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Altitude Sickness Prevention and Efficacy of Comparative Treatments (ASPECT)



We are getting smarter about traveling to high altitude. The incidence of acute mountain sickness (AMS) is now half of historical norms at the most popular trekking routes on the Everest approach; and on the Annapurna circuit researchers at the Himalayan Rescue Association are seeing one case of AMS every *other* day. The distressing constellation of symptoms that comprise AMS (headache, sleep disturbance, fatigue, dizziness, and gastrointestinal distress) often resolve within 1 – 2 days after arrival at high altitude, however the disease can be debilitating, ruin an adventure, and if left unrecognized or untreated can progress to potentially fatal high altitude cerebral edema.

While the decreasing rates of AMS is great news for trekkers, the lower incidence of AMS negatively effects power calculations and makes it nearly unfeasible to run large clinical trials. So where in the world can one go to study altitude illness? Certainly a trip to Mt Kilimanjaro with over 50,000 annual visitors and a terrifying 40 fatalities a year is ripe for education and interventions, but the lack of infrastructure and logistical challenges of Tanzania makes it a daunting venue. Colorado is a great option complete with a drive-up 14er, but baseline acclimation of Denverites and the lack of high altitude lodging have made things difficult. Alternatively, the White Mountain Research Center ([WMRC](#)) in California has been serving up an approachable and comfortable option for high altitude research for nearly 60 years. Established in 1950 just outside of Bishop, California, WMRC has lodges at 4,100', 10,200', and 12,500' and is located on the flanks of White Mountain – the 3rd highest peak in California at 14,252' with a gorgeous ascent path.



With the generous support of the American Alpine Club's 2015 Research Grant, Wilderness Medical Society's Herbert N. Hultgren Grant, and the Institute for Altitude Medicine, this past August we studied the inhaled asthma medication budesonide for AMS prevention compared to the standard AMS prophylactic acetazolamide (diamox) versus placebo. This was a double blind, randomized, placebo controlled trial. Considered the most rigorous type of research methodology, the trial was run by [Stanford Wilderness Medicine](#).



ASPECT enrolled 103 participants, resulting in the largest North American AMS prevention trial to date. We witnessed AMS rates ranging from 56% to 72%, with severe AMS of 46%. Imagine the worst hangover of your life replete with pounding headache, stupefying nausea, and a rapid resting heart rate with low oxygen levels that would set off alarm bells in a sea level emergency room. That is severe AMS.

While budesonide did not appear to work any better than a placebo, diamox worked wonders, especially on preventing severe disease. This was significant both statistically and clinically, with a 20 – 30% reduction of disease over both placebo and budesonide. The laboratory space and on-the-grid infrastructure at 12,500' Barcroft Lodge allowed us to run ultrasound testing and pulmonary function tests to analyze the physiologic changes seen with rapid ascent to high altitude. Having study participants provide forced expiratory tests in a low oxygen state made all the researchers profoundly appreciative of the volunteer's time and effort! The initial analyses point to increased total body water in those suffering from AMS, findings that may provide greater insight into causation of the disease itself.



Diamox (125mg twice / day) is usually ingested the night prior to ascent to allow time for maximal effect. Interestingly, ASPECT was one of the few studies to examine diamox beginning the morning of ascent, in a rapid ascent profile (4,100' to 12,500') that is common in most hikers, climbers, as well as tactical and search & rescue personnel. The robust protective effect of diamox in this setting is generalizable to ascents found in the continental US and Western Europe, which may allow diamox to be utilized in a new manner. While diamox was not directly compared to ibuprofen, it appeared to work as well as ibuprofen at identical altitudes and ascent rates (600mg taken three times a day, started morning of ascent), which was the subject of our prior study at WMRC, the [Prevention of Altitude Illness with Non-steroidal anti-inflammatory Study](#) (PAINS). While the potential for a new prevention drug for AMS in budesonide appears to be a non-starter, we were able to confirm the high rates of AMS at WMRC that hopefully will make this an epicenter of future high altitude clinical trials. Every study often poses more questions than answers, and future work may find us comparing diamox to ibuprofen to make definitive conclusions of the efficacy of these two popular drugs.

