National Science Foundation
WHERE DISCOVERIES BEGIN

ECOLOGY AND EVOLUTION OF INFECTIOUS DISEASES — A SPECIAL REPORT

Overview: Infectious Diseases Spreading

West Nile virus. Hantavirus. Lyme disease. All are infectious diseases spreading in animals, and in humans. Is our interaction with the environment somehow responsible for the increase in incidence of these diseases?

A joint National Science Foundation (NSF) and National Institutes of Health program--Ecology and Evolution of Infectious Diseases (EEID)-- supports efforts to understand the underlying ecological and biological mechanisms behind human-induced environmental changes and the emergence and transmission of infectious diseases. Projects funded through the EEID program and other NSF programs allow scientists to study how large-scale environmental events--such as habitat destruction, invasions of non-native species and pollution—alter the risks of emergence of viral, parasitic and bacterial diseases in humans and animals.

Pathogens, or disease-causing microbes, rarely cause extinctions in the species they infect. There are a few examples, however, where a pathogen may have resulted in the extinction of a species. Frogs in El Cope, Panama, affected by a fungus called *Batrachochytrium dendrobatidis*, are a case-in-point. One frog species there that lived along riverbanks disappeared completely in one month.

Credit: Nicolle Rager Fuller, National Science Foundation

Researchers supported in the EEID program are advancing basic theory related to infectious diseases and applying that knowledge to improve our understanding of how pathogens spread through populations at a time of increasing global change.

The benefits of research on the ecology of infectious diseases include development of theories of how diseases are transmitted, improved understanding of unintended health effects of development projects; increased capacity to forecast disease outbreaks and knowledge of how infectious diseases emerge and reemerge.

Disease transmission is a complex process that involves the disease organism, disease vectors, disease hosts and the predators of those hosts. It links relatively pristine areas with human habitations and human-dominated areas.

Credit: Nicolle Rager Fuller, National Science Foundation

"Virtually all the world's terrestrial and aquatic communities have undergone dramatic changes in biodiversity due primarily to habitat transformations such as deforestation and agricultural intensification, invasions of exotic species, chemical contamination and climate-change events," said Sam Scheiner, EEID program director at NSF. "The coincidence of broad-scale environmental changes with the emergence of infectious diseases may point to underlying and predictable ecological relationships."

Examples of studies funded by the EEID program include research on the origin and spread of the aspergillus-gorgonian coral disease and how climate and environment may have worked as facilitators of the disease; effects of human-induced change on the ecology of human pathogens in North Carolina's Neuse River estuary, which is polluted by excess nutrients from human activities; the microbial community ecology of tick-borne human pathogens; plague as a model for disease dynamics; ecological reasons for rodent-borne disease outbreaks; and how social organization influences an infectious disease outbreak.

Further information about EEID program support is available in the latest program solicitation.

By Cheryl Dybas

Rare Infectious Cancer

The following is part seven in a series on the NSF-NIH Ecology and Evolution of Infectious Diseases (EEID) Program. See parts one one, two, three, four, five, six, eight, nine and 10.

Taz, was his name, the Tasmanian devil of Warner Bros. cartoon fame. A scrappy omnivore who ate anything and everything, he spun in a vortex and bit through everything in his path.

The devil was short-lived, however, making television appearances for a few years in the late 1950s and early 1960s before disappearing from view. In 1991, Taz got a reprieve: His own show, "Taz-Mania," which ran for three seasons. Then he was gone for good.

From the screen to the wild

Tasmanian devils in the wild are no less imperiled. Carnivorous marsupials, they're found only on the Australian island of Tasmania. With a stocky build, black fur, keen sense of smell and ferocity when feeding, "real-life" Tasmanian devils and their cartoon namesake have much in common.

The size of small dogs, Tasmanian devils became the largest carnivorous marsupials in the world following the 1936 extinction of thylacines (*Thylacinus cynocephalus*), known as Tasmanian tigers or Tasmanian wolves. Thylacines lived on continental Australia, Tasmania and New Guinea.

Not all Tasmanian devils are docile; many share traits with the cartoon character "Taz."

Credit: Government of Tasmania

Will the fate of *Sarcophilus harrisii*, the scientific name for the Tasmanian devil, mimic that of the thylacine?

"If a way isn't found to stop devil facial tumor disease, or DFTD," says disease ecologist Andrew Storfer of Washington State University, "models predict that Tasmanian devils could be extinct in as few as10 years."

And vanishing with them, valuable clues to diseases in other species, including humans.

DFTD is an aggressive, non-viral, transmissible parasitic cancer that is 100 percent lethal, says Storfer. "In short," he says, "it's bad news."

Can we save the Tasmanian devil?

To study DFTD and find ways of understanding its emergence and spread, Storfer has received a grant from the National Science Foundation (NSF)- National Institutes of Health (NIH) Ecology and Evolution of Infectious Diseases (EEID) Program.

Collaborators include Paul Hohenlohe of the University of Idaho, Hamish McCallum of Griffith University, Menna Jones of the University of Tasmania and Elizabeth Murchison of the Wellcome Trust Sanger Institute.

The NSF-NIH EEID Program supports efforts to understand the ecological and biological mechanisms that link environmental changes and the emergence and transmission of infectious diseases.

Projects funded through the program allow scientists to study how large-scale environmental events--such as habitat destruction, invasions of nonnative species and pollution--alter the risks of emergence of viral, parasitic and bacterial diseases.

Storfer's research may lead to new insights about the spread of flu in humans. It also may help scientists understand other infectious diseases in animals such as bats, and how certain cancers progress.

"This study provides an excellent test-bed for understanding the spread of infectious diseases," says Sam Scheiner, EEID program director at NSF. "The results may help us control the spread of seasonal flu in people, West Nile virus in birds and white-nose syndrome in bats, among many other diseases."

Tasmanian devils: extinction on the horizon

The first official case of devil tumor facial disease was reported in 1996. Since then, Tasmania's devil population has declined by 70 percent. Findings reported in 2010 show that 80 percent of the remaining devils are affected.

"Tasmanian devils that live in high-density populations may suffer drastic reductions a few years after emergence of the disease," Storfer says.

DFTD has been slowly moving from east to west across Tasmania for the last 17 years; it's now approaching the west coast. "Soon there may be no known uninfected devils," says Storfer.

The disease is spread when Tasmanian devils bite each other's heads while fighting over food, during territorial interactions and when they spar during mating season.

Devils that contract the disease develop lesions around their mouths that become cancerous tumors. The tumors may spread from their faces to their entire bodies. Devils almost always die within six to nine months.

Devil facial tumor disease likely began in what are called Schwann cells. Schwann cells are found in the peripheral nervous system; they produce myelin and other proteins essential for the functions of nerve cells.

In response to DFTD, Tasmanian devils have changed their reproductive habits. Before the outbreak, females started breeding at two years old. Now they breed by the end of their first year--and often die of DFTD soon afterward.

There's a ray of light, however, in this dark day for devils. Some devils have been found with partial immunity to the disease. Breeding in captivity is underway to try to save the species.

"Emerging infectious diseases like DFTD are one of the great scientific challenges of the 21st century," says Storfer. "Infectious diseases are now the sixth leading cause of species extinctions."

Answers in Tasmanian devils' genomes?

Extensive research by Storfer and others, including thousands of samples taken before and after devil die-offs, has given scientists a rare opportunity to study the genomic interactions of

an infectious disease and its host--the devils--across an entire species' range.

"The research will tell us about the genetic basis of Tasmanian devils' susceptibility to the tumors," says Storfer, "providing environmental managers with information about which particular devils would be best suited for captive breeding programs."

Knowledge of the rates and direction of past tumor spread will enable scientists to uncover the likely locations of future infections.

Although only a few infectious cancers have been documented, Storfer says, "this disease shares properties with human cancers.

"Our research, especially genetic studies, may reveal the underlying reasons why DTFD is so prevalent and can hold on for so long in a population, perhaps providing information on cancer recurrence in humans."

To test predictions of the course of the epidemic, he and colleagues plan to meld what they call "devil contact network modeling" with genomic studies of Tasmanian devil populations expected to become infected.

"The answers will help in developing responses to this and other disease outbreaks in Tasmanian devils--and potentially in people," says Storfer.

Taz may be gone, but, says Storfer, "Hopefully it's not too late for the real Tasmanian devil."

Frogs VS. Trout

Ecology of infectious diseases data gathered over seven years have played a key role in convincing the National Park Service and the California Department of Fish and Game to remove trout from high-altitude lakes in California's Sierra Nevada. The trout are causing the disappearance of the mountain yellow-legged frog.

Funded through the EEID program, biologist Vance Vredenburg of San Francisco State University showed that introduced-trout have devastated native frog populations over the past 50 years in formerly fish-free, high-Sierra lakes, but that removing the fish can allow the frogs to flourish once more.

"The mountain yellow-legged frog used to be the most common inhabitant of the high Sierra, but frog populations have declined dramatically enough to put it on the endangered species list," said Vredenburg.

Mating season (June 2004) in Sixty Lake Basin. The large lake in the foreground is a frog population source and the three lakes in the background are trout removal lakes now colonized by large frog populations.

Credit: Rob Bingham, University of California, Berkeley

"The worldwide decline in frog and salamander populations is a harbinger of more serious threats posed by the current rapid environmental changes our planet is undergoing," said Sam Scheiner, EEID program director at NSF. "Possible culprits include the spread of disease, increased UV radiation and predation by introduced species. This study helps to tease apart those complex causes and shows that, in these frogs, the decline is due to increased predation. For these populations, removing the trout will save the frogs. Such studies provide hope that we can reverse the large environmental changes we're causing."

As part of the research, Vredenburg removed trout from five lakes and documented a rebound in the frog population in all of them. Three years after trout removal, the frog populations in all five lakes were indistinguishable from populations at lakes that had never seen a trout.

"The response was incredibly dramatic and rapid," Vredenburg said. "Every time you plant hundreds of thousands of fish, you're hammering a nail in the frogs' coffins."

Vredenburg has also teamed up with other researchers to determine the effect of a chytrid fungus, *Batrachochytrium dendrobatidis*, on the mountain yellow-legged frog. The fungus, which is threatening frog populations around the world, attacks tadpoles as well as adults, and can kill adult frogs. It was discovered in the Sierra Nevada in 2001.

Loss of wetland habitat has also reduced populations of frogs and toads and endangered several species of amphibians with restricted ranges. Alarming new events have added to these trends. For example, frog and toad populations have declined dramatically in the past several years, many in high-altitude places in the United States, Puerto Rico, Costa Rica, Panama, Colombia and Australia. Studies suggest that these population declines may be caused by infections, perhaps promoted by environmental stressors.

For more information on studies of the chytrid fungus, please see Outbreak: Rapid Appearance of Fungus Devastates Frogs, Salamanders in Panama.

A California Department of Fish and Game airplane stocking fingerling trout in the Sierra Nevada wilderness. This practice continues in parts of the Sierra Nevada.

Credit: © Stephen Ingram

A mating pair of mountain yellow-legged frogs.

Credit: Vance Vredenburg, University of

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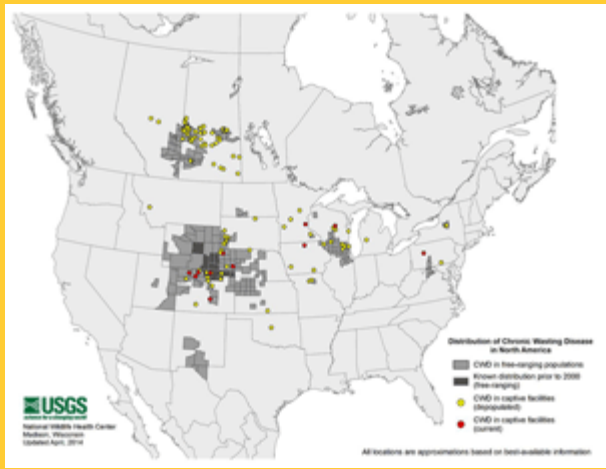
Deer Susceptible to Disease

Researchers funded through the EEID program recently found that chronic wasting disease (CWD) can be transmitted through environments contaminated by whole carcasses or by excrement of animals infected with the pathogen that causes CWD. CWD is rampant in Western states like Colorado.



The extent of chronic wasting disease in the U.S., as of 2012.

Credit: USGS

"Diseases like CWD are poorly understood and of rising concern," said Sam Scheiner, EEID program director at NSF. "This new knowledge will substantially alter how we manage the disease in wild and domestic animals."

CWD is a fatal neurological ailment of elk, white-tailed deer and mule deer. Researchers believe the disease is caused by an aberrant prion protein that misfolds in the brain, destroying brain tissue as it progresses. The disease is always fatal and there is no known cure or treatment.

Although live deer and elk still seem the most likely way for CWD to spread geographically, environmental sources could contribute to maintaining and prolonging local epidemics, even when all infected animals are eliminated, said biologist Tom Hobbs of Colorado State University. "Through the EEID program, we hope to develop models that will predict the behavior of the disease, shedding light on how potentially complex these epidemics may be in natural populations."

Lyme Disease on the Rise

Lyme disease incidence is rising in the United States and is in fact far more common than West Nile virus and other insect-borne diseases. Forest fragmentation could explain the increase.

Areas of patchy woods, which are very common in cities and suburban and rural areas, may have higher populations of Lyme-disease carrying ticks than forest fragments, which generally have fewer species than continuous habitat. This is because some species thrive in smaller places.

White-footed mice, for example, are more abundant in forest fragments in some parts of the country, likely because fewer predators and competitors remain there. These mice are particularly abundant in patches smaller than about five acres, which could spell trouble for people living nearby: the mice are the main carriers of Lyme disease-causing bacteria. In the eastern and central United States, Lyme disease is contracted via blacklegged ticks that feed on infected mice, then transmit the bacteria when the ticks bite people. As a result, says biologist Felicia Keesing of Bard College in Annandale, New York, Lyme disease is concentrated in areas where people live near forests with blacklegged ticks.

Keesing, scientist Richard Ostfeld of the Cary Institute in New York and other researchers found that smaller forest fragments had more infected ticks, which could translate to more Lyme disease. Forest patches that were smaller than three acres had an average of three times as many ticks as did larger fragments, and seven times more infected ticks. As many as 80 percent of the ticks in the smallest patches were infected, the highest rate the scientists have seen. These ticks may also be infected with other emerging diseases--Babesiosis, Anaplasmosis and Powassan encephalitis--therefore, forest fragmentation might also be contributing to other serious illnesses, Ostfeld says.

"Our results suggest that efforts to reduce the risk of Lyme disease should be directed toward decreasing fragmentation of deciduous forests of the northeastern United States, particularly in areas with a high incidence of Lyme disease," says Keesing. "The creation of forest fragments smaller than five acres should especially be avoided."

For more information, see Lyme Disease: Ten things you always wanted to know about ticks.