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Studies Offer New Insights Into How Deadly Amphibian Disease Spreads and Kills

Scientists have unraveled the dynamics of a deadly disease that is wiping out amphibian populations across the globe. Chytridiomycosis is caused by a microscopic aquatic fungus called *Batrachochytrium dendrobatidis* (Bd) that attacks the skin of amphibians. This disease was discovered in 1998 and has already caused the decline or extinction of hundreds of amphibian species across the globe. This impact was recently described by scientists as "the most spectacular loss of vertebrate biodiversity due to disease in recorded history."

The new findings, from two separate studies published in today's online edition of the Proceedings of the National Academy of Sciences (PNAS), suggest that infection intensity -- the severity of the disease among individuals -- determines whether frog populations will survive or succumb to chytridiomycosis. The research identifies a critical tipping point in infection intensity, beyond which chytridiomycosis causes mass mortalities and extinctions.

"We found that mass frog die-offs only occur when the severity of Bd infection reaches a critical threshold among the individual frogs," said Vance Vredenburg, lead author of one of the studies and an assistant professor of biology at San Francisco State University. "Now that we know this limit, conservation efforts may be able to save susceptible frog species by preventing the disease from reaching this

point."

UC Santa Barbara's Cheryl J. Briggs, professor of Ecology, Evolution and Marine Biology and the Duncan and Suzanne Mellichamp Chair in Systems Biology, is lead author of the second study and a co-author of the first study. Other collaborators from UCSB were Roland A. Knapp, a research biologist with the Marine Science Institute, and graduate student Tate S. Tunstall.

In the first study, Vredenburg and colleagues tracked the invasion and spread of Bd among frogs in California's Sierra Nevada mountains during a 13-year period, focusing on two species of the mountain yellow-legged frog (*Rana muscosa* and *Rana sierrae*). The study described the initial invasion of Bd into the study areas and its subsequent spread to all mountain yellow-legged frog populations. Within weeks of when Bd infection intensities reached the critical threshold, frog populations experienced mass die-offs. Two to three years after Bd arrival, dozens of frog populations were extinct.

"Mountain yellow-legged frogs can naturally occur at such high densities that when Bd hits previously uninfected populations, transmission and re-infection occur at such rapid rates that the severity of infections on all frogs rapidly reach the lethal level, and the frog population goes extinct," said Briggs.

Some previous studies have argued that Bd may be ubiquitous in the environment and that recent observations of frog die-offs due to chytridiomycosis were a consequence of frogs becoming more susceptible to Bd, perhaps due to changing environmental conditions. The finding in the current study -- that Bd was not present in the study areas prior to the die-offs -- suggests instead that Bd is a novel pathogen to which frogs have not been previously exposed.

But not all mountain yellow-legged frog populations that become infected with Bd are driven extinct. In the companion study, Briggs and colleagues used mathematical models and individual-based infection data to explore why the disease drives most frog populations to extinction, while a few survive with the disease.

Although differences between frogs in their susceptibility or between Bd strains in their virulence both have the potential to contribute to these different disease outcomes, Briggs and the other researchers demonstrate that neither of these differences is necessary to explain the long-term persistence of infected frog populations. Instead, the alternative disease outcomes observed in natural

populations may result solely from density-dependent, host-pathogen dynamics.

An unusual feature of Bd, which can help explain the different outcomes in different populations, is that it is relatively ineffective at replicating on a frog's body in the same way as cancer or a viral infection. A key part of the Bd life cycle involves a swimming fungal spore that must either re-infect the same frog host after it is released outside the body, or find a new host to continue growing.

Both studies found that infection intensity, which escalates through frogs being re-infected, is central to understanding how to save amphibians from mass extinction caused by chytridiomycosis. High population densities in naïve frog communities could promote re-infection, causing the infection to reach a dangerously high level. The importance of population density is supported by evidence from surveys in Kings Canyon National Park where patterns of infection spread were consistent with frog movement patterns, suggesting that frogs help to re-infect each other through contact.

The authors suggest that conservation efforts should focus on limiting the severity of the fungal infection on individuals during an outbreak of chytridiomycosis. For example, treating individual frogs with anti-fungal compounds, or probiotics -- temporarily removing tadpoles or reducing population density -- might lower infection intensity and allow some frogs to survive an epidemic. Such interventions could promote a stable relationship with the disease where the infection reaches an endemic steady state.

"These results are about more than just frogs," Vredenburg said. "They are about disease, how and why it spreads, and how some populations can be wiped out by a disease while others survive. This is important to all of us, considering that 60 percent of emerging diseases in humans come from wildlife. The models we have provided may be adapted by ecologists to better understand similar diseases that affect humans or cattle or corn, for example."

"Dynamics of an emerging disease drive large-scale amphibian population extinctions" was authored by Vredenburg, in collaboration with Knapp, Tunstall, and Briggs. "Enzootic and Epizootic Dynamics of the Chytrid Fungal Pathogen of Amphibians" was authored by Briggs, in collaboration with Knapp and Vredenburg.

This research was supported by the National Science Foundation Ecology of Infectious Disease Program.

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