High and Mighty

New discoveries by CWRU anthropologist Cynthia Beall continue to unravel the mystery of how humans have adapted to high altitude living.

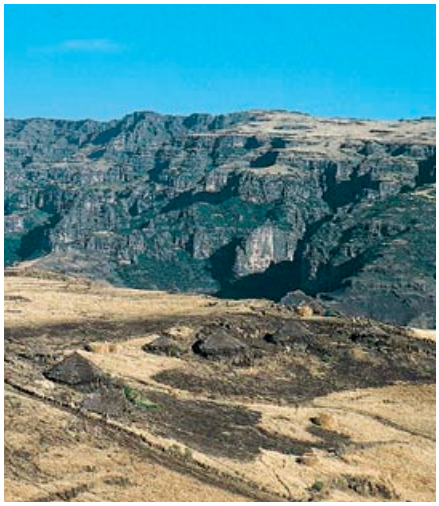
In her hematological study of villagers in the Semien Mountains of Ethiopia, she found that this population differs biologically from people on the Tibetan and Andean plateaus, but in a couple of key aspects does not differ from people at sea level.

Prof. Beall, CWRU's Sarah Idell Pyle Professor of Anthropology, reported the research findings in the article "An Ethiopian Pattern of Human Adaptation to High-Altitude Hypoxia" in the *Proceedings of the National Academy of Sciences* (PNAS). Also contributing to the project were colleagues from CWRU, Emory University, and Columbia University.

Twenty years ago, her research on Tibetans began to overturn the long-held model of the "Andean man," with a large barrel chest and high concentrations of hemoglobin, the oxygen-carrying molecule in the blood. Despite high hemoglobin concentrations, the Andean highlanders have low oxygen saturations of hemoglobin relative to sea level.

Prof. Beall discovered Tibetans had normal sea-level hemoglobin with low oxygen saturations, but there is a variation among some Tibetans, who have a genetic allele (one of two or more alternative forms of a gene) for higher oxygen saturation of hemoglobin.

In her recent research, another way to survive highland living was found among a sample of Ethiopian people, who have normal sea-level hemoglobin and normal sea-level oxygen saturations–a distinct combination of traits, according to Prof. Beall.



Dynamic landscape: A group of local houses near the area in Ethiopia where Prof. Beall collected data

She made the discovery from data collected in a field study of 313 native residents (at 11,650 feet of altitude) between the ages of 14 and 86 years from the Ambaras Region of the Semien Mountains National Park in Ethiopia. The Ambaras people are farmers of barley and herders of cattle, goats, and sheep. They live in small villages scattered across the plateau in northeastern Ethiopia.

Arresting Elephantiasis

Researchers at CWRU have reached an important milestone in learning how to halt a major mosquito-borne disease affecting 120 million people around the world.

Under attack: Elephantiasis can lead to dramatically swollen and disfigured legs, arms, breasts, and genitals.

The disease, called lymphatic filariasis and commonly known as elephantiasis, is a leading cause of physical disfigurement, social ostracism, and economic loss throughout Africa, Asia, South America, and islands of the Pacific Ocean. The disease can lead to dramatically swollen and disfigured legs, arms, breasts, and genitals.

Treating 2,500 residents in a remote area of Papua New Guinea in the South Pacific, the researchers from CWRU's School of Medicine, University Hospitals of Cleveland, and Papua New Guinea Institute of Medical Research found dramatic results with four annual mass treatments of single doses of safe and inexpensive anti-filarial (anti-worm) drugs.

There was a greater than ninety-five-percent decrease in mosquito transmission, nearly complete prevention of new infections in children, reduction of infection rates in the communities to less than one percent, and, remarkably, a cure of severe disease manifestations such as extremely enlarged arms and legs and genital disfigurement.

Combined with conclusions drawn from mathematical analysis of the interrelationships between the potentials of mosquito transmission and human infection, a report, which appeared in the December 5 issue of the *New England Journal of Medicine*, demonstrated that annual mass treatment with safe and inexpensive medications can go a long way toward eliminating this devastating disease.

"Until this study, it was not clear that eradication and significant decreases in mosquito-borne transmission and disease severity

Passing by: A group of young boys and men from the area whom Prof. Beall met in her travels. While the young boys were herding, the older ones had come to watch her work.

With the assistance of Amha Gebremedhin, from the Department of Internal Medicine at Addis Ababa University, and local peasant associations, Prof. Beall made contact with the villagers and gathered blood samples for analyses of their hemoglobin content as well as erythropoietin, a hormone that stimulates the production of stem cells in the bone marrow to produce blood cells. Erythropoietin is also an indicator of hemoglobin levels.

Because the Ambaras have experienced famines and other hardships, Prof. Beall ruled out anemia, infections, and inflammations that might skew the findings.

Healthy sea-level dwellers have saturations of oxygen in their blood that vary from 92 to 100 percent. In the Ambaras sample, the oxygen saturation averaged 95 percent, which surprised Prof. Beall, because the oxygen saturation in the Andean and Tibetan highlanders at similar altitudes was in the mid to high 80s.

"This raised the question of how did they achieve this?" Prof. Beall says. "We looked to see if they had normal hemoglobin or a special form of hemoglobin, but they did not. It seems that people living at high altitude in Ethiopia have very little hypoxic stress. These findings suggest there are three patterns of adaptation to high-altitude hypoxia among indigenous populations."

Learning why this is the case will require two lines of future investigation: looking at the biological mechanisms and underlying genetics that allow for successful high-altitude living, and investigating the evolutionary process that produced these adaptation patterns.

Susan Griffith

Photography, by Cynthia Beall, courtesy of the photographer

Double threat: This painting by Jakura, an acclaimed Papua New Guinea artist, represents the two major infectious diseases spread by mosquitoes: malaria and lymphatic filariasis

could be realized even on a small scale," says James Kazura, the paper's senior author, who is a professor of medicine at CWRU and UHC and director of the Center for Global Health and Diseases at the University.

Lymphatic filariasis is caused by microscopic juvenile parasitic worms that are transmitted to humans by mosquitoes containing these infective parasites.

In many rural areas of Papua New Guinea, Africa, and India, nearly ten percent of the population suffers from elephantiasis by adulthood, and large numbers of men develop such swelling of the scrotum that it can reach the size of a grapefruit.

Building on more than twenty years of research and clinical investigations on filariasis, the study was conducted in Papua New Guinea, where transmission of filariasis and other serious infectious diseases such as malaria reach the highest levels seen anywhere in the world.

"Performance of a study in this setting to determine whether inexpensive and safe medications could decrease transmission of filariasis and control its clinical outcomes represents an extraordinarily tough test or 'proof of principle' of the Global Plan to Eradicate Lymphatic Filariasis," Dr. Kazura says. Launched by the World Health Assembly in Geneva in 1997, the plan calls for filariasis to be exterminated, on a global level, by 2020.

"This study provides essential guidelines to control this infectious disease and points the way to the ultimate eradication of filariasis on a global level," Dr. Kazura adds. "The work also poses interesting and challenging new research questions that should enable the testing of new hypotheses on how genetics and immunity determine infection susceptibility in humans and contribute to the development and ultimately prevention of lymphatic disease."

George Stamatis

Photograph and painting courtesy of Dr. Kazura