

CONSERVATION

Amphibians on the brink

Preemptive policies can protect amphibians from devastating fungal diseases

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Over the past three decades, the emergence of a globalized pandemic lineage of chytrid fungus (*Batrachochytrium dendrobatidis*) has caused declines of amphibian species in Central America, Europe, Australia, and North America (see the figure). By 2004, where documented, 43.2% of amphibian species globally experienced some level of population decrease, and the amphibian chytrid fungus was identified as a major contributing factor for hundreds of species (1). The recent discovery of a related but functionally distinct chytrid fungus, *Batrachochytrium salamandrivorans*, that has begun exterminating salamanders in Europe (2) fulfills predictions that further infectious fungal pathogens will continue to emerge (3). The threat of chytrids and similar fungal

pathogens to areas where they have not yet emerged—for example, in New Guinea—is of critical conservation concern.

Initial conservation action in response to the amphibian chytrid fungus was impeded by a dearth of information, lack of policy experience, and the insidious nature of the disease. That frog declines were global was not recognized until 1989, several decades after regionalized declines had begun (4). The causal agent of the wave of declines was not identified until 1998 (5) and described the year after; the idea of a disease causing mass global extinctions was not consistent with doctrine and met with skepticism. Lack of predecline sampling has restricted the capacity of scientists to conclusively link pathogen arrival with frog declines (6). We now have over two decades of evidence and experience to inform decisions on the management of remaining amphibian refugia in which chytrids have not yet emerged.

Although the mechanisms of pathogen emergence are often difficult to determine, it is now clear that chytrid fungi can remain infective on a range of hosts and media, providing pathways to transmission (7).

Transmission to remote areas, particularly to islands, may be slower than across forested areas, whereas transmission along roads and other pathways may be faster (8). These findings suggest that stringent biosecurity to eliminate the transmission of potentially infective media can reduce the probability of, or at least delay, arrival. The high risk to biodiversity when parasitic chytrid fungi invade novel areas, however, suggests a need to also establish a postinvasion plan before arrival. Some frog populations that declined as a result of the amphibian chytrid fungus have recovered, suggesting great potential for conservation actions such as genome storage and assisted reproduction, which can buy time for populations to adapt (9). Other populations require captive breeding in order to avoid extinction.

Evaluations of responses to emerging infectious disease have identified the benefits of forecasting disease outbreaks and using adequate surveillance before disease spread. Such a preemptive approach was implemented in Madagascar after an unsubstantiated detection of the amphibian chytrid fungus (10). A chytridiomycosis working group was formed to coordinate a preemptive national monitoring plan and enact timely and strategic disease surveillance, which led to the identification of infected areas and a means to investigate mass mortality events.

On a larger scale, the emergence of the salamander chytrid fungus in Europe has evoked timely preemptive action in the United States, Canada, and Switzerland (11),

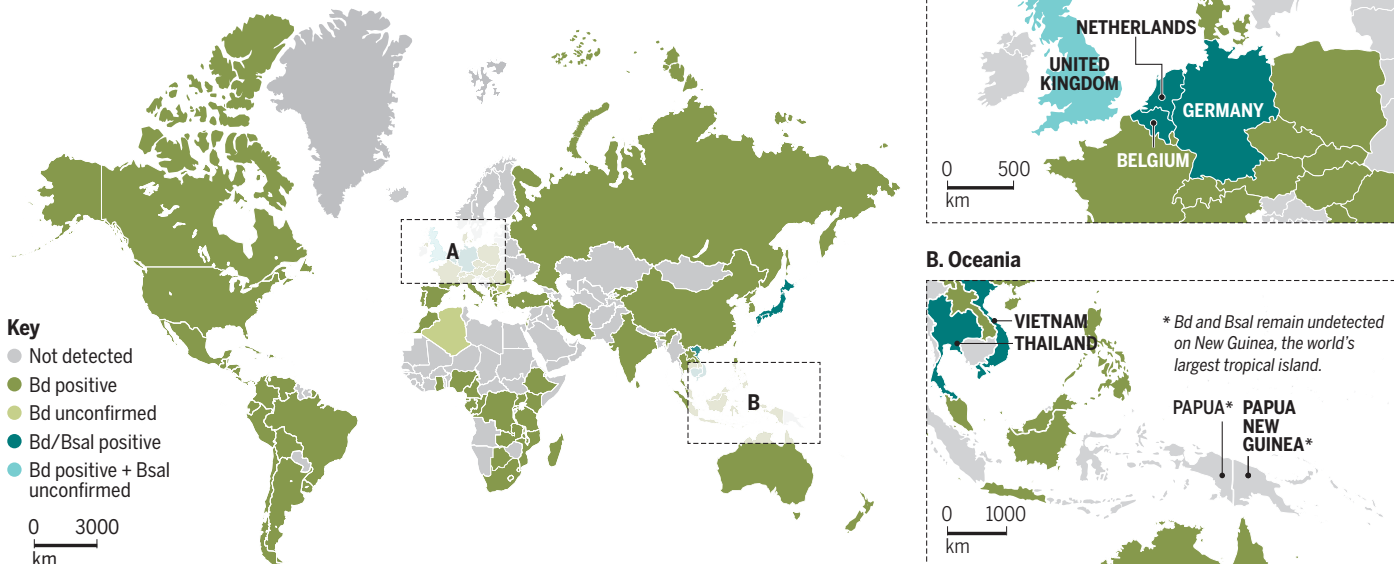
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Parasitic vertebrate chytrids around the world

Parasitic chytrid fungi from the lineage *Batrachochytrium dendrobatidis* (Bd) have been detected in many countries around the world. More recently, *B. salamandrivorans* (Bsal) has been found in Europe and several Asian countries. Efforts to prevent further spread and to develop early response plans in currently uninfected regions are a key priority.



each of which have native salamanders. Immediate research into modes of transmission, susceptible species and habitats, and available treatment options enabled accurate risk assessments to inform policy (12). Importation of salamanders through the pet trade posed the greatest risk of pathogen introduction, and this threat led to lobbying for an importation ban by academics, government officials, and nongovernment organizations, supported by the private sector. Resulting legislation banned the import of 20 salamander genera; a voluntary moratorium by the Pet Industry Joint Advisory Council included additional genera. This example illustrates the power of multiple stakeholders to imple-



The frog species *Litoria auae* is endemic to Papua New Guinea, where no parasitic chytrid fungi have been detected to date.

ment meaningful regulations and voluntary measures in a timely fashion in order to reduce the threat from chytrid fungi.

At the time of writing, salamander chytrid fungus has not been detected in the United States. However, this does not reduce the need for a more comprehensive and permanent legislative solution to wildlife health issues and a mature postinvasion plan should the fungus be detected. Both prevention and options for mitigation need to be part of a considered response to this threat. Furthermore, recent reports that the salamander chytrid fungus can infect hosts other than salamanders suggest that it may emerge even in areas without native salamander fauna, such as Australia and southern Africa (12).

Many areas of the globe still remain naïve to emerging parasitic chytrid fungi (see the figure). For example, disease surveys in New Guinea suggest that its frog fauna (which represents 6% of global frog species) may not yet have been exposed to amphibian chytrids, despite the fact that this remote island is climatically suitable for the parasitic fungi (13). Although the data are sparse, they suggest that New Guinea may be one area where

preemptive disease mitigation could save species such as *Litoria auae* (see the photo) from decline and possible extinction.

There is a distinct opportunity for rapid, preemptive action for policy, legislation, and management informed by a strategic investment to protect the biodiversity of remaining refuges from parasitic chytrid fungi. Although significant outcomes arose from preemptive responses to the threat of the salamander chytrid fungus in the United States, greater impact (such as from comprehensive and permanent legislative solutions) is still hindered by lack of disease policy, fragmented management responsibility, multiple competing objectives, and few effective options for postemergence control (14). These problems are likely to be magnified in developing countries, where many species are undescribed and their ecology is unknown, providing an additional hurdle to effective conservation. Aid and scientific expertise from international sources must flow to regions that are a last remaining refuge for a large proportion of the world's amphibian species.

Comparatively cheap measures, such as lobbying for protective legislation to avoid introduction of wildlife diseases and strategically developing early response plans, will be more effective than post hoc attempts at species salvation. Estimates for effective conservation of 29 threatened frog species in Australia were costed at AU\$15 million over 5 years (15). Wildlife disease is often an additional threat to species already exposed to overexploitation, habitat loss, and climate change; approaches to conservation need to be approached strategically. Efficient management of remaining refugia requires immediate collaboration among scientists, policy-makers, managers, and local landowners together with commitment and funds. By acting now to identify remaining refugia, document fauna, improve biosecurity, and plan contingency responses, funds, and species can be saved long term. ■

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METABOLISM

Targeting an energy sensor to treat diabetes

New activators of AMPK have beneficial effects in type 2 diabetes mellitus

By D. Grahame Hardie

Obesity occurs when whole-body energy intake exceeds energy expenditure for prolonged periods. This is a major public health issue because obesity increases the risk of disorders such as type 2 diabetes mellitus (T2DM). The liver and muscle store excess energy in the form of fat, leading to resistance to the hormone insulin. Released when blood glucose rises after meals, insulin normally promotes glucose uptake by muscle and represses glucose production by the liver, thus rapidly returning blood glucose to normal. However, this process is impaired in insulin-resistant individuals, who may eventually develop persistently elevated blood glucose (i.e., T2DM), which can cause debilitating or life-threatening complications. Because the energy sensor AMPK (adenosine monophosphate-activated protein kinase) promotes muscle glucose uptake by insulin-independent mechanisms, it was proposed in 1999 that AMPK-activating drugs might represent a novel approach to treating T2DM (1). Representing the culmination of more than 15 years of developing this concept, a study by Myers *et al.* (2) on page 507 of this issue and a study by Cokorinos *et al.* (3) show that compounds that bind to a unique site on AMPK can promote glucose uptake by muscle, and hence reverse elevated blood glucose in animal models of T2DM.

AMPK senses cellular energy status by monitoring the levels of AMP, ADP, and ATP (adenosine mono-, di-, and triphosphates) (4). ATP and ADP can be likened to the chemicals in a rechargeable battery, with a high ATP:ADP ratio being equivalent to a fully charged battery; AMP is a breakdown

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