Why is it that Boulder, Colorado is the city with the lowest obesity rate in the United States --12.4%, compared with the national average of 35.7%? [1] Boulder also has very low rates of diabetes, cardiovascular disease and other metabolic disorders. Is it because residents eat a good diet and get lots of exercise? Or is it something else? While health is multi-factorial, an examination of alpine populations around the world reveals the surprising fact that lower levels of atmospheric oxygen contribute to lower rates of obesity and diabetes. [2,3,4]

Maps of the U.S. and Europe show a close correspondence between altitude and obesity, diabetes and longevity. [5,6] A survey of 422,603 adults across the U.S.—controlling for age, sex, race, ethnicity, education, employment, ambient temperature, diet, physical activity and smoking—found the odds of being obese for those who live at sea level are 4-5 times higher than for those living at 10,000 feet or higher. [2] Another U.S. study showed that those living above 4,900 feet lived longer than those at sea level. [3,7] Obesity rates of Tibetans are halved at higher altitudes. [8] This strengthens the altitude-obesity hypothesis because Tibetans are homogeneous genetically, culturally and economically.

People living at higher altitudes breath air that has a reduced oxygen concentration--a condition known as hypoxia. Several studies show an association between hypoxia and reduced incidence of cardiovascular disease and diabetes. [3,4,7] But what causal mechanisms can explain this association?

Hormesis is a biphasic biological stimulatory response to low dose stressors, which are inhibitory at higher doses; it has been extensively documented in animals, plants and microbes. [9,10] Moderate hypoxia activates several hormetic processes that improve health measures. Activation of the metabolic "stress sensor" PGC-1α, initiates a cascade of changes, including increased mitochondrial biogenesis, thermogenesis, leptin sensitivity and BDNF, with attendant suppression of appetite and increased urge to exercise. [4,11,12]

The good news is that we don't need to move to the mountains to harness the power of hormesis. Several other environmental "stressors"--including calorie restriction, exercise, and cold exposure--activate the very same PGC-1α cascade triggered by the hypoxia of high altitude. [11.13] Before the modern era, our ancestors followed a lifestyle in which these particular hormetic environmental stressors were ubiquitous. [13,14] We should think about how to improve our healthspan by employing these practices in daily life.

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