Ocean Fever Heralds African Epidemics

In late 1997, heavy rains in East Africa unleashed a viral epidemic called Rift Valley fever that killed tens of thousands of livestock and hundreds of people before the outbreak faded. Next time, however, Kenya and its neighbors won't be caught off guard.

Scientists report in the July 16 SCIENCE that they have developed a strategy for predicting outbreaks of Rift Valley fever several months in advance. Data going back to 1950 indicate that water temperatures in the Indian and Pacific Oceans start rising long before the extreme rains wash over East Africa and trigger the disease. Carried by infected mosquitoes, the virus spreads first to wild animals and livestock and then to people.

"It's potentially possible that if you can predict an outbreak, all of the [health] organizations could be mobilized to curtail or somewhat lessen an outbreak," says study leader Kenneth J. Linthicum of the Water Reed Army Institute of Research in Washington, D.C.

A medical entomologist, Linthicum studied Rift Valley fever in Kenya in the 1980s and returned to the country during the recent outbreak, in late 1997 and 1998. The epidemic coincided with the record-breaking El Niño warming in the Pacific, raising the prospect that scientists could use ocean temperatures as a prediction tool. Linthicum teamed up with Kenyan geographer Assaf Anyamba of NASA's Goddard Space Flight Center in Greenbelt, Md., and others to test this concept.

The researchers studied records of viral attacks and ocean temperatures going back to 1950. Pacific temperatures on their own did not reliably indicate when Rift Valley fever would erupt. The researchers, however, found a consistent pattern when they considered the Indian and Pacific Oceans together: If water temperatures in both areas surged, a viral outbreak followed in 2 to 5 months.

Satellite measurements can also help by pinpointing which areas face the greatest risk, they report. Instruments on weather satellites routinely track changes in vegetation color, providing a way to sense where particularly intense rains are falling in East Africa.

Nations in that region could take a number of steps if scientists forecast the appearance of Rift Valley fever, says Linthicum. He and his coworkers have experimented with spreading insecticides in mosquito-breeding sites before the arrival of rains, a tactic that could stem the spread of the disease. An effective livestock vaccine exists that must be given a month before exposure to the virus. The U.S. military is now testing an experimental human vaccine.

While disease specialists applaud the new study, some wonder about its utility. "I'm a little skeptical about what you could do with the information," says Thomas G. Ksaizek of the Centers for Disease Control and Prevention in Atlanta, who worked in Kenya and Tanzania tracking the recent epidemic.

The disease spread across such a broad region that it would be difficult to apply enough insecticide to prevent such an outbreak, he says. Relatively wealthy livestock owners could vaccinate their large herds, says Ksaizek, but he holds less hope for reaching small rural communities and nomadic herders.

Others see more possibilities arising from forecasts of Rift Valley fever. "This technique could permit us to become proactive," says David L. Heymann of the World Health Organization in Geneva, noting that it would take a month to obtain the resources for combating a predicted epidemic.

"It would be extremely helpful," agrees Paul R. Epstein, who studies tropical public health at Harvard Medical School in Boston.

The recent fever outbreak harmed the economies of East Africa because other nations blocked livestock exports from affected areas, says Epstein. Kenya and neighboring nations, therefore, have a strong motivation to combat the disease.

The latest El Niño sparked disease outbreaks across the world, including cholera, encephalitis, malaria, and Dengue fever. This episode may provide a foretaste of the future, says Epstein. If climatic disruptions increase as expected, the changes will often benefit the insects, rodents, and other animals that spread such diseases. *—R. Monastersky*

Immune blockade impedes blood poisoning

Each year, roughly a half million people in the United States come down with sepsis—blood poisoning that is usually caused by bacteria. The consequences can be dire: One-third to one-half of these patients die from the disease, despite massive doses of antibiotics.

The body doesn't handle sepsis well in part because key white blood cells called neutrophils, whose job it is to destroy bacteria in the blood, tend to shut down when it strikes. Researchers have now engineered an antibody that blocks this neutrophil deactivation in rats with sepsis, extending their survival. The research, reported in the July NATURE MEDICINE, suggests that a similar antibody might work in human disease.

Sepsis, also called septicemia, is a blood infection that can arise from trauma or disease. In past centuries, plagues, battle wounds, and unsanitary surgery caused many cases.

Neutrophil deactivation in sepsis stems from a tragic misfire in the complement system, a complex cascade of protein interactions that guides many immune responses. In a normal immune response, some complement proteins activate neutrophils to combat bacteria.

Scientists became curious, however, when they found large amounts of a complement-protein fragment called C5a attached to neutrophils in blood from people with sepsis. While C5a normally incites neutrophils to do battle, too much of it shuts them down, says study coauthor Peter A. Ward, a pathologist at the University of Michigan in Ann Arbor.

Despite the complement system's apparent role in sepsis, many scientists have hesitated to tamper with these proteins because their immune functions are critical, if poorly understood, he says. Changing or blocking one protein risks upsetting the balance of the system.

Nonetheless, by devising an antibody that blocks the action of C5a, Ward and his colleagues have ventured into the complement realm. C5a breaks off from a complement protein called C5. The antibody that the researchers engineered recognizes C5a and binds to it—preventing the overload of C5a that would deactivate neutrophils. However, the antibody doesn't recognize C5a until it splits from C5 and so doesn't interfere with that protein's normal function.

"We developed an antibody that turned out [to be] very fortuitous," Ward says.

Preserved neutrophil function greatly aided rats in the study. The researchers perforated the large intestine in 43 rats, causing sepsis to develop. Of 10 rats getting the new antibody that blocks C5a, half survived beyond 10 days, Ward says. Nineteen of 21 rats receiving another antibody died within 8 days, and 12 rats getting no antibody all died within 5 days.

"The data in this paper are very impressive," says Kevin J. Tracey, a neurosurgeon at North Shore University Hospital in Manhasset, N.Y. "It's an important study that could lead to . . . development of new therapeutics for sepsis." Indeed, Ward and his colleagues are now trying to devise an antibody to use against human sepsis. *—N. Seppa*