Where Are 'New' Diseases Born?

They may come out of the forest when the forest is cleared for economic development. That hypothesis is now being put to the test in Papua New Guinea and in the Amazon

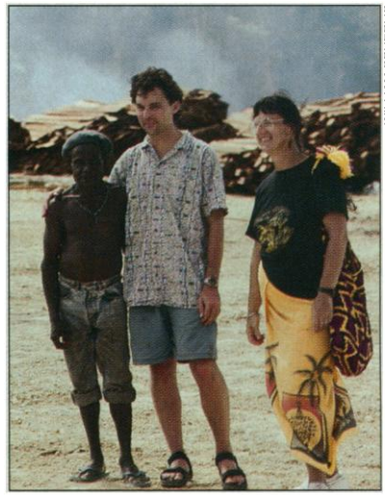
WEWAK, PAPUA NEW GUINEA—One night last March, a Malaysian ship dropped anchor off a quiet beach at the edge of a dense tropical forest here, and sent ashore a convoy of bulldozers, jumbo-sized trucks, and road graders. By the time local villagers heard the rumble of the engines the next day, the bulldozers had cleared the beach of palms and hardwood trees and started to cut a dusty highway through the lush forest—all in preparation for one of the largest logging operations in Papua New Guinea in recent years.

Little did the loggers know that night that, by opening a road into the forest, they were also paving the way for an ambitious medical experiment aimed at addressing a major question in epidemiology: What causes the emergence of seemingly "new" pathogens that periodically sweep through human populations often causing serious, even fatal diseases? The most devastating recent example, of course, is AIDS, but there are lots of other examples: the hantavirus that killed 16 people, mostly Navajos, earlier this summer in the southwest United States and the tick-borne bacterium that has infected thousands of people in the Northeast with Lyme disease, as well as the virus that causes dengue fever.

In recent years, epidemiologists have come up with new theories that blame the emergence of these killers on changes in human behavior and on devastation of the environment—especially intrusion of humans into new ecological settings, such as the rain forest, along with construction of roads that allow viruses and other infectious microbes to spread rapidly to huge numbers of people. The theories are new and intriguing, but so far, there has been little more than circumstantial evidence to support them.

That's where the logging operation in Papua New Guinea could be of help. With 70% of its land covered by tropical forest and one-third of its people living in traditional tribes that hunt and gather most of their food in the forest, the country constitutes a natural laboratory where medical scientists can do the prospective studies needed to pin down the effect of human activities on the emergence of infectious diseases. Funded by an $180,000 grant from the MacArthur Foundation, an international team led by medical anthropologist Carol Jenkins of the Papua New Guinea Institute of Medical Research will follow what happens to the health of the local people over the next 3 to 6 years to see how they are affected by logging and the intrusion of outsiders.

"This is important work," says Amherst College evolutionary biologist Paul Ewald, who is one of the pioneers of the new thinking about environmental devastation and disease. Ewald is referring to Jenkins' work, along with a similar study in the Amazon led by Yale virologist Robert Shope, which is due to get under way this month. Says Ewald: "We will benefit a lot if we get a better understanding of how these disease organisms spread from their animal hosts to humans." And indeed, the benefits could be large: Optimally, such studies could provide public health workers with clues about how to detect—even prevent—the emergence of new pathogens.



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Microbe hunters. Carol Jenkins, shown with graduate student John Leedom and a local man, leads a study of emerging viruses in Papua New Guinea.

For many years, the scientists who were trying to understand how "new" infections arise suddenly in humans focused their attention on mutations in the viruses or other microbes. These mutations might, for example, enable the pathogens to move from animals to humans, or convert an innocuous agent into a dangerous one. But 4 years ago, at a landmark meeting on emerging viruses (*Science*, 19 January 1990, p. 279), it became clear that there was growing evidence that pointed not to changing pathogens, but to changing environments as the main cause of emerging infectious diseases. One of the organizers of that meeting, Rockefeller University virologist Stephen Morse, explains that most "new" viruses that have emerged in humans are in fact old viruses that have been around for centuries in other host species; as examples, Morse cites the AIDS, Ebola, Marburg, and yellow fever viruses that probably were first in monkeys, Rift Valley fever in cattle, sheep, and mosquitoes, and Hantaan in rodents.

These pathogens probably lurked relatively undisturbed in their animal hosts in the tropics, jumping to humans only in rare cases. They had little opportunity to adapt to humans, who usually were a "dead end" host species, because the viruses would fizzle out once they swept through a small population at the edge of the forest. But once large numbers of humans moved into the forest, that picture changed. "We've created new pathways for these viruses to travel rapidly from place to place," says Morse. "Social changes gave rather isolated and very specialized viruses opportunities to get to people in the cities."

One of the first, and most dramatic indications that humans were disrupting the balance between pathogens and hosts came in the 1950s, when Brazil built a highway from the city of Belém on the coast to the new capital, Brasilia, deep in Amazonian jungle. At the time, the Rockefeller Foundation's Virus Program had a lab in Belém that was part of a worldwide network whose goal was to isolate and identify unknown viruses. Soon after construction of the highway, researchers from the Belém facility isolated viruses from the blood of highway workers. Some of these viruses were unknown, others had been found only in animals, according to Shope, who was head of the lab at the time. Among the new specimens was a rare virus known as Oropouche, found in the blood of a sloth dead on the side of the Belém-Brasilia highway in 1960. At the time, Oropouche was not known to be responsible for epidemics in humans or animals, but by 1961 the virus had spread to Belém, causing a flu-like epidemic in 11,000 people who suffered from high fevers, severe headaches, and muscle aches.

While it was clear that Oropouche was to blame for the epidemic, it was not clear how a virus never seen in human beings before had leaped from the jungle fauna to the residents of Belém. Solving that mystery took 19 years of epidemiological detective work, but by 1980 researchers had the answer: In that year, they isolated the virus from biting midges, which proved to be the missing link.

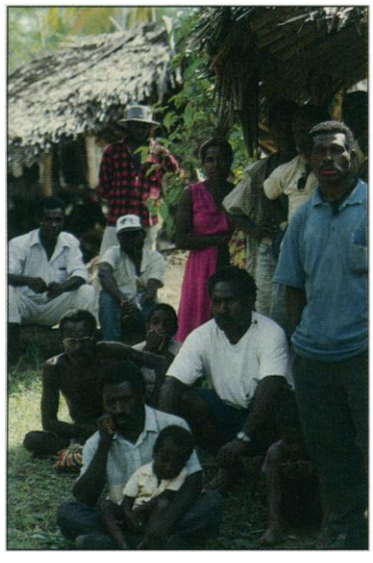
The forest-dwelling midges, it seems, had gone through a population explosion when the settlers started clearing the forest and planting cacao for chocolate. After the farmers harvested their cacao beans, they discarded the hulls in piles that were an ideal breeding ground for midges, which spread the virus to humans all along the Amazon roads.

During the time when this mystery was being solved, many other examples came to light of pathogens emerging when a natural habitat is cleared. Those findings made such an impression on the field that by 1992 a panel of infectious disease experts produced a report for the Institute of Medicine stating that "environmental changes probably account for most emerging diseases."

Yet the evidence for that conclusion was—and is—largely circumstantial. "A lot of this is hypothetical," says Jenkins. "We look back after disease has broken out and try to project mechanisms for how this occurred." To prove the hypothesis, prospective studies are needed in place of the retrospective ones Jenkins is describing. In prospective studies, the population's health would be followed closely not only after a project that alters natural habitat, but also before and during the disruption. That is what Jenkins and her team are up to in Papua New Guinea: "What we're trying to do is go in before the logging begins and then watch for changes in the health of people living in the area for 3 years, maybe 6 years."

Jenkins learned from contacts in the government that Sovereign Hill Pty. Ltd., a subsidiary of the giant Malaysian logging company Rimbunan Hijau, had been given permission to exercise logging rights bought from villagers in the Hawain River valley north of Wewak. Before the loggers landed, Jenkins met with villagers in the region to get permission to study them. The plan for her network of graduate students, Peace Corps workers, and researchers from the Christensen Research Institute and the University of Papua New Guinea was to study people from four villages—two in the logging region and two in areas that remain pristine—to see how logging affects the villagers' health.

By the time the loggers arrived, Jenkins' team was mostly in place. The researchers had to move quickly to get baseline health data on 1000 people in the four villages before their environment was disturbed. They began by collecting blood to search for antibodies to a series of viruses, including those that cause AIDS, herpes infections, and those carried by mosquitoes, such as Ross River and Dengue fevers. Emerging viruses are just part of the picture, however—they also will test for other nonviral microbes, such as the bacteria and parasites that cause typhoid and malaria. And they will be on the alert for the spread of sexually transmitted diseases, because where there are all-male logging camps, there usually are prostitutes.



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Control data. People from the village of Arin—in an unlogged area—serve as a control in Jenkins' study.

At the same time, entomologists and a virologist on the team are scrutinizing mosquitoes and other insects that might transmit diseases. Institute of Medical Research virologist Ray Sanders has started to isolate viruses carried by mosquitoes, which should give researchers an idea of what to look for in humans and a way to identify emerging arboviruses (viruses carried by insects and other arthropods). Bioiogists have netted dozens of birds, rodents, bats, and other forest-dwelling creatures to sample their blood. Predicts Sanders: "I suspect we'll find some completely new viruses—or variants of known species."

While Jenkins' study was getting under way, Shope was making plans to return to Brazil to help start another study that may provide data on how the diseases of the Amazon are spread to humans. The Rockefeller Foundation has provided $600,000 in funding for the first year of the 3-year study, which is a collaboration with the School of Forestry and Environmental Studies at Yale and Brazilian researchers.

The researchers will focus attention on inhabitants of islands in the Amazon, 60 kilometers inland from Belém. The settlers who live there have been clearing the forests so they can plant fruit trees, including the acai fruit that is a staple of their diet. As in the Papua New Guinea study, researchers will aim at determining how deforestation affects human health. They will start with baseline studies of the health of about 300 people in the municipality, Abaetetuba, with particular emphasis on malaria, Leishmaniasis, Leptospirosis (a disease that plagued British troops in the jungle of Malaya), and arboviruses, of which more than 150 types are known in Brazil, some 30 disease-causing. At the same time, biologists will collect insects and wild animals to see what pathogens they harbor.

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Viral nursery? Forest cleared by logging in Papua New Guinea could be a source of "new" infectious diseases.

The study has one extra dimension that takes it beyond observation of what is happening when nature is devastated by development. The Yale and Brazilian researchers are setting up an experiment to find out how farmers can grow their crops with the least damage. "The goal is to find out how to grow crops in the forest without destroying the forest—and to keep the best public health possible," says Shope.

The team will divide the study area into four experimental plots. On one, settlers will cut down the forest and plant cash crops, as they always have done. On the second, they will do the same—but also mix into their usual crops fruit trees native to the forest. On the third, only a small part of the forest will be cut down to make room for the planting of more native fruit trees. The fourth will serve as a control; the forest will be left intact. As settlers tend their plots, the researchers will check the health of the farmers three to four times a year, as well as draw blood from insects and wild animals.

Shope hopes the data the team collects will not only pin down the relation between deforestation, agriculture, and the spread of disease, but will provide information the Brazilian government could use to formulate policy recommendations on how to settle that region of Amazonia with the least possible destruction.

The studies by Shope and Jenkins are just now getting off the ground, and it will be at least 3 years before conclusions can be drawn. But when those results do arrive, Morse at Rockefeller is hopeful they will provide "scientifically valid data" that will help nail down theories about emerging infections and viruses. "I'd like to see more studies like these," says Morse. "Only by fully understanding how viruses interact with their hosts can we hope to rationally devise effective preventive and therapeutic strategies." And in the age of AIDS, that isn't a trivial outcome of research.

–Ann Gibbons