Elevated nitric oxide in blood is key to high altitude function for Tibetans

October 30 2007

How can some people live at high altitudes and thrive while others struggle to obtain enough oxygen to function?

The answer for Tibetans who live at altitudes around 14,000 feet is increased nitric oxide (NO) levels. High levels of NO circulate in various forms in the blood and produce the physiological mechanisms that cause the increased blood flow that maintains oxygen delivery despite hypoxia—low levels of oxygen in the ambient air and the bloodstream.

Researchers from Case Western Reserve University and the Cleveland Clinic report that Tibetans have 10 times more NO and have more than double the forearm blood flow of low-altitude dwellers. The findings from a comparison of NO levels in the high and low altitude dwellers are reported in the article, “Higher Blood Flow and Circulating NO Products Offset High-altitude Hypoxia among Tibetans,” in the current *Proceedings of the National Academy of Sciences*.

The low barometric pressure of high altitudes generally causes low arterial oxygen content among Tibetans, yet the researchers have found that Tibetans consume oxygen at normal rates.

“We asked how that could be done,” said Cynthia Beall, the S. Idell Pyle Professor of Anthropology at Case Western Reserve University. For two decades, Beall has been one of the world’s leading researchers in the studies of high altitude adaptation in different populations in Ethiopia, South America and Tibet.

Beall collected blood samples and blood flow readings from the forearms of 88 Tibetans during a 2002 research trip that was funded by the National Science Foundation. The blood flow data and blood samples were brought back to the United States where Serpil Erzurum, chair of pathobiology, Cleveland Clinic, and the paper's lead author, analyzed the information. In Erzurum's lab, Allison Janocha, a Case Western Reserve graduate, performed many of the technically challenging analyses.

For comparison, the scientists collected the same information from 50 near sea-level dwellers from the United States who participated in the study at the General Clinical Research Center at the Cleveland Clinic.

The combined increase in NO and blood flow levels resulted in double the amount of oxygen delivered to the capillary beds in the Tibetans' arms.

The researchers hypothesize that Tibetans have a genetic mutation that allows high NO production. Genetic studies and comparable data on sea-level populations living at high altitude would be needed to test that hypothesis, said Beall.

During the study, the researchers also recognized another population difference: Tibetan women were found to have higher nitrite and lower nitrate levels than those of Tibetan men, whereas no gender differences were found in sea-level dwellers.

In this research, blood flow is determined by the length, number and width of the diameter of blood vessels. These numbers are determined partly by NO, which is a dilator of the vessels and prevents high blood pressure, which would result from increased blood flow in restricted blood vessels. NO also helps in the release of oxygen to tissues. NO reacts in the blood to produce nitrite, nitrate, nitrosothiol proteins and á-nitrosyl hemoglobin, which can be used as indicators of NO production.

To confirm the increases in NO, the researchers subjected the Tibetan samples to sensitive high performance liquid chromatography, where the results verified the 10-fold increase of NO in the blood.

This study continues to unravel the mysteries of high altitude adaption and follows Beall's 2001 study, published in Nature, on the NO levels in exhaled breath of Tibetans, which were found to be 25 percent greater than that of local Cleveland residents. There was also a related paper on NO and pulmonary blood flow in 2005 in the Journal of Applied Physiology. Brian Hoit of the department of medicine at the Case Western Reserve School of Medicine was the lead author on that paper.

Source: Case Western Reserve University