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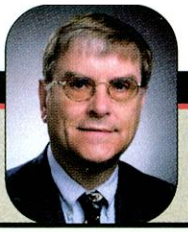
Robots confront disaster



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Academic freedom in Austria

EMERGING DISEASES

New Arenavirus Blamed for Recent Deaths in California

Hemorrhagic fever. The words conjure up images of people in far-off places dying horrific deaths from diseases like Ebola and Lassa fever. Now, researchers say a similar viral disease is endemic—but at very low levels—in the western United States. Last week, the California Department of Health Services announced that a recently discovered virus carried by wood rats and pack rats killed a 14-year-old girl in April; moreover, the department says, there's strong evidence that the virus has caused at least two other deaths within the last 14 months.

The agent, called the Whitewater Arroyo virus, probably infects humans when they inhale aerosolized rat urine. Hantaviruses, another family of rare viruses carried by rodents, infect people by a similar route. Although the evidence isn't airtight yet, researchers say two of the three patients' symptoms—high fever, internal bleeding, and liver problems—suggest that the new disease is indeed a hemorrhagic fever. If the Whitewater Arroyo virus is the culprit, that would be true to form: The virus is an arenavirus, a family that includes Lassa as well as several South American viruses known to cause hemorrhagic fever.

"People don't need to be alarmed," says Carol Glaser, an infectious-disease physician at the state's Viral and Rickettsial Disease Laboratory in Berkeley. "We think this is a rare event." At this stage, researchers don't know how widespread the virus is: So far, it has been found in rodents in six western states. Nor do they have any idea how many people infected with the virus go on to develop disease. Even so, Glaser and others suspect that more people may have succumbed to the disease in recent years—which is why they plan to go back and look at blood and tissue samples from patients who died of unexplained illnesses that bear some hallmarks of hemorrhagic fever.

Some arenaviruses are treatable with a drug called ribavirin, raising hopes that future patients may be saved if the disease is diagnosed in time. "It's not like with hantavirus, where you can only sit by the bedside and hope to God they get through it," says Charles Fulhorst, a virologist at the University of Texas Medical Branch (UTMB) in Galveston, who worked with Glaser to nail down the new virus as the culprit. "We may actually be able to do something." In addition, other arenaviruses have been known to cause secondary infections when hospital workers come into contact with blood from infected patients, which can occur easily because they're often bleeding extensively, says Robert Tesh, also of UTMB. Patients with hemorrhagic fever–like symptoms should probably be handled with extra care, says Tesh, who has studied South American arenaviruses such as Guanarito and Junin, which cause Venezuelan hemorrhagic fever and Argentine hemorrhagic fever, respectively.

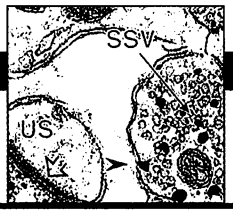
Rat reservoir. Wood rats carry the newly discovered Whitewater Arroyo virus, which is thought to resemble other arenaviruses, such as Cupixi *(inset)*.

North America had seemed blissfully free of dangerous arenaviruses until now. Although there are at least 14 arenaviruses known in South America, four of them deadly, the only previously discovered North American member of the family—the Tamiami virus, found in cotton rats in South Florida in 1970—doesn't seem to make anyone sick. But in 1996, Fulhorst, then at the Centers for Disease Control and Prevention (CDC) in Atlanta, discovered the Whitewater Arroyo virus—named after the site in New Mexico where it was first found—in several rat species of the genus *Neotoma*. Over the past 3 years, Fulhorst, working with rodent-control officials in several states, discovered the virus in western Oklahoma, Colorado, Utah, Texas, and California. Explains Fulhorst: "The next question then became, Does it also make people sick?"

The first clue came last year, when Glaser's lab was asked to test a blood sample from a middle-aged woman from Riverside County, east of Los Angeles, who had died in June 1999 of a disease resembling hantavirus pulmonary syndrome. She tested negative for hantavirus, as well as for dozens of other infectious agents. The case might have gone into the record books as another undiagnosed fatality if it hadn't been for Michelle Jay, a veterinarian at the lab who happened to be familiar with Fulhorst's work. She suggested that he test the sample for the arenavirus. Using the polymerase chain reaction, Fulhorst soon found traces of the virus's genetic material in the woman's blood, suggesting she died from an infection. Fearing the test might be a false positive, Fulhorst and Glaser decided not to go public yet.

Stronger evidence came when a 14-year-old girl in Alameda County, in Northern California, died with similar symptoms in April. In her blood samples, Fulhorst not only found traces of the virus's RNA that matched that of the Whitewater Arroyo virus found in Californian rats; he also isolated the virus itself—sufficient proof, Fulhorst says, that it was indeed the culprit. And just when the team was preparing to announce those findings in June, a 30-year-old woman died of similar symptoms in Orange County.

CREDITS: (LEFT TO RIGHT) R. SIMPSON/VISUALS UNLIMITED; C. S. GOLDSMITH AND M. D. BOWEN/CDC



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Glutamate transporter found at last

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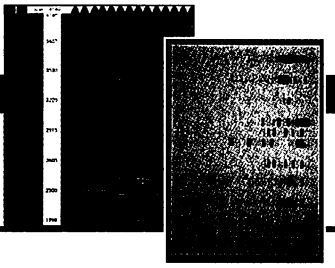
Special Report: Forensic science



Again, Fulhorst found genetic traces of the virus; he is now trying to isolate the agent itself from the samples—a task that could take a couple of weeks. But with one case nailed down and strong evidence in two others, the researchers did not want to wait to go public. "A new patient may be walking into the hospital next week," says Fulhorst.

"From what I've seen, the data look pretty compelling," says Thomas Ksiazek, acting chief of CDC's Special Pathogens Branch. Although the disease doesn't seem to pose a big public health threat, he says, CDC plans to step in by developing new diagnostic tests and disseminating them to state labs, and by putting together a case definition so that doctors will know what to look for when they see possible new patients. The agency will also assist in finding out how widespread Whitewater Arroyo infections may be by looking at old blood and tissue samples from California and other states, says Ksiazek. Meanwhile, the one confirmed case emphasizes the importance of avoiding rodent-infested places or taking precautions to prevent exposure to rat urine—a CDC warning already in place since the Sin Nombre virus, a hantavirus, was discovered after an outbreak in 1993. Since then, more than 250 people have come down with hantaviruses.

The new finding also drives home a point infectious-disease experts have been making for years: If they have the resources to monitor for new viruses and track their distribution before they cause disease, researchers are much better prepared when an outbreak does occur. During the 1993 Sin Nombre outbreak in the Four Corners area, says Fulhorst, no one had a clue what the causative agent was, and a small army of epidemiologists, microbiologists, and toxicologists was sent in to find out in a rush. Only afterward did researchers realize that the Sin Nombre virus had been around, occasionally killing people, for years. "With this one, it's exactly backward," says Fulhorst. "We said we thought there may be arenaviruses out there; we showed they were in the rats; and now we're saying they're causing disease."

There may be much more to discover this way. During his rodent surveys, Fulhorst says he found a third North American arenavirus, this one in deer mice in California. The agent, whose discovery hasn't been published yet, has been called the Bear Canyon virus; whether it makes people sick is, at this point, anybody's guess. **–MARTIN ENSERINK**

AGRICULTURAL BIOTECHNOLOGY

Monsanto Donates Its Share of Golden Rice

Monsanto Co. has agreed to provide royalty-free licenses to speed up work on a genetically modified rice that could alleviate vitamin A deficiency around the world. Researchers welcomed last week's announcement, but warn that a thicket of intellectual property claims surrounds the technology and that significant legal hurdles remain before the rice can become widely available to farmers in developing countries.

"Monsanto is the first company with the good will to offer this technology free for humanitarian purposes," says Ingo Potrykus, a plant molecular biologist at the Institute for Plant Sciences of the Swiss Federal Institute of Technology in Zurich. "I hope I can use this to convince other companies to give up their intellectual property rights," adds Potrykus, who developed the variant in collaboration with Peter Beyer of the Center for Applied Biosciences at the University of Freiburg in Germany (*Science*, 13 August 1999, p. 994; and 14 January, p. 303). Monsanto CEO Hendrik Verfaillie says his company, a subsidiary of Pharmacia Corp., is taking this step "to minimize the time and expenditure associated with obtaining licenses needed to bring 'golden rice' to farmers and the people in dire need of this vitamin."

Potrykus's team transferred into rice the multiple genes needed to create a synthesis pathway for β-carotene, which the body converts into vitamin A. It marked the first time a trait requiring multiple genes had been transferred into a plant. The enriched rice, which has a golden hue, promises to help alleviate a widespread public health problem: vitamin A deficiency, which afflicts 400 million people and can lead to vision impairment and increased susceptibility to disease.

Before the promise can be realized, however, the β-carotene pathway must be transferred to the different varieties of rice grown in each region. Potrykus's group has tried to hasten the process by offering to make its germ plasm and related technology freely available. The offer drew interest from several national rice research labs, as well as the International Rice Research Institute (IRRI) in the Philippines.

But claims of intellectual property rights have kept the technology bottled up in Potrykus's lab. Two outside studies have found that between 25 and 70 proprietary techniques and materials are involved in the gene transfer. Potrykus says Monsanto's most important claim is on the 35*S* promoter, which boosts the expression of the genes introduced into the rice. That change makes possible a high level of β-carotene synthesis.

But other important pieces of the puzzle lie outside Monsanto's control. Incorporated into the golden rice, for example, are two "bits of DNA" acquired, says Potrykus, under separate agreements that require the donors' consent to be passed on to third parties. The agreements have prevented him from distributing the germ plasm to any of the rice breeders interested in working with it.

Potrykus has spent a year negotiating with the two companies that hold rights to the DNA to enable the technology to be used by public-sector research groups. He declined to identify the companies to avoid jeopardizing what he calls a "delicate stage" of the negotiations, which he hopes will be concluded "within 2 months." Potrykus and others hope that Monsanto's announcement—made at an agricultural

CREDIT: MONSANTO CO.

Golden gift. Monsanto is making available its technology on new, vitamin-rich rice aimed at improving nutrition in the developing world.