EPIDEMIOLOGY

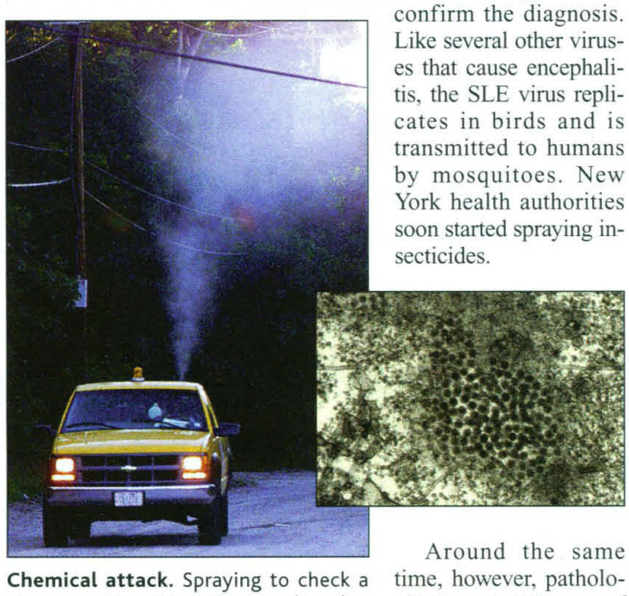
Groups Race to Sequence and Identify New York Virus

Two scientific groups are racing to sequence the DNA of the lethal virus that sowed panic in New York City last month, hoping to pin down its precise identity—which at this writing is still uncertain. The virus triggered an outbreak of encephalitis that killed four people and sickened at least 33 others in New York and surrounding communities. The culprit looks like one of the flaviviruses, a family of agents that cause dengue and yellow fever as well as encephalitis. But experts are not sure exactly which member of the family is to blame. After a false start, they are now moving with caution.

Shortly after the first cases emerged in late August, the Centers for Disease Control and Prevention (CDC) in Atlanta announced that the outbreak was St. Louis encephalitis (SLE), caused by a flavivirus endemic in the southeastern United States. The CDC changed its diagnosis 2 weeks ago, however, after genetic tests indicated the virus might be the so-called West Nile virus, endemic in Africa. Since then, the agent has been provisionally called "West Nile–like" virus. But a competing research group led by molecular biologist Ian Lipkin of the University of California, Irvine, believes it may be more closely related to the Kunjin virus of Australia and Southeast Asia.

Lipkin's group and a CDC team led by Duane Gubler are both sequencing the virus's entire genome. Although Kunjin and West Nile are about 80% the same genetically, the differences between them are important to researchers trying to determine how the virus ended up in New York. A second reclassification would be awkward for the CDC, which has already drawn fire for sticking to a faulty diagnosis for weeks. "In retrospect, it's embarrassing," says Jack Woodall, an emerging diseases investigator at the Federal University of Rio de Janeiro, Brazil.

When the first patients in New York City came down with fever, swollen glands, and headaches, the symptoms seemed consistent with SLE. Tests of antibodies appeared to confirm the diagnosis. Like several other viruses that cause encephalitis, the SLE virus replicates in birds and is transmitted to humans by mosquitoes. New York health authorities soon started spraying insecticides.



Chemical attack. Spraying to check a virus resembling West Nile type (*inset*).

Around the same time, however, pathologist Tracy McNamara of the Bronx Zoo noticed that birds there were dying from what looked like a neurological disorder. McNamara sent tissue samples to the U.S. Department of Agriculture (USDA) National Veterinary Services Laboratories in Ames, Iowa. The USDA isolated and cultured the virus, ruling out some of the usual suspects of sudden bird mortality, such as avian influenza and Newcastle disease. But the lab was unable to make a final identification, and on 20 September it sent the virus to CDC's lab for insect-borne diseases in Fort Collins, Colorado. Suspecting a link to the human epidemic, CDC started sequencing snippets of the viral genome and concluded that the New York birds were dying from something that resembled the West Nile virus, which had never before been found in the Western Hemisphere. Soon afterward, the CDC confirmed that the human patients were infected with the same virus. Fort Collins researchers think the close genetic resemblance between the SLE and West Nile viruses produced a high degree of cross-reactivity in blood tests, which led scientists astray.

As CDC was examining the virus from birds, Lipkin's lab, which had been asked by New York state health authorities to conduct an independent investigation using tissue from patients, also ruled out St. Louis encephalitis. Genetic tests suggested the agent was Kunjin virus. Based on the sequence of three regions, says Lipkin, who will publish his first results in this week's *Lancet*, the New York isolate shows 86% to 87% similarity with the Kunjin virus, and only 80% to 82% with West Nile. Lipkin is calling it the Kunjin/West Nile–like virus for the moment. Both the CDC and Lipkin expect to have the entire genome sequenced in the next couple of weeks. "We won't know what virus it is until we have that complete sequence," says virologist Vincent Deubel of the Institut Pasteur in Paris, France. Some researchers were miffed that the CDC announced its own findings without mentioning the contributions of the USDA and Lipkin. "We were a little bit astounded," says the USDA's Beverly Schmitt.

The confusion hasn't in any way hampered attempts to control the outbreak; the St. Louis, West Nile, and Kunjin viruses are all transmitted by mosquitoes, and spraying of insecticides is a good preventive measure. But some experts say that CDC could have avoided its mistake by isolating the virus and ruling out other candidates more quickly. "They didn't do anything wrong, but they didn't do all the right things," says Charles Calisher, a former head of CDC's Fort Collins lab who is now at Colorado State University. But CDC spokesperson Tom Skinner says that the lab followed standard protocols by first considering four or five U.S. types of encephalitis. "West Nile virus has never been seen before in the United States," says Skinner, "so why would we have thought that this would be the first time?"

Researchers are still trying to figure out where the virus came from. One possibility is that an infected person arrived in New York and was bitten by a mosquito there, which transmitted the virus through birds to other New Yorkers. But the zoo epidemic prompted New York health authorities to focus on the possibility that recently imported birds

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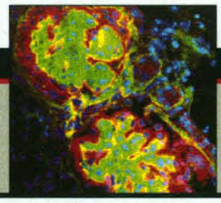


brought the virus. It's also possible that the virus was lurking in or around the city for years without being noticed, says Woodall.

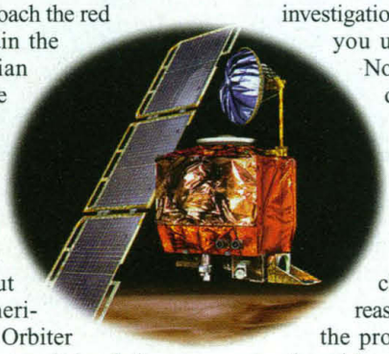
The disease may disappear from view as temperatures drop and mosquitoes die. But it's unknown whether infected eggs might hatch next year, or whether migratory birds might spread the disease to southern U.S. states this fall—a worrying possibility because those states have mosquitoes all year round. Woodall warns: "It could become established in the South if it gets there."

–MARTIN ENSERINK

PLANETARY SCIENCE

More Than Missing Metric Doomed Orbiter

Mission planners have long postulated a martian gremlin who lies in wait for unsuspecting spacecraft that approach the red planet. How else to explain the atrocious record of martian exploration? Humans have launched 28 missions to Mars, but only 9 or 10 could be considered successes. Most of the failures—at least 14 out of 16 attempts—befell Soviet and Russian missions, but last month it was the Americans' turn. Mars Climate Orbiter (MCO) swooped in too low as it headed for Mars orbit, dipped too deeply into the atmosphere, and was never heard from again. Early investigations put the blame on a mismatch of units, with one team of flight engineers reporting measurements in English units that another team assumed were metric.



While that kind of snafu may be as scary as any gremlin, observers are pointing to a variety of problems with MCO. The metric-English confusion was one of them, says an engineer familiar with the MCO navigation operation, "but I think there were other [problems] along the way, and all of them together caused the loss." Whatever the causes, three review panels are rushing to sort them out well before Mars Polar Lander, which may be susceptible to some of the same problems, arrives on 3 December.

The metric-English problem arose between the MCO's navigation team at the Jet Propulsion Laboratory (JPL) in Pasadena, California, and the spacecraft team at Lockheed Martin Astronautics in Denver. The JPL team determined from tracking data where the spacecraft was and how its trajectory should be corrected. The Lockheed Martin team told the spacecraft how to fire its thrusters to make those corrections. Besides nudging the trajectory, the thrusters had to blast once or twice a day to counteract the twisting effects of sunlight hitting the single, off-center solar panel. Inevitably, those adjustments or "momentum dumps" would nudge MCO ever so slightly off course in some random direction. When the Lockheed Martin team told the navigators how much force the thrusters had applied to the spacecraft, they used units of pounds; JPL assumed the data were in newtons, a smaller unit of force. Applying those forces to the tracking data, JPL navigators concluded that MCO was closer to its intended course than it indeed turned out to be.

How such confusion arose is still under investigation. "The general rule is you use metric," concedes Noel Hinners, vice president for flight systems at Lockheed Martin Astronautics in Denver. NASA began to metrify its operations in the 1970s, he notes, and JPL uses metric exclusively, but "for some reason [some companies in] the propulsion industry have continued to use English units." According to sources, the use of metric units for MCO was spelled out in a written agreement between JPL and Lockheed Martin.

Although the use of pounds may have been a fatal error, other factors could have been crucial as well. Momentum dumps occurred frequently for MCO because the spacecraft carried only a single solar panel, placed off center. According to John McNamee, an MCO project manager at JPL, that solar panel arrangement was necessary to give the spacecraft's two instruments, a camera and a radiometer that required wide fields of view, unobstructed looks at Mars. In contrast, the NEAR spacecraft on its way to the asteroid Eros has a symmetrical design and need make no momentum dumps at all.

Once the units errors slipped in, they were difficult to discern in MCO's behavior, navigation specialists note. Tracking data reveals only what the spacecraft is doing in the line of sight between Earth and the spacecraft, so that subtle shifts of the spacecraft in the plane perpendicular to the line of sight, like those imparted by momentum dumps, take time to show up. Only in the last days, as Mars bent MCO's trajectory toward itself, would the changing angle between the line of sight and the trajectory let such subtle changes become more obvious.

In the end, the tracking data did throw up a red flag, indicating that the spacecraft might be coming in below its 140-kilometer target point above the surface. The navigation team recommended raising the low point of the approach—if MCO came in too low, probably around 85 kilometers, atmospheric drag would destroy it—but JPL managers decided against it. "We were considering that," says project manager for operations Richard Cook of JPL, "and we chose not to do that." Cook will be discussing his reasons only with investigators, but some lessons learned are already obvious. The burden of "eternal vigilance" cannot be avoided, says Hinners. "You can never, never take anything for granted." Especially with Mars Polar Lander—and several more missions—getting ready to run the gremlin gauntlet.

–RICHARD A. KERR

NUCLEAR ACCIDENT

Special Treatment Set For Radiation Victim

As life returned to normal this week in Tokaimura, the site of Japan's worst ever nuclear accident, the worker who received the highest dose of radiation was being readied for an experimental procedure using blood stem cells in an attempt to save his life. Meanwhile, government and police investigators were gathering evidence expected to result in charges of criminal negligence

Helping hands. Medics transport plant worker to the hospital after the Tokaimura accident.

CREDITS: (TOP) JPL/NASA; (RIGHT) KYODO NEWS AGENCY/UPI