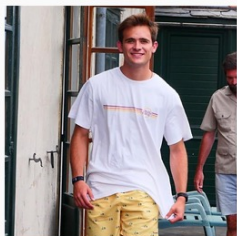
Heather McAdam



Anya Tan



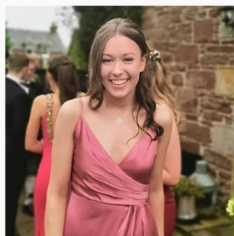
Darcey Smyth



Jaime Garcia Fer...



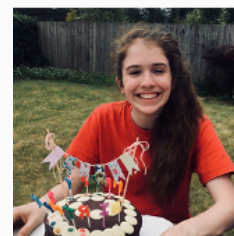
Jonathan Lang



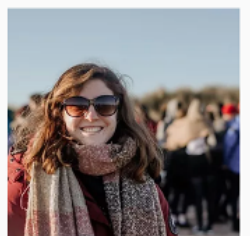
Sarah Barrie



Karolina Futera



Bethan MacDonald



Becky Lillicrap



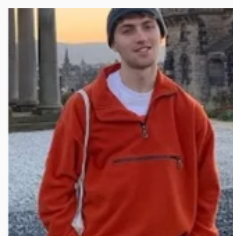
Ella Andrea



Calum Weir



Harry Henriksen



Ben Harrison



Pierre Lardet



David Geddes



Robert Zhan



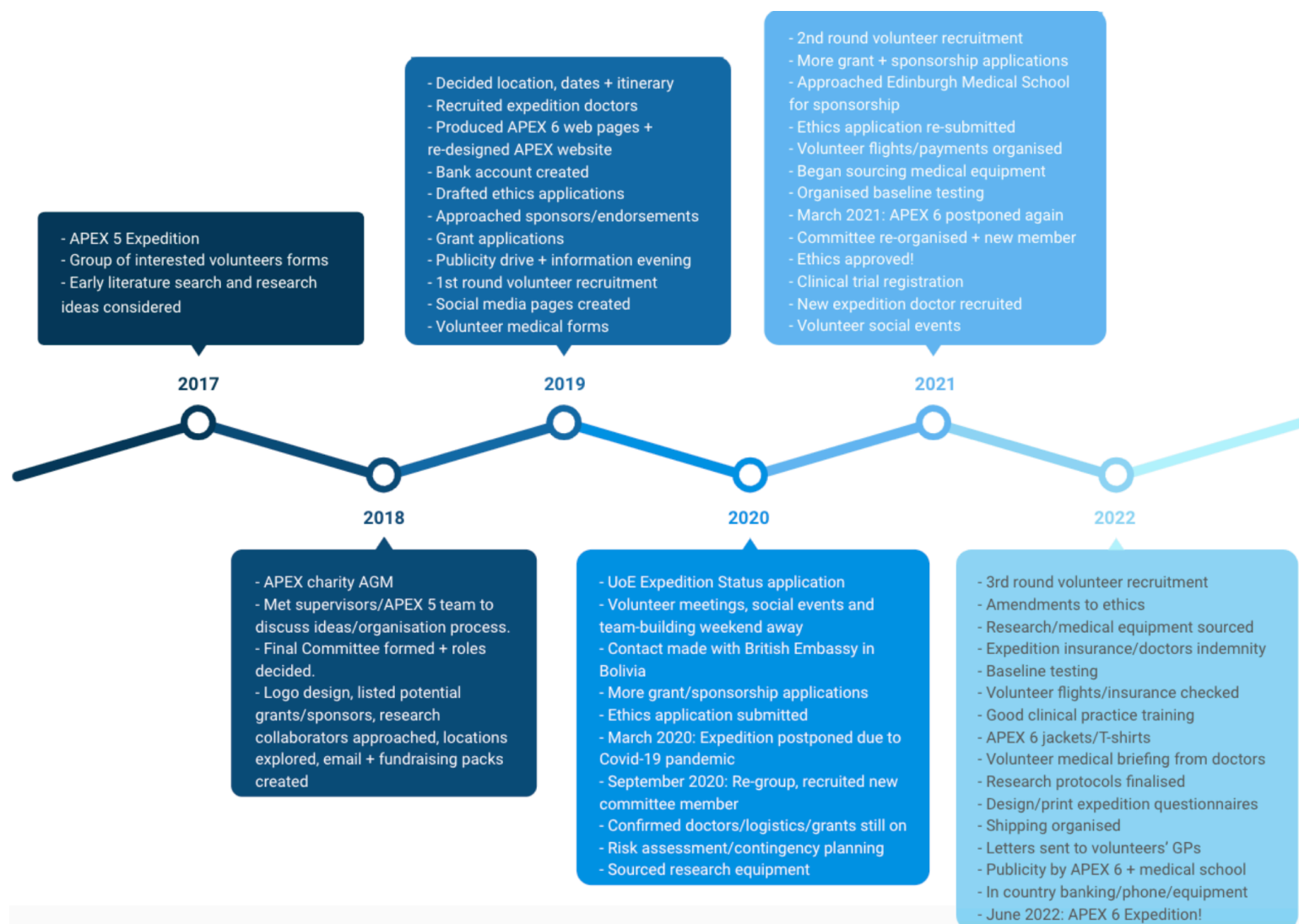
Chloe Wightman



## 4. Expedition Organisation

### Timeline

The twice-postponed APEX 6 expedition went ahead in 2022 after five years of planning. The organisational timeline is outlined below:



**Figure 2:** Timeline of APEX 6 Organisation

### Organising Committee

The expedition organising committee was initially formed in 2018 from interested volunteers from the APEX 5 expedition in 2017. The committee initially comprised six University of Edinburgh undergraduate medical students. Following expedition postponements in 2020-21, the organising committee changed due to some members graduating from university and new members were recruited from the pool of APEX 6 volunteers. Past and present APEX 6 organising committee members are highlighted in Section 3.

The committee met regularly throughout the planning process, utilising both in person and online meetings. The success of the final expedition was the result of a phenomenal amount of planning, teamwork and the help and support of many fantastic organisations and individuals listed in the acknowledgements section of this report.



The committee was supervised and assisted by Professor Kenneth Baillie, Dr Roger Thompson (both previous APEX expedition leaders) and Dr Nina Rzechorzek (Team Leader, APEX 2), as well as the organising committee of the APEX 5 expedition.

### **Research**

Much of APEX 6 builds upon research carried out on APEX 5 and preceding APEX expeditions, namely the studies on neutrophil hypoxia and eQTLs; as well as exploring new areas of high altitude research such as: eye function; circadian rhythms (body clocks); lung function and menstruation. The committee is extremely thankful for the practical help and support of all research supervisors involved throughout the planning process. All research projects are explored in detail in Section 7.

### **Logistics**

Early consideration was given to the location of the APEX 6 expedition, with various sites explored. It was decided that locations around La Paz were most feasible due to contacts built up over previous expeditions, as well as the proximity of emergency medical care to accessible high altitude sites, which is not replicated to our knowledge in other geographical locations. Safe access was no longer available to Chacaltaya Ski Lodge, the location of APEX 4. Additionally, we considered Chacaltaya Cosmic Physics Lab, the location of early expeditions, however, communication difficulties with the site discounted this option. Huayna Potosí base camp was chosen for the expedition as this location was found to be more pleasant for volunteers during APEX 5, with lower risk of severe altitude sickness. Here, Refugio Casa Blanca was chosen which was larger than the refugio used previously and could be booked exclusively for our expedition party.

APEX 6 was the first expedition to use Bolivian Mountains as our logistics company who were helpful and professional throughout the planning process, and very accommodating to multiple changes to final expedition dates.

Due to political unrest in Bolivia in 2019 and 2020, we developed a fully costed contingency plan to relocate the expedition to neighbouring Peru. This plan involved acclimatisation in Cusco (3370m) with the high altitude expedition taking place near Ollantaytambo (4300m). Changes in the political situation and the onset of the COVID-19 pandemic meant that this option was not utilised, but may present an alternative option for future expeditions should Bolivia not be a suitable destination.

### **Recruitment**

Initial volunteer recruitment took place in December 2019, recruiting volunteers from the University of Edinburgh student population. We promoted the expedition to prospective volunteers using posters, pre-lecture announcements, online announcements, social media and a stall at the University's 2019 Welcome Week. We held an Information Evening for prospective volunteers in October 2019. Recruitment was a two stage process with online applications shortlisted before some applicants were invited to in-person interviews. When recruiting volunteers we focussed on both motivation and interest in altitude research, as well as recruiting a team who we felt would cope well together under difficult conditions on the expedition.

The postponement meant that many volunteers initially recruited were unable to come on the 2022 expedition. For insurance purposes we were only able to take students currently studying at the University of Edinburgh, therefore volunteers who graduated in the interim were unfortunately unable to travel on the postponed expedition. Two further rounds of recruitment took place in 2021 and 2022 following a similar format to the initial recruitment drive; online interviews replaced in-person ones due to the pandemic. Across the three recruitment cycles, APEX 6 received 171 volunteer applications, with 114 interviews completed. Eventually, 34 volunteers, 4 committee members and 2 expedition doctors were able to embark upon APEX 6.



## Volunteering and Team-building

The expedition volunteer group comprised undergraduate and postgraduate students at the University of Edinburgh. Although a medical education was not a prerequisite, the vast majority of volunteers recruited were medical students, with a small number of volunteers from other backgrounds including mathematics and computer science.

Volunteers were encouraged to get involved with research if they wished and two volunteers from the first round of recruitment later joined the organising committee. Every effort was made to involve volunteers including in data collection for the eye function project, assisting with laboratory skills for the neutrophil hypoxia project and assistance with clinical skills for a number of other studies. One of the primary aims of APEX expeditions is to train students in designing and conducting their own medical research. We hope that through involving our volunteers in research it will further their academic development, and that some of them may go on to organise their own expeditions or research projects.

In order to integrate the group prior to the expedition we organised information events including a medical briefing from expedition doctors, evening socials and two team-building weekends. During the pandemic we also utilised online social events.



*APEX 6 Team Building Events (Spring 2022)*

## Baseline Testing and Consenting for Research

Although APEX 6 was primarily a research expedition, there was no requirement for expedition volunteers to consent to take part in any research study. Volunteers were first recruited to take part in the expedition. Participant information sheets for all of the research studies were then circulated in March 2022 and volunteers were invited to attend the Queen's Medical Research Institute (QMRI), Edinburgh in April 2022 in order to consent to take part in any research studies they were both eligible for, if any. All volunteers and committee members consented to take part in one or more of the studies.

A number of research projects were completed as part of APEX 6. Detailed summaries of these can be found in Section 7 of this report. Each project required baseline sea level data to be collected to some extent and this was completed following consent being obtained at the QMRI. Some of this data collection took place immediately (blood tests, baseline observations), with further data taken at various points before or after the expedition.





*Consenting and Baseline Testing, Queen's Medical Research Institute, Edinburgh (April 2022)*

### University and Ethical Approval

Ethical approval was sought for the expedition from the Edinburgh Medical School Research Ethics Committee (EMREC) and granted in November 2021. Further information can be found in Section 7 of this report.

Accreditation for the expedition was sought from the University of Edinburgh Expeditions Committee. The Committee has the responsibility for evaluating proposed expeditions and recommending to the University Court which expeditions should be officially recognised and approved by the University. APEX 6 was delighted to be successful in achieving this status in May 2022 following the submission of an extensive application and risk assessment.

### Budget and Finance

Finances were managed using an APEX 6 RBS Business Account. Early budgeting and fundraising targets were based on the actual costs of the APEX 5 expedition. We received grants from several funding bodies as well as financial support and equipment from several sponsors. These are listed in the acknowledgements section of this report. Furthermore, a full breakdown of expedition income and expenditure is provided in Appendix A.

### Publicity

APEX 6 focussed primarily on online publicity. The organising committee updated the APEX website ([altitude.org](http://altitude.org)), which is a well-used online resource developed by APEX for general information on altitude sickness as well as past and present APEX expedition publicity. We regularly utilised Facebook, Instagram and Twitter to reach a wider audience and to publicise expedition sponsors, endorsements and grants. Social media was also invaluable in recruiting expedition volunteers.

Additionally, members of the expedition committee spoke at the British Mountain Medicine Society Science day in November 2019, the Birmingham Medical Research Expeditionary Society Conference in September 2021, and APEX Annual General Meetings in 2019, 2020 and 2021.

We were very grateful to receive the following endorsements which were invaluable for expedition publicity:



*"I am delighted to endorse APEX 6. APEX has been hugely successful over the past years, with much exciting research being done into the intricate effects of altitude and hypoxia on the human body. This year, students will take on this challenge once again, with a further aim of collaborating with local Bolivian researchers. The group have my full support, and I wish them all the best on this journey."*

*- Sir Chris Bonington, Mountaineer*

*"I am proud to support APEX 6. The Bolivian mountains are amongst the more beautiful in the world, but they are also a real test of human endurance. The work of the APEX 6 team will be invaluable in gaining better understanding of the effects of altitude on the human body. I wish them a safe and successful expedition."*

*- Tom Avery, Polar Explorer and Mountaineer*



*"I wanted to say a few words of encouragement and support to everybody involved with APEX 6. I am delighted to hear about the expedition... and I wish you all the very best for a successful trip. I hope you learn some new facts through your research, I hope you have a great time and I hope you all return safely back afterwards. Good luck with it and we are very proud of you, all the best."*

*- Professor Peter Mathieson, Principal and Vice-Chancellor of the University of Edinburgh*

## **COVID-19**

The COVID-19 pandemic represented an astronomical and unforeseen challenge for the organisation of this expedition. As a result of the postponement, more than 50% of volunteers could no longer be involved, and 4/6 members of the original expedition committee were unable to continue due to graduation from University or other commitments. The psychological impact of twice cancelling APEX 6 only a few months prior to the expedition, as well as a considerable amount of additional work created as a result of the pandemic, makes us extremely proud and grateful that we were eventually able to orchestrate a successful and worthwhile expedition in 2022.



## 5. Expedition Itinerary

### Pre-Expedition Events

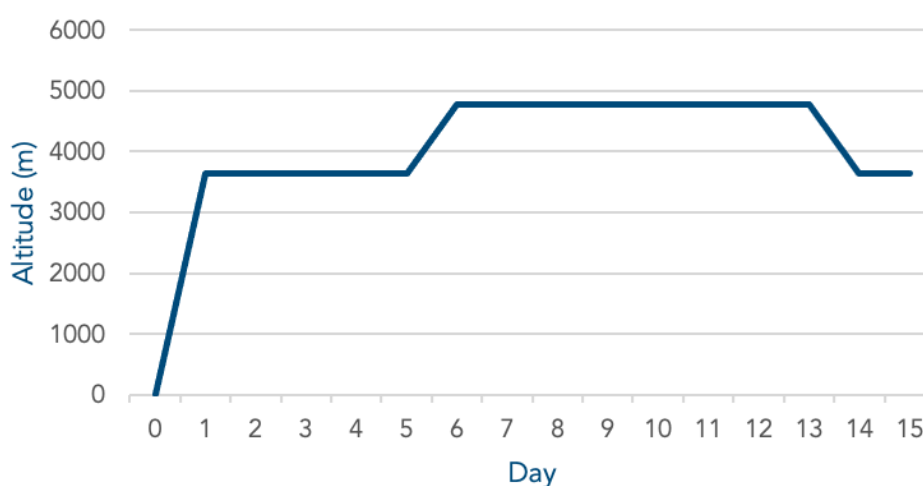
First Recruitment Cycle	November 2019 – December 2019
Second Recruitment Cycle	December 2020 – January 2021
Third Recruitment Cycle	December 2021 – February 2022
Team-building Weekend	2nd April 2022 – 3rd April 2022
Baseline Research Testing	20th April 2022 – 22nd April 2022, 6th June 2022

### Expedition

24th June 2022 (Day 0) – 8th July 2022 (Day 14)

Day	Location	Activities
-1	Europe	Departure of expedition members
0	In transit	Transfer via Frankfurt/Bogota/Madrid/Santa Cruz
1	La Paz (3640m)	Arrivals 00:00-12:00
2	La Paz (3640m)	Acclimatisation, exploration of local area, teambuilding, medical talk
3	La Paz (3640m)	
4	La Paz (3640m)	
5	La Paz (3640m)	
6	La Paz/Huayna Potosí Base Camp	Ascent via vehicle (2h30)
7	Huayna Potosí Base Camp (4775m)	Research activities, free time, organised walks, stargazing
8	Huayna Potosí Base Camp (4775m)	
9	Huayna Potosí Base Camp (4775m)	
10	Huayna Potosí Base Camp (4775m)	
11	Huayna Potosí Base Camp (4775m)	
12	Huayna Potosí Base Camp (4775m)	
13	Huayna Potosí Base Camp/La Paz	Descent via vehicle (2h00), debrief, group photo, end of expedition meal
14	La Paz (3640m)	End of expedition 00:00 Onward travel/return to UK

### Ascent Profile



## 6. The Expedition

### Location and Accommodation

APEX 6 took place in the Bolivian Cordillera Real, split over two locations. The first five nights were spent acclimatising in urban La Paz, with the final seven nights spent at a remote refuge.

Acclimatisation took place at Hostal República located at 3,640m in the historic centre of La Paz. Expedition members shared dorm-style accommodation where breakfast was provided. During this acclimatisation period, expedition members received important information and safety briefings as well as enjoying the opportunity to explore the city and experience Bolivian culture. Leaders took time to finalise plans, inventory equipment and undertake a reconnaissance visit to the high altitude location. Expedition members who consented to take part in research undertook sampling for some of the research studies.

The expedition team ascended to the high altitude refuge by vehicle. Most members and equipment were transported by bus, with the remainder moved by two four-wheel drive vehicles. The 1,135-metre ascent took approximately two hours and thirty minutes, including a brief stop for picture taking. This was an ascent of approximately 7.6 metres per minute.

The high altitude portion of the expedition took place at Refugio Casa Blanca, located at 4,775m in the shadows of Huayna Potosí. The refuge usually serves as accommodation for climbers on their way to the summit of Huayna Potosí, however, due to an abundance of communal space, it was adapted to serve as both accommodation and a research laboratory. Most expedition members slept in a large open-plan upstairs bedroom with a small number located in bunk beds downstairs. One communal area was used for dining and socialising, with the other used as a research laboratory. There were two kitchen areas used for food preparation.

The expedition was fortunate to experience only dry weather, with a mixture of overcast and clear sunny days. The temperature in La Paz was reported to range from 0°C to 15°C, with nighttime temperatures experienced at high altitude well below freezing.

Google Maps accuracy was observed to be of a high standard, with roads and buildings indicated appropriately. Satellite imagery largely accurate, although the glacier Northwest of the refuge was seen to have receded. Footpaths within the area are not shown on Google Maps.



*Refugio Casa Blanca (Summer 2022)*





**Figure 3:** Ascent Route from Hostal Reubública to Refugio Casa Blanca (44.8km) (Google Maps)



**Figure 4:** Satellite Image of Refugio Casa Blanca at the Base of Huayna Potosí (Google Maps)





**Figure 5:** Image of Huayna Potosí glacier (July 2022)

### **Infrastructure**

The refuge was well-connected to La Paz and El Alto by dirt track which was well-maintained in most areas. The narrow nature of the road in some areas made passing other vehicles difficult. Once a few kilometres from the city, mobile phone reception is poor, with satellite phone the only reliable method of communication. There was a continuous power supply to the refuge, with no outages experienced. There was no water supply to the refuge, with water instead collected in tanks and used to supply toilets and sinks. There is no waste disposal service in the region and so rubbish was sorted into recyclable waste, non-recyclable waste, clinical waste, and sharps waste. The clinical and sharps waste was disposed of at a local medical facility, with the other waste disposed of in communal city bins in La Paz.

### **Security**

The expedition team was warned that violent robbery on the roads between El Alto and Huayna Potosí occurred occasionally, particularly during the hours of darkness. For this reason, local drivers are reluctant to drive at night in the region. There is a Police checkpoint near Refugio Casa Blanca, however, the risk remains. UK Foreign Commonwealth and Development Office (FCDO) advice was sought and adhered to with regards other risks in the area.

### **Communication and Language**

The primary language spoken in Bolivia is Spanish, with the Quechua and Aymara languages spoken by indigenous people, sometimes exclusively. The expedition was fortunate to have several Spanish speakers who were able to act as translators, aiding with the smooth running of in-country logistics. A few staff at our accommodation and logistics partners spoke a good level of English, further aiding smooth communication. Expedition members were encouraged to learn basic Spanish phrases prior to coming on the expedition,



not only to aid them during their time in Bolivia, but also for onwards travel around the majority Spanish-speaking continent.

Prior to the expedition, all communications were by email, translated into Spanish as required. Our main contact was Matty Sowinski, a British national at Bolivian Mountains, who coordinated accommodation and logistics in Bolivia. We maintained regular communication with University of Edinburgh staff, the British Embassy in La Paz and APEX charity committee members.

In La Paz, we primarily communicated with expedition members and in-country contacts through WhatsApp, the preferred method of communication in Bolivia. Accessing the internet was easy, with most cafes, restaurants and hostels providing WiFi free of charge, although speeds were variable. Expedition leaders purchased Bolivian SIM cards to ensure they always had internet access in case of emergency. At high altitude, we were able to communicate with contacts in Bolivia and La Paz via satellite phone (which was tested but never required) and via WhatsApp, with a slow WiFi hotspot connection available from the refuge's owner for a short period each day. This was only accessible by expedition organisers.

### **Food, Water and Hygiene**

Food was sourced locally by Bolivian Mountains, catering to a range of food allergies, intolerances, and preferences. It was transported to high altitude with the expedition team and prepared by three expedition cooks. The food was of a high standard and provided a balanced diet. Bottled water was brought up from La Paz in large reusable containers which were returned upon descent. Given the substantial risk of transmission of infectious diseases, expedition members were encouraged to both wash and sanitise their hands prior to handling any food. Copious quantities of hand sanitiser and liquid soap were placed throughout the hostel and refuge.

### **Travel and Transport**

All expedition members were required to arrive at La Paz El Alto Airport (LPB) within a 12-hour window with a maximum 36-hour travel time. This was to ensure consistency in altitude exposure and impact on body clocks for research purposes. All departures were from Europe with all individuals transiting Bogotá, Colombia or Santa Cruz de la Sierra, Bolivia during their journey. Expedition equipment was taken as excess baggage with expedition leaders via Bogotá.

Transport from LPB to Hostal República was by private taxi. Ascent to and from Refugio Casa Blanca was by coach and two four-wheel drive vehicles. Two drivers and the two four-wheel drive vehicles were stationed on site at Refugio Casa Blanca, with one required to remain there at all times in case of evacuation. Drivers' vehicle reports and licenses were inspected prior to the expedition. Expedition blood samples were returned to the UK with World Courier, facilitated by Inbolcarga in Bolivia. They were shipped on dry ice, topped up frequently in transit. The remaining equipment was either used, disposed of, donated, or returned as excess baggage with expedition leaders.

### **Customs and Approvals**

Approvals were sought for the temporary import of equipment into Bolivia as well as for the samples to be returned to the UK. Letters of approval were sought from the University of Edinburgh Expeditions Committee, the College of Medicine and Veterinary Medicine. Letters were also sought from those who had lent the expedition equipment or were supervising research. Finally, an authorisation letter was sent on our behalf by the British Embassy in La Paz to the Bolivian Ministry of Foreign Affairs. Upon presentation of this documentation at the Bolivian border, expedition leaders were able to temporarily import the expedition equipment with ease. No further approvals were required.

## Research Equipment and Training

A considerable amount of equipment was brought into or sourced in Bolivia. Wherever possible, equipment was borrowed to reduce cost, encourage collaboration, and reduce waste. The key research equipment was as follows:

Body clocks research	34x ActTrust 2 actigraphy watches, 9x ActDock, Condor prototype reaction timer
Eye function research	Portable field dark adaptometer (PFDA), RETeval Electroretinogram Stimulating and Recording system (ERG), ERG electrodes
White blood cells research	Heraeus Labofuge 200, SciSpin Micro Centrifuge, 2 x EasySep™ Magnets, EasySep™ Direct Human Neutrophil Isolation Kit, SciQuip Vortex device, P10, P100 and P1000 micropipettes, Pipetboy, inverted microscope, Worthington CX100 Cryogenic dry shipper
Lung Function research	1x i-STAT Alinity handheld blood analyser, 70x i-STAT CG4+ cartridges, 12m <sup>3</sup> medical oxygen
eQTL research	40x Tempus® vacutainer tubes

There was a substantial quantity of consumable and other equipment taken on the expedition. Details of this can be found in the 'Equipment List', available upon request.

Training in the use of equipment was organised as follows:

- Alastair Woodhead was trained in the use of the ActTrust 2, ActDock, ActTention and Psychomotor Vigilance Task (PVT) software by their manufacturer, Condor Instruments.
- Oliver Vick and Suzanne Green were trained in the use of the i-STAT Alinity and CG4+ cartridges by Christopher Elms, a representative of Abbott.
- Isla Petrie was trained in the use of the PFDA by its creator, Professor Alain Labrique, Johns Hopkins University. She was additionally trained in the use of the ERG by Professor Omar Mahroo, University College London.
- Alexander Thomson was trained by staff at the Centre for Inflammation Research, University of Edinburgh in the use of the white blood cells research equipment. He also observed and took part in pre-expedition sampling, developing techniques required at high altitude.

## Finance

In-country expedition money was held in two separate bank accounts (Revolut, Starling) with the aim of minimising currency conversion fees. Debit cards for these accounts were held by expedition organisers and Bolivianos (local currency) withdrawn as required. Card payments were preferred and widely accepted, with cash only used when necessary. 870 US dollars in cash was also held and split between expedition organisers to avoid any individual carrying large amounts of cash. Payment for accommodation and logistical services was primarily made by international bank transfer from our UK RBS business account.

## Health and Safety

A thorough risk assessment process was carried out both as part of the preparation for the expedition as well as for the approvals processes and funding applications outlined in Section 4. Risk assessments were reviewed by a number of senior administrators, clinicians and academics. Risk assessments highlighted a number of altitude- and non-altitude-related risks.

Serious altitude-related illnesses were highlighted as some of the more significant risks of the expedition. Specifically, the risk of fluid building up on the brain (high altitude cerebral oedema) and lungs (high altitude pulmonary oedema) were identified as two key risks of rapid high altitude ascent. Efforts were made to reduce these risks through extending the acclimatisation period in La Paz (3640m) as well as building the



capacity to respond quickly to them through the provision of medical cover and of 24-hour evacuation with rapid descent possible within 30 minutes. These risks were carefully and fully explained to all participants. Fortunately, APEX 6 did not experience any cases of serious altitude-related illness.

Common but less serious consequences of ascent to high altitude include headache, shortness of breath, increased heart rate, sleep disturbance and reduced appetite. These were experienced by most expedition members to differing extents, however, no medical management was required beyond basic over-the-counter treatments such as painkillers.

Non-altitude-related risks were considered, particularly the risk from poor hygiene. Good hand washing practices were encouraged, with soap and alcohol gel provided at all hand washing and dining areas. Clean bottled water was provided to all expedition members and high standards of hygiene were practised when preparing group meals. The APEX 6 committee and doctors also provided advice on road and personal safety and encouraged all expedition members to familiarise themselves with the UK Foreign, Commonwealth and Development Office advice for Bolivia and any other countries they intended to transit through or visit. There were a small number of risks identified specific to the research projects carried out and these were considered and approved by EMREC as outlined in Sections 4 and 7.

APEX 6 was incredibly fortunate to have two highly-qualified doctors supporting the expedition. Dr Ben Warrick, a consultant anaesthetist and Trust Trauma Lead for Royal Cornwall Hospitals NHS Trust and Dr Katie Flower, a senior registrar in anaesthetics, volunteered two weeks of their time in order to support the physical and mental wellbeing of all expedition members. The doctors were equipped with an extensive supply of equipment and medications, sufficient to treat and manage the illnesses and injuries which could be anticipated ahead of this high altitude expedition. The doctors also reviewed the medical and vaccination histories of all expedition members in advance of the expedition and sought advice and clarifications were necessary. All expedition members were required to bring a basic first aid kit including basic medications. The doctors also held a supply of expedition members' personal medications throughout the expedition. Arrangements were made with a local hospital in order to receive any unwell expedition members if necessary.

Comprehensive insurance was sought from and approved by the University of Edinburgh for the expedition in respect of medical treatment, personal and public liability and participants took out their own policies against travel-related costs and disruption. Additional University insurance was also put in place in respect of research equipment and its transit.

### **The Volunteer Experience**

Volunteering on APEX 6 afforded individuals three key opportunities: to gain exposure and training in medical research; to experience and immerse themselves in new and vibrant cultures; and to get to know and collaborate with other students they may not otherwise have met.

When not participating or assisting with research, volunteers enjoyed a lot of free time. In La Paz this enabled them to explore the beautiful city, try the local food and to bond with fellow volunteers. At Refugio Casa Blanca, they were able to disconnect from the world, explore the dramatic landscape and take time to relax and recharge in the company of likeminded individuals. When involved in research, they were able to see firsthand how primary research translates into clinical practice as well as learn new skills and perspectives. One of our volunteers has explained the impact volunteering on APEX 6 had on them:

*"Following recruitment to the originally planned expedition in 2020, I have been able to follow the growth of all the projects, getting to know the team all the way to final expedition in 2022. This experience was extremely unique compared to anything else I had experienced at university, both personally and as a medical student, and I am extremely glad I was able to stay involved throughout.*

*On a personal level, the expedition encouraged me to work with fellow volunteers from a range of backgrounds and year groups. This was exceptionally rewarding as we could get to know each other outside of a tutorial or campus setting, making long term friendships. It also encouraged me to explore a continent I had never had the opportunity to explore before, making me a better informed global citizen. The skills I developed through the volunteer and funding application processes also made me feel better equipped to face the world post-graduation.*

*Secondly, as this was a medical expedition, it really helped contextualise the impact what we are learning can have not just in hospitals, but on a research level too. The expedition itself encouraged me to learn about the process, from planning and pre-expedition tests to traditional 'wet-lab' approaches and how to face challenges along the way. Being a volunteer also emphasised the human side to research as we had to support each other in extremely challenging environments. I believe this will help me become a more empathetic doctor, improving my resilience and the outlook I have on the world."*

*- Heather McAdam, APEX 6 Volunteer*

### **Post-Expedition Travels**

Following the conclusion of the expedition at 00:00 on Friday 8th July 2022, expedition members were free to travel around South America. Some chose only to stay on the continent for a few days, others for many weeks. Most chose to spend more time in La Paz before departing for destinations such as Cusco, Peru, the Bolivian Amazon and Asunción, Paraguay. A number of individuals decided to return to the location of the expedition and summited Huayna Potosí (6,088m). There was also a large group trip to the Salar de Uyuni in the South of Bolivia. Many took the opportunity to visit Machu Picchu, one of the New Seven Wonders of the World and there were many reports of expedition members 'bumping' into one another around the continent.



(L-R) Summit of Huayna Potosí, Machu Picchu, Salar de Uyuni (Summer 2022)



## 7. Research

### Introduction

Our research expedition will inform two important but very different areas of medicine. Firstly, high altitude research allows us to study the effects of hypoxia in humans, which is a feature of several medical conditions from various specialties (e.g. critical care medicine, respiratory medicine, cardiology, and anaesthetics). In the intensive care setting, for instance, patients with low blood oxygen levels have poorer outcomes, with a mortality rate as high as 40%. We hope that a greater understanding of body clock adaptation, lung oxygenation quantification, menstrual bleeding, white blood cell gene expression and cell death will allow for better treatment options for patients with low blood oxygen concentrations at sea level. Secondly, high altitude research is directly applicable to those individuals who ascend to altitude for recreation, employment, or other purposes (over 35 million per year). Improving our understanding of the impact of high altitude on the body will improve the safety and wellbeing of these individuals.

### Planning and Approvals

Research on APEX 6 builds upon previous expeditions, in particular projects investigating hypoxia and white blood cells and expression quantitative trait loci (eQTLs); as well as exploring new research areas including circadian rhythms, eye function, lung function and menstrual bleeding. Research projects were conceived by the APEX 6 organising committee in conjunction with prominent researchers based in Edinburgh, Cambridge and London. Orchestrating six separate research elements on one expedition took considerable planning, and a substantial portion of the expedition budget was spent on research equipment and transportation of equipment and samples (see Appendix A). Additionally we were extremely grateful to receive sponsorship for and loan of much of our research equipment.

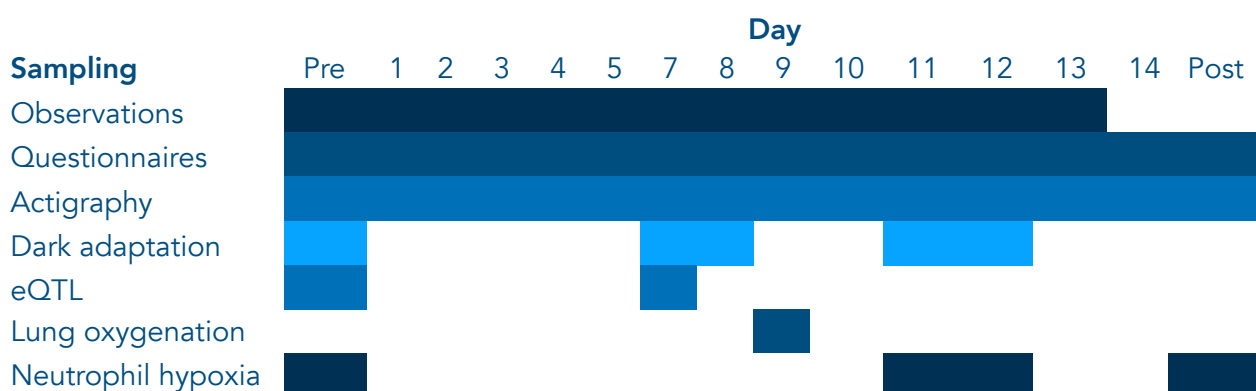
Ethical approval was originally sought from EMREC (Edinburgh Medical School Research Ethics Committee) in February 2020, and was granted in November 2021 following considerable delay and amendments necessitated by the COVID-19 pandemic. Ethical approval was sought as two separate applications due to the RESET intervention being a clinical trial (detailed below). RESET was granted clinical trial registration from the ISRCTN Registry in November 2021.

Reference numbers: 21-EMREC-043 (all study elements except RESET trial), 21-EMREC-044 (RESET trial). ISRCTN76074900.

### Research Schedule

Day	Location	Research
Pre-expedition	Europe/South America	Actigraphy Observations and questionnaires Dark adaptation Venous blood for neutrophil hypoxia
1	La Paz (3640m)	Actigraphy Observations and questionnaires
2	La Paz (3640m)	Actigraphy Observations and questionnaires
3	La Paz (3640m)	Actigraphy Observations and questionnaires
4	La Paz (3640m)	Actigraphy Observations and questionnaires
5	La Paz (3640m)	Actigraphy Observations and questionnaires

6	La Paz/Huayna Potosí Base Camp	Actigraphy Observations and questionnaires
7	Huayna Potosí Base Camp (4775m)	Actigraphy Observations and questionnaires Venous blood for eQTL study Dark adaptation
8	Huayna Potosí Base Camp (4775m)	Actigraphy Observations and questionnaires Dark adaptation
9	Huayna Potosí Base Camp (4775m)	Actigraphy Observations and questionnaires Lung oxygenation
10	Huayna Potosí Base Camp (4775m)	Actigraphy Observations and questionnaires
11	Huayna Potosí Base Camp (4775m)	Actigraphy Observations and questionnaires Dark adaptation Venous blood for neutrophil hypoxia
12	Huayna Potosí Base Camp (4775m)	Actigraphy Observations and questionnaires Dark adaptation Venous blood for neutrophil hypoxia
13	Huayna Potosí Base Camp/ La Paz	Actigraphy Observations and questionnaires
14	La Paz (3640m)	Actigraphy Observations and questionnaires
Post-expedition	South America/Europe	Actigraphy Questionnaires Dark adaptation Venous blood for neutrophil hypoxia



### Baseline Testing

Baseline testing took place in Edinburgh from 20th-22nd April, and on the 6th June 2022. Volunteers were consented at baseline testing, having been provided with information about each research project (Participant Information Summary) in advance. Volunteers were consented for each research element individually, and there was no requirement for volunteers to consent to any research element in order to take part in the expedition. We took basic clinical measurements (height and weight, and also blood oxygen levels and heart rate using pulse oximetry, temperature using an ear thermometer, and a simple clinical test



to assess blood supply to the hand). Additionally blood samples were taken and questionnaires completed in order to collect baseline (sea level) data for the various research elements (detailed below).

Pulse oximetry and temperature were measured twice daily during the expedition. Volunteers also completed a number of questionnaires once daily, with further details later in this section.

## **Hypoxia and Circadian Rhythms**

*Led by Alastair Woodhead*

*Supervised by Dr Nina Rzechorzek, MRC Laboratory of Molecular Biology, Cambridge*

### Background and Significance

Biological clocks regulate how our body works, and they must synchronise to our 24-hour world. Environmental timing cues feed into a 'master clock' in the brain, which then synchronises clocks throughout the body. Light-dark cycles, meal times, and steroid hormones form the strongest cues, tuning our internal clocks to the day-night rhythm. Genetic variation determines how our body clocks align with this rhythm, thus resulting in different 'chronotypes' (i.e. 'morning larks' and 'night owls').

Annually, millions of people stretch the limits of their body clock by rapidly crossing multiple time zones. Temporary misalignment between an individual's body clock and local time in their destination produces 'jet lag', the symptoms of which subside as the body clock adapts to the new time zone. Disruption of our body clocks—as occurs with jet lag and shift work—has far-reaching health effects, playing a role in cancer, diabetes, heart disease, and dementia. If we could rapidly reset the body clock to better accommodate our modern lifestyles, this could have enormous health benefits.

An intense challenge is faced by visitors to high altitude, since exposure to a low-oxygen environment often coincides with jet lag. A prominent feature of both jet lag and ascent to high altitude is sleep disturbance. Most studies of sleep at altitude have failed to control for individual chronotype and body clock function—factors which could substantially modify the body's adaptation to a new time zone. Research on APEX 6 addresses an important knowledge gap; the impact of individual chronotype and jet lag on how the body copes with high altitude. The RESET trial builds on this by testing whether a multi-factorial intervention can accelerate resetting of body clocks and improve sleep function in healthy volunteers exposed to jet lag and high altitude.



### Methods

#### *Hypoxia and body clocks*

All volunteers could participate in this research element. Volunteers were asked to wear an activity wristwatch for a total of approximately 25 days (7 days prior to departure to Bolivia, 11 days on the expedition, and for 7 days from the day of their departure from South America). The actigraphy device measured rest/activity and sleep patterns, different types of light exposure, and skin temperature.

### *The RESET Trial Intervention*

The RESET trial was an extension of research being conducted into body clocks at high altitude during the APEX 6 expedition. Taking part in the trial meant that, after baseline testing, each volunteer was randomly assigned to one of two intervention sequences, and received the RESET intervention on either the outbound or return leg of travel to South America.

The RESET intervention lasted 72 hours and consisted of five components, each optimally timed to promote rapid resetting of the body clock to the new time zone. Components included restrictions on the timing of (1) exposure to light, (2) food consumption, (3) physical exertion, and (4) sleep opportunity, and (5) a single, oral dose of synthetic steroid (dexamethasone) to suppress the volunteers' 'stress' axis and thus reset their internal rhythm of steroid hormone. Exact timings were dictated by each volunteer's flight schedule and chronotype (determined in advance using questionnaires and actigraphy).

Volunteers were asked to complete questionnaires in the lead up to, and each day during the expedition. These documented their chronotype, sleep patterns, sleep quality, mood, cognition and any symptoms of altitude sickness.

### *Primary research question:*

Can a novel, evidence-based, combinatorial intervention accelerate re-adjustment of body clocks in healthy volunteers flown across several time zones?

### *Secondary research questions:*

These include all objectives/questions relating to the 'Hypoxia and body clocks' research element (1-5), plus some that are specific to the RESET trial (6-10):

1. Is chronotype predictive of changes in sleep quality upon acute exposure to high altitude?
2. Is chronotype predictive of changes in any of the following parameters upon acute exposure to high altitude: acute mountain sickness (AMS) score, mood, or cognitive function?
3. Does chronotype affect how quickly APEX 6 expedition participants can 're-entrain' their body clock to a new time zone (how quickly they can overcome 'jet lag')?
4. Is chronotype linked to genetic variation (as determined by QTL mapping) in APEX 6 participants?
5. By controlling for individual body clock variation, can chronotyping data be used to clarify outcomes of other research projects on the expedition?
6. Can the RESET intervention improve sleep function in APEX 6 expedition volunteers?
7. Can the RESET intervention improve (a) cognitive function or (b) mood in APEX 6 expedition volunteers?
8. Can the RESET intervention improve altitude-related clinical outcomes (AMS score) in APEX 6 volunteers?
9. Is there a relationship between chronotype and response to the RESET intervention?
10. Does exposure to high altitude hypoxia affect sleep or circadian function measures at sea level (comparing pre- and post-expedition data)?

### **Eye Function**

Led by Isla Petrie, Sarah Lewis and Denisa Strončeková

Supervised by Dr Ian MacCormick, University of Edinburgh and Professor Omar Mahroo, University College London

### Background and Significance

The brain is extremely sensitive to low oxygen levels (hypoxia). The retina, the light-sensitive tissue layer which lines the back of the eye, is formed as an outgrowth of the developing brain, and is similarly sensitive to hypoxia.



Visual impairments have been widely reported by those exposed to hypoxia including mountaineers and pilots ascending to high altitude. Investigations under simulated hypoxic conditions and in the field have outlined the negative effect of hypoxia upon vision, demonstrating these effects to be most prominent in low light conditions. Despite this, measuring the retina's ability to adjust to low light conditions, namely dark adaptation (DA), has not previously been performed at high altitude. This is likely due to the requirement for a dark room and logistical difficulties of transporting large equipment. The development of a Portable Field Dark Adaptometer (PFDA) provides the opportunity to accurately and objectively assess retinal functions such as dark adaptation at altitude.

Other methods of measuring retinal function include electroretinography (ERG) which measures the electrical response of various cells of the retina in response to light stimuli. Although ERG has been performed at high altitude, it is not yet known if ERG measurements change as the body acclimatises to high altitude.

Sight is critical for orientation, movement, and balance and so visual function is clearly essential for the safety and performance of pilots, mountaineers, and athletes training at high altitude. Furthermore, as the only visible part of the brain, studying retinal function at high altitude provides a unique opportunity to objectively assess the effects of hypoxia on the brain.

### Methods

All volunteers were eligible to take part in this study. DA and full-field ERG were undertaken on days 7 and 11 for half the participants, and on days 8 and 12 for the other half. DA was measured using a PFDA. Volunteers were exposed to a bright baseline retinal bleaching flash. Dark adaptation then occurred as these photo pigments regenerated and the sensitivity of the retina increased. After a period of 10 minutes, volunteers were exposed to a series of 9 light stimuli which increased in brightness. An infrared digital camera within the PFDA recorded pupil diameter immediately before and after each light stimulus.

Retinal function was measured using a portable full-field ERG (RETeval®) device. Skin electrodes were positioned and volunteers were asked to look at a fixed point, or alternatively, look ahead and hold a steady gaze. The dark-adapted protocol was performed first, followed by the light-adapted protocol. In the dark-adapted protocol, volunteers underwent dark adaptation in a dark room for 20 minutes minimum, and consequent actions were performed under dim red light. Volunteers were exposed to a series of white light stimuli of increasing light intensity. The responses to each light intensity were recorded as an average of 5 readings. In the light-adapted protocol, volunteers underwent light adaptation in a light room for 10 minutes. They were then exposed to a single white flash on a white background. 10 readings were averaged, and the interval between flashes will be 0.5 seconds. This was followed by a flickering light. 30 readings were averaged and the interval between stimuli was 300 milliseconds. Pupil diameter was noted before and at the end of ERG.



### *Objectives:*

1. To determine if high altitude-induced hypoxia affects how well our eyes adapt to the dark
2. To determine whether high altitude-induced hypoxia affects the electrical activity of the retina
3. To determine whether eye function improves upon acclimatisation to high altitude and/or return to sea level
4. To determine if any changes seen in dark adaptation and electrical activity of the retina correlate with each other or with body oxygen levels
5. To determine if changes in eye function can correlate with measures of AMS

### **Lung Oxygenation**

*Led by Oliver Vick and Suzanne Green*

*Supervised by Professor J Kenneth Baillie, University of Edinburgh*

#### Background and Significance

Accurate measurement of lung oxygenation is vital for the classification of disease severity, as well as quantification of outcomes in clinical trials.

In severely hypoxic patients (such as patients in critical care settings, or those ascending acutely to high altitude), direct measurement of 'lung shunt' provides the most accurate quantification of reduced lung oxygenation. Shunt measures the fraction of blood which passes through the lungs without being oxygenated. The best way to measure this is by directly measuring oxygenation of the blood in peripheral arteries, and in arteries bringing blood to the lungs to be oxygenated (pulmonary arteries), however the latter is rarely available. Currently, there are two widely used methods to measure lung oxygenation ( $\text{PaO}_2:\text{FiO}_2$  ratio (P/F) and alveolar-arterial (A-a) gradient). Without pulmonary arterial blood, these methods have been shown to be unreliable in estimating lung shunt, though they remain widely used.

We have developed a new method of estimating lung shunt from arterial blood gases without the need for additional invasive measures (this 'effective shunt' method has been shown to be more accurate and reliable than commonly used measures when analysing existing arterial blood gas data from critical care patients). We aim to compare the accuracy of these three measures to predict lung shunt at high altitude. This will allow us to model hypoxia in critical care patients whilst eliminating various confounding factors known to change arterial oxygen levels, such as changes in posture and urine production. Our results should demonstrate the superiority of 'effective shunt' over widely used methods in a cohort of healthy volunteers, and under controlled conditions. This may help us to introduce a more accurate method of measuring lung oxygenation to clinical environments, with potential benefit to patients in critical care environments, and to researchers carrying out clinical trials.

#### Methods

Eight volunteers took part in this study. Blood samples were collected from an artery on day 9 of the expedition. This involved volunteers lying down with an expedition doctor inserting an arterial line using local anaesthetic to minimise pain. The procedure lasted a maximum of 1.5 hours, taking five 1ml samples from the cannula in total. Volunteers were asked to sit calmly for ten minutes breathing room air, whilst blindfolded and listening to calming music to minimise changes in breathing. After ten minutes, a 1ml sample of blood was taken from the arterial line and analysed using a portable blood gas analyser (iSTAT Alinity®). These results were used to calculate lung shunt using the three different methods described previously. Volunteers were then given oxygen to breathe via an oxygen mask. After ten minutes, a further 1ml sample of blood was taken from the arterial line for analysis. The above was repeated after breathing increasing concentrations of oxygen from 28 to 100% oxygen. The arterial line was then removed and pressure applied until five minutes beyond the point at which bleeding stopped.



### Objectives:

1. To investigate how well a new, minimally-invasive method of predicting lung oxygenation ('effective shunt') performs under conditions of high altitude-induced hypoxia
2. To compare the performance of the new method for predicting lung oxygenation against other widely used methods of quantifying lung function: PaO<sub>2</sub>:FiO<sub>2</sub> ratio (P/F) and alveolar-arterial (A-a) gradient



### Menstrual Bleeding

Led by Ella Crowther and Erin Bennett

Supervised by Dr Jacqueline Maybin, University of Edinburgh

#### Background and Significance

Heavy menstrual bleeding (HMB) affects 20-30% of females of reproductive age, with over 800,000 females in the UK seeking specialist medical help for this condition every year. This poses a major socioeconomic burden. HMB has a significant impact on these patients' quality of life, particularly as the medical treatments available are often deemed unsatisfactory due to side-effects or a lack of efficacy. As a result, 43% of females who visit the hospital for HMB will opt for surgical intervention within a year of first attending. There is a clear unmet need for more effective medical treatments for HMB.

Hypoxia in the uterus (womb) has been linked to effective cessation of bleeding and repair of the uterine lining in experimental models. Additionally, levels of the protein HIF-1 $\alpha$ , the product of a gene whose activity is enhanced by hypoxia, is lower in uterine biopsies of females with HMB than those with normal menstrual bleeding. This study will evaluate the effects of altitude and the subsequent total body hypoxia on the female menstrual cycle, contributing towards a body of work looking to address the problems associated with menstrual bleeding. This work is important to help understand menstruation and to find better treatments for conditions such as HMB.

#### Methods

All female volunteers were invited to take part in this study. Volunteers completed a pictogram chart to note the number of tampons/towels used for each day of menstruation, tallying next to the pictogram representing the appropriate volume of blood loss for one cycle before, one cycle during, and two cycles after the expedition. This method was used to measure changes in menstrual blood loss pre-, during and post-exposure to high altitude. Volunteers on any form of contraception not aforementioned were given calendars to note changes in breakthrough bleeding or 'spotting'.

### Objectives:

1. To investigate whether high altitude-induced hypoxia reduces the volume of menstrual blood loss
2. To determine whether high altitude-induced hypoxia also affects the duration of menstrual blood loss

## White Blood Cells

Led by Alex Thomson

Supervised by Professor Sarah Walmsley, University of Edinburgh

### Background and Significance

Our research follows previous work conducted in mice. Upon infection and exposure to hypoxia (hereafter referred to as “challenged”), mice become severely sick, with the majority dying after 24 hours of exposure. However, mice are protected from this sickness if they lack the expression of a protein called hypoxia-inducible factor (HIF) in a portion of their white blood cells. Mice also avoid this sickness if they are exposed to hypoxia one week before challenge (“pre-conditioned” with low oxygen levels). Interestingly, this protection is maintained if mice are returned to normal oxygen levels for one month after pre-conditioning.

We proposed that a prolonged period of exposure to low oxygen levels (during the expedition) will result in a similar pre-conditioning response in humans. Before and after the expedition, we exposed human white blood cells, isolated from venous blood samples, to acute low oxygen levels/infectious stimuli. Evidence for a pre-conditioning response to low oxygen levels in a human population would be highly significant to clinical practice: evidence of a ‘genetic memory’ in white blood cells to low oxygen levels has the potential to improve treatment outcomes amongst patients with low blood oxygen levels and infection.



### Methods

Up to 20 volunteers could take part in this study. Blood was sampled at baseline testing, and on days 11 and 12 of the expedition and at post-expedition testing. Multiple tests were run on these samples for different studies. From the blood samples, we plan to analyse gene activity in white blood cells (i.e. which genes are ‘turned on’). We will also investigate the control of gene activity (partly controlled by a process called DNA methylation) and measure the amount of various proteins present in white blood cells. For the cell death experiments we will analyse the numbers of neutrophils that are alive or dead after they are grown in conditions that simulate low oxygen levels and infection. At baseline testing and post-expedition testing, we measured the degree of cell death using a microscope and a technique called flow cytometry. Some volunteers may be asked to return for a further blood sample in 2023. This may allow us to investigate how long changes to genes last after being exposed to hypoxia.

### Objectives:

1. To investigate whether prolonged exposure to hypoxia change gene activity in neutrophils and alter their lifespan or function
2. To investigate changes in gene expression and regulation in whole blood and neutrophils that are associated with exposure to systemic hypoxia
3. To characterise changes in leukocyte and neutrophil gene expression, lifespan and function in response to hypoxia and infectious stimuli before and after the expedition
4. To investigate changes in the amount of proteins released from neutrophils and other white blood cells into the blood (plasma) associated with exposure to systemic hypoxia



## **Expression Quantitative Trait Loci (eQTLs)**

*Supervised by Professor J Kenneth Baillie, University of Edinburgh*

### Background and Significance

It is well known that exposure to low oxygen levels changes gene activity in the body. However, the impact of variation in regions of the genome, known as expression quantitative trait loci (eQTLs), remains unclear. eQTLs are known to influence the activity of one or more genes, and their presence varies amongst individuals. By collecting human genomic DNA (gDNA), we will be able to identify genomic regions that may differentially regulate activity of gene messages and resultant protein levels in hypoxia, potentially revealing important information about an individual's response to altitude and their risk of altitude illness.

### Methods

All volunteers could take part in this study. Part of the venous blood sample taken at baseline testing was frozen for its genome to subsequently be sequenced. We will be looking for the impact of genetic variation in DNA (specifically "expression quantitative trait loci") on gene activity measured in the blood samples taken at high altitude on the expedition. These were frozen and shipped back to the UK.

### Objectives:

1. To investigate the impact of variations in the genetic code (known as eQTLs) on gene activity under conditions of high altitude-induced hypoxia.
2. To determine whether variations in the genetic code (eQTLs) are associated with individual differences in the response of the body to high altitude, and the likelihood of suffering from high altitude-related illness.

### **Early Research Conclusions**

Data analysis from the APEX 6 expedition is in progress, and we aim to present our work at national and international conferences, and publish our work in due course. All APEX publications to date and future publications are listed at [altitude.org/publications](https://altitude.org/publications). We intend to update this expedition report to reflect APEX 6's findings when the outcomes become clear. This will also be available on our website.

## 8. Conclusions and Next Steps

### Conclusions

APEX 6 aimed to further our understanding of human physiology at high altitude whilst involving and exposing future generations in the hope they will go on to do the same.

Through investigating pertinent research areas and through designing and completing complex research studies at 4,775m, the expedition has hopefully gone some way to furthering our understanding of human physiology and under conditions of high altitude hypoxia. APEX 6 uniquely studied a new method of measuring lung oxygenation using arterial blood gases, dark adaptation of the eye at altitude using both electroretinography and a portable field dark adaptometer and used actigraphy devices to assess body clocks at altitude. A study also looked at the ability of a small dose of dexamethasone to reset the body clock. APEX 6 further investigated neutrophil hypoxia and expression quantitative trait loci (eQTL), building upon findings from previous expeditions. In time, once analysis is complete, we will share findings from these unique studies with interested colleagues and identify any new areas of potential research.

The expedition was also successful in training future generations to conduct medical research in challenging environments. This will help advance our mission to better understand human physiology under hypoxic conditions. APEX 6 enabled 34 new individuals to experience high altitude medicine and Bolivian culture who otherwise may not have. Feedback shows how valued an opportunity this was.

### APEX 7

Following on from the enthusiasm shown by APEX 6 volunteers both in high altitude research and organisation of an expedition, we anticipate that some will go on to lead their own future expedition. We wish them every success in doing so.



## 9. Feedback and Development

APEX 6 compiled post-expedition feedback from volunteers focussing on the execution of the expedition and its contribution to their student experience. Feedback was overwhelmingly positive, with some constructive suggestions for improvements received. Below are some highlights from feedback received:

**What do you think went well with this expedition?**

"People helped each other when they were struggling and it was just a great team to be a part of."

"The expedition leaders were very thorough and detailed in their planning, which helped greatly on the expedition. The group was very enthusiastic and committed to the project and the expedition."

"The group dynamic was really supportive and contained a wide variety of individuals."

"Everyone was made to feel at home, included and valued. There were great opportunities to be challenged and put out of our comfort zones in an incredibly supportive environment."

**How do you think this expedition has enhanced your University experience?**

"It gave me an insight into medical research and also introduced me to an amazing group of people who I hope to keep in touch with as I go through university and beyond."

"Being a participant of APEX6 has exposed me to a side of medicine seen rarely within the traditional medical curriculum."

"Apex has given me the opportunity to see what it means to be a research participant as well as researcher."

"I got the opportunity to meet loads of people on my course, develop skills that will be useful to me in my professional career, and majorly boost my confidence."

**Has this trip influenced your sense of wellbeing/community? How?**

"I think that staying in the same place with so many people for such a long period of time did bring us closer and gave us a sense of community. It also made us understand that it is important to look after our own wellbeing as well as regularly check in with other people."

"I got to know a really diverse group of people and it has really expanded my group of friends."

"[APEX 6] made me realise the benefit of taking time away to look after myself so I can more effectively interact with others."

"It was great to meet people with different experiences and learn from them and to take away friends from the expedition."

### Has this trip developed and/or enhanced your learning? How?

"This trip has given me a greater understanding into what needs undertaken to be involved in a research project, building on research and evidence based medicine which is seen throughout the MBChB course."

"It has enhanced my learning and understanding of altitude for sure. Experiencing high altitude and its effect on myself will give me a better understanding of what hypoxic patients are feeling."

"Being able to chat to the doctors has widened my perspective of what [a career in] medicine can be."

### Is there anything in particular you enjoyed from a research perspective?

"I enjoyed helping out with carrying out the research and seeing how my own body was affected by altitude."

"Getting to be involved with the data input meant I felt much more a part of the research."

"It was enjoyable to be part of the dark adaptation study and help take measurements from other participants."

"I enjoyed... how tasks were shared and delegated because it was fulfilling to work as a team."

### Is there anything we could do better in future years?

"Have a more diverse set of volunteers - a lot were from a similar background."

"Even more opportunities to get involved with research and trip planning."

"[Recruit] more people not studying medicine / more international students so there is greater diversity."

"More socials and time to get to know people before the trip."

"Less cabbage soup!"

### Key Themes Highlighted

Volunteers particularly appreciated the extent to which they were involved in research. A strong effort was made to identify any areas where volunteers could engage with and participate in research, aside from participating as research subjects. Opportunities were made available within all of the research projects, with opportunities including the processing of neutrophil samples, recording questionnaire data, completing key aspects of the eye function study and oversight of reaction tests.

The ability to both bond and travel with a group of likeminded people was highlighted as a particular strength of the expedition. Although the expedition team aimed to recruit volunteers entirely on their own merits, those who showed particular interest in travel, research and teamwork were more likely to be

successful in being selected. APEX 6 was thus able to unite likeminded people from all years of study at the University of Edinburgh, introducing students to others who they may otherwise never have met or engaged in conversation with.

An area highlighted for improvement was with regards to the diversity of the group. Feedback highlighted that involvement of more international and non-medical students would have been beneficial. This was also identified as an area for improvement by the expedition leaders. As recruitment took place largely during periods affected by COVID-19, promotion and recruitment campaigns occurred almost exclusively online. APEX 6 faced significant difficulty reaching out to non-medical students, with social media and email communications largely only reaching medical students. Further thought should be put into how best to reach non-medical students in future expeditions. APEX is open to all students and non-medical perspectives would undoubtedly be beneficial to future planning, research and team building.

The supportive nature of the group was highlighted in a number of comments, and it was very pleasing to see how comfortable individuals felt in what was a relatively large group. This is particularly testament to the qualities of the participating volunteers, who were open and supportive to their colleagues.



# 10. Acknowledgments

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Notes



