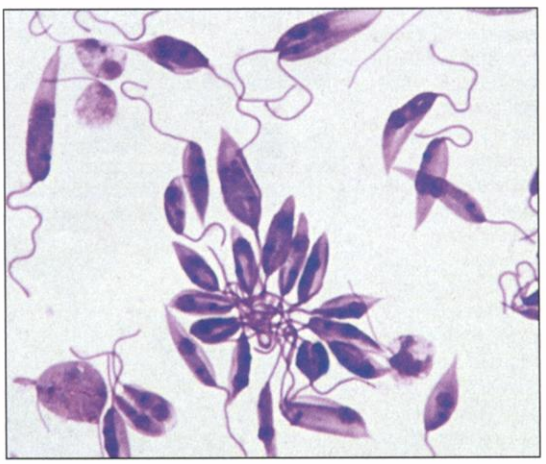
INFECTIOUS DISEASES

Has Leishmaniasis Become Endemic in the U.S.?

Believed to be all but absent from the U.S., the *Leishmania* parasite has infected more than 1000 hunting dogs

Since its surprise attack in New York City last year, the West Nile virus has become the most infamous new pathogen in the United States. But a handful of researchers and public health authorities are now worrying about another new bug on the block. Since last January, they have discovered that hunting dogs in 21 U.S. states and the Canadian province of Ontario are infected with the parasite that causes visceral leishmaniasis—a protozoan thought to be all but absent from the United States. Visceral leishmaniasis is an infection of the liver, spleen, and bone marrow; it can affect humans as well as dogs and can be lethal when untreated.



Unwanted visitor. *Leishmania* parasites can kill.

Nobody is claiming that the disease is about to run riot among the U.S. population. But the widespread outbreak in dogs has experts wondering whether visceral leishmaniasis—which sickens over half a million people yearly in South America, Africa, the Mediterranean, and India—has become an endemic disease in North America. If so, scattered human cases are possible, says Peter Schantz, a researcher at the Centers for Disease Control and Prevention (CDC) in Atlanta: "It's certainly something to be concerned about." To gauge that risk, Schantz and his colleagues are trying to find out how the parasite—identified as *Leishmania infantum* by the Institute of Public Health in Rome, Italy—spreads in North America. And they're still flummoxed by how the parasite could have become so widespread in the first place.

Dogs are *Leishmania*'s main reservoir, although most of them can be infected for years without severe symptoms. The parasite is spread to humans and other mammals by sandflies of the Phlebotomidae family, blood-feeding insects about a fourth the size of a mosquito with a nasty bite. Travelers occasionally return from the tropics with an infection. And sporadic cases of *Leishmania*-infected dogs have occurred in the United States, says Schantz; most were pets brought here by military families returning from a base in the Mediterranean. In the 1980s and early 1990s, a few foxhounds that had never been in an endemic area were also diagnosed with the disease in the southern United States. Nobody could determine how they became infected, but few bothered to look very thoroughly.

That changed in late 1999, when foxhounds at an exclusive hunt club in Millbrook, 130 kilometers north of New York City, came down with symptoms such as bleeding, wasting, seizures, hair loss, and kidney failure. Almost two dozen died, and club members spared no expense to find out what was killing their companions. Because the area is infested with ticks, the club's veterinarian called in Edward Breitschwerdt of North Carolina State University (NCSU) in Raleigh, an expert in tick-borne infections. But Breitschwerdt and his colleagues couldn't find anything in the dogs' blood. When the club finally drove two ailing dogs down to Raleigh for a thorough checkup, however, the researchers found *Leishmania* parasites in the animals' joint fluid.

Since then, researchers from NCSU, CDC, and the Walter Reed Army Institute of Research in Silver Spring, Maryland, with the aid of the Masters of Foxhounds Association of America, have tested almost all of the 11,000 foxhounds in U.S. hunt packs. About 12% of them, from the eastern United States, have antibodies to *Leishmania*—even though the vast majority are asymptomatic. Researchers have also tested almost 50 stray dogs from around Millbrook; none had the disease, says Schantz. In addition, CDC researchers have examined old blood samples from 450 dogs from several states; they too were negative.

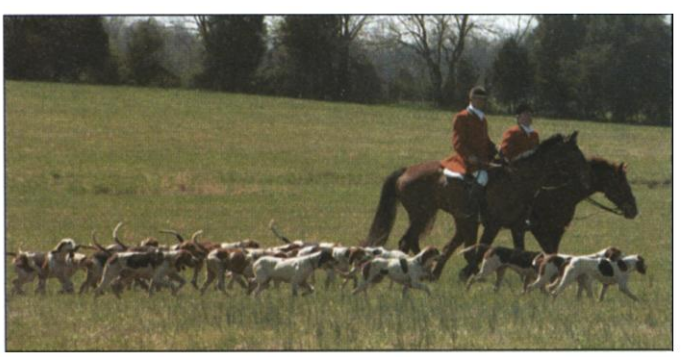
Those findings leave a big riddle: How is the infection transmitted? At least four species of sandflies inhabit the United States, says Edgar Rowton, a medical entomologist at Walter Reed. But they have never been found farther north than New Jersey, hundreds of kilometers south of Millbrook. So how could the disease have ventured as far north as Michigan and Canada? And why didn't other dogs, or even humans, become infected?

Schantz posits an unusual mode of transmission. Foxhounds live close together in hunt club kennels, he points out, and they may infect each other without the help of sandflies—for instance, through sexual contact, or through wounds sustained when they tear through the forest.

Other experts disagree. Although direct transmission between dogs has been shown to occur rarely, concedes Robert Killick-Kendrick, a leishmaniasis researcher at Imperial College in London, he doesn't believe that could explain the high prevalence among U.S. foxhounds. He thinks sandflies are the main vector, just as they are everywhere else. Foxhounds, he points out, often travel for joint hunts, training, or dog shows with other clubs. On one of these visits south, the northern dogs may have been bitten by sandflies, he says. (The New York pack indeed were frequent travelers.) A closer look may reveal that other dogs have been bitten and infected in the south as well, he says.

Another possibility is that there are sandflies in the north that nobody has ever seen, says Rowton, because nobody has looked carefully. Rowton, for one, has studied sandflies from endemic areas extensively but is only now beginning to look at North American varieties. Yet another possibility is that other insect vectors exist.

The debate is not just academic. If sand-



Fly bites dog? Normally, *Leishmania* is transmitted by sandflies, but it's not clear how U.S. foxhounds become infected.

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flies are spreading the disease, there's a chance they may also infect humans; in fact, that may already have happened, says NCSU's Breitschwerdt. Because a few foxhound cases occurred in the 1980s, "we probably uncovered a smoldering epidemic that has been in this country for 20 years or more," he says. Doctors could have easily missed a few scattered human cases of visceral leishmaniasis, whose symptoms include fever, malaise, and weight loss. But there is no reason to panic, says Killick-Kendrick. The *Leishmania infantum* strain isolated from the Millbrook dogs is the same one found throughout the Mediterranean; there, about 20% of all dogs are infected, yet human cases are rare, and an effective treatment exists. Most at risk are people with a weakened immune system. "From what I know from about the Mediterranean, the risk is very low indeed," says Killick-Kendrick. "I would be very upset if a scare erupted about this."

The route of transmission will also determine whether the disease can ever be wiped off the continent. If *Leishmania* is transmitted directly among foxhounds, it might be eradicated by simply culling all infected dogs. In fact, some hunt clubs have already started putting down their sick animals. But if sandflies are involved, they have likely already infected other dogs, foxes, or coyotes, making it impossible to stamp out *Leishmania*. "That's the fear," says Breitschwerdt. "If the disease has become endemic in the United States, then we can't eliminate it, and we'll have to live with it." **–MARTIN ENSERINK**

MATHEMATICS

Taking the Measure of the Wildest Dance on Earth

By exploiting the symmetry of randomness, three mathematicians have revealed the geometric underpinnings of Brownian motion

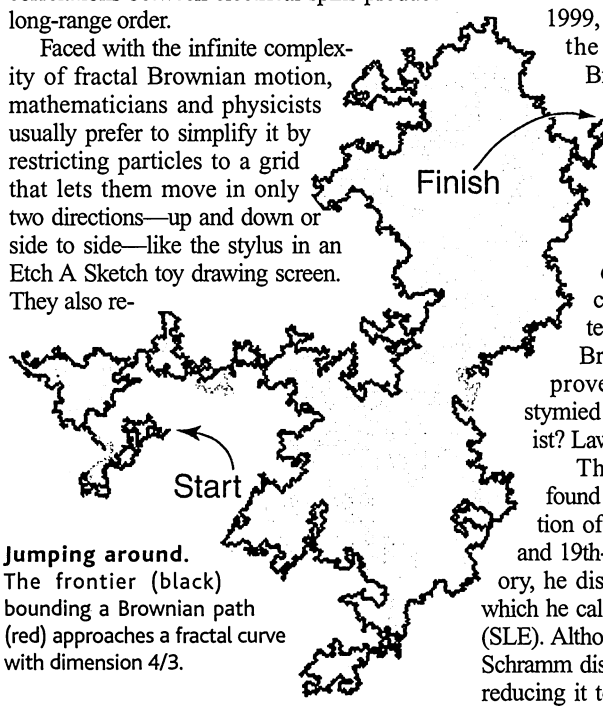
If you could watch an individual air molecule, you would see a dance that puts the wildest mosh pit to shame. Slamming into its neighbors, rebounding, ricocheting without letup, each humble particle traces out a path so jittery that nothing can tame it. The slowest slow-motion camera, the most powerful zoom lens, would only bring quicker and smaller lurches into view.

Now, a trio of American and French mathematicians has proved that the frenetic random dance called Brownian motion has geometric properties that can be calculated as exactly as the circumference of a circle. The methods they used to prove that counterintuitive notion seem likely to apply to other random processes, some as familiar as the flow of water through a filter. The proof, presented at the recent Current Developments in Mathematics 2000 conference* sponsored by Harvard University and the Massachusetts Institute of Technology, is drawing rave reviews. Says Yuval Peres, a mathematician at the University of California, Berkeley, "I feel their work is one of the finest achievements in probability theory in the last 20 years."

The proof by Gregory Lawler of Duke University, Oded Schramm of Microsoft Research, and Wendelin Werner of the Université de Paris–Sud describes the probability that two or more neighboring air molecules, trapped in a plane, will escape to a large distance apart without crossing one another's tracks. In theory, the molecules could travel in straight lines, avoiding collisions with other particles; in practice, however, it is infinitely more likely that they will get jostled into tangled fractal paths.

Whether those paths cross has little physical significance: "Particles in the real world aren't worrying about where they've been," Lawler notes, and they usually are not confined to a plane. But the numerical parameters that describe the likelihood of crossing, called intersection exponents, interest physicists intensely, as they model a variety of systems near a phase transition. In the study of magnetic materials, for example, similar "critical exponents" describe how short-range correlations between electrical spins produce long-range order.

Faced with the infinite complexity of fractal Brownian motion, mathematicians and physicists usually prefer to simplify it by restricting particles to a grid that lets them move in only two directions—up and down or side to side—like the stylus in an Etch A Sketch toy drawing screen. They also require the particles to move only in discrete steps. The finer the grid is, the more closely the Etch A Sketch squiggle resembles true Brownian motion.



Jumping around. The frontier (black) bounding a Brownian path (red) approaches a fractal curve with dimension 4/3.

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Unfortunately, such simplified "finite-lattice models" have not led to a rigorous derivation of the long-sought intersection exponents. "[Brownian motion] problems have been studied to death on the lattice using combinatorial methods, and no exact solution is in sight," says John Cardy, a theoretical physicist at Oxford University. Lattice models also lack some crucial characteristics of true Brownian motion. For example, in the lattice version, a strong enough magnifying glass would reveal the underlying graininess of the motion. Real Brownian motion when magnified still looks like Brownian motion—even if the magnification varies from point to point, as in a funhouse mirror.

That extremely strong symmetry property, called "conformal invariance," may actually make the fractal Brownian paths easier to work with than their lattice imitations. In 1999, Lawler and Werner showed that the intersection exponents for Brownian motion are determined by its symmetry properties alone, regardless of what physical process produces the motion. Any other random, conformally invariant process that doesn't get distorted by edge effects (a condition called "locality") would have the same intersection exponents. Such a non-Brownian random process might prove a mathematical godsend to stymied researchers. But did it even exist? Lawler and Werner had no idea.

Then, independently, Schramm found it. Using an ingenious combination of 20th-century probability theory and 19th-century conformal mapping theory, he discovered a wholly new process, which he called stochastic Loewner evolution (SLE). Although SLE looks two-dimensional, Schramm discovered a mathematical trick for reducing it to one dimension—as if the two knobs of an Etch A Sketch toy were secretly controlled by a single master dial. That made the intersection exponents for SLE much simpler to compute. Werner, Lawler, and Schramm then showed that SLE was also conformally invariant and local, thus confirming that its exponents were the same as the expo-

*17–18 November, Cambridge, Massachusetts.