

# Army Scientists Isolate Deadly Virus

In early August, Army virologists isolated and cultured a deadly hantavirus likely associated with a disease outbreak that began in the southwestern United States last May. However, the viral isolate came not from the Southwest, but from the Deep South.

Researchers isolated the virus in autopsied tissues from an 8-year-old Mississippi girl, says Peter B. Jahrling, chief scientific adviser of the Army Medical Research Institute of Infectious Diseases in Frederick, Md. The girl died May 25, after being ill for less than a week.

Since the initial Southwest outbreak, similar hantavirus-related deaths have occurred sporadically across much of the United States. Researchers at the Centers for Disease Control and Prevention (CDC), in Atlanta, have identified cases not only in the Southwest, but also in rural parts of the West, the Northwest, and the Southeast. At least 25 people have died and the CDC is investigating another 55 suspicious cases in 24 states.

The sudden outbreak (SN: 6/12/93, p.374) and the growing geographic distribution of cases raise the question of whether this is an emerging, rapidly spreading viral disease or a long-time killer that previously went unnoticed. Having an isolate of the virus in hand may help researchers begin to answer that question, Jahrling says.

Although other researchers have yet to replicate the Army results, Gregory Gurri Glass, an infectious disease expert at Johns Hopkins University School of Hygiene and Public Health in Baltimore, says that the results "look fairly conclusive."

If the results hold up, the viral isolate should be useful in a number of ways. "Materials from the virus could be used to develop accurate diagnostic tests," says Stephen Ostroff, an epidemiologist with the CDC. Currently, doctors diagnose the disease primarily by assessing a patient's symptoms. However, these symptoms are often deceptive. What appears to be a common, flu-like ailment can rapidly turn into a catastrophic failure of the lungs. Having a definitive diagnostic test available when a patient walks into a clinic could save lives.

Researchers could also use the viral isolate to study the disease in animal models. Such studies may help explain why this disease seems so radically different from that caused by hantavirus strains in Asia and Europe, Ostroff says. Those strains cause hemorrhagic fever along with kidney disease; the new U.S. variant seems primarily to attack the lungs. One strain, common in China, infects about 100,000 people annually,

killing about 10 percent. The Southwest type appears, at least initially, to have a mortality rate of about 70 percent.

"The major groups of rodents each have hantavirus, and each virus seems to be different," Glass notes. Urban rats, country mice, and meadow voles are among the rodent groups that carry the virus. And, although a milder strain of hantavirus found in city rats causes mortality rates of up to 3 percent in humans, last spring's disease outbreak was the first known instance of the hantavirus causing acute respiratory infection in the United States. Rural deer mice appear to carry the Southwest strain.

Deer mice range across most of the continental United States — except the Southeast. Therefore, an unidentified rodent species must have carried the virus that infected the Mississippi girl, Glass says. Furthermore, initial genetic studies of the Mississippi virus, using polymerase chain reaction, indicate that it may be slightly different from that found in the Southwest, says Jahrling, who isolated the virus.

The finding of yet another hantavirus variant would not be surprising, Glass

says. However, only close scrutiny of the isolate's genetic material will reveal whether it is distinct, where it came from, and whether it is new. If new, it may be the result of recombination between separate hantavirus strains or the mutation of an existing one.

To assess these possibilities, scientists will need to isolate and compare viruses from different parts of the country. "If all the isolates are the same, the implication will be that it is spreading and extremely virulent," Jahrling says. However, a finding of multiple, closely related variants would suggest that rodents have carried the virus for some time, long enough for it to have differentiated in separate populations, he says.

In that case, rather than the virus being new, "maybe the circumstances are new and the conditions are right to suddenly start epidemics," Glass says.

It is also possible, he suggests, that the virus has been causing death and disease for years, something public health officials are only now discovering. Perhaps, Glass says, "the only reason we haven't found it before is we didn't go looking."

—B. Wuethrich

## Unstable enzyme underlies inherited ALS

*In March, researchers announced they had pinpointed the faulty gene in the familial form of amyotrophic lateral sclerosis (ALS), often called Lou Gehrig's disease (SN: 3/6/93, p.148). Mistakes in that gene's sequence lead to alterations in an enzyme called superoxide dismutase.*



*Typically, this enzyme becomes active when two identical "subunits" link up (as shown) to form a "dimer" and disarm potentially harmful oxygen free radicals by converting them to hydrogen peroxide or molecular oxygen.*

*Using X-ray crystallography and computer graphics techniques, John A. Tainer and his colleagues at the Scripps Research Institute in La Jolla, Calif., found that enzyme alterations (the most common in red; others, in gold) do not affect the sites (orange and blue) where this chemical conversion occurs. Instead the alterations weaken the dimer linkage, causing it to fall apart easily. Thus the enzyme scavenges fewer free radicals, says Teepu Siddique of Northwestern University Medical School in Chicago.*

*He and his colleagues measured the enzyme's activity in the red blood cells of 15 ALS patients from seven families with inherited ALS. The enzyme worked between one-third and one-half as well as normal, they and collaborators from several institutions, including Scripps, report in the Aug. 20 SCIENCE.*

*"Now we know this disease is caused by free radicals," Siddique says. These results strongly suggest that therapy involving this enzyme or some surrogate compound (not simple antioxidants such as vitamins) may help slow both the inherited and noninherited forms of the illness.*

Tainer/Scripps