

## Xtreme Everest Update – October 2015

Ever since XE1 in 2007, when I trekked to Everest Base Camp as part of the legendary Group G, I've maintained an interest in the various twists and turns of the project, not least because I still give talks about it. Occasional visits to the website have kept me abreast of the follow-on expeditions and research initiatives, but I'm afraid I'm in the slow readers group when it comes to medical publications and papers. That's why I jump at the chance of attending the Walk and Talk events, including the latest at Langdale Youth Hostel on 26<sup>th</sup>/27<sup>th</sup> September 2015.

After a slightly restless night in the youth hostel dormitory – how can someone snore that loudly without waking themselves or causing structural damage – I joined trekkers from 2007 and 2013 settling down to hear from an impressive team of speakers – including one, Andrew Murray, who'd been a fellow trekker in 2007.

With apologies to the researchers for mangling their words and concepts, what follows is my interpretation of the science updates we received, interspersed with generous helpings of tea and cake.

Mike Grocott kicked proceedings off with the XE Story to date.

It seems the story started 2.8 billion years ago, when a single-celled organism began producing oxygen. Unfortunately, the gas proved toxic to most other inhabitants of the planet, and 200 million years later, caused the Great Oxygenation Event, a mass extinction. Luckily, a life form that had adapted to use oxygen survived. And here we are.

However, the legacy of cells being damaged by oxygen remains. Patients in intensive care must have the gas, but it seems that the less some receive, the better they'll fare, the amount being determined by many factors, including genetics. So, wouldn't it be marvellous to identify the optimum oxygen level for every patient – their sweet spot – and to modify it as their treatment proceeds?

Research on patients is tricky, whilst that in labs or on animals has only limited read across. Which is why, in the early Noughties, researchers had the idea of taking a group of humans from sea level to, in some cases, the summit of Everest. On the way, they'd follow the oxygen trail, from the respiratory to the circulation and micro-circulation systems, to the mitochondria turning it into energy for use in the muscles and organs. Armed with the data accumulated, they'd work toward achieving the read across into critical care.

Cue Xtreme Everest.

Denny Levett explained that the huge amount of data from all the studies was still being analysed, and that the task becomes ever more Herculean as new research methods open the prospect of further tests on samples and data from as far back as XE1 in 2007.

What has been shown is that, at altitude, the reduction in exercise performance (35%) cannot wholly be attributed to the 30% reduction in the efficiency of respiration and circulation. (Gender and age had no effect, although the performance of fitter guinea pigs deteriorated by more than their less fit peers.)

So, it seems that the micro-circulation and mitochondria components of the oxygen delivery system have a significant part to play in the reduction in performance.

Dan Martin provided graphic evidence of this, his films of microcirculation at altitude showing capillaries disappearing, while the flow of blood through those that remained slowed dramatically. Meanwhile, having adapted to altitude for at least 21,000 years, the Sherpas showed no reduction in capillary density or flow rate. Researchers are about to start looking at micro-circulation in patients.

Dan's final bombshell was that we all need to start adapting like Sherpas, but in a much shorter timescale. A little-publicised prediction of studies into climate change is that the oxygen level in the Home Counties is likely to reduce to that of Base Camp – in a mere 4,000 years.

Andrew Roberts explained the process by which mitochondria turn oxygen into energy, and how it can be measured to show the heart's energetics. We lost mitochondria as we climbed, killed off by an increase in free radicals, but those that remained became more efficient – burning glucose rather than fat. Again, the Sherpas seem naturally to have fewer but more efficient mitochondria.

Loss of energetics can be a predictor of heart failure and, after a heart attack, any reduction seems to be irreversible. However, the reduction in our heart energetics as we climbed to Base Camp was reversed in 6 months. Could loss of energetics in some heart patients be due to hypoxia, and could there be a way to promote a recovery similar to that seen in XE subjects?

As with all of the XE research, watch this space!

Kate Mythen and her daughter, Alice, went through the conduct of the Young Everest expeditions, an element that generated much media interest, and which has since appeared in school curriculums and textbooks – complete with pictures of Alice and her siblings!

Mark Wilson explained how XE results had fed through from mountain to bedside and the treatment of head injuries.

About a litre of blood enters your head every minute and, of course, it also has to drain away. Any restriction in the outflow can cause a rise in Inter Cranial Pressure. With altitude, our blood vessels dilated and their flow rate increased to maintain oxygen levels. It seems that those who suffered headaches had narrower veins draining blood, which points to hypoxia causing the venous system to become constricted, in the case of trauma as well as AMS.

Mark's final message was that if you find an accident victim, you may have to counter the instinct to leave them alone to prevent spinal damage, and move them to allow the blood to drain from their head, the danger from this being the alligator nearest the boat.

Finally, Kay outlined where the project is now, fitting into a wider network of partners, such as CASE and Duke University, and where it may be headed, becoming the Xtreme Everest Oxygen Research Consortium, perhaps with charitable status.

In the short term, it's unlikely that we'll all have the chance to take part in another large expedition to Nepal, but there will continue to be events in London and elsewhere to maintain our interest, including an anniversary conference in Namche Bazaar in May 2017. And some of us may be asked to volunteer for further studies to see how we've fared since our initial involvement.

Of necessity, I've skated over much of the detail contained in the various talks. Suffice to say, I found it all fascinating and I remain incredibly grateful to Kay and her assistant, Sarah, for organising the event, and to the whole team for taking the time to travel to the Lake District and bring us up to date with their various avenues of research.

With a final apology for any mistakes, I wish the team all the very best as they move forward with their lives and careers.

Ron Powell, XE1, Group G