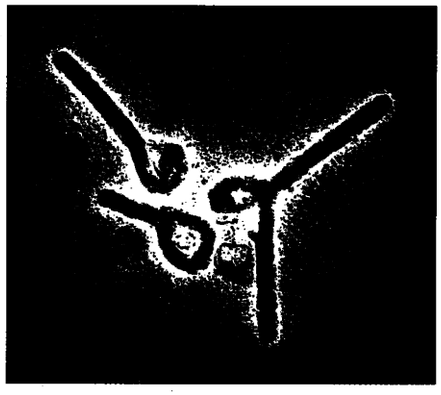
make an avian retrovirus containing the Ebola glycoprotein. They then used fluorescent antibodies that bind specifically to the glycoprotein to trace the virus's interactions with various kinds of cultured cells. The glycoprotein, they found, preferentially binds to human endothelial cells, allowing the retrovirus, which would not normally infect human cells, to enter them. Presumably, this protein also helps the Ebola virus infect endothelial cells, making them fragile and leading to hemorrhaging.

Antibodies also helped the group work out the role of the secreted version of the glycoprotein. Sanchez's team had discovered this protein in the late 1980s in the blood of infected patients. It is a truncated version of the protein found on the virus, and researchers had thought that this similarity might allow the secreted protein to serve as a decoy, sopping up immune cells and antibodies that might otherwise attack the membrane glycoprotein on the virus.

But the Nabel team found that the secreted glycoprotein attaches not to the immune cells that might specifically attack the virus, but to neutrophils, which trigger inflammation, an early general assault in which scavenger cells clear the body of foreign bodies. These results suggest, says Nabel, that rather than serving as a decoy, the secreted glycoprotein actively blocks an inflammatory response that might otherwise stamp out the virus. "It's as if the virus is throwing darts at the neutrophil," he says.



ANTHONY SANCHEZ

Demon virus. Researchers are getting a handle on Ebola virus's high pathogenicity.

No one has shown that the Ebola virus proteins behave the same way in animals as they do in cell cultures, although experiments to find out are under way in monkeys. And even if the cell-culture results hold up, nagging questions may remain. One strain of Ebola, for instance, kills with unusually severe symptoms but makes relatively little soluble glycoprotein, raising doubts that it is always critical for causing the disease. Another unknown is the identity of the endothelial cell receptor to which the membrane glycoprotein binds—information crucial to devising therapies that might block Ebola's binding to these cells.

But even as researchers work to answer those questions, Nabel's team is already exploring another possibility: adding the Ebola virus membrane glycoprotein to a harmless virus that could then carry therapeutic genes specifically to endothelial cells. With such a tool, notes Bloom, doctors might someday treat cardiovascular disease.

Gene-carrying viruses equipped with the Ebola glycoprotein might be used, for example, to deliver growth-factor genes that could trigger the growth of new blood vessels to circumvent damaged ones. Because cardiovascular disease alone afflicts hundreds of millions of people worldwide, that would be an astounding achievement, and it could even give a lift to Ebola's macabre reputation. Says Bloom: "As I read the paper, I started cheering."

–Ingrid Wickelgren

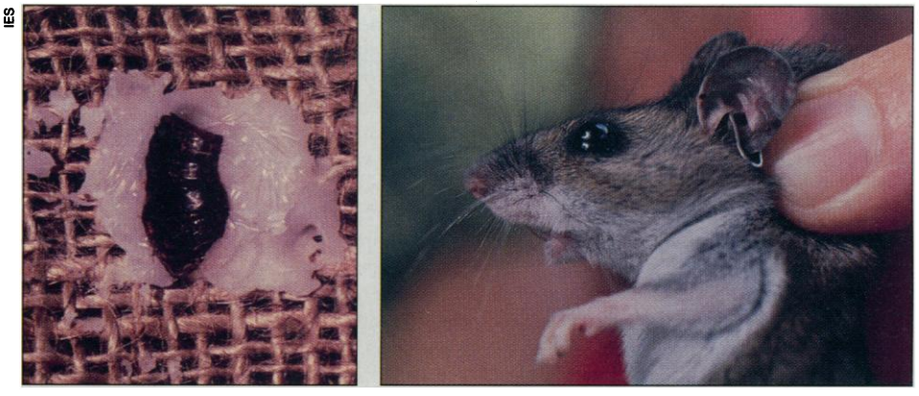
ECOLOGY

Of Mice and Moths—and Lyme Disease?

Charles Darwin once speculated that English cat lovers might unwittingly be setting off an ecological domino chain that leads to prettier gardens. Cats eat the mice that normally pillage the nests of bumblebees, so Darwin reasoned that more cats would mean more bees—and more of the red clover and purple-and-gold pansies, called heartsease, that the bees pollinate. "It is quite credible," Darwin playfully digressed in his 1859 treatise, *The Origin of Species*, "that the presence of a feline animal in large numbers in a district might determine ... the frequency of certain flowers in that district!"

Neither Darwin nor anybody else apparently tested this idea, but ecologists have now unraveled an equally intriguing, albeit less picturesque, skein of interactions that may govern upsurges of Lyme disease and tree-ravaging gypsy moths. In a 3-year study described on page 1023, a team led by Clive Jones and Richard Ostfeld of the Institute of Ecosystem Studies (IES) in Millbrook, New York, traced the links between several forest species to show that bumper crops of acorns lead to an explosion of mice. The mice in turn protect the oak trees by eating gypsy moths, but they also host ticks that can spread Lyme disease, a sometimes disabling human infection.

To tease out these links, Jones and Ostfeld had to manipulate large forest patches by trapping mice or adding acorns—an effort other ecologists are applauding. "It's a wonderful example of how perturbing the system produces results that you wouldn't have expected to be there, unless you'd done the experiments," says Princeton University ecologist Andrew Dobson. But some epidemiologists say too many other factors determine Lyme disease outbreaks for the work to have much predictive value for now. "People are talking about the acorn connection with Lyme disease risk, and it's not established," cautions Yale Lyme disease expert Durland Fish.



IES IES

Sic 'em. More mice munch more gypsy moth pupae *(left)* but may mean more Lyme disease.

Jones and Ostfeld's team, collaborating with Jerry Wolf of Oregon State University in Corvallis, initially set out to learn what controls populations of gypsy moths, a European invader that plunders eastern U.S. forests every decade or so. The researchers knew that white-footed mice are important predators of gypsy moth pupae. The mice also eat acorns, and their population booms after "masting"—the term for an abundant acorn season that occurs naturally every 2 to 5 years. To the ecologists, it seemed plausible that masting would check moth populations, which would take off only a few years after mouse populations crashed.

Jones's team tested this idea in upstate New York in the summer of 1995, 1 year after a masting, when mice were abundant. They removed most mice from three unfenced 2.7-hectare forest patches. Next, they compared the survival rate of moth pupae in

the study areas and control plots. They found about 45 times more of these pupae and moth egg masses in plots with fewer mice. Using freeze-dried pupae attached to wax, which picked up tooth marks, they were able to confirm that mice were eating the pupae in the control plots.

After firming up that link, the researchers simulated a masting. With help from local Girl Scouts, they spread 3500 kilograms (nearly 4 tons) of acorns on their experimental plots. Mouse populations skyrocketed. "Our data show that the key trigger [for moth outbreaks] is this relationship between the acorns and the mice," Jones says.

Along the way, the researchers kept an eye on ticks, because white-footed mice are a reservoir of the Lyme disease spirochete, which they transmit to tick larvae. More mice wouldn't necessarily mean more ticks: Ticks of reproductive age live on deer, not mice. But the summer after the masting, the team found far more tick larvae—an eightfold rise—in the acorn-rich plots compared to other plots. The acorns had apparently attracted tick-bearing deer and boosted mouse numbers as well, Jones says. And the adult ticks, in turn, had spawned more offspring, which infested more mice: The mice in the acorn-rich plots bore 40% more tick larvae than those in other plots.

More acorns, more mice, more deer, more ticks: It adds up to a larger Lyme disease risk, the researchers argue. "It suggests that you may be able to warn people when the risk of Lyme disease is high," Ostfeld says. But the study also highlights the challenge of managing ecosystems, because in this case trying to cut down on Lyme disease by, say, chemically suppressing acorn production could send gypsy moth numbers soaring. "Once we start tinkering with nature, we could get in a wonderful mess," Dobson says.

Fish and other epidemiologists, however, interpret the study more cautiously. They point out that a high larval tick count the summer after a masting may not necessarily mean more infected juvenile ticks a year later. Indeed, Jones's group members didn't measure infection rates on their plots last summer. "The question is still open," says Joseph Piesman, who heads the Lyme disease vector branch at the Centers for Disease Control and Prevention in Fort Collins, Colorado. Many other factors, such as rainfall and competing parasites, also affect the abundance of ticks carrying the Lyme disease spirochete, Piesman says. So nailing down any acorn link, he adds, may take at least a decade of observing mastings and tick outbreaks.

Most experts agree, however, that the work underscores ecology's importance in studying vector-borne diseases. "The entire genetic sequence of the organism wouldn't tell you this," Dobson says.

–Jocelyn Kaiser

SEISMOLOGY

A Slow Start for Earthquakes

If seismologists had their way, every earthquake would have a prelude—days or weeks of preparations along the fault that was about to break. Quake prediction would then be a matter of watching for the right signals. Theoretical and lab studies have suggested that faults should give off such warning signs as they edge toward rupture, but no one has yet found them. Now, researchers using a seemingly roundabout method—testing for the effects of tides on quake timing—offer the strongest evidence yet that some faults do start to slip, rapidly concentrating stress, for hours or days before the full-blown rupture. "The good news is that something must be happening before earthquakes," says seismologist Thomas Heaton of the California Institute of Technology in Pasadena. However, there's no guarantee of successful prediction, he cautions. "The bad news is that it may be so small it's useless."

R. A. KERR

Tidal test-bed. Earth tides don't affect the timing of small quakes on the San Andreas fault, buried beneath these hills near Parkfield.

Seismologist John Vidale of the University of California, Los Angeles, and his colleagues coaxed this bit of good news from the timing of more than 13,000 small to moderate quakes on California's San Andreas fault, near the town of Parkfield, and on one of the great fault's branches, the Calaveras. The ultimate driver of earthquakes on these faults is the slow march of the tectonic plates to either side, which continually adds stress at about 0.1 millibar per hour, building over the years toward the 1 bar to 100 bars needed to rupture a fault. But the gravitational tugs of the moon and sun, which raise tides in the earth just as they do in the ocean, also vary the stress—much faster than tectonics does. As the tides wax and wane, they alternately increase and relieve stress on faults at a rate of several millibars per hour.

If the steady buildup of stress from tectonics and the rapid variations from tides were the only factors involved, Vidale's team reasoned, the tides should sometimes trigger quakes on faults already close to the breaking point. The effect would be subtle—most seismologists long ago rejected schemes to predict earthquakes from tides. Nevertheless, the seismic events should be more common when the tidal pull is strongest, for example during full and new moons. They could occur randomly with respect to tides only if some third process rapidly loads stress onto faults just before quakes, overwhelming the tidal effects.

To test for any trace of tidal influence, Vidale and colleagues included only quakes on straight segments of the two faults, which amounted to 13,042 earthquakes of magnitude 1 to 6. The large number of events together with the known fault orientations—which allowed the tidal stresses to be calculated reliably—gave the study unprecedented sensitivity. Still, they found no correlation between the two phenomena. Of the 13,042 quakes, only 95 more occurred when tidal stresses favored fault failure than when they discouraged failure—not a significant result. Some other short-term stress source must have overwhelmed the tidal effects. "The lack of a tidal correlation argues that there is some preparation process over the days before an earthquake," says Vidale. During the final hours before such an event, stress must build many times faster than it does during a tidal cycle—at least 150 millibars per hour, he adds.

Can seismologists catch this preparatory movement in action and so predict earthquakes? No one knows yet. In theory and lab experiments, the stress-inducing process is a slow but accelerating slip on a small patch of fault. That slip causes stress to build up faster and faster around the edge of the patch, until a larger area of the surrounding fault ruptures in an earthquake. "What we don't know is the size" of the patch, says theoretician and experimentalist James Dieterich of the U.S. Geological Survey in Menlo Park, California. Estimates range from a patch a few hundred meters across before a magnitude 5 quake, which might be detectable by strainmeters buried near the surface, or one only a few meters in size, in which case detection would be hopeless.

Researchers may get an answer from the next magnitude 6 quake to hit the heavily instrumented Parkfield area (*Science*, 19 February 1993, p. 1120) or from a proposed project to monitor a small patch of the fault at Parkfield that regularly fails in frequent magnitude 1 quakes. The answer could make or break earthquake prediction forever.

–Richard A. Kerr