White-Nose Syndrome: Human Activity in the Emergence of an Extirpating Mycosis

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ABSTRACT
In winter 2006, the bat population in Howe Cave, in central New York State, USA, contained a number of bats displaying an unusual white substance on their muzzles. The following year, numerous bats in four surrounding caves displayed unusual winter hibernation behavior, including daytime flying and entrance roosting. A number of bats were found dead and dying, and all demonstrated a white, powdery substance on their muzzles, ears, and wing membranes, which was later identified as the conidia of a previously undescribed fungal pathogen, Geomyces destructans. The growth of the conidia gave infected bats the appearance of having dunked their faces into powdered sugar (Fig. 1A). The disease was named white-nose syndrome (WNS) and represents an emerging zoonotic mycosis, likely introduced through human activities, which has led to a precipitous decline in North American bat species (3, 4).

The genus Geomyces (teleomorph Pseudogymnoascus) consists of 11 described species within the Ascomycota (5). Prior to the emergence of WNS, we knew very little about this fungal genus other than its general role as a soil saprobe (5). Geomyces spp. have been isolated from a number of diverse environments across a wide geographic region, from the Arctic to the Antarctic (5–9). The association of Geomyces with temperate and low-temperature (as low as −11°C) environments has suggested that members of the genus are either psychrotolerant or psychrophilic, while their close association with keratinaceous materials (10) and old wood (11, 12) suggests that the genus contains important keratin and cellulose degraders (5).

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INTRODUCTION
Although One Health is often associated with transmission of disease from animals to humans, white-nose syndrome (WNS) of bats is an example of how humans and environment can influence the transmission of a devastating disease to wildlife. In winter 2006, the bat population in Howe Cave, in central New York State, USA, contained a number of bats displaying an unusual white substance on their muzzles (1). The following year, numerous bats in four surrounding caves displayed unusual winter hibernation behavior, including daytime flying and entrance roosting. A number of bats were found dead and dying, but all demonstrated a white, powdery substance on their muzzles, ears, and wing membranes, which was later identified as the conidia of a previously undescribed fungal pathogen, Geomyces destructans (2).

The growth of the conidia gave infected bats the appearance of having dunked their faces into powdered sugar (Fig. 1A). The disease was named white-nose syndrome (WNS) and represents an emerging zoonotic mycosis, likely introduced through human activities, which has led to a precipitous decline in North American bat species (3, 4).

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Despite the histological observation of an invasive fungal mycosis in infected bats, initial attempts to isolate the WNS pathogen were difficult due to overgrowth by
commensal fungal species (D. S. Blehert, personal communication, 2008). Nonetheless, the pathogen was successfully cultured from the guard hairs of infected bats by growth at low temperatures (3 to 6°C). This new species, named *Geomyces destructans*, is closely related to *Geomyces pannorum* var. *pannorum* (2), a fungal species that has been associated with superficial infections of the skin, nails, and hair in humans and other mammals, including both immunocompetent and immunocompromised patients (13–16). Infections with *G. pannorum* are extremely rare and are generally confined to superficial mycoses, although an inflammatory response can lead to irritation for the patient. Treatment of *G. pannorum* is difficult and often involves systemic treatment with antifungals (itraconazole) for extended periods of time (>6 months) (13, 14). Unlike *G. pannorum*, *G. destructans* is unable to cause disease in endothermic mammals due to its temperature restriction (<19°C); however, bats become susceptible due to their drop in body temperature during torpor.

Torpor in hibernating mammals is a period of unconsciousness in which the animal enters a hypometabolic state, allowing its body temperature to drop to ambient conditions (generally <12°C). This cooling is associated with a drop in the metabolic rate, with the breathing and heart rates falling to <1% of normal (17) and a suppression of the innate and adaptive immune responses, including a drop in complement, phagocytic, cytokine, and lymphocyte activities (18). Arousal naturally occurs in hibernating bats, in which bouts of torpor are punctuated with short periods (<8 hours) of activity every 6 to 14 days, depending on the bat species (19). The role of arousal in bats is still contested, with some investigators suggesting that it allows the individual to urinate/defecate, change roost position, mate, and even sleep (20). Other researchers have postulated that arousal plays a critical role in immune avoidance, allowing reactivation of B- and T-cell populations to screen for disease, a hypothesis supported by the rapid mobilization of lymphocyte populations from secondary lymphoid organs in arousing mammals (21). Whatever the physiological driver, arousal comes at a significant energetic cost: during arousal the bat must increase its body temperature from ambient to euthermic (36°C), which can consume critical fat reserves stored for hibernation. In a small bat, such as the little brown bat (*Myotis lucifugus*), arousal consumes 108 mg of fat—an amount that could support a bat in torpor for 67 days (17).
WNS

During hibernation, keratinophilic *G. destructans* targets the keratin-rich areas of the bat, including the muzzle, ears, and wing membranes (Fig. 1A). Initially infection is superficial with no inflammatory response, presumably due to immune suppression during torpor (1). The continued superficial growth of the fungus on the skin and wing membranes results in the production of curved, nonmelanotic, aerial conidia (Fig. 1B), which give the animal the characteristic appearance of having been dipped in powdered sugar (Fig. 1A).

It is unclear how this comparatively superficial *G. destructans* infection kills the bat; however, during an experimental infection with *G. destructans*, Warnecke et al. (2012) observed that infected bats roused from torpor more frequently than uninfected bats, with an arousal rate 3 to 4 times greater than control animals (22). This increase in arousal could lead to the acute inflammatory response observed in infected bats, as well as the depletion of essential fat reserves before the end of the winter; starvation is an important arousal trigger in bats, causing the animals to wake in search of food (22). An alternative WNS pathology has also been proposed, based on observed changes in the structure of the bat’s wing membrane (23). The wing membranes of bats are remarkably elastic, allowing them to balloon out and contract, increasing flight efficiency and providing the remarkable maneuverability that enables a bat to capture insects in flight (24). The wing membranes also play an important role in physiology, being responsible for up to 10% of total gas exchange (both O2 and CO2) during flight and providing an important mechanism for water adsorption during hibernation (25, 26). Hydration during hibernation is critical to survival and an important arousal trigger: even reducing the humidity of the hibernaculum by 15% (from 97 to 82%) can lead to a 20% mortality rate in *M. lucifugus* populations (22). Cryan et al. (2010) observed dramatic structural changes in wing membranes from *G. destructans* infection: previously malleable and elastic tissue became brittle and dry, with the consistency of tissue paper (23). As *G. destructans* infection causes such gross structural changes to the wing membrane, including the loss of internal vasculature (Fig. 1B) (23), it is possible that wing damage prevents water homeostasis during torpor in these animals.

The unusual behavior often seen during winter in bats with WNS, including entrance roosting and day flying, could therefore be indicative of starvation or dehydration, prompting arousal. The bats then emerge onto the winter landscape in search of food and water; in the midst of a northeastern U.S. winter, the frozen water, lack of food, and frigid temperatures quickly lead to death. Indeed, WNS produces greater declines in bat populations at higher latitudes, where the hibernation season is longer and winter temperatures are colder (cave-hibernating *M. lucifugus* bats demonstrate a much higher mortality rate in New York [91%] than in Virginia [79%] (22)). In southern states such as Tennessee, the observed high rates of WNS morbidity do not correlate with high mortality, suggesting that the length of the hibernation season is critical to the outcome of disease (22). Thus, while *G. destructans* itself is not directly fatal, the physiological changes induced by the pathogen ultimately lead to its host’s death.

DETECTION

Although gross diagnostic identification of WNS is possible, the aerial conidia of *G. destructans* are easily damaged during handling of infected bats and confirmatory analyses are necessary (28). Due to the invasive nature of *G. destructans* in the pathogenesis of WNS, histology remains the gold standard for differentiating WNS infections from other, more generic mycoses. As WNS develops, *G. destructans* hyphae invade the hair follicles and associated sweat glands of infected bats (2), breaching the basement membrane and invading the regional tissue (Fig. 1C). This leads to gross morphological changes in the wing membranes that are characteristic of WNS, including devascularization, loss of connective tissue, and ulceration (Fig. 1B and C) (23). The fungus also creates a characteristic cupping: cup-like lesions in the wing membrane that are often filled with conidia (Fig. 1B) (23, 28). PCR methods have been developed to detect *G. destructans* on suspect animals, with a detection limit of ~100 conidia (29); however, the presence of PCR-detectable *G. destructans* on an animal does not confirm the development of the WNS pathology, but simply the presence of the fungus. It is therefore necessary to confirm all PCR-based findings with histology before a diagnosis of progression to WNS can be made (29). These same PCR methods have also been used to successfully detect *G. destructans* in contaminated hibernacula, although such methods find the fungus only in sediments closely associated with WNS-infected bats (30).

EPIDEMIC WNS

Upon the first detection of WNS, it was unclear whether this emerging infectious disease was the result of a mutation in an endemic organism or the introduction of a
foreign pathogen to a susceptible community. Nonetheless, as long as the 1970s, bat biologists in Europe had been describing a white substance on the muzzles of hibernating bats (31), although these bats did not display any signs of infection, wing damage, behavioral change, or increased mortality (32). Following the identification of WNS in the United States, a comprehensive microscopic and PCR analysis of this substance on European bats led to the identification of _G. destructans_ in numerous European countries, including the Czech Republic, France, Germany, Hungary, Slovakia, Switzerland, and Romania (32, 33). Genetic comparisons of the European _G. destructans_ across a large geographic range suggest that _G. destructans_ is endemic to Europe and closely related to North American _G. destructans_ (34), although the vast mortalities in North American bat populations could not provide a more dramatic contrast between the two strains. The differences in mortality rate may stem from the pattern of European bats hibernating as solitary individuals or in small (two to three animals) groups, rather than as thousands of animals clustering together as in North America (35), suggesting that alternative hibernation patterns in the European bat population may reflect an adaptation to past epidemics.

Warnecke et al. demonstrated that both European _G. destructans_ and North American _G. destructans_ are able to cause morbidity and mortality in North American bat species, suggesting that the survival of European bats includes an intrinsic resistance to the pathogen (22). Of particular interest in this study was the finding that European _G. destructans_ was more pathogenic in bats than North American _G. destructans_, indicating that despite its short history in North America, North American _G. destructans_ has already become less virulent (22). This supports an origin for WNS in the European bat population (22, 34); with mortality rates in infected bat populations reaching 100% in North America, North American _G. destructans_ must adapt to allow the host to survive long enough to be transmitted to new susceptible individuals.

After the initial identification of 18 infected bats in New York in February 2006, the winter of 2007–2008 saw the infection zone increase to >100 miles,
with bat mortality rates exceeding 75% and an estimated 500,000 animals dead (Fig. 2) (A. C. Hicks, personal communication, 2008). This rapid expansion has continued, with the epidemic appearing to follow bat migration patterns along the Appalachian Mountains in the United States (Fig. 2). Currently the Great Plains of the central United States, which extend from Montana down through northern Texas, serve as a natural barrier to the westerly movement of WNS by migrating bat species; however, the early detection by PCR assay of G. destructans in a cave bat (Myotis velifer) (D. S. Blehert, personal communication, 2010) confounded this pattern (Fig. 2). The significance of this case is important, as M. velifer’s range extends to the southwestern United States and down through Mexico into Central America. Infection in M. velifer would greatly increase the potential spread of G. destructans into the cooler climates of the western United States, which is home to the highest diversity of hibernating bat species in the Americas (19). Nonetheless, in the 2 years since the detection of G. destructans in Oklahoma, WNS has not been detected at or around the original site. This suggests that either M. velifer is resistant to a progressive WNS infection or that the G. destructans detected did not constitute a minimum infectious dose.

ROLE OF HUMANS IN TRANSMISSION

The identification of European G. destructans raises the question of how the pathogen arrived in North America. There have been numerous hypotheses as to the transport of G. destructans, with human activities central to all of them (3). The human-vectored transport of Old World mycoses to North America has an inglorious past and includes import of chestnut blight from invasive Cryphonectria parasitica; Dutch elm disease caused by three species of Ophiostoma; and Batrachochytrium in amphibians, which has spread rapidly and is threatening numerous species globally (3). Similar human activities are likely responsible for the movement of G. destructans, although our currently limited understanding of G. destructans transmission and infectious dose makes it difficult to distinguish whether it was moved through human travel or the movement of bats via trade. To dissect the differences between the two, and hence the likelihood of the transmission of G. destructans elsewhere, it is important to understand the survival and environmental resistance of the pathogen as well as potential vectors, fomites, and reservoirs.

The activity of bats within the hibernacula covered with G. destructans spores likely spreads the fungus on air currents, bringing it into contact with surfaces, water, or other animals in this environment. Although we have little information on the propagation of G. destructans on surfaces, we do have some clues based on the physiology and survivability of the Geomyces. It is known that G. destructans can be detected both in the sediments and on the walls of WNS-impacted hibernacula (30, 34), and members of the Geomyces appear to be common residents of cave environments, being found on speleothems, in guano, and in the air (36). These data suggest that Geomyces may have a saprophytic lifestyle within caves, feeding on cellulose-rich organic detritus or the keratinaceous remnants of decaying arthropods. G. destructans itself has a narrow growth temperature range (from 0 to 19°C) (2) and requires high humidity, making it ideally suited for growth in caves (19). Anecdotal evidence suggests that once contaminated, an infected hibernaculum can serve as a reservoir for WNS: 2 years following the loss of all bat species from a WNS-impacted mine, the reintroduction of naïve bats to the same location led to a 100% mortality from WNS (Fig. 3) (A. C. Hicks, personal communication, 2010). The ability of infected hibernaculum to serve as reservoirs for G. destructans will have a profound impact on the recovery and/or reintroduction of bat species following the WNS epidemic; while the ability of G. destructans to grow as a saprotroph within hibernacula can increase the overall virulence of the pathogen, freedom from the constraints imposed by reliance on a host for continued survival may allow G. destructans to drive its host species to extinction (3).

Subterranean hibernacula are often shared with other animals, including troglobenes (cave visitors) and troglobites (obligate cave residents) (37). If bats disperse G. destructans through their in-cave activities, it is likely that cave-inhabiting species would also come into contact with the pathogen, although to date no other animals have demonstrated the ability to develop a progressive G. destructans infection. Further, troglobenes and troglobites are generally restricted to one or a group of closely related caves, making it unlikely that they could serve as vectors to spread the pathogen over long distances (37). The potential to transmit the fungus via water is possible, and water does flow through WNS-impacted caves; however, cave conduits often form part of regional groundwater flow, flowing toward the regional aquifer or watershed rather than to other caves and susceptible populations (38). This again limits the potential of water to play a role in transmission.

The only other potential vectors of G. destructans in hibernacula are humans (Fig. 3). After visiting a tourist...
cave, humans pick up >1 × 10⁶ fungal spores on their feet (H. A. Barton, unpublished data), while cave explorers (cavers) visiting a WNS-infected site can pick up *G. destructans* spores on their equipment (J. C. Okoniewski, personal communication, 2010). This suggests that human clothing and equipment can serve as fomites for the movement of *G. destructans*. The question remains as to whether these fomites can in turn serve as sources of *G. destructans* infection of bats or seed *G. destructans* into caves to create new reservoirs (Fig. 3).

The successful introduction of any xenobiotic species into an ecosystem is generally limited by resource competition, nutrient availability, and in the case of *G. destructans*, the nonconducive geochemistry of cave and mine environments (39). Therefore, the ability of a human to serve as a vector for WNS depends on a number of currently unknown factors, such as the survivability of the fungus/spores during transport, the minimum infectious dose for bats, and the inoculum size that is permissive of the establishment of *G. destructans* in a new site (Fig. 3). At this time, much of this information is lacking, other than the known susceptibility of *G. destructans* to heat (40) and the general tolerances of the *Geomyces* to cold and freezing (6).

Recreational cave exploration is common throughout North America and Europe and is particularly popular in many of the countries where European *G. destructans* is endemic, including France, Germany, Romania, and the Czech Republic. Indeed, cavers have been visiting North America from these countries since the 1940s. The first detected site of WNS is within 200 feet of Howe Caverns, a commercial cave open to both tourists and cavers since 1843 and receiving upwards of 200,000 visitors a year. While it is not surprising that such a site could serve for the introduction of an invasive species, other commercial caves in North America have been open for as long and receive much larger numbers of international visitors (~8% of total visitation) (National Caves Association, personal communication, 2012). Wind Cave (South Dakota, opened 1891) receives >600,000 visitors/year, Mammoth Cave (Kentucky, opened 1838) >500,000 visitors/year, and Carlsbad Caverns (New Mexico, opened 1915) >400,000 visitors/year. WNS has not been seen in any of these caves.

**FIGURE 3** Known and postulated mechanisms of *G. destructans* transmission and WNS establishment. Bat-to-bat transmission has been demonstrated in laboratory experiments and based on epidemiology. Cave-to-bat and bat-to-cave transmission has been shown anecdotally. Fungal spores can be picked up by human activities in caves, while the ability of humans to pick up spores and serve as vectors for *G. destructans* transmission remains speculative. Black arrows demonstrate known fungal transport, with the thickness of the arrow indicative of the known significance of transfer. Gray arrows indicate as yet unknown mechanisms. doi:10.1128/microbiolspec.OH-0008-2012.f3
despite their significant bat populations and long history of international visitation. These data may suggest that while the human-vectored transport of G. destructans is possible, disease establishment itself must be quite rare.

Bats are obvious vectors of G. destructans, and bat-to-bat transmission of WNS is well established and demonstrable under laboratory conditions (Fig. 3) (41). The fungus produces abundant conidia on the wings and fur of infected bats (Fig. 1A), which routinely come into contact with other bats through swarming, grooming, and mating events prior to and during hibernation. Indeed, bats routinely change roost positions and even hibernacula during arousal periods (19), thus providing a mechanism of G. destructans movement from both bat to bat and cave to cave. Given that G. destructans is unable to infect naïve bats segregated from WNS-infected bats by a wire mesh (allowing airborne movement of the fungus) and that laboratory infection studies require $1 \times 10^5$ spores, it is possible that the minimum infectious dose of G. destructans is high (41). This, along with the epidemic spread of WNS along bat migration paths (Fig. 2), opens up the possibility that bats themselves moved G. destructans movement from Europe to North America. While bats are not capable of transoceanic flight, bats migrating across bodies of water have occasionally been blown off course during storms and forced to seek refuge on any object they find, including ships (42). These bats then ride along on the vessel to its final destination. Such travel has been recorded in cases of North American bats ending up in Europe and Russia (42). Bats are also known to roost in shipping containers, only to become trapped on an oceangoing vessel and transplanted to the final port of call. The translocation of bats in this way has been documented from Asia and Europe to North America and vice versa (42). Given that Howe Caverns is within 40 miles of Albany, NY, one of the busiest shipping ports in North America, this opens the possibility that G. destructans may have been transported by a European G. destructans-infected bat.

**IMPACT**

Whatever the mechanism of transfer, G. destructans is now in North America and is having a profound impact on bats and the environment. Bats have a remarkable environmental distribution and range of potential food sources, including vegetarian, omnivorous, insectivorous, and nectarivorous diets (very few species are hematophagic), allowing them to colonize virtually every available habitat, from desert to coastal and tropical to the Arctic Circle (19). With such a wide distribution and variety of foodstuffs, it is not surprising that bats play an important role in the ecosystem, including in pest control, the pollination of plants (including agaves, mangoes, guavas, and bananas), and seed dispersal. Adaptive behavioral patterns also allow insectivorous bats to migrate during the winter when food is unavailable (Mexican free-tailed bats, Tadarida brasiliensis, can migrate as far as 2,000 km) or hibernate in situ until favorable conditions return (19). Of bats that hibernate, those that choose subterranean (mines and caves) sites are susceptible to WNS. Of the 47 bat species in North America, 12 species are currently found within the WNS epidemic range, including the little brown bat (M. lucifugus), Indiana bat (Myotis sodalis), gray bat (Myotis griseus), northern long-eared bat (Myotis septentrionalis), southeastern bat (Myotis austroriparius), eastern small-footed bat (Myotis leibii), big brown bat (Eptesicus fuscus), tricolored bat (Perimyotis subflavus), Virginia big-eared bat (Corynorhinus townsendii virginianus), eastern red bat (Lasiusus borealis), and Rafinesque’s big-eared bat (Corynorhinus rafinesquii). Of these, L. borealis and C. rafinesquii do not hibernate in caves and mines, limiting their exposure to the fungus. Of the remaining 10 species, all except C. townsendii virginianus are experiencing population declines from the WNS epidemic (27).

Insectivorous bats are voracious hunters, able to feed on a diverse range of insects, from small midges (Chironomidae at $\sim$2 mm) up to large beetles (Coleoptera at $\leq 5$ cm); a nursing female M. lucifugus can consume up to 30% of her body weight during one evening, catching up to 520 insects/hour (43). The insects consumed by WNS-impacted bat species include members of the Diptera (true flies), Trichoptera (aquatic caddisflies), Lepidoptera (moths), and Homoptera (including cicadas and aphids) (43). These are important agricultural pests that lay eggs on crops, which hatch into caterpillars and other larval forms with ravenous appetites. With the current loss of 6.7 million bats translating into an additional 5,000 to 10,000 metric tons of insects per year, the potential agricultural impacts are staggering. Boyles et al. (55) estimated in 2011 that current declines in the bat population would result in more than $3.7 billion per year in crop losses and increased costs of pesticide application.

The other commercial impacts of WNS have yet to be calculated. In the United States, there are 142 commercial caves and 14 national parks containing caves, with an annual visitation of $\geq 32$ million people/year generating local revenues of more than $549 million and employing an estimated 10,000 people directly or indirectly.
(National Caves Association, personal communication, 2012; K. Castle, personal communication, 2012). While no show caves have been closed during the WNS epidemic, increasing pressure has been placed on these businesses to limit the potential human spread of G. destructans. In addition, the perception by the general public that caves are closed or that G. destructans itself poses a danger to human health has severely affected the operations of these caves (P. Youngbaer, personal communication, 2012). Income is also generated by the activities of recreational cave explorers. With an estimated 50,000 active recreational cavers spending more than $50 million annually on cave exploration (through travel and equipment), as well as >1 million cave visits by youth groups including Boy Scouts, church groups, etc., annual losses from the WNS epidemic in cave-rich areas could be as high as $700 million.

The WNS epidemic can also affect humans beyond simple economics. The diet of M. lucifugus consists of 10 to 20% mosquitoes (Culicidae), with a daily intake of 200 to 800 (43). This means that the current losses of M. lucifugus alone correspond to an extra 200 billion mosquitoes/year. West Nile virus, an introduced viral pathogen vectored by mosquitoes, has been responsible for >1 million human infections since its introduction in 1999, including >1,300 deaths (44). With a significant increase in the mosquito population, there may also be a dramatic increase in the incidence of and morbidity from West Nile virus, which could be particularly significant in states such as New York, which has been heavily affected by both West Nile virus and WNS (44).

RESPONSE

The ability of a superficial mycosis to cause a fatal infection in an immunocompetent, endothermic mammal is rare (3). As a result, WNS was originally thought to be caused by an underlying regional or environmental factor, such as an immunosuppressive virus or unidentified pesticide (43). This problem was compounded by the difficulty in culturing the pathogen and establishing the environmental conditions necessary for both fungal growth and bat hibernation. Because of this, it took 4 years beyond the emergence of WNS before Koch’s postulates were satisfied for G. destructans (41). Nonetheless, Chaturvedi et al. used random amplified polymorphic DNA analyses to demonstrate that G. destructans isolates from WNS-infected bats had shared genetic loci over a geographically wide area (46). This identity, demonstrated using five different random amplified polymorphic DNA primer sets, indicated that a single source organism was responsible for all WNS cases and argued for the epidemic spread of a single etiologic agent (46). At this point, biologists realized they were witnessing an emerging zoonosis on an epidemic scale, and the questions immediately focused on controlling the epidemic.

While humans have been unable to constrain or eradicate a single epidemic mycosis (3), the pressure from business stakeholders and the general public in the face of such a devastating epidemic required action on the part of federal and state agencies. But there are limited options available to wildlife and land managers in the face of such devastating epidemics, and the response to WNS has mirrored that to other infectious mycoses: research results are often outpaced by population declines, with the result that some type of action has to be perceived to be happening (2). Initial efforts were directed toward limiting transport of the pathogen. While it is impossible to control bat movement and migration, it is possible to limit human activities that could transport the fungus. In states affected by WNS, caves were closed to visitation, while a nationally adopted disinfection protocol against the fungus was developed (40). Initial indications show that these measures may have contributed to the absence of new disease epicenters, particularly in the more vulnerable western United States.

Other intervention options are limited. As a superficial mycosis, G. destructans does not generate a strong adaptive immune response, so vaccination may have limited impact (1). Antifungal agents are often deleterious to bats themselves, through both toxic and endocrine effects, limiting the usefulness of treatment. If an antifungal agent that did not harm bats was found, bat activity during hibernation, such as grooming, would remove any superficial application, while repeated administration would lead to a WNS-like disturbance mortality. Therefore, any effective treatments would require a long-lasting antifungal agent, which would have to be administered directly to each bat. As bats hibernate in nooks and crevices, often high in the ceiling, with colonies that can exceed thousands of individuals, such direct administration efforts are extremely difficult on an environmental scale. Remaining options that have been tried are even more dramatic, including the culling of infected individuals, particularly in newly identified WNS sites. Modeling of such action has shown that, given the difficulty in identifying all infected organisms, culling would not prevent the spread of WNS and would actually prevent the emergence of naturally resistant communities (47, 48).
With the impending extirpation of certain bat species, biologists are working toward methods of maintaining genetic diversity, including the establishment of “Ark” communities: colonies of individuals that are maintained until the WNS epidemic has passed. A similar approach has been developed for threatened amphibians in the face of the chytrid fungus (49). The establishment of such colonies would allow the reintroduction of bats post-WNS; however, if *G. destructans* can survive in a saprophytic lifestyle in hibernacula, even this approach may be limited in its effectiveness. Further, a preliminary attempt to maintain a small, exploratory community of *C. townsendii virginianus* in captivity resulted in the complete loss of the colony, reflecting the difficulty in maintaining healthy bats in nonnative environments.

Some researchers have pushed for the disinfection of hibernacula to break the chain of transmission and to prevent reinfection of bats. This approach is fraught with problems, the primary being the as yet unknown impact of biocides on the subterranean ecosystem: caves represent intricate ecosystems, including a great diversity of cave-adapted and endemic species (37), of which fungi play an important role in nutrient mobilization (50). Indeed, the use of disinfectants to limit the spread of xenobiotic species has a dire history, and such attempts have been devastating (51). Lascaux Cave, France, is a culturally important cave due to its extensive Neolithic paintings. In 2000, an invasive fungus, *Fusarium solani*, began to colonize surfaces within the cave. In an attempt to control this fungus, biocides including quaternary ammonium compounds were applied in the cave. Unfortunately, the use of these disinfectants destroyed the native microbial flora of the cave, selecting for disinfectant-resistant entomophilous fungi that were previously contained by the endemic microbial community (52, 53). The results were disastrous for both the cave ecosystem and, through the increased and rapid growth of these introduced fungi, the paintings themselves (51). Antifungals therefore have the potential to collapse the cave ecosystem, a difficult problem given the other threatened and endangered species that share this environment (37).

**FUTURE**

The fate of bats in North America currently hangs in the balance. The rapid rate of spread and the high mortality of WNS have led to a dramatic decline in cave- and mine-hibernating bat species. At the time of this review, WNS has spread to 22 U.S. states and four Canadian provinces, spreading as far south as Alabama and as far north as Ontario, Canada (Fig. 2). The most recent estimates have put bat mortality at >6.7 million animals, although with the difficulties in accurate counting, this number could be significantly higher (54). At the current rate of decline, it is almost certain that the once common *M. lucifugus* may go extinct within the northeastern United States (4). Other species already on the endangered species list have their entire populations within the WNS epidemic area, including *M. sodalis*, *M. grisescens*, and *C. townsendii virginianus*. These species may well go extinct without human intervention.

But still, there is reason for hope. The high mortality in states such as New York, where WNS was first discovered, has led to the almost complete loss of hibernating bat species. However, in certain hibernacula, remnant populations of bats have been observed to return to the site year after year despite the presence of WNS. This includes *M. lucifugus*, one of the populations hardest hit by WNS, and suggests the emergence of a resistant population (48). Some species, such as *C. townsendii virginianus* and *E. fuscus*, hibernate in caves in which other species have experienced dramatic declines from WNS. Yet members of these species demonstrate little to no observable signs of the disease (G. G. Turner, personal communication, 2011), suggesting that natural resistance to *G. destructans* is present. While this is encouraging news for the persistence of these species, healthy individuals from WNS-impacted sites may act as superspreaders, carrying the disease to uninfected caves and promoting the infection of vulnerable species.

A hindrance in mobilizing resources to combat the WNS epidemic has been the misconceptions of the general public about the importance of bats and bat behavior: the common notion that bats are blood-sucking, flying rodents that get caught in your hair could not be further from the truth. Bats are members of the *Chiroptera*, which share an evolutionary lineage with primates and represent >20% of all known mammalian species. With >1,100 bat species identified, bats are second only to rodents in diversity (19). Their excellent spatial awareness through echolocation, acrobatic flight capabilities, and good eyesight make them the least likely to accidentally land on anyone’s head. Bats play an important part in our ecosystem, and the education of the public on the importance of these mammals is critical to their continued survival.

**CONCLUDING REMARKS**

Perhaps more than any other recent epidemic, WNS exemplifies the impact that infectious agents can have on
animals, our environment, and human health. The response to this epidemic demonstrates the necessity of collaboration across a wide range of disciplines, including bat biologists, wildlife managers, veterinary researchers and pathologists, medical mycologists, and environmental microbiologists—together emphasizing the importance of a functioning, holistic approach to emerging diseases and the demonstration of a functioning One Health initiative. The outstanding questions in WNS and G. destructans pathology similarly cannot be answered by one discipline alone, but require the shared resources and integrative tools of the medical, veterinary, and environmental sciences.

Whatever the source of WNS or the future of bats in North America, G. destructans is here to stay. As we move forward, an integrative approach may allow for the protection or conservation of bat species, but perhaps more importantly, help us to understand the transfer of such devastating mycoses and how future epidemics can be prevented.

REFERENCES


Human Activity in the Emergence of White-Nose Syndrome


