

# Hidden Worlds Collide

## How one deadly epidemic flushed another from hiding

By STEVE STERNBERG

**V**eteran trainer Vic Rail had never seen so many horses so sick. Fourteen of the 21 thoroughbreds in his Brisbane, Australia, stable could scarcely breathe. A pregnant mare had died, blood spouting from her nostrils.

Rail invited government veterinarians to examine the horses, but they were as perplexed about the ailment as he. Moreover, the 49-year-old trainer and one of his stable hands—a 40-year-old who had comforted the dying mare—had some of the initial symptoms of the horses' disease.

Rail died of pneumonia after spending 6 days in Brisbane Royal Hospital's inten-

had never seen before. The viruses also turned up in tissue from Rail's kidneys.

The researchers named the microbe Equine Morbillivirus (EMV) and published their results in the April 7, 1995 SCIENCE. Their next challenge was to find out where the virus normally resides. Researchers soon identified its host as the fruit bat, also known as the flying fox.

Then, while testing a bat for EMV, they apparently found something else, one of the most dread viruses known to man—rabies.

**A**t that moment in the spring of 1996, Australia and Antarctica were considered the only two rabies-free continents in the world. Australia had had a few brushes with the virus in animals and people who had been infected elsewhere; the only possible exception was a Tasmanian child thought to have been bitten by a rabid dog in 1867.

Rabies strikes with the stealth of a practiced assassin, lying dormant in the body for weeks, even years before any symptoms appear. Victims typically become depressed, restless, and feverish. Soon, their malaise turns to aggressiveness. A powerful thirst sets in, yet drinking even a swallow of water becomes a torment, causing inflamed nerves in the throat to constrict in painful spasms. Sufferers recoil from water, a reaction so pronounced the disease has been called hydrophobia.

Although the lethality of rabies seems self-defeating, since any virus that kills its host ultimately destroys its own environment as well, the course of the disease is part of the microbe's survival strategy. The rabies virus can infect someone only through a break in the skin—the kind that occurs with a bite. Insane, aggressive individuals are more inclined to bite, which suits the virus perfectly.

"No other disease so completely manipulates its stricken host, while barely leaving a trace of its presence," veterinarian Cynthia Mills asserts in the January-February THE SCIENCES.

The stage of the rabies life cycle in

which the virus hides in the victim's tissues is known as the eclipse phase. Where the virus goes and what it does during this phase remain uncertain, says Charles E. Rupprecht of the rabies laboratory at the Centers for Disease Control and Prevention in Atlanta.

Ultimately, Rupprecht says, the virus sheds its outer layers and injects its genetic material—five genes made of ribonucleic acid (RNA) bound with protein—into the host's nerve cells.

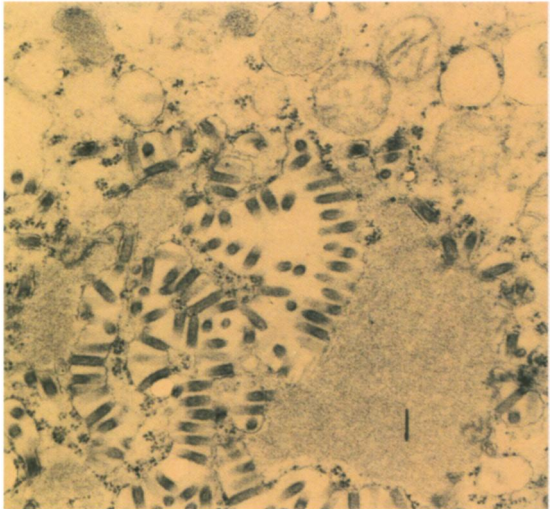
The virus then creeps from nerve cell to nerve cell toward the brain at a pace of 10 millimeters a day, Mills reports. Once it arrives, it begins to replicate. The exploding population of viruses causes encephalitis, an inflammation of the brain marked by swollen, leaky blood vessels. The virus makes its way back down the nerves to the salivary glands, where it awaits entry into a new host.

For many people, rabies conjures up an image of snarling, slavering, insanely vicious dogs. Packs of abandoned dogs are ideal hosts for the rabies virus. In developed nations, however, the required vaccination of pets has virtually eliminated this threat.

On the weight of this evidence, many people think the human disease has ceased to be a problem. In the United States, fewer than two people, on average, die of rabies each year. Yet this benign picture is incomplete. Worldwide, 40,000 to 100,000 people, most of them in developing nations, die of rabies annually.

Deprived of its canine hosts, the rabies virus takes up residence in coyotes, skunks, raccoons, and bats. One recent study linked 15 of the 17 U.S. rabies deaths in the last 15 years to insect-eating bats. Among the victims was a 4-year-old girl in Washington whose parents found a bat clinging to the ceiling of her bedroom. The girl insisted she had had no contact with the bat, so doctors did not treat her—with tragic consequences.

Bats are wide-ranging travelers. North American species regularly visit Bermuda, 600 miles away. If a rabies virus entered the bat population in Indonesia or Southeast Asia, it could easily turn up in Australia.



Classic rabies virus (magnified 23,000 times) in a dog's brain appears as bullet-shaped particles budding from Negri bodies, abnormalities in nerve cells caused by rabies infection. No visible differences exist between classic rabies and the Australian Lyssavirus.

sive-care ward. His stable hand was more fortunate. He recovered, slowly.

The outbreak in September 1994 prompted researchers at the Australian Animal Health Laboratory (AAHL) in East Geelong to investigate the mysterious illness. In the horses' tissues, they found bloated cells clinging to the interior walls of blood vessels in all the major organs. Within these cells, they found viruses they

Several weeks after Rail's death from EMV, an Australian wildlife enthusiast found a 5-month-old black fruit bat lying under a fig tree. She took it to the New South Wales Department of Agriculture in Wollongbar to find out whether the creature had a contagious disease. There, veterinary pathologist Graeme C. Fraser killed the bat and sliced it open. The bat had encephalitis.

Fraser knew that a 35-year-old farmer named Mark Preston and two horses had recently died in the only other known outbreak of EMV. Preston lived near the woman who had brought in the bat. Moreover, unlike Rail and the other victims of EMV, Preston had encephalitis.

Intrigued, Fraser asked Peter T. Hooper, a veterinary pathologist at AAHL, to test the bat's brain tissue for EMV. A positive test would suggest that encephalitis is a typical complication of EMV.

The EMV test was negative.

Then, because the bat had encephalitis, the two men decided to test it for rabies. "We knew bats were important animals insofar as rabies and rabieslike diseases were concerned," Hooper says, "but we also knew a positive result was highly unlikely."

The test for rabies, like the test for EMV, relies on antibodies. The first antibody seeks out the rabies virus; the second bears a chemical, biotin, that attaches to the first and turns brown when the enzyme peroxidase is added. If tissues don't contain the rabies virus, the antibodies won't stick and the tissue keeps its normal color.

When Hooper put his eye to the microscope and saw the brown stain, he felt the hairs on the back of his neck prickle. "I was excited and horrified at the same time," he says. "Rabies is a terrifying disease, and this was the first recognition of rabies or rabieslike disease in Australia."

Keith Murray, head of the AAHL and a member of the team that isolated EMV, contacted CDC to learn how to conduct surveillance for the rabieslike virus and how to protect people from being exposed to it. Murray also asked what the outcome might be if someone were exposed.

The answer came all too soon.

Patricia Paget, a 39-year-old mother of four, liked caring for wild animals and often plucked sick bats from the bush to nurse them back to health. She knew that sick animals could be dangerous, but the risks did not deter her.

In the 2 months before her death on Nov. 15, 1996, Paget was bitten by animals several times—twice by a brush-tailed possum, once by a yellow-bellied sheath-tail bat, and at least twice by flying foxes. Her first symptoms were fever, headaches, muscle aches, dizziness, vomiting, and agitation. Her vision doubled, and her eyes lost their focus. Doctors found her spinal fluid flooded with white blood cells, a sign of central nervous system infection.

On the sixth day of her illness, paralysis set in. Doctors treated her with rabies vaccine, but it was too late. Paget could no longer breathe without the aid of a ventilator. She lapsed into a coma from which she never recovered.

Rabies belongs to a branch of the Rhabdovirus family known as Lyssavirus. Until the AAHL researchers conducted their test, the classic rabies virus was thought to have just four close relatives: Lagos bat virus, Mokola virus, Duvenhage virus, and European bat virus.

The AAHL researchers wanted to add to the Lyssavirus family tree both Fraser's virus and a virus from a bat dissected in 1995 and recently proffered for testing by a Townsville wildlife biologist.

Allan R. Gould of AAHL sequenced the genes of the two viruses and compared them. The 1995 and 1996 viruses were identical, indicating that the virus had been in Australia for at least a year. The virus differed from classic rabies by only 8 percent.

The researchers considered this good news because rabies vaccines, given after exposure but before symptoms appear, might prevent infection by the

new virus. They published their findings in the October-December 1996 EMERGING INFECTIOUS DISEASES.

Fraser named the new rabieslike virus *Pteropid lyssavirus*, after the species of bat in which it was found. It has since been identified in three other species living along more than 2,000 miles of Australia's east coast. Researchers still don't know where the virus came from, when it arrived, or how it reached Australia.

Nevertheless, Chief Australian Veterinarian Gardner Murray told the World Health Organization that since the new lyssavirus differs slightly from classical rabies, "Australia should continue to be regarded as a rabiesfree country."

Paget is the only person who has died of *Pteropid lyssavirus*. Another woman exposed to the virus was treated in time to save her life.

Likewise, EMV has not developed into an epidemic, as was feared. All 14 of Rail's horses, which were found to be infected with the virus, died or were put to death. Tests of 150 men and about 5,000 horses—including 90 from Preston's farm—have turned up no other infections. □

## Unusual cargo sparks U.S. rabies epidemic

Many of the trucks rumbling north from Florida on Interstate 95 in the late 1960s and early 1970s carried Indian River Oranges, grapefruit, sugar, and other produce.

Some carried a livelier cargo—raccoons.

Entrepreneurs were shipping these inviting targets to hunting preserves. At that time, Georgia and Florida were the only states in the nation where rabies was endemic in raccoons. State conservationists knew some of the raccoons were rabid but saw the hunters as an effective instrument of rabies control. The strategy backfired, kindling a rabies epidemic in raccoons that has spread up the East Coast and is now pushing westward into Ohio.

"When we became aware of semi trucks hauling out raccoons, we notified the destination states. A few were interested enough to try to intercept the shipments. Most were not," says Gerald Hoff, who fought animal epidemics for the Florida Department of Health and Human Services and now works as chief of communicable disease control for the Kansas City, Mo., health department.

Last year, raccoons accounted for half of the 7,881 animal rabies cases in the United States, according to a study by the Centers for Disease Control and Prevention in Atlanta. The findings appeared in the Jan. 3 MORBIDITY AND

MORTALITY WEEKLY REPORT.

Although no people have developed rabies from contact with raccoons, the cost of prevention nationwide each year ranges from \$230 million to \$1 billion, CDC researchers reported in the October-December 1995 EMERGING INFECTIOUS DISEASES.

In New York State alone, the number of people vaccinated after exposure to rabies from 1990 to 1995 surged from fewer than 100 to more than 10,000. The series of five shots costs from \$1,500 to \$3,000.

To curb the epidemic, officials in New York, New Jersey, Massachusetts, Virginia, and Pennsylvania are testing the effectiveness of scattering vaccine-saturated raccoon bait along the perimeters of local epidemics. Studies have shown that this creates a swath of immunized raccoons that serve as a sort of firebreak, stopping the infection from spreading further.

With so few human cases of rabies, such activity represents a massive overreaction, argues the National Audubon Society's Edward P. Bruggemann in the October 1992 *BIO SCIENCE*.

"You can forget rabies is a problem [only] because of the amount we spend on rabies control—it's a multi-million-dollar industry," counters Charles Rupprecht, a CDC epidemiologist. "We want to find out if it's feasible to control [rabies] at its source." —S. Sternberg