UC San Diego to Lead New Malaria Research Center in South America

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Multi-national effort targets control and eventual eradication of mosquito-borne scouge

Tropical disease specialist Joseph Vinetz, MD, of the University of California, San Diego School of Medicine will lead an ambitious multi-national effort to help control and eventually conquer malaria, establishing a new Peruvian/Brazilian International Center of Excellence in Malaria Research Center (ICEMR) with a seven-year, $9.2 million grant from the National Institutes of Health.

The grant is one of 10 awards announced July 8 by the National Institute of Allergy and Infectious Disease, part of the NIH. All of the grants support ICEMR projects located in seven major geographic regions of the world where malaria is an endemic, significant public health problem. The ultimate goal is global eradication of the disease.

Joseph Vinetz, MD

Vinetz, a professor of medicine at UC San Diego, will be principal investigator of the Peru/Brazil ICEMR, whose mission will be to comprehensively study and understand the complete disease cycle of malaria in the Amazon basin. Collaborating with UC San Diego scientists will be colleagues from the University of Sao Paulo, Brazil; the Universidad Peruana Cayetano Heredia in Lima, Peru; the Federal University of Acre and the Universidade Estadual Paulista, both in Brazil; the U.S.-based Wadsworth Center of the New York State Department of Health; the Johns

Hopkins School of Public Health in Baltimore, Md.; and the U.S. Naval Medical Research Center Detachment in Lima.

Except for cases contracted elsewhere and brought here, the disease of malaria has largely been eliminated in the United States. It was officially declared eradicated in 1949. In other parts of the world, however, malaria remains a persistent and deadly affliction. More than 3 billion people – almost half the world's population – live in regions of the world where they are at significant risk, primarily in parts of Africa, Asia and South America. An estimated 1 million malaria-related deaths and 300 million infections occur annually. The vast majority are children under the age of 5 and pregnant women. Travelers who lack immunity are also vulnerable when visiting areas with a high rate of malaria transmission. There is no vaccine, and the cause of the disease – a parasitic microorganism transmitted to humans by the bite of an infected mosquito – evolves constantly to resist drug treatments.

"At a time when eradication is the ultimate goal of malaria control strategies, it remains unclear why malaria has proven so difficult to control across the Amazon Basin," said Vinetz, who has spent more than 20 years investigating malaria, much of that time in the Peruvian Amazon.

"We have assembled an impressive team of specialists who are prepared to look at all aspects of malaria transmission in this region, to improve the diagnosis, the treatment and the prevention of infection. Over the long term, we share the NIH's goal of generating research findings that can be translated into effective public health interventions and that lead to the audacious goal of global malaria eradication."

Marcelo Ferreira, MD, PhD, of the University of Sao Paulo and a world-recognized malaria parasitologist who will oversee the Brazil-based part of the grant, said "our focus will be on studying the great reservoir of malaria-infected people who have no clinical symptoms of disease. This will allow us to direct malaria control efforts at the sources of infection: asymptomatically infected humans. This focus will drive vaccine- and drug-based control strategies."

Alejandro Llanos Cuentas of the Universidad Peruana Cayetano Heredia, a tropical disease specialist who will direct the grant in Peru, added:

"In Peru, with the control measures implemented in the last 5 years, there has been an 80% reduction in malaria cases in the Amazon. Nevertheless, this reduction is an unstable equilibrium because of limitations of current control strategies and the great risk of new outbreaks and epidemics. Our purpose is to develop new understandings of determinants of transmission, disease manifestations and immune protection, especially regarding malaria due to *Plasmodium vivax*, with the goal of long-term control."

Professors Ferreira and Llanos Cuentas both underscored the enormous and unprecedented opportunity for new research created by the equal partnership among collaborators in Brazil, Peru and the United States.

Investigators in the Peru/Brazil ICEMR will operate from bases across the geographically and culturally diverse Amazonian basin, from agricultural settlements in the Brazilian state of Acre to villages near the city of Iquitos, Peru, deep in the heart of the rain forest to the mining region of Madre de Dios/Puerto Maldonado in Peru, where new highway projects and deforestation are creating new and problematic exposures for malaria transmission.

Planned projects will include studies of the biology and ecology of the mosquitoes that carry the malaria parasite, the biology of malaria transmission from human to mosquitoes, mechanisms underlying clinical manifestations of the disease in patients, environmental factors contributing to spread of malaria, and overall prevalence and incidence of the disease in the Amazon region.

- → According to Vinetz, the danger of disease spread and the risk of epidemic are as real as the many factors that contribute to the continuing emergence and re-emergence of the disease

throughout the Amazon. As a result, the Peru/Brazil ICEMR will focus on key questions and issues in the region. For example:What are the characteristics of the area's most prominent malaria-transmitting mosquito species? And why do they appear in previously non-infested areas following deforestation associated with agriculture and mining?

"It is critically important to correctly identify the vector species in order to assess its contribution to malaria transmission in Amazonian localities altered by anthropogenic activities," said Jan Conn, PhD, of the Wadsworth Center of the New York State Department of Health and one of the project leaders. "This knowledge, combined with information on the ecologies and behaviors of distinctive vector species can be used to effectively reduce human-vector contact."

- → How does resistance or adaptation to insecticide spraying and other forms of insect control develop and spread?

- → What are the travel patterns of infected humans, including people with asymptomatic infections who inadvertently introduce strains of the malaria parasite into new locales and populations;
- → How does medical science deal with the emergence of drug-resistant strains of the parasite?
- → Can a rapid diagnostic test be developed to differentiate malaria from other infections, one that could be used remote, rural areas where medical treatment may be delayed or limited?

The knowledge gained from resolving these questions and the research involved in the broader multidisciplinary programs will form the basis for clinical trials of new drugs and vaccines, said Vinetz. A key element, he added, will be the engagement of participating countries, in particular local scientists, doctors, health workers and students.

Other project and scientific leaders participating in the Peru/Brazil ICEMR are Monica Da Silva Nunes, MD, PhD of the Federal University of Acre, Brazil; Kezia Scopel of the Universidade Federal de Juiz de Fora in Brazil; Paulo Ribolla, PhD of the Universidade Estadual Paulista, Brazil; Dionicia Gamboa, PhD and Jorge Arevalo, PhD of the Universidad Peruana Cayetano Heredia in Peru; Andres G. Lescano PhD, Paul Graf, PhD, and Kirk Mundal, PhD, of the U.S. Naval Medical Research Detachment, Lima and Iquitos, Peru; and Robert Gilman, MD, Margaret Kosek, MD, and Pablo Penataro Yori, RN, MPH of Johns Hopkins Bloomberg School of Public Health.

More about malaria

Malaria is a parasitic disease caused by a single-celled protozoan in the genus Plasmodium, which is transmitted to humans through the bite of the *Anopheles* mosquito, the latter serving as the parasite's incubator and transport from human to human. Symptoms of the disease include fever, chills, headache and vomiting. Four different *Plasmodium* parasites cause human malaria, and some human cases are caused by a parasite associated with monkey malaria recently identified in Southeast Asia. Different species of *Anopheles* mosquitoes are present in different parts of the world. Severity of the disease varies, depending upon the type of malaria parasite and access to appropriate treatment. The most deadly cases occur in sub-Saharan Africa, which accounts for 85% of all malaria deaths. Two types of *Plasmodium* species are prevalent in the Amazon, where the death rate is not as high as in Africa, but where the disease can lead to both acute and chronic illness. Infected pregnant women have a much higher incidence of problem pregnancies, and a higher risk of fetal or newborn death. Currently, there is no vaccine against the disease.

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