INFECTIOUS DISEASE

West Nile's Surprisingly Swift Continental Sweep

Scientists are trying to understand why the West Nile epidemic has exploded this year—and how the virus might be stopped

CAMBRIDGE, MASSACHUSETTS—It's a glorious September morning in this city of brick and ivy—but you'd never know that from where Paul Reiter is working. Wearing waders and brandishing a flashlight, Reiter is making his way through thigh-deep, murky water in one of the city's storm sewers. The concrete pipe, so narrow it forces him to stoop like a hunchback, is a claustrophobe's nightmare. But Reiter doesn't mind. "It smells rather sweet today," he says, cheerfully forging ahead. "It's usually more fecal."

Reiter carefully scans the curved concrete surrounding him with his flashlight: He's looking for mosquitoes that have chosen to overwinter in this netherworld. A mosquito expert at the Centers for Disease Control and Prevention (CDC) currently stationed at Harvard University, Reiter hopes to shed more light on the insects' life cycle—and with it, on the spread of the West Nile virus, which is now taking North America by storm.

When a Los Angeles woman was diagnosed with West Nile last week, it marked the virus's arrival on the West Coast, barely 3 years after it was first detected in New York City. With more than 1400 cases so far and 66 deaths, the 2002 outbreak is also remarkably vicious; there were only 149 cases and 18 deaths in the three previous seasons combined. Adding to the worries, several people recently became ill after receiving blood from a West Nile–infected donor, sparking alarm about the safety of the blood supply.

The outbreak is straining CDC's resources, and it has jolted state and local health authorities as well as academic researchers into action. But researchers have trouble answering some basic questions about the epidemic, such as these: How does the virus spread so fast? Why is this year's epidemic so intense? And how best to control it? Reiter says studying the secret lives of mosquitoes might help find some answers. He's focusing on *Culex pipiens*, an abundant species that transmits the virus among birds in the northern United States.

Cambridge is as good a place as any to study mosquitoes, he says. Elsewhere in the city, Reiter and Harvard entomologist Andrew Spielman have turned a typical street—upscale, tree-lined Lexington Avenue—into an urban field site. Students walk into backyards there every morning to collect mosquito eggs and to hoist pigeons, housed in cages that double as mosquito traps, high into the canopy. The residents—many of them Harvard faculty members and retirees—find it all quite interesting and seem happy to help.

Viral blitzkrieg

The West Nile virus has now been found in 42 of the lower 48 states—up from 28 last year—as well as in four of Canada's 10 provinces. Although most researchers expected it to keep spreading after its surprising arrival in 1999—from the Middle East, genetic studies suggest—"it's really amazing to me how fast it's going," says Laura Kramer, a virologist at the New York State Department of Health in Guilderland.

Tunnel vision. Paul Reiter and Andrew Spielman look for overwintering mosquitoes in a storm sewer in Cambridge, Massachusetts.

CREDIT: GRAHAM GORDON RAMSAY

Part of the explanation is that the virus landed on fertile ground in North America, says David Rogers of Oxford University, U.K. It has been found in over 70 bird species and more than 40 mosquito species, Rogers says—many more than anybody expected. (West Nile is essentially a disease of birds; humans and several other mammals can get sick when they're bitten by an infected mosquito, but they usually do not pass the virus on.)

For its long-haul travel, the virus seems dependent on migratory birds. When these get infected just before taking off, they might still be infectious upon arrival a few days later, ready to seed a new outbreak. But infected mosquitoes might occasionally hitch a ride on planes, trains, or trucks, some researchers speculate, and spark new outbreaks elsewhere. Such insect tourism might explain, for instance, how the Los Angeles patient became infected, because so far, no infected mosquitoes or birds have been found in California. Usually, birds start dropping dead in an area long before people get sick.

Some of the surge in new cases might be due to increased awareness, which leads people with even a mild case to seek medical attention. The fact that only 4.5% of cases have been fatal this year—compared with 14% in 1999—seems to support that theory. But the number of deaths indicates that the outbreak really is more severe. Researchers have no hard data to explain this or the fact that Illinois and Louisiana, with 358 and 238 cases, respectively, are bearing the brunt of the outbreak. Similarly vexing patterns have been found for other, closely related insect-borne viruses, such as St. Louis encephalitis. "People have been trying to study these kinds of epidemics for years," CDC's Lyle Petersen said last week at a press briefing. They've never been very successful, he added.

Nor does experience elsewhere in the world offer much guidance. West Nile is endemic in Africa, from where it has made occasional inroads into southern and eastern Europe, after which it usually withdrew—perhaps because European birds are less susceptible to the virus. But a series of severe outbreaks since 1996—in Romania, Israel, and Russia—has suggested to some that both Europe and the United States are dealing with a recently mutated, more virulent form of the virus. This remains speculation.

Another theory to explain this year's U.S. explosion posits that, like St. Louis encephalitis, West Nile thrives after dry, hot spells of the type many U.S. regions went through last spring and early summer. That seems paradoxical, because mosquitoes breed in water. But a drought concentrates organic pollutants in water reservoirs and creates the eutrophic environment beloved by *C. pipiens* and its southern counterpart, *C. quinquefasciatus*, CDC's Reiter says. Moreover, heat speeds up mosquitoes' life cycles. This could fuel the epidemic among birds, and it would eventual-

Bird Advocates Fear That West Nile Virus Could Silence the Spring

ROCKVILLE, MARYLAND—Ellen Paul is cruising this Washington, D.C., suburb looking for crows. Thousands of the birds once gathered here in raucous roosts every night, but this evening, just three or four are flapping aimlessly above the strip malls as Paul, executive director of The Ornithological Council, a coalition of 10 major bird research groups, peers through her windshield.

The empty sky might be due to West Nile virus. Wildlife researchers are increasingly worried that the virus could take a big toll on wild birds, including some endangered species. It has already killed at least 100,000 crows, blue jays, and other birds, some scientists estimate. And they know it has infected at least 120 North American species, from tiny black-capped chickadees to hefty bald eagles, since it was first detected in New York City in 1999. (For a list, see www.nwhc.usgs.gov/research/west_nile/wnvaffected.html.)

But so far, most reports of absent avians are anecdotal, like Paul's drive-by survey, or are based on sketchy data. But that could change if some researchers get their way. Next week, at the 3rd North American Ornithological Conference in New Orleans, Louisiana, the council is expected to call for a major new federal effort to understand West Nile's impact on wild birds—which would also help scientists study its potential threat to humans.

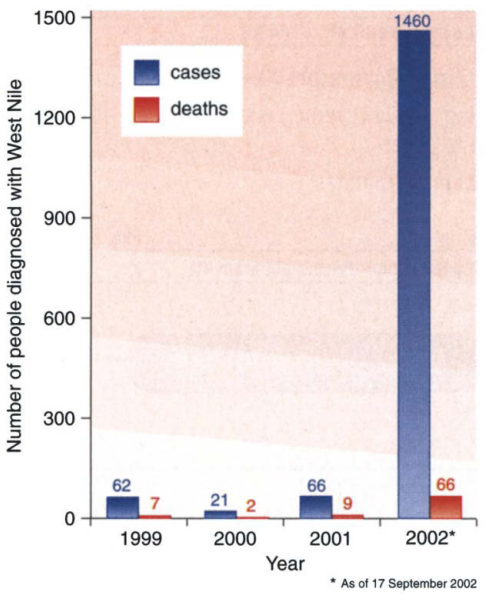
Although finding funding is expected to be a challenge, there are plenty of questions such an initiative might tackle, notes Peter Marra of the Smithsonian Environmental Research Center in Edgewater, Maryland. Researchers strongly suspect that migrating birds carry the virus to new areas, for instance, but it hasn't been proven. The Centers for Disease Control and Prevention (CDC) in Atlanta has funded Marra and colleagues at the New York State Department of Public Health's Wadsworth Center near Albany to screen migratory birds arriving in several Caribbean nations that are free of the virus. If the arrival of infected birds is followed by infections of humans or nonmigratory birds, Marra notes, it would be strong evidence that migrating birds can spread the virus.

It's also not clear whether wild birds need to be bitten by a virus-carrying mosquito to become infected. They might acquire the virus from each other or by eating tainted prey, suggest preliminary laboratory experiments by Robert McClean of the U.S. Department of Agriculture's National Wildlife Research Center in Fort Collins, Colorado, and Nicholas Komar of CDC in Fort Collins. If so, species that feed on sick animals or roost together could be at risk.

Infected. Antibodies for the virus have been found in at least 120 species, including the great horned owl.

Researchers aren't sure which species are most vulnerable to the virus. Infected crows and their corvid kin have suffered nearly 100% mortality in lab experiments, McClean and Komar note, raising fears for endangered crows in the Pacific Northwest and Hawaii. Other kinds of birds, such as gulls and pigeons, have proved relatively resistant. Marra and others are now combing through long-term census data—mostly collected by amateur bird watchers—to see if they can spot any trends in the wild. **–DAVID MALAKOFF**

ly spill over to humans. But there are no hard data to support this, says Harvard's Spielman. And Massachusetts has more cases than last year but fewer mosquitoes. During his trips into the storm sewers, Reiter finds very few of them; a year ago, the concrete would be "furry with mosquitoes."



Leap year. The number of cases exploded in the virus's fourth summer in the United States.

CREDITS: (TOP TO BOTTOM) GEORGE W. ROBINSON/CALIFORNIA ACADEMY OF SCIENCES; SOURCE: CDC

Know your enemy

One of the goals of Reiter's work is to find out how best to control West Nile virus. Despite public opposition to spraying—which runs strong here in New England—many local authorities fight the virus with aerosols of insecticides from trucks. But surprisingly little is known about how useful spraying is, Reiter says, and there are reasons to doubt its efficacy. Spray trucks produce a relatively narrow swath of insecticide, whose dispersion is further blocked by buildings and vegetation. Furthermore, insecticides kill only flying mosquitoes; those that are resting—which might be the majority—survive.

To provide an answer, Reiter and Spielman are comparing mosquito activity in Massachusetts towns where spraying takes place with ones where it doesn't. But Reiter believes that improved control will require a better understanding of the intimate details of the mosquito life cycle. Where and when exactly do they feed? How long do they live, and when do they stop biting and start hibernating? And how does the virus get into overwintering mosquitoes, even though they usually don't bite before retiring to the underworld? Much of this is unknown, and the answers can be surprising.

When Reiter's team suspended caged pigeons a meter and a half above ground level, for instance, few mosquitoes came to bite the birds; but when they were hoisted 15 meters into the air, they attracted 150 to 200 mosquitoes per night. Apparently, the insects are canopy feeders, says Reiter—an important fact if you're trying to kill them.

Still, Reiter acknowledges that *C. pipiens* is just one part of a huge puzzle. South of a line that runs roughly through Atlanta and Los Angeles, *C. quinquefasciatus* is the most important vector, and it has its own peculiarities. *C. pipiens*, moreover, is an important catalyst for the epidemic among birds but only a minor player among the so-called bridge vectors: mosquitoes that bite both birds and mammals and are able to infect humans. Species with such catholic tastes, such as *Aedes vexans*, have different habits and require different control methods.

That complexity makes battling West Nile a bewildering problem—and makes watching the outbreak unfurl fascinating for researchers. "It's like a chess game," Reiter says, as he waits for the opponent's next surprise move. **–MARTIN ENSERINK**