Amphibian Decline and Emerging Disease

What can sick frogs teach us about new and resurgent diseases in human populations and other species of wildlife?

Joseph M. Kiesecker, Lisa K. Belden, Katriona Shea and Michael J. Rubbo

Frog 1: length 45 mm. There is a shortened left leg that is twisted at the knee. It also does not appear to have a knee joint.

Frog 2: length 39 mm. The left rear leg on this frog is missing. There are no knobby traces of an underdeveloped leg that was found on other frogs. The right leg is bent the wrong way. It also has two bone growths coming out of the [frog's] back.

Frog 3: length 45 mm. The only thing wrong with this frog is that there is a bony projection coming from [its] butt.

These are excerpts from the field notebook of Betsy Croon, who was a middle school student in rural Le Sueur, Minnesota when her class stumbled on the misshapen leopard frogs in the summer of 1995. They alerted the Minnesota Pollution Control Agency, who determined that 30 to 40 percent of the frogs in Ney Pond were deformed. Nothing like this episode had ever before been seen in Minnesota, and the story shocked the public. Suddenly, the students were featured in print and broadcast media across the country—including the children's magazine *Earth Focus*, where this record appeared.

The problem was not unique to Ney Pond, or to the leopard frogs that the students observed or even to the Midwestern United States. Across the globe hundreds of species of frogs, toads, salamanders and newts are in dramatic decline. At the same time, new and often serious infectious diseases seem to be sickening people. Might these unhappy developments be connected? Might they indeed share a root cause: the changes in our world brought about by a growing human population? From several lines of inquiry, evidence is accumulating to support such a conclusion—that environmental degradation wrought by people is contributing to both trends.

The human species now numbers 6.3 billion, and collectively we have altered between one-third and one-half of the Earth's land surface. After being stable for millennia, atmospheric carbon dioxide has increased by 30 percent in the last two centuries. Our actions fix more nitrogen than all natural terrestrial sources, and we utilize over half of all accessible surface freshwater. These are dramatic changes, even though we can't always determine their long-term significance. The immediate consequences seem to be disproportionately borne by frogs, which have suffered massive mortality in recent years.

Along with many other scientists around the world, our research group studies this surge in amphibian deaths. While many cases can be linked directly to single, proximate factors such as habitat loss, numerous populations have declined in protected parks and nature reserves, even in remote wilderness areas—places that are removed from our modern effluvium and that ought to be insulated from human influence. Yet across the globe, many amphibian species have experienced increased disease- and parasite-prevalence, causing massive mortality. Developmental malformations associated with parasitic infection are also frequent: In some groups 90 percent are severely deformed, with extra or missing limbs.

The origins of these catastrophic losses are complex. Several agents can act synergistically to endanger a population. Depending on the specific locale, forces such as climate change, habitat destruction, environmental chemicals, fertilizer runoff and the introduction of exotic species have all been implicated in the threat.

So how is the global decline of amphibians related to increased disease prevalence among humans and wildlife? The link is suggestive, not proven, but there are compelling similarities between recent disease outbreaks in many animals. Amphibians have been hit particularly hard because of their life cycle and physiology: Frogs and salamanders are exquisitely sensitive to environmental changes. This property casts them in the role of biological Cassandras, prophesying a pessimistic message of environmental degradation that we don't want to hear. Like Homer's Trojans, we've mostly ignored their warnings.

Joseph M. Kiesecker received his Ph.D. in zoology from Oregon State University in 1997. After postdoctoral research at Yale University, he joined the biology department at the Pennsylvania State University as an assistant professor in 1999. He has spent the last 10 years trying to understand the factors responsible for disease outbreaks and how disease can contribute to the decline of threatened species, above all amphibians. Lisa K. Belden studied how environmental stressors alter disease susceptibility in amphibians as a postdoctoral fellow in the biology department at Penn State. She recently joined the biology department at Virginia Polytechnic Institute and State University as an assistant professor. Katriona Shea is an assistant professor in the biology department at Penn State, where her primary research interest is the use of ecological theory in conservation, harvesting and the control of invasive species. Michael J. Rubbo is a Ph.D. candidate in biology at Penn State studying the interface between ecosystem-level processes and community dynamics, using temporary forest ponds as a model. Address for Kiesecker: Department of Biology, 208 Mueller Laboratory, Pennsylvania State University, University Park, PA 16802. Internet: jmk23@psu.edu

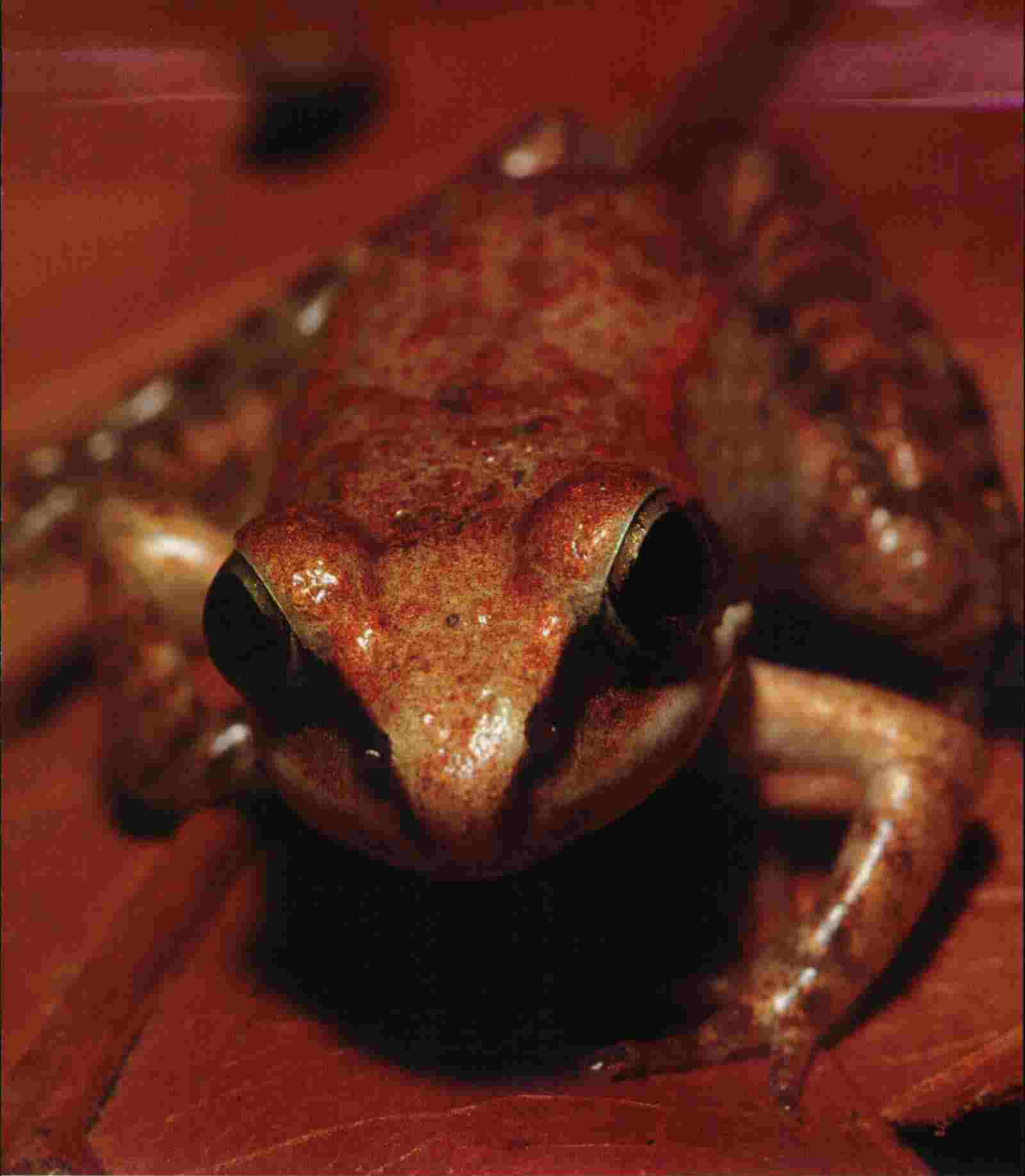

Figure 1. Many amphibian species, including the wood frog *(Rana sylvatica, above),* are experiencing increased rates of deformities or serious population declines. Several studies, including those of the authors, show that this mortality is tied to a variety of human-induced environmental changes. This result is concerning because amphibians are seen as indicators of environmental health—they have permeable skin without scales, feathers or hair; their embryos are fully exposed to the environment without the benefit of shells or other protection; and their life cycle often exposes them to both aquatic and terrestrial hazards. So the widespread amphibian decline could be a warning of environmental degradation. Furthermore, the same forces that have threatened amphibian populations might also be driving the emergence and reemergence of human infectious diseases such as West Nile virus and cholera. (All photographs courtesy of the authors.)

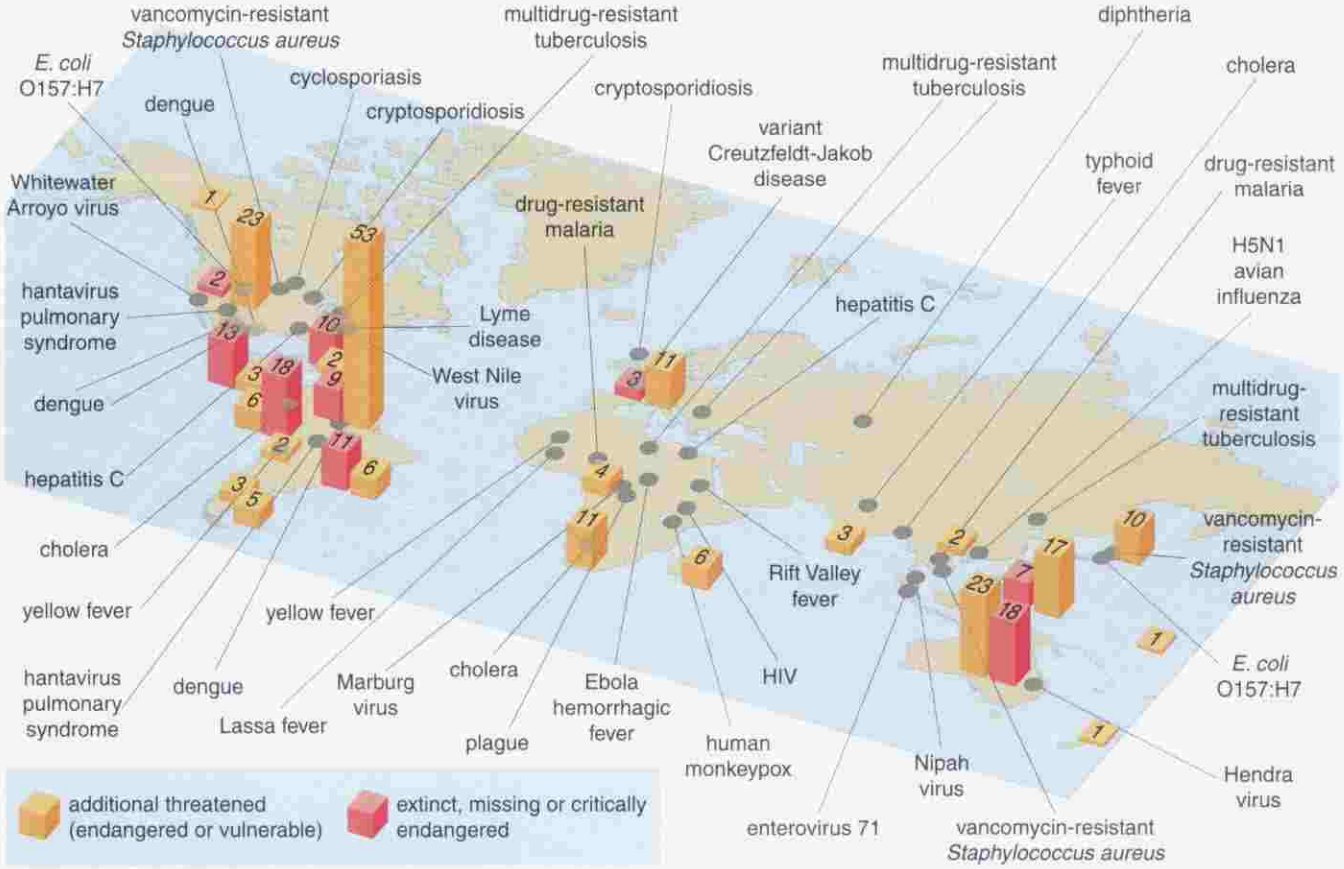

Figure 2. Global declines in amphibian populations have coincided with a sharp rise in new and resurgent human infectious diseases. In this map, red bars represent the number of amphibian species that have recently become extinct, missing or critically endangered; orange bars indicate the number of endangered or vulnerable species. The ranges and sites of origin for many emerging human diseases are also indicated. Amphibian data are from Hero and Shoo 2003. Human disease data are from Fauci 2001.

Amphibian Examples

The relevance of wildlife (including frog) health to human health has only come to be appreciated recently, as similar patterns began appearing among many species. For people, at least 20 major diseases have reemerged in more virulent forms in the past two decades. Over roughly the same period, more than 30 new diseases, including Ebola, AIDS and SARS, have emerged. Among other animals, several wildlife species have been killed in large numbers in the past 10 years by new "epizootics" of diseases such as canine distemper virus, which affects African wild dogs, lions and other carnivores. In the case of amphibians, the toll from microbial and parasitic infection is especially severe, even though the global decline in frogs, toads and salamanders went mostly unnoticed until 1989. Since then, over 125 species of amphibians have become severely threatened or gone extinct.

Emerging diseases are those that have increased in incidence, virulence or geographic range, have shifted hosts or have recently evolved new strains. Diseases emerge when a new pathogen is introduced into a naive host population or when an external factor somehow increases the vulnerability of current hosts.

Understanding the factors that drive emergence of infectious disease in amphibians is central to understanding contagion in human and wildlife populations for several reasons. Amphibians are especially sensitive to subtle changes in their environment. Because the origins of most new frog and toad pathogens have been linked to human-induced environmental change, conditions that cause outbreaks among amphibians could have similar effects on other organisms. Also, wild and domesticated animals are relevant to human diseases because they serve as reservoirs for pathogens that can be transmitted between humans and animals. These so-called zoonotic diseases make up many of the emerging infectious agents in humans. Thus, increased pathogenic infection in wildlife populations could translate into increased risk of human infection.

Here we consider a few cases of widespread amphibian mortality and deformity that have been tied to new surges in disease. These examples demonstrate specific ways in which the global decline in amphibians could relate to the larger phenomenon of emerging pathogens in humans and wildlife. Although there are many mechanisms leading to the rise in infectious diseases, we will focus on environmental stressors and introduced pathogens to illustrate how general factors have promoted specific disease outbreaks among many species.

A Plague of Frogs

Environmental changes can shift the range and distribution of pathogens, and they can increase host susceptibility to disease by altering the ability of hosts to resist infection. Global warming is particularly threatening to amphibians. During the past 50 years, surface temperatures have risen by about half a degree Celsius, resulting in altered precipitation patterns and increased frequency and severity of extreme weather in many areas. One such

event is the El Niño-Southern Oscillation (ENSO), a phenomenon that originates over the tropical Pacific Ocean but impacts weather patterns over the entire globe. During an El Niño event, the cold, nutrient-rich water that normally covers most of the equatorial Pacific is replaced by warm, nutrient-deficient water. This shift happens every two to seven years. La Niña, the opposite of El Niño, refers to a blanket of extremely cold water over the equatorial Pacific. In the last quarter-century, ENSO events appear to have increased in frequency, duration and intensity. In the United States, precipitation patterns in the Pacific Northwest are closely tied to ENSO cycles, which decrease winter rain and snowfall in the area.

This part of the U.S. has also experienced catastrophic mortality of amphibian embryos associated with the pathogen *Saprolegnia ferax*. Several investigators hypothesized that these outbreaks were related to increased exposure to ultraviolet radiation caused by depletion of the upper-atmospheric ozone layer. This scenario is partly true: A particularly harmful component of ultraviolet light, UV-B, may contribute to the decline of amphibian species. However, climate change in the form of altered rainfall patterns may have a greater effect than ozone depletion on the amount of UV-B exposure among aquatic organisms. This is because lower water levels or reductions in dissolved organic matter reduce the absorption of ultraviolet wavelengths by the embryo's aquatic environment.

In the late 1980s, we suggested that amphibians that breed in shallow, high-elevation lakes and ponds might be particularly susceptible to this kind of climate-induced change in UV-B exposure. Those embryos that develop in such montane lakes and ponds are often exposed to direct sunlight, so they depend on the overlying water column to attenuate ultraviolet radiation. When there is less precipitation, less water covers the egg clutches, enhancing UV-B exposure. We believed that the increasing frequency and magnitude of El Niño events might have raised the incidence and severity of *Saprolegnia* outbreaks by increasing the extent to which embryos are exposed to sunlight in shallow water.

To test the theory, the Kiesecker lab along with colleagues at Oregon State University compared pathogen-mediated embryo mortality of the western toad, *Bufo boreas*, with climate fluctuations in Oregon's North Cascades mountain range. For more than 10 years we measured mortality and water depth at natural egg-deposition sites, and we compared these data with annual precipitation and the Southern Oscillation Index (SOI). Using a combination of observation and experimentation in the field, we wanted to test how *Saprolegnia*-caused mortality was related to the water depth in which embryos develop, how water depth at oviposition sites is related to ENSO cycles and how *Saprolegnia* outbreaks were related to UV-B exposure.

We found that El Niño-induced fluctuations in the depth of high-elevation pools did influence the amount of UV-B radiation that reached developing embryos and that higher levels of UV led to greater susceptibility to *Saprolegnia*. More than half of the embryos that developed in shallow water (less than 20 centimeters deep) contracted the pathogen, but when toad eggs developed in deeper water (depths greater than 45 centimeters), mortality associated with *Saprolegnia* was never more than 19 percent. This water depth was related to the amount of winter precipitation, which was itself a function of the ENSO from 1990 to 1999. We also demonstrated that eggs that were screened from UV-B radiation showed low levels of *Saprolegnia* infection—even if they were laid in shallow water.

Amphibious Assault

The *Bufo boreas* results are concordant with other studies that point to recent Pacific warming as a threat to amphibians. Because their survival is tied closely to water availability, climate changes that alter hydrology may set the stage for similar losses in other parts of the world. One example is the Monteverde Cloud Forest of Costa Rica, the site of one of the most notable cases of amphibian decline. In 1999, Alan Pounds of the University of Miami and his colleagues at the Golden Toad Laboratory for Conservation reported massive population crashes in approximately 40 amphibian species, including the apparent extinction of the golden toad *(Bufo periglenes)*. They suggested that the deaths were linked to a warmer, drier climate, which raised the altitude at

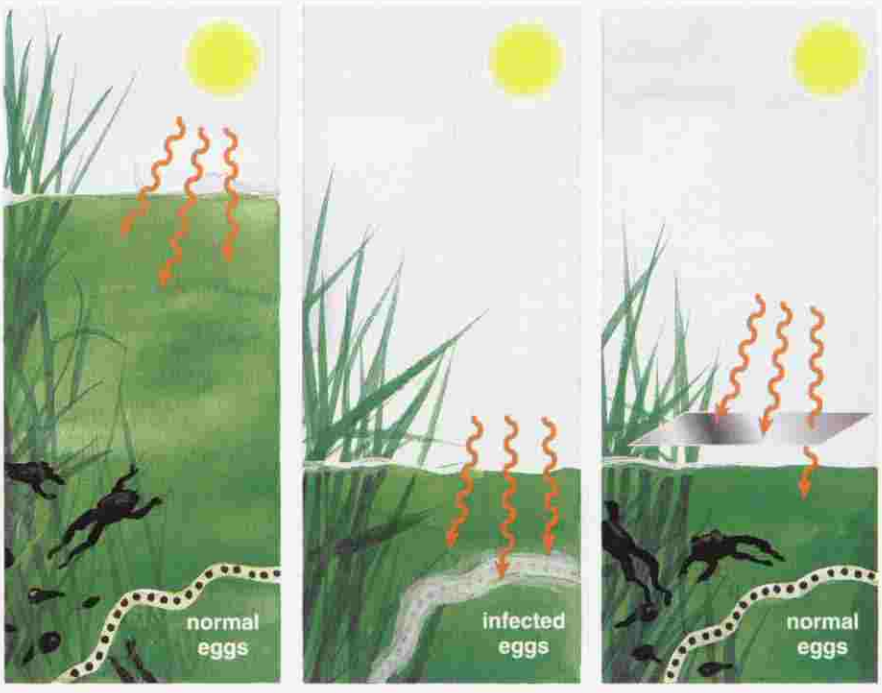

Figure 3. Western toad embryos suffer greater mortality from ultraviolet radiation and infection when rainfall patterns are disrupted. During a decade-long study, years with normal winter precipitation *(left panel)* had a low rate of infection by the pathogenic mold *Saprolegnia ferax*. But during increasingly frequent El Niño years, less precipitation falls in the Cascade Mountains, so the toads lay their eggs in shallower lakes and pools *(center panel)*. The shorter water column above the egg clutches does not screen ultraviolet rays as well as deeper water, and the UV-B wavelength makes embryos more susceptible to infection by *S. ferax*— causing more than 50 percent mortality during those seasons. However, when the egg clutches were screened from UV-B rays, the embryos developed normally, even when they had been laid in shallow water *(right panel)*.

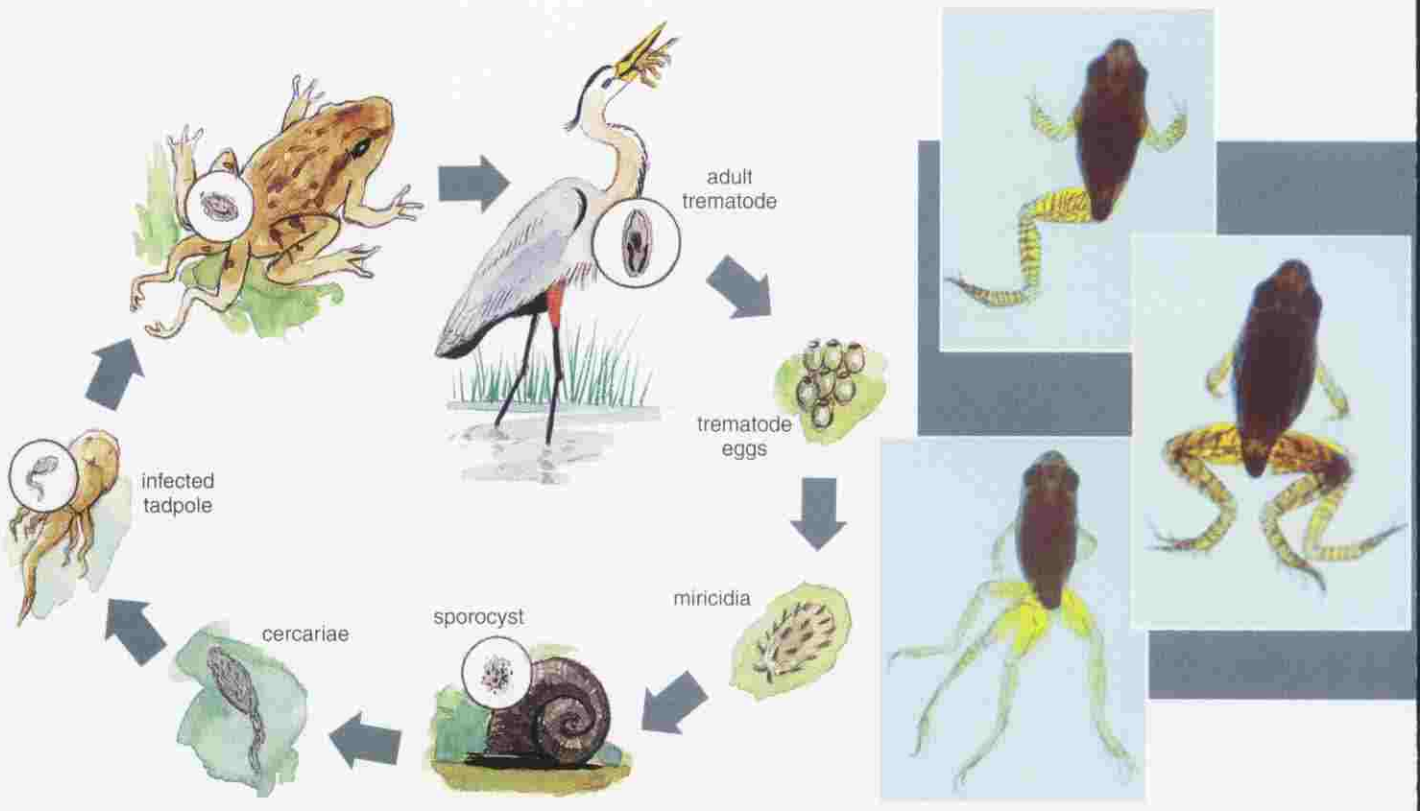

Figure 4. Trematodes like *Ribeiroia* cause developmental deformities in several amphibian species. During the life cycle of this flatworm parasite, adults live and reproduce in the digestive systems of birds *(left)*. Trematode eggs are released with the bird's feces, hatching into free-swimming miricidia that infect snails and develop into sporocysts. Within the snail hosts, each sporocyst produces many infectious cercariae, which leave the snail and burrow into the bodies of amphibian larvae, where they form cysts in and around the hindlimb buds. This disrupts normal development, producing deformities such as duplication or deletion of the rear legs, as seen in wood frogs from central Pennsylvania *(right)*. Infected animals are readily caught and consumed by the bird hosts to complete the cycle.

which clouds formed, thereby diminishing the amount of moisture in large portions of the cloud forest. Pounds hypothesized that the stress from their drier surroundings made individuals more susceptible to infection. Even as some species shifted their habitat into the remaining moist areas, the increased amphibian density in these oases facilitated the spread of a waterborne pathogen.

These associations between disease outbreaks and weather patterns are not limited to amphibians. Global warming also influences the course of certain human diseases. For example, cholera is a water-borne bacterial disease that has reemerged as an epidemic problem. In 1988 there were approximately 50,000 cases of cholera worldwide. Three years later, that number had increased to 600,000. What was the cause of the outbreak? There were many contributing factors, but a major one was the presence of the 1991 El Niño event. The incidence of cholera infection in humans, like *Saprolegnia* in the western toad, is correlated with global climatic cycles such as ENSO, perhaps because local warming of shallow bodies of water led to conditions that were more favorable to the transmission of the bacterium or because of indirect effects on human water usage and sanitation.

Among the important lessons that emerge from these studies is this: The local consequences of large-scale climate shifts—as well as their effects on living systems—are varied. As a result, the way that changes in the weather impact amphibians (and humans) will probably be different for each environment and species.

Fluke of Nature

A great variety of parasites are dependent on freshwater environments. The parasitic, platyhelminthic flatworms called trematodes or flukes are prominent examples. Members of this class usually adopt free-swimming aquatic forms for part of their life cycle, and they later rely on an intermediate host that is often a freshwater organism. Several well-known human diseases, including but not limited to schistosomiasis, echinostomiasis and cercarial dermatitis, result from infection with various flukes. Collectively, these diseases affect hundreds of millions of people around the world. However, trematodes have also received close attention recently because of their role in outbreaks of amphibian deformities.

Amphibian deformities, particularly those related to limb development, have been reported in 46 states in the U.S., five provinces in Canada, and several other countries. They aren't a new phenomenon: Reports from the early 1700s document similar specimens, suggesting that whatever causes the deformities has been present for centuries. These historical records describe one or two affected frogs in a population, and scientists usually regard a small number of deformities, less than five percent of the population, to be normal. However, the frequency of such malformations has skyrocketed in recent decades. Contemporary reports describe an extremely high incidence of developmental abnormalities in some areas—from 15 to 90 percent—often affecting multiple species at a site.

Several studies have shown that infection by the trematode *Ribeiroia* causes many of these deformities. During its life cycle, *Ribeiroia* depends on several hosts, including pond snails. When their snail hosts are present, free-swimming trematode larvae, called *cercariae*, reach the next step of their life cycle by targeting tadpoles and burrowing into their bodies. In some cases the cercariae develop into cysts called *metacercariae*. When the cercariae encyst in developing limb buds, the cysts disrupt the normal growth patterns and cause duplication or deletion of legs in the adult frog.

In 2002, Pieter Johnson of the University of Wisconsin and his colleagues suggested that *Ribeiroia* occurrence and limb deformities were associated with highly productive artificial ponds situated near agricultural areas. These pools were extremely nutrient dense because of fertilizer runoff and cattle manure, leading to increased algal growth and greater snail density. Amphibians and birds—the other necessary hosts for *Ribeiroia*—also used these environments readily. This type of artificial wetland has become much more common with changes in agricultural land-use patterns associated with the so-called "green revolution" in the 1960s and the current trend toward large-scale corporate farming.

Farm ponds aren't the only sites where habitat manipulation is altering the incidence of trematode diseases. Most epidemiologists, parasitologists and health professionals now recognize that several human parasites have thrived after anthropogenic changes were made to freshwater ecosystems. An example is schistosomiasis, a trematode disease that contributes to the death of about a million people each year. The incidence of this parasitic infection is growing because various human activities, including dam construction, deforestation and irresponsible agricultural practices, have multiplied the amount of suitable habitat for the parasite's snail hosts. This is a common theme: Many emerging-disease hotspots have been linked with changes that led to population booms in critical hosts. These findings illustrate how human beings have altered the environment in ways that have inadvertently increased the risk to our own health.

Chemical Compromise

The same kinds of environmental degradation that result in increased snail densities can also increase amphibian exposure to pollutants such as pesticides. Many deformed frogs have been found in agricultural areas where, in addition to fertilizer, herbicides and insecticides accumulate. Such chemicals are nearly ubiquitous in modern agriculture: Since their early use in the mid-1940s, the worldwide application of pesticides has grown from 50 million kilograms per year to approximately 2.5 billion kilograms per year.

Our research group recently investigated the role of chemical contamination in trematode-mediated limb deformities among wood frogs *(Rana sylvatica)* in central Pennsylvania. As expected, we found that the parasites caused limb deformities in the frogs: When we prevented trematode cercariae from getting to the developing tadpoles, the malformations never occurred. However, in the wild populations there was great variation in the incidence of limb deformities depending on which pond the frogs came from. The animals that lived in ponds receiving pesticide runoff developed abnormalities much more often that animals from ponds without agricultural runoff—even though all the ponds had comparable levels of *Ribeiroia*.

We thought that stress, in the form of pesticide exposure, might have decreased the host tadpoles' ability to resist infection, resulting in higher parasite loads and higher risk of limb deformities. To test the idea, we put *R. sylvatica* tadpoles in a controlled labora-

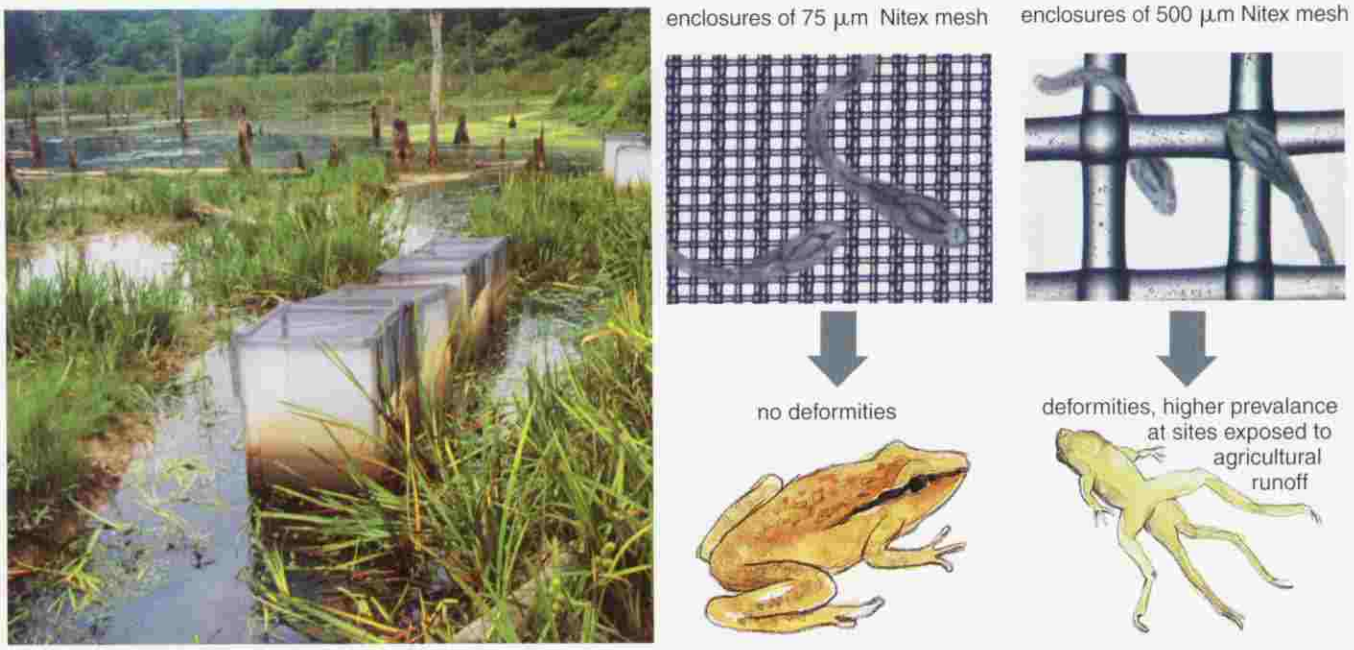

Figure 5. Trematode infection leads to limb deformities, but the infection rate is higher at sites that receive agricultural runoff. The authors reared groups of tadpoles inside screened enclosures *(left)* at six ponds where *Ribeiroia* was present. Three of the ponds were contaminated by runoff containing agricultural pesticides. Different mesh sizes were used to exclude the parasite from some groups and permit access to others *(right)*. For the frogs housed behind finer mesh, the absence of cercariae prevented developmental abnormalities at all six locations. As expected, frogs that were reared in the larger-mesh enclosures were exposed to the parasite and developed limb deformities. However, the infection rates were significantly higher in the ponds that received agricultural runoff—despite the fact that the densities of *Ribeiroia* were comparable.

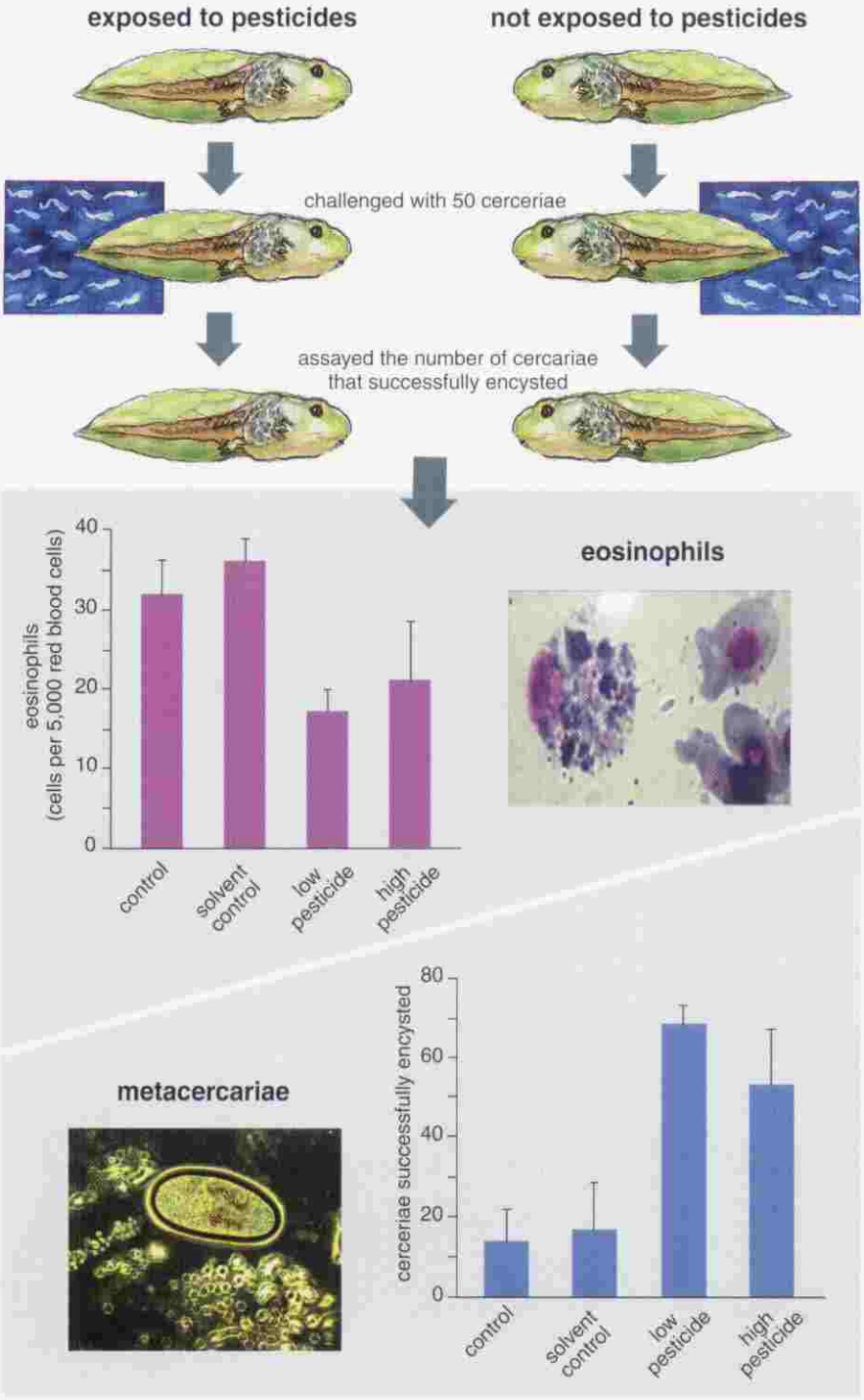

Figure 6. In the laboratory, tadpoles exposed to even low levels of pesticides (the U.S. Environmental Protection Agency maximum for human drinking water) had fewer eosinophils, a type of white blood cell—potentially indicating a weakened immune system—and much higher rates of parasitic infection than controls.

tory environment and exposed them to one of three different pesticides (atrazine, malathion or esfenvalerate) at concentrations equal to the U.S. Environmental Protection Agency maximum for drinking water. We measured the immunocompetency of each group of animals by challenging them with cercariae and by examining a blood sample for the number of eosinophils, a cell type that may help resist macroparasite infection. For the atrazine and esfenvalerate groups, even these supposedly safe levels had dramatic effects on the wood frogs, and malathion had similar consequences at higher concentrations. The animals that were exposed to these pesticides showed sharp increases in the proportion of encysted cercariae and significantly fewer eosinophils.

These findings parallel other analyses of disease outbreaks in the midst of environmental stress. An example is the 1988 introduction of phocine distemper virus into North Sea pinnipeds. The virus is endemic to its usual host, the harp seal, which lives on the Arctic pack ice. However, as the host population shifted its range southward in response to overfishing, the virus passed to the native seal species of northern Europe and inflicted catastrophic losses. Two separate investigations into the animal epidemic, or epizootic, suggested that the seals might have been particularly vulnerable because their immune systems had been compromised by exposure to pollutants such as polychlorinated biphenyls (PCBs). Other studies of marine vertebrates have also indicated that some pollutants, particularly pesticides, can have immunotoxic properties, which impair the ability to rebuff infectious agents.

Old Fungi, New Hosts

One of the consequences of our domination of the Earth is massive biotic homogenization. Worldwide transport of people, plants and animals has become routine, resulting in the breakdown of biogeographic boundaries that historically maintained distinctive flora and fauna in different regions. People move organisms for conservation, agriculture and hunting, in addition to accidental transport, on a global scale. This steady traffic represents a constant influx of exotic infectious agents to humans and wildlife. Such foreign introductions are often referred to as "biological pollution," and they have universally diminished local biodiversity.

One example of this kind of introduced pathogen is a newly discovered fungal disease of amphibians, chytridiomycosis, caused by infection with *Batrachochytrium dendrobatidis*. The chytrids are the oldest fungi we know of, based on fossils from the Rhynie Chert in northern Scotland (see *Marginalia*, page 120). These ancient, still ubiquitous fungi are found in moist soil and aquatic habitats where they act primarily as detritivores. Parasitic members of this group infect plants, protists and invertebrates, but *B. dendrobatidis* is the first chytrid known to infect vertebrates. It has caused mass die-offs of juvenile and adult frogs from Australia, Central America and the western United States. The pathogen was first described in 1998 from dead and

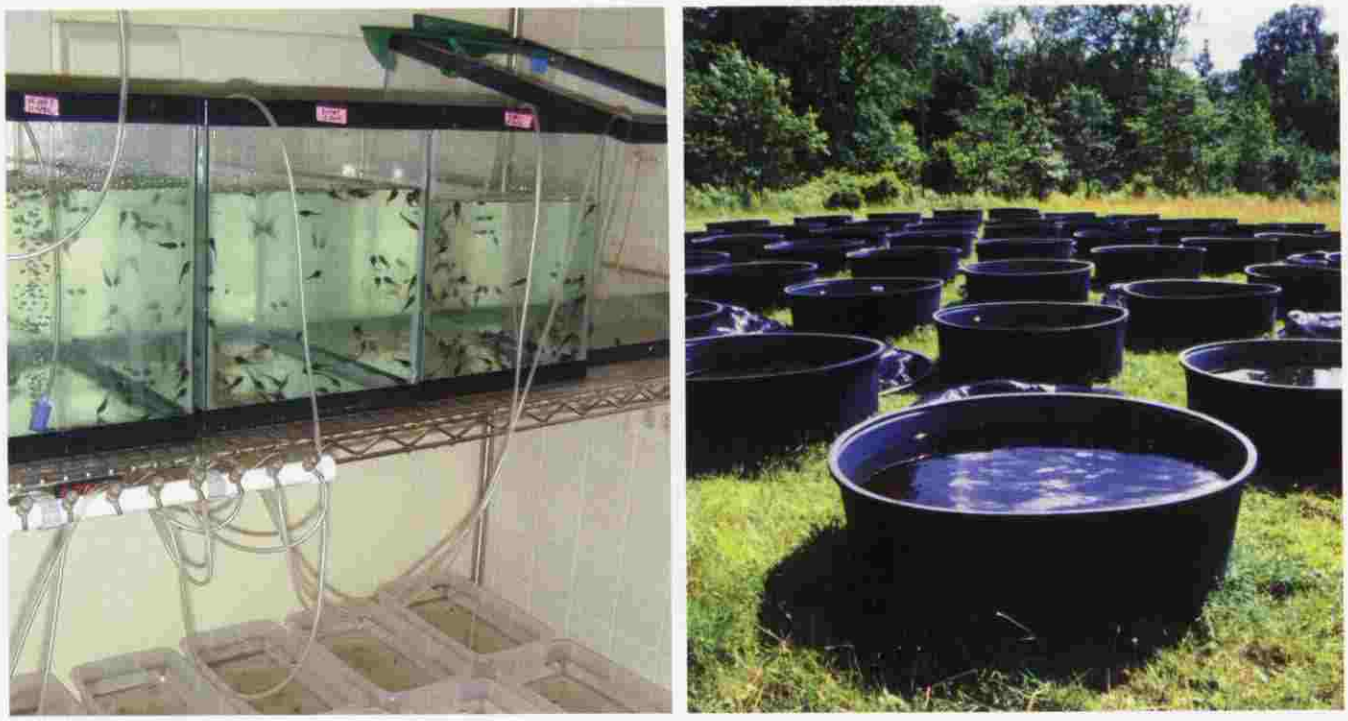

Figure 7. Amphibians are particularly sensitive to the environmental changes responsible for emerging diseases, a property that also makes them ideal models for understanding the mechanisms of infection. Amphibians are amenable to experimental manipulation, not only in wetland settings, but also in well-controlled laboratory environments *(left)* and readily manipulated "mesocosm" experiments *(right)*. This flexibility allows investigators to combine natural settings with precise control of environmental variables and specified levels of infection to probe disease dynamics in the most realistic and powerful way.

dying amphibians in Australia and Panama. Infected animals develop gross lesions and hemorrhages of the skin, which has led some scientists to suggest that the *Batrachochytrium* has specialized to use amphibian keratin as a prime nutrient.

The epidemiological patterns of chytridiomycosis infection are characteristic of a virulent pathogen spreading through a naive host. In Central America and Australia the mortality has been severe, ravaging entire populations over the course of a few months and leaving few survivors. Such high death rates are often associated with introduced pathogens, and other signs also point to a novel agent as the cause of this outbreak. For example, Peter Daszak of the University of Georgia and his colleagues showed that specific DNA sequences from chytrid isolates from around the world were much less divergent than expected for a wild strain, and some samples collected in opposite hemispheres were identical. Further evidence that *B. dendrobatidis* has recently emerged comes from preserved amphibian specimens collected prior to the onslaught. Not one Australian or Central American specimen examined in the 10 years before local crises showed evidence of chytrid infection. But in a strange twist to the story, an examination of preserved frogs that were collected during population collapses in the western United States during the 1970s *has* found evidence of a type of *Batrachochytrium* infection. If this is true, it raises a number of pressing questions. Did the new strain emerge twice? If so, where has it been all this time? Most importantly, why did it subside?

The animal pandemic, or *panzootic*, of chytrid infection is relatively recent, and the field of amphibian biology is still struggling to understand the phenomenon. So while the findings to date are consistent with a novel, introduced pathogen, other factors can't yet be excluded from an explanation of these massive crashes. So the chytrid hypothesis, which states that the declines of highland amphibians in Central America and Australia are due solely to chytrid infection, is likely to be an oversimplification. Even the population declines in amphibians of the Monteverde cloud forests—which were strongly linked to climatic warming—have occurred synchronously with nearby waves of chytrid infection, even as the specific pathogen in Monteverde has yet to be identified. Another puzzling detail is that some of the mortality among Central American frogs has been accompanied by simultaneous declines in reptiles and birds. The aquatic chytrid fungus is unlikely to attack terrestrial vertebrates, so the relationship between these deaths remains a mystery.

Puttin' the Flava in Flavivirus

Despite the uncertainty that remains, chytrid infection has followed the paradigm of novel pathogen, naive host in an exemplary way. We're familiar with the script for this kind of onslaught because the pattern has been repeated so many times. The template was followed when Spanish explorers introduced smallpox and measles to the Americas, and it is still being played out in today's newspaper headlines. Among wildlife, chronic wasting disease is spreading through wild ungulate populations as infected elk are transported among game ranches, and duck plague threatens the future of North American wildfowl after being introduced repeatedly from abroad.

For humans, the West Nile virus provides a more urgent example. This microbe is a mosquito-borne flavivirus that infects people, horses and birds. Although it is widespread in Africa, Asia and the Middle East, its appear-

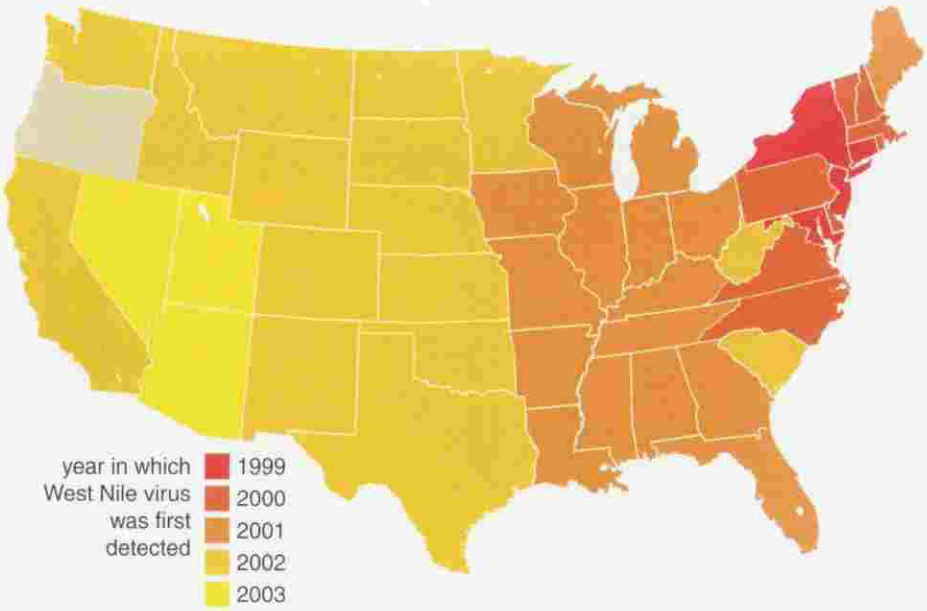

Figure 8. The outbreak of West Nile virus in North America illustrates the rapidity with which a novel pathogen can infect a naive population. This "zoonotic" virus infects birds, mosquitoes, humans and horses. In the five years since it was first detected, it has spread to all but one of the 48 contiguous United States.

ance in North America is quite recent, with the first human cases diagnosed in 1999. Initial cases in the northeastern United States coincided with a large epizootic in captive exotic and native wild birds. West Nile virus could have entered through a number of avenues, including travel by infected humans, importation of infected domesticated birds or the unintentional transfer of infected mosquitoes. In the four years since its introduction, the virus has spread extremely quickly and now covers most of North America. During 2002 and 2003, 13,000 cases of West Nile infection were reported to the Centers for Disease Control and Prevention, resulting in nearly 500 human deaths. West Nile virus illustrates the rapid rate at which a novel pathogen can spread once it encounters a fresh host population.

Low Biodiversity, High Disease Risk

Biodiversity advocates often argue that animals, plants and microbes are valuable as sources for new medicines or other useful products. Seldom mentioned is the benefit of species diversity in mitigating human disease risk, a hypothesis called the "dilution effect," which was proposed by Richard Ostfeld and his colleagues at the Institute of Ecosystem Studies in Millbrook, New York. Their model evolved to explore the relationship between humans, wild mammals and the deer tick, which transmits the spirochetal bacterium that causes Lyme disease. In a 2000 article, they explained that in diverse communities, many ticks do not carry the disease because some vertebrate hosts that offer perfectly good blood meals are inefficient at transmitting the spirochete to the feeding ticks. However, degraded habitats lose many species of tick hosts, leaving the ticks to feast on the few remaining mammals that are well adapted to disturbed areas. One of these species, the white-footed mouse *Peromyscus leucopus*, also happens to be the most effective reservoir for the spirochete. In 2003, the same group demonstrated that increased species diversity could buffer the risk of Lyme disease transmission by providing hosts other than white-footed mice for ticks to feed on. More diversity in macrofauna would, presumably, lead to lower rates of tick infection and therefore lower risk of human exposure.

The proposed relation between species diversity and infection risk is new, but we have seen similar patterns in our own most recent work with amphibians. We observed that variably urbanized wetlands showed an inverse relation between the diversity of amphibians, trematodes and snails, and the degree of urbanization. At the same time, snail density and the number of trematode infections among individual amphibians was higher in the more disturbed ponds. Although these data are preliminary, the mechanism responsible for this pattern could be similar to the dilution effect. However, we cannot rule out the contribution of other factors that might co-vary with diversity in explaining the data. Consequently, the higher trematode susceptibility may not be driven by a loss of diversity *per se* if the same factors that decrease diversity also increase infection. If future data can substantiate the connection between species diversity and disease risk, then the biodiversity debate will become much more tangible and pressing.

Conclusion

Species extinction and the emergence of infectious disease are two of the most serious global concerns we face. These processes are tightly intertwined, with parasitic and microbial infection acting as a cause for and consequence of biodiversity loss.

There is no doubt that the world's climate patterns are changing. Although some scientists maintain that these alterations cannot yet be conclusively linked to human actions, none contest that global biodiversity has sharply decreased in recent decades. However, not all organisms are negatively affected by such environmental changes. Indeed, many organisms, including hundreds of pathogens and parasites, have been great beneficiaries of these alterations. If current trends continue, these life forms are likely to experience continued prosperity. Unfortunately, the outlook for animals, including people, is somewhat dimmer.

The rapid global declines in amphibian populations have led some observers to believe that such massive decimation of frogs and toads is somehow separate from the overall biodiversity crisis. This is a fallacy. It is now clear that the loss of amphibians is part of a larger phenomenon that is also increasing the prevalence of infectious disease in human and wildlife populations.

If we hope to extricate ourselves from this situation, we must gain greater insight into the origins and mechanisms of future disease outbreaks. The complexity of the problem presents a daunting obstacle to the task of reversing the trend of accelerating emergence of infectious disease. However, it seems clear to us that we need a better understanding of the environmental cofactors that facilitate the

spread of disease or the susceptibility of hosts. At the very least we need a much better understanding of how humans intentionally or inadvertently disperse disease-causing organisms.

Amphibians make ideal subjects to investigate these issues because they have proved to be particularly sensitive to the environmental cofactors that trigger disease outbreaks. This sensitivity makes them an early warning system of environmental degradation and disease emergence—the canaries in our planetary coal mine. In addition, frogs are amenable to experimental manipulations, allowing controlled experimentation to assess the influence of key environmental variables on disease emergence. In many ways it seems fitting that although amphibians have been so severely affected by the conditions that promote disease emergence, they might also serve as a most promising tool to understanding this process.

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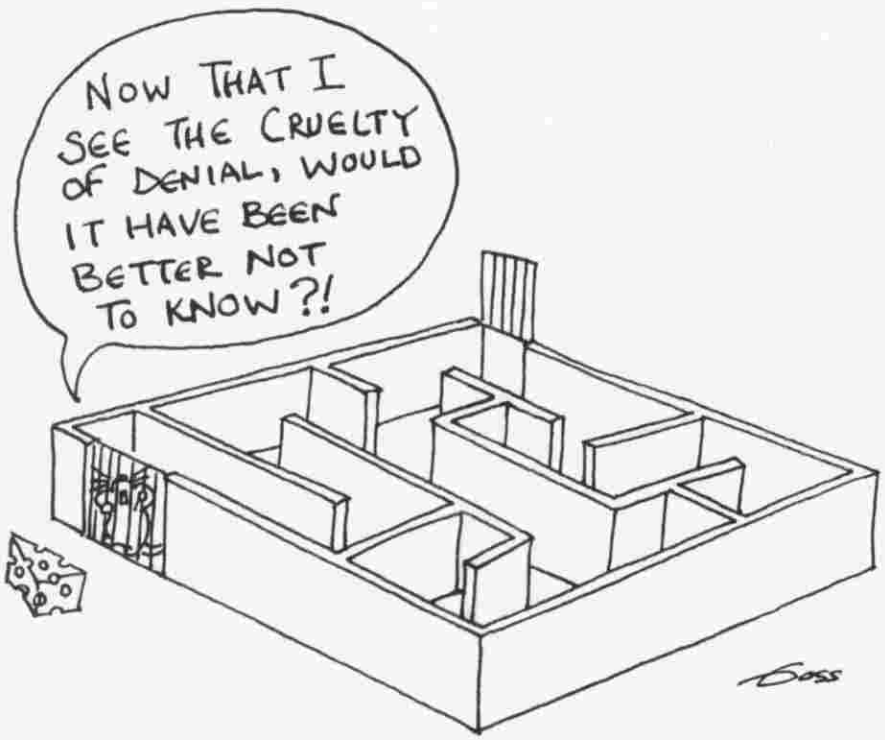

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