Darwin's Necessary Misfit and the Sloshing Bucket: The Evolutionary Biology of Emerging Infectious Diseases

Daniel R. Brooks · Eric P. Hoberg

Abstract Evolutionary studies suggest that the potential for rapid emergence of novel host–parasite associations is a "built-in feature" of the complex phenomenon that is Darwinian evolution. The current Emerging Infectious Disease (EID) crisis is thus a new manifestation of an old and repeating phenomenon. There is evidence that previous episodes of global climate change and ecological perturbation, broadly defined, throughout earth history have been associated with environmental disruptions that produce episodic bursts of new host–parasite associations, each of which would have been called an EID at the time of its first appearance. This perspective implies that there are many evolutionary accidents waiting to happen, requiring only the catalyst of climate change, species introductions, and the intrusion of humans into areas they have never inhabited before.

Keywords Darwinism · Complexity · Ecological fitting · Emerging infectious disease · Sloshing bucket · Coevolution

D. R. Brooks (✉)
Department of Ecology & Evolutionary Biology,
University of Toronto,
Toronto, ON M5S 3G5, Canada
e-mail: dbrooks@zoo.utoronto.ca

E. P. Hoberg
US National Parasite Collection,
Animal Parasitic Diseases Laboratory,
US Department of Agriculture, Agricultural Research Service,
BARC East 1180, 10300 Baltimore Avenue,
Beltsville, MD 20705, USA
e-mail: ehoberg@anri.barc.usda.gov

Introduction

The human population grows daily, expanding geographically and carving a deep technological footprint on this planet. We accelerate landscape alteration and ecological perturbation by inserting ourselves and other species into novel regions of the world, leading to potentially irreversible changes in the biosphere. This is the biodiversity crisis as it is usually viewed—a crisis of habitat loss and species extinction. It is, however, also a crisis of emerging infectious disease (EID) (Brooks and Hoberg 2006, 2007a, b). In popular parlance, "emerging infectious disease" usually means primarily viral, sometimes bacterial, infections of humans that appear in novel places infecting novel hosts. Highly publicized EIDs include West Nile Virus, introduced to North American birds by an infected tourist visiting New York from the Mediterranean, and the Ebola virus, introduced to humans when population increases resulted in encroachment on African forest.

Restricting the phrase "emerging infectious disease" to a subset of species of human health concern gives a misleading, falsely comforting, impression of the scope of the crisis. Thinking that EIDs are likely to be rare, much attention is given to managing each EID as it has emerged, but little attention is paid to the origins of EIDs, beyond a search for the taxonomic identity of the parasite acting as the pathogen, and its immediate reservoir, if there is one. Rhetoric used to deny the EID crisis stem from the assumption that nothing like this has happened before, so it is premature to suggest that there is anything particular to worry about. Similar rhetoric is used to report unfolding crises of global climate change and biodiversity, based on similar assumptions that they are rare phenomena that have originated only recently and are unique to human activities.

Simplicity and Complexity in Scientific Explanations: Why Biology is Different from Physics

More than 50% of the known species on this planet are parasites of some form, including known pathogens of humans, livestock, and wildlife (Price 1980). That alone should give us pause. Are EIDs something novel or have they always been part of the evolutionary saga? Which of those parasitic species alive today represent potential EIDs? Answering these two questions is complex, and when scientists are faced with complex problems, they usually fall back on some form of the following mantra.

> The universe is structured by laws, and science is the search for theories providing powerful general explanations couched in terms of those general laws.

This belief has guided the development of western science for nearly 2,500 years, embodied in the *principle of parsimony* (Latin *parcere*, to spare). Aristotle (350 B. C.E.) articulated the ontological view of the principle of parsimony, the postulate that "nature operates in the shortest way possible" and "the more limited, if adequate, is always preferable". The principle of parsimony is also linked with the English philosopher and Franciscan monk William of Ockham (ca. 1285–1349), who advocated the use of what is known as "Ockham's razor": "Pluralitas non est ponenda sine neccesitate" ("plurality should not be posited without necessity") and "non sunt multiplicanda entia praeter necessitatem" ("entities should not be multiplied unnecessarily"). In this sense, the principle of simplicity obliges us to favor theories or hypotheses that make the fewest unwarranted, or *ad hoc*, assumptions about the data from which they are derived. This version of the principle does not necessarily imply that nature itself is parsimonious. Indeed, despite the best efforts of philosophers for more than 700 years, no link between parsimony and truth has ever been established.

Nonetheless, ever since the Enlightenment, scientists and philosophers have favored simple, elegant theories. Time and again, simple theories have won out over more complex ones by explaining a myriad of phenomena as different manifestations of the same underlying process. Darwinian evolution has been a notable exception to this trend. From the beginning, Darwinism drew criticism from philosophers and physicists for not being a proper theory, by which was meant a simple theory based on invariant laws. For a century after the publication of the *Origin of Species*, biologists proposed simpler evolutionary theories in response to those critics, including neo-Lamarckism and Orthogenesis (Bowler 1983) and neo-Darwinism (Eldredge 1985, 1995), but none of them have been fully successful at explaining the scope of biological form and function en-compassed in Darwinism, which was characterized by George Gaylord Simpson as

> ...in every part of the whole, wonderful history of life, all the modes and all the factors of evolution are inextricably interwoven. The total process cannot be made simple, but it can be analyzed in part. It is not understood in all its appalling intricacy, but some understanding is in our grasp, and we may trust our own powers to obtain more. (Simpson 1953)

The simple Newtonian laws of physics are taught in school as a model of scientific achievement. Nevertheless, physicists have recently "discovered" complexity and made it socially acceptable within the broad community of scientists. The cosmologist Stephen Hawking has even dubbed the 21st century the century of complexity, leading a parade of physicists who began to think about "complexity science" in the latter decade of the 20th century. Evolutionary biologists can help physicists navigate this sea change in their understanding of the nature of science and the universe, because Darwinism was likely the first modern complexity theory proposed. Consider the following statement from the *Origin*

> ... there are two factors: namely, the nature of the organism and the nature of the conditions. The former seems to be much more the important; for nearly similar variations sometimes arise under, as far as we can judge, dissimilar conditions; and, on the other hand, dissimilar variations arise under conditions which appear to be nearly uniform. (Darwin 1872)

Many consider this passage no more than a general repudiation of Lamarckism, but we believe it is far more significant. Darwin proposed that evolution is an emergent property of interactions between two different causal agents (the nature of the organism and the nature of the conditions), each with its own properties, that are asymmetrical in strength (the nature of the organism is more important than the nature of the conditions), producing outcomes that are not readily predictable from the knowledge of the properties of either agent, because they are also the result of particular events at particular places and times, not repeating episodes of the same outcome derived from one or a few simple laws.

Darwin thought that organisms were historically and developmentally cohesive wholes, and therefore it was in the "nature of the organism" to produce offspring that were all highly similar (but not identical) to each other, to their parents, and to other ancestors. He also postulated that re-production occurred without regard for environmental conditions and therefore it was in the "nature of the organism" to produce offspring in numbers far exceeding the

resources available for their support. When this inherent overproduction produced a variety in critical characters, natural selection would favor the versions that were functionally superior in that particular environmental context (Darwinian adaptations). Whenever an environment changed, those organisms that already had the adaptations necessary to survive would do so, whereas those lacking appropriate adaptations would not. The production of organismal diversity thus required that organisms be at once autonomous from, and sensitive to, the environment, another example of complexity.

Darwin's conceptual framework also required that the nature of the organism embody a strong degree of conservatism. Darwin called the tendency for offspring to closely resemble their parents "simple inheritance." Genetics has shown us that replication rates are much higher than mutation rates, allowing us to see the conservative nature of the organism on a generation-to-generation basis, that is, in real time. We can also see evidence of this conservatism at higher levels of diversity, where traits shared among different species indicate their history of common ancestry. For example, all organisms having hair are thought to form an evolutionary group descended from a single ancestral species that was the first species in which hair evolved. And, as anticipated by Darwin even before the emergence of knowledge about genetics, inheritance explains an aspect of Darwinian evolution that seems paradoxical. We call this *Darwin's Necessary Misfit* (Brooks 1998, 2000; Brooks and Mclennan 2000).

The conservative nature of inheritance suggests that organisms cannot change as rapidly as the environment, so they will always "lag behind" environmental changes. In addition, the organisms in any given species population need not be perfectly fitted to their environments to survive and reproduce—they only have to be adequate. And there appears to be a wide range of adequacy. Thus, populations of organisms will always exhibit variability, much of which is historical baggage. This means they cannot all be perfectly adapted to the conditions in which they find themselves during their lives. Natural selection has the greatest power to affect evolutionary change when populations of organisms are not particularly well adapted to their conditions. The conservative nature of inheritance means that there will always be a misfit between organisms and their environments, so natural selection will always be operating. This is the reason biologists can demonstrate its effects so easily in laboratory studies. However, the conservative nature of inheritance also means that long-term, permanent, or irreversible effects of selection will not be very predictable. The late great evolutionary biologist John Maynard Smith coined the term "evolutionary lag load" (Maynard Smith 1976) as a means of trying to quan-

tify the amount and form of selection necessary to effect permanent evolutionary change in a population, given its historical baggage.

The Evolutionary Biology of Hosts and Parasites

Darwin visualized the complexity of evolution using two metaphors, the phylogenetic tree (the only illustration ever to appear in any edition of *Origin of Species*) and the tangled bank. The phylogenetic tree points to complexity arising from the conservative nature of inheritance that is the core part of the nature of the organism. This is because all the stems and branches of the Tree of Life are held together by inherited traits that are shared by two or more species, that is, by traits that evolve more slowly than new species are formed. By referring to species as "communities of descent", and placing them in a single "Tree of Life," Darwin emphasized that the fundamental explanatory principle in evolution is shared history among organisms and species.

The tangled bank, by contrast, points to a complexity arising from ecological associations among coexisting species:

> It is interesting to contemplate a tangled bank, clothed with many plants of many kinds, with birds singing on the bushes, with various insects flitting about, and with worms crawling through the damp earth, and to reflect that these elaborately constructed forms, so different from each other, and dependent upon each other in so complex a manner, have all been produced by laws acting around us. (Darwin 1872)

We are intrigued by one aspect of tangled bank complexity, asking how associations between particular parasites and particular hosts come into existence, and what role historical conservatism plays in maintaining them and allowing them to change over time. Species do not exist in isolation; they form ecological associations, within which each species experiences a wide range of interactions with other organisms representing both close and distant relatives. Our perspective gained from about 60 years of combined experience with host–parasite systems in boreal, temperate, and tropical ecosystems is that the explanations for such associations are likely to be complex rather than simple, but not necessarily so complex as to be unbelievable.

An understanding of how we should conceptualize and approach the EID crisis requires the explicit use of evolutionary biology. No matter where a given species evolved in the first place, its inherited functional abilities may allow it to survive in a variety of places under a variety of condi-

tions through arbitrary amounts of time, and in association with other species. In other words, species and their conservative traits may disperse through time and space. This interaction between the past history of the species and their present day associations is called "ecological fitting" (Janzen 1985; Agosta 2006). Brooks and McLennan (2002) discussed a number of manifestations of ecological fitting. A parasite species might be a resource specialist, but also might share that specialist trait with one or more close relatives. That is, specialization on a particular resource can be a persistent ancestral characteristic of an entire group of parasites. As a result, a given host species occurring in more than one area might be inhabited by two different species of related parasites, each of which became associated with the host at a different time and under different circumstances.

Alternatively, conservative traits are commonly coopted to perform novel functions. Trouvé et al. (1998), for example, reported that many life history traits of parasitic flatworms (flukes and tapeworms) do not differ from life history traits of their closest free-living relatives, indicating that these species do not have a "parasitic mode of life" but rather a particular variant of a "flatworm mode of life" that has been coopted to function in the context of parasitizing vertebrates. Persistent ancestral traits also might be "anachronisms" (Janzen and Martin 1982), i.e., traits that evolved in an evolutionary or coevolutionary context that no longer exists.

Finally, parasites may have very specific host resource requirements, but if those resources are evolutionarily conservative traits of hosts, they may occur in many host species in many different places. In such cases, a given parasite might inhabit more than one species of host. Even more importantly, conservatism in parasite biology and in host biology could create a very large arena for host switching, even without the evolution of novel capabilities for host utilization.

A species of trematode, or fluke, called *Haematoloechus floedae* inhabits the lungs of two native leopard frog species, *Rana taylori* and *R. cf. forreri*, from the Area de Conservación Guanacaste, in northwestern Costa Rica (Brooks et al. 2006a). *Haematoloechus floedae* is native to the southeastern United States, where it lives in the lungs of the bullfrog, *Rana catesbeiana*. Although we have not been able to find official records of *R. catesbeiana* being introduced to Costa Rica, biologists in the country recall attempts in the 1960s to farm bullfrogs in the San Jose region and two specimens of *R. catesbeiana*, collected in Alajuela, a suburb of San Jose, are in the natural history collection of the University of Costa Rica. Since then, there have been no reports of bullfrogs in Costa Rica, despite intensive amphibian monitoring projects across the country.

Haematoloechus transmission dynamics, although specialized, are conservative across the genus, in each case involving a freshwater pulmonate snail, a dragonfly nymph, and a relatively large aquatic frog. Although most lung flukes are known from only a single snail species in natural infections, a number are capable of infecting a broader range of snails from the superfamily Lymnaeoidea in the laboratory. The larvae, called cercariae, that emerge from the snail infect the second intermediate host, which, for all species studied to date is an anisopteran odonate (dragonflies). Members of the Lymnaeoidea and the Anisoptera are widespread throughout North American and Mesoamerica. Evolutionary conservatism in the physiology and ecology would allow the parasite to expand into novel territory; all that would be required is a species of lymnaeoid pond snail and a species of anisopteran dragonfly. Leopard frogs appear to be the ancestral frog hosts for *Haematoloechus* species. Within that historical context, however, *H. floedae* itself appears to have originated through a switch to bullfrogs, so the original host for *H. floedae* is bullfrogs. *Rana taylori* and *R. cf. forreri*, the hosts for *H. floedae* in Costa Rica, are leopard frogs. Parasite species can thus retain ancestral host utilization capabilities, even when they are not being used, which allows "new" associations to be formed through "retrocolonization" (Janz and Nylin 1998; Janz et al. 2001; Hoberg 2005a; Nylin et al. 2000; Nylin and Janz 1999).

Ecological fitting seems to be a fundamental property of species, so the potential for rapid emergence of new interspecific ecological associations seems great. The patterns of transmission from host to host, the parts of the host in which parasites live, and the range of suitable hosts are all evolutionarily conservative for parasites. Likewise, the diet and habitat preferences of host species are evolutionarily conservative. This conjunction of evolutionary conservatism on the part of parasites and hosts seems to explain pronounced ecological similarities in entire communities of platyhelminth parasites of frogs (including *H. floedae*) occurring in such widely divergent environments as temperate deciduous forests, temperate grasslands, and two different sets of tropical dry forest and tropical wet forest (Brooks et al. 2006b). But what drives changes in geographical distribution or local ecology that produce actual episodes of this type? The answer appears to be two manifestations of the *sloshing bucket* (Eldredge 2003; see also article by Niles Eldredge in this issue).

First, ecological associations of many different species exhibit complex geographic distributions. These distributions are the result of alternating episodes of expansion and isolation of biotas. Geological phenomena, such as tectonic changes, and phenomena related to changing climates on a local or regional scale, drive these episodes, which seem to
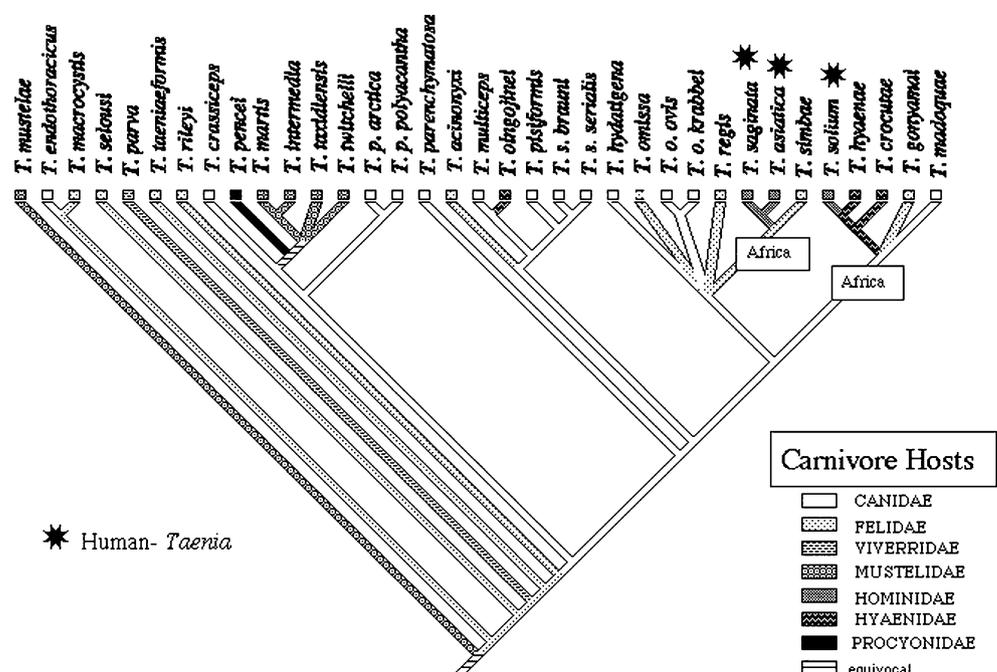
have been the primary agent of evolutionary radiations and production of regional biotas (Brooks and Hoberg 2006, 2007a, b; Erwin 1979, 1981; Lieberman and Eldredge 1996; Lieberman 2000, 2003; Halas et al. 2005).

Second, during biotic expansion phases, previously unexposed hosts may come into contact with parasites they can host. Under such circumstances, parasites and hosts that seemed made for each other, and each other alone, may establish new intimate relationships without any evolutionary innovation. Niklas Janz and colleagues have recently proposed that host-dependent groups (this works for parasites and for plant-eating insects that have specific plant host requirements) evolve through alternating episodes of increasing numbers of host species followed by isolation on restricted numbers of host species. They called this the *oscillation hypothesis* (Janz et al. 2006; Janz and Nylin 2007).

Evolution and the Emerging Infectious Disease Crisis

Now we come to the crux of the matter—how does the evolutionary biology of host–parasite associations relate to EIDs? First and foremost, our perspective suggests that today's EID crisis is "new" only in the sense that this is the first such event that human scientists have witnessed directly. There is evidence that previous episodes of global climate change and ecological perturbation, broadly defined, throughout earth history have been associated with environmental disruptions that have repeatedly led to EIDs (Hoberg and Brooks in press).

When ancestral humans moved out of the African forest and onto the savannah during the late Pliocene and early Pleistocene, they made a rapid transition from herbivory to facultative carnivory to active predation (Jurmain et al. 2005; Leakey and Lewin 2000; Lewin 1987). During that time, humans apparently shared more than just food with other apex carnivores, becoming hosts to species of cestodes, e.g., *Taenia* spp., whose closest relatives inhabit hyenas, large cats, and African hunting dogs (Jurmain et al. 2005; Leakey and Lewin 2000; Lewin 1987) (Fig. 1). This pattern is repeated in two nematode groups, hookworms (*Oesophagostomum* spp.) and pinworms (*Enterobius* spp.). Despite long-term associations between these parasites and hominoids, one-third of their host associations are the result of host switches, most of which occurred during episodes of biotic expansion between Africa and Eurasia since the Miocene (Hoberg 2006; Hoberg et al. 2000, 2001). The taxon pulse pattern exhibited by these parasites (Brooks and Ferrao 2005) is congruent with the taxon pulse dynamic exhibited by hominoids, proboscideans (elephants and their relatives), and hyenas since the Miocene (Folinsbee and Brooks 2007). Further, similar associations for host and geographic colonization by carnivores from Eurasia to Africa and from Eurasia to the Nearctic are implicated in the diversification of *Trichinella* nematodes (Zarlenga et al. 2006). At the time of their origin, each of these host switches would have created an Emerging Infectious Disease. These results indicate that EIDs affected human ancestors, but other studies indicate that EIDS resulting from ecological fitting and the sloshing bucket of taxon pulses and host range oscillation have a much longer and continuous history.

Fig. 1 Phylogeny and host associations for species of *Taenia*, redrawn and modified from (Hoberg et al. 2000, 2001). Those species that are specific parasites in human definitive hosts, *T. saginata*, *T. asiatica*, and *T. solium* are denoted by stars). Among those species, *T. saginata* and *T. asiatica* are sister species and share a relationship with *T. simbae* a parasite circulating in lions and antelopes in Africa. In contrast, *T. solium* represents a discrete lineage and is the sister-species of *T. hyaena* a parasite in hyenas, African hunting dogs, and ungulates in Africa

Alfred Russel Wallace, co-discoverer of the theory of natural selection, explained the larger number of species in the tropics as opposed the boreal regions of the world, not as the result of higher rates of species formation in the tropics, but the higher rate of extinction in the boreal regions. Recent research in the world's boreal regions, especially Beringia, has yielded evidence of a long and continuous history of the dynamic we have outlined (Cook et al. 2005; Hoberg 2005b; Hoberg et al. 2003). The boreal regions are not just places species go to die.

The Tetrabothriidea is an archaic lineage of tapeworms that is older than the modern orders of seabirds, cetaceans, and pinnipeds, their contemporary hosts. This means they were already distributed in marine environments when the first marine birds arrived in the Cretaceous. The first tetrabothriids were likely parasites of earlier archosaur marine relatives of birds, especially pterosaurs or crocodilians, and seabirds acquired these tapeworms from those hosts. Saurians (icthyosaurs, plesiosaurs, mosasaurs), non-avian archosaurs (pterosaurs and crocodilians), and marine birds co-occurred in oceanic habitats during the Mesozoic. Marine birds were the last of these host groups to appear on the scene, but they acquired tetrabothriids before all other marine tetrapods went extinct, by the end of the Cretaceous. This scenario is not unlike the situation with *Haematoloechus floedae* and the introduced bullfrogs in Costa Rica. Tetrabothriids persisted across the K/P boundary as relictual parasites of birds. Subsequent diversification of tetrabothriids involved host switching from birds to toothed and baleen whales, and from toothed whales to pinnipeds (seals and sea lions and their relatives).

Species of the tetrabothriid genus *Anophryocephalus* are obligate parasites in pinnipeds distributed throughout the Holarctic. Their history of diversification is limited to the Pliocene and Quaternary—the genus appears to have originated through colonization of pinnipeds by parasites of toothed whales less than 5.0 MYA. The oldest living members of the group are historically linked to the North Atlantic, and Pacific members apparently resulted from two independent invasions of the North Pacific coinciding with sequential marine transgression of Beringia and the formation of the Bering Strait during interstadials (a period of glacial retreat of approximately 10,000–100,000 years within a stadial, or a period of glacial advance) within the last 2–3 MY. Cyclical processes at Beringia resulted in alternating periods of biotic expansion, geographic colonization, host switching, intense isolation, and rapid speciation for assemblages of worm parasites in pinnipeds and among seabirds moving from Pacific to Atlantic and the reverse.

Sequential geographic and host colonization during periodic extremes of climate variation and ecological perturbation during the past 2.5–3.0 MY characterize all members of the northern marine parasite fauna (tape-

worms, roundworms, and flukes) in seabirds and pinnipeds. Interestingly, it was at this time that we find evidence of carnivores (including canids, felids, mustelids, and ursids), ungulates, and hominoids participating in their own episodes of biotic expansion across the Bering Land Bridge during periods of diminished sea level. The Beringian nexus has thus alternately served as a barrier or pathway for the expansion of marine and terrestrial faunas and as a center for diversification over the past 4–5 MY for hosts, pathogens, and parasites (Cook et al. 2005; Hoberg 2005b; Hoberg et al. 2003). Ecologically and phylogenetically disparate terrestrial faunas as the roundworms inhabiting lagomorphs and artiodactyls, those inhabiting carnivores and tapeworms inhabiting rodents and pikas all exhibit patterns of episodic biotic expansion between the Palearctic and Nearctic at different specific times during the late Tertiary and Quaternary (Waltari et al. 2007).

The general explanation for all these bursts of widespread host switching is ecological fitting coupled with episodic regional or global climate change leading to cycles of biotic expansion, followed by isolation followed by new expansion (Janz et al. 2006). During such episodes, specialist parasites will act like generalists as geographic expansion brings an array of host species carrying the required resource into contact with them. This explains why most pathogens can inhabit multiple hosts and yet produce disease in only some of them. Episodes of biotic expansion alternate with episodes of biotic isolation, during which time specialist parasites act like stereotypical specialists, inhabiting the only one suitable host (or small number of hosts) occurring within their isolated range. This condition is problematical for public health and biodiversity specialists because, despite appearances in the field, the specialist parasite is not nearly as host specific as they appear Brooks and McLennan (2002) called them "faux specialists"). Such species may be difficult to control if moved to an area containing new hosts with the appropriate resource. After introduction the specialist will colonize as many of these hosts as it can, spreading rapidly against all "predictions" based on its apparently restricted one host association.

As we noted in the "Introduction," strategic approaches for dealing with EID are predicated on explicit or implicit models of host–parasite relationships that imply particular relationships between climate change, biodiversity, and EID. Those models need to be explicitly evolutionary because we must learn the lessons of those past events if we are to cope with the future in a timely and economical manner. *Pathogen pollution*, the negative impact of anthropogenically introduced diseases on endemic biodiversity (Daszak et al. 2000), is a growing problem. It begins with outbreaks of disease on local spatial and fine temporal scales, leading to what John Thompson calls "mosaics of emergence" (Thompson 2005) arising against a background

of established associations, followed by emergence of new associations through geographic or host colonization, potentially associated with disease (Erwin 1979). This has been demonstrated for nematode–gastropod–ungulate systems in the Arctic, and are likely widespread already (Cook et al. 2005).

The potential for rapid emergence of novel host–parasite associations, or EIDs, appears to be a "built-in feature" of the complex phenomenon that is Darwinian evolution. This implies that there are many, not few, of these evolutionary "accidents waiting to happen," requiring only the catalyst of climate change, species introductions, and the intrusion of humans into areas they have never inhabited before. All of these are happening right now. An old aphorism states that to be forewarned is to be forearmed. A modern version is that anticipating a problem is always more time- and cost-effective than responding in crisis mode. Ignoring the evolutionary basis of EIDs is tantamount to mortgaging our children's future.

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