EMERGING VIRUSES

Cause of Fatal Outbreak in Horses and Humans Traced

"Excellent. Absolutely superb." Those are the words Frederick Murphy, an expert on emerging viruses at the University of California, Davis, used to describe the detective work—published in this issue of *Science*—that ran to earth a previously unknown virus that created a veterinary and medical nightmare in Australia last fall.

On 22 September 1994, health authorities in Brisbane confronted a scenario that's now familiar from a welter of books and movies: A presumed exotic infection was on the rampage. Eleven horses had died of a mysterious disease, and their trainer was also extremely ill, apparently from the same cause. The killer had to be found quickly and steps taken to prevent a plague from descending on Australia.

While that fear never materialized, the initial carnage did trigger a furious search that captured the quarry within a week. On page 94, the Australian team, including Keith Murray, chief of the Commonwealth Scientific and Industrial Research Organization's (CSIRO's) top-security Australian Animal Health Laboratory in Geelong, near Melbourne, and Linda Selvey, a medical epidemiologist at the Queensland health department in Brisbane, describe their find: A previously unknown morbillivirus, a viral group that includes canine distemper virus, seal plague virus, rinderpest virus, peste des petits ruminants, and—the only one previously known to infect humans—the measles virus.

It's not just the pace of the chase that leads to superlatives such as Murphy's; it's the novelty of the virus—now referred to as equine morbillivirus (EM)—and the many mysteries that remain unsolved. "It's as mysterious as Ebola," says Murphy. "We have no idea of where it came from, or where it's going to ... but the odds are it will reappear." And until EM's natural host is identified, he warns, there's no telling where that will be.

Murray first got the warning call about the outbreak on Thursday, 22 September. Tissue samples collected from the horses that had died were rushed from Brisbane across Australia to the CSIRO labs near Melbourne. The cause of the deaths was unknown. One possibility was poison; a more worrisome possibility was that a virulent virus was on the loose. Australia's Consultative Committee on Exotic Animal Diseases, the national network that deals with disease outbreaks in animals, imposed a "category III" alert, its highest emergency category.

By the fourth day of the outbreak, suspicions about a viral pathogen were confirmed. The CSIRO team had a virus growing in culture. A mere day later, they were able to harvest it. When virologist Alex Hyatt examined the virus under the electron microscope, he found it had the characteristic shape of the Paramyxoviridae, a large viral family whose members include the morbilliviruses. Just as the CSIRO team appeared to be gaining on its quarry, however, the race took a much-feared twist: Vic Rail, the horses' trainer, died. Three days after Rail's death, the CSIRO team had a firmer fix on the identity of the new virus. Analysis of its RNA revealed that the virus is a novel morbillivirus.

CSIRO AUSTRALIAN ANIMAL HEALTH LAB

Suited up. Vets working with infected horses wear breathing hoods to protect them from the new virus.

But, in fact, EM has some notable differences from other members of the morbillivirus group. For a start, it looks different, with a very distinct double fringe of projections sprouting from its surface; all other Paramyxoviridae appear to have a single fringe. It is also extremely virulent, killing about 70% of infected horses. EM wreaks its damage by causing cells lining the blood vessels to clump, creating holes in the vessel walls so that they leak into the lungs and other tissue. "Fluid pours into the lungs," says Selvey, and the horse or human "more or less drowns in its own fluid." And whereas other morbilliviruses infect only a single species, EM "was pathogenic to humans and horses," says virologist Frank Fenner of the Australian National University in Canberra. (The CSIRO team confirmed that EM killed Rail by recovering the virus from his kidneys because his lungs were too ravaged.)

The identity of the pathogen wasn't the only thing that the Australian team came up with in a hurry. By the seventh day of the emergency, the CSIRO group had devised a test for antibodies to the virus. Within a month, they surveyed 1600 horses and 90 humans in the vicinity of the outbreak and found that none were infected. With that, the outbreak was officially declared at an end.

Although the Australian team tracked down the new virus at lightning speed, they've had less luck finding its source in nature. Murray speculates that EM benignly infects a native Australian animal and that it causes disease only when it jumps to horses or humans. "But why it has [jumped] to horses 200 years after they were introduced into Australia is a mystery," points out Fenner.

Veterinarians from the Queensland Department of Primary Industry in Brisbane are about to start gathering information that they hope will resolve that conundrum. They plan to catalog every animal species in the Brisbane suburb of Cannon Hill where the first horse become infected and collect blood from representative animals for analysis by the CSIRO labs. They hope that EM's animal reservoir can be pinned down within 6 months—but realize it could take far longer or even prove impossible.

Whenever the answer comes, the hope is that Murray's hunch is right, and that EM turns out to be a harmless freeloader on a native Australian mammal—preferably one that rarely comes in contact with horses or humans. The fear is that if EM naturally infects livestock, Australia's meat and livestock export business would be destroyed as other countries ban imports. Finding that the lethal virus's natural host is a species that occurs outside of Australia would also mean that EM is far more likely to pop up elsewhere.

Either way, EM will almost certainly not be the last new killer to emerge apparently out of nowhere. "There's been at least one major new disease episode each year," says Murphy. "And with more and more human crowding and ecological infringement," he says, the situation is likely to get worse.

In the end, the destruction caused by the Brisbane EM outbreak was relatively minor. The virus killed 13 of 21 horses and one of two humans that became infected naturally, plus four horses that the CSIRO team inoculated in their search for the mysterious agent. At the time, however, the CSIRO team could not predict whether the unidentified agent that was killing horses and humans would go on to wreak havoc of historic proportions. Despite those fears, says Murray, the hunt was exhilarating.

"It's very exciting. It's wonderful," he says. "You can dump all the paperwork into the bin and get down to the real thing." Now all the CSIRO team has to worry about is who gets to play them in the movie.

–Rachel Nowak