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Emerging infections in animals—potential new zoonoses?

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Today, there is widespread recognition that our most powerful enemy may not be the next world war, a nuclear bomb, or even acts of terrorism, but rather Mother Nature. A new disease with high transmissibility and mortality could emerge from an unnoticed quarter and drastically reduce the human population before sufficient resources and expertise could be marshaled. It is likely that such a new and deadly disease would have its origin in the animal world. In fact, a full 75% of emerging diseases of humans come from animals. As the human population expands, and we hop from continent to continent; as we mix various species together for trade, personal satisfaction, or to advance our technology, we are certain to move more microorganisms into novel niches, with pathogenic results.

Many outbreaks of emerging disease in humans are preceded by a similar emergence in an animal population. In general, emerging disease agents can be broadly defined to include three groups: known agents appearing in a new geographic area, known agents or their close relatives occurring in a hitherto unsusceptible species, and previously unknown agents detected for the first time. This review seeks to describe some of the emerging diseases of animals and their relations to the corresponding and subsequently emerging diseases in the human population. As a framework, diseases will be clustered into one of the three groups listed above: agent in a new geographic area, agent in a new species, and previously unknown agent detected for the first time.

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Emerging zoonotic disease—occurrence in a new area

Some of the most worrisome infectious diseases are those that are already recognized as endemic in one area, so that current control practices keep these diseases in check and off the international public health radar screen. With globalization, pathogen distribution patterns become redrawn in haphazard and unpredictable ways. Almost invariably, the new host region is taken by surprise. Two examples are Rift Valley fever, an African disease that recently emerged with ferocity for the first time outside Africa, and alveolar echinococcosis, a smoldering and highly fatal parasitic infection that is making insidious moves from its historic home in the Arctic to many new and more southerly climes.

Rift Valley fever

Rift Valley fever (RVF) is a mosquito-borne viral disease that causes mass mortality among newborn ruminants, especially sheep, and a flu-like illness in humans. The disease had always been confined to the African continent. Then, in 2000, a severe epidemic occurred in the Arabian peninsula. In this outbreak, the unusual presentation of disease, the high human case-fatality rate, and the presence of multiple potential mosquito vectors made the disease a serious cause for concern.

RVF virus was first isolated in 1930 in an epizootic situation among sheep on a farm near Lake Naivasha in Kenya's Rift Valley [1]. A characteristic feature of the disease is hepatic damage, as described in the original report, ''Enzootic hepatitis or Rift Valley fever.''

RVF virus can infect a very wide host range; severe, often fatal disease has been documented in lambs, calves, goat kids, puppies, kittens, mice, and hamsters. Moderate disease has been seen in many other species [2]. The incubation period is 2 to 6 days. The virus replicates primarily in hepatocytes. Clinical signs in ruminants include weakness, anorexia, jaundice, and death. Pregnant animals will abort or give birth to malformed young. The disease is usually more severe in sheep than in cattle. Most infections in humans are asymptomatic. Those who become clinically ill most commonly experience a flu-like illness. Photophobia and symptoms of hepatic impairment may be evident. Approximately 5% of clinically ill people will develop complications, which are often grave. These include encephalitis, retinopathy, hepatorenal failure, and disseminated intravascular coagulation leading to massive hemorrhage. Disease in humans is almost invariably noted after mass mortality among animal species.

RVF is transmitted by mosquitoes. At least 30 species of mosquitoes in eight genera can effectively carry the virus from one mammalian species to another. This lack of ''monogamy'' with respect to vector competence ensures that RVF could easily become established in a number of areas outside its historic range. Transovarial transmission occurs, and the virus

can remain in dormant eggs oviposited in dry areas. With rainfall, eggs hatch, and the resulting mosquitoes can transmit the disease. Outbreaks usually occur subsequent to climatic conditions that favor an increase in the vector population. Ruminants are considered to be amplifier hosts and can experience a significant viremia. This animal infection results in expansion of the infected vector populations, with the disease spreading to the human population.

Before 1977, RVF was confined to Africa south of the Sahara; however, the construction of the Aswan Dam and the subsequent development of flood plains for agriculture resulted in a large outbreak in Egypt in the late 1970s. Likewise, construction of the Diama Dam on the Senegal River precipitated an outbreak in Mauritania in 1987. Excessive rainfall, largely brought about by the El Niño Southern Oscillation Effect, created moist, mosquito-enhancing conditions that contributed to an outbreak in Kenya and Somalia in 1997 to 1998 [3]. In each of these instances, mass mortality in animals preceded human infections. Then, in September of 2000, the Ministries of Health in both Yemen and the Kingdom of Saudi Arabia received reports about acute disease in humans that was compatible with RVF. The focus of disease was the northwestern region of Yemen and the southwestern corner of Saudi Arabia. Just before reports of human disease, there were records of extensive morbidity and mortality among livestock, predominantly sheep.

In Saudi Arabia, there were a total of 886 suspected cases during the outbreak. Laboratory confirmation was attempted on 834 of the patients; positive results were obtained on 683 (81.9%). The male-to-female ratio was 4:1. Of these 683 laboratory confirmed cases, 95 died, for a case-fatality rate of 13.9%. Seventy-seven of the 683 cases were Yemenis living and working in Saudi Arabia; the case-fatality rate for these patients was 26%. The higher case-fatality rate for Yemenis may be related to the lack of affordable access to health care and thus to late presentation [4]. Also, most of the Yemenis living in Saudi Arabia were male rural workers, who proved to be the highest risk group.

Clinical and epidemiologic data from Yemen are not as readily available. According to Centers for Disease Control and Prevention records, between August and November 2000 there were 1087 suspected cases, including 121 deaths [5]. Three quarters of the patients reported exposure to sick animals, handling an aborted fetus, or participating in slaughter of animals.

The key presenting complaints in the outbreak in Saudi Arabia were nausea, vomiting, abdominal pain, and diarrhea, all related to the acute hepatitis developing. In addition, renal failure was a common complication, occurring in one fourth of the patients. That factor makes this outbreak quite different from what has been seen in past outbreaks in Africa, where the majority of cases were reported as flu-like illness. The case/fatality rate also was much higher than that reported in previous outbreaks [4]. The reasons for the higher death rate may be related to underreporting of mild

or asymptomatic cases, or to pre-existing subclinical liver disease caused by the schistosomiasis and viral hepatitis that are known to exist in this part of Saudi Arabia [6].

The genetic sequence of the virus obtained from this outbreak is closely related to that of the virus that was circulating and causing disease in Kenya and Somalia in 1997 to 1998, a fact suggesting that it was introduced into the Arabian peninsula from eastern Africa [7]. The lack of variation among isolates from this outbreak indicates that the agent had only recently been introduced to the area. The suspected route of introduction is in infected livestock. Rainfall had been heavy the previous year, as aerial surveys and satellite images revealed an increased vegetations index [8].

This outbreak of RVF in the Arabian peninsula underscores the interconnectedness of human and animal populations. The blurring interface created by trade, combined with favorable climatic factors, made possible a portal of entry and subsequent amplification, creating first an emerging disease in livestock, then a significant public health crisis for the region.

Alveolar echinococcosis

Alveolar echinococcosis is a chronic disease caused by infection with the intermediate form of the tapeworm *Echinococcus multilocularis*. This parasite is geographically distributed in the northernmost part of the northern hemisphere, including areas of western Europe, Asia, China, northern Japan, Alaska, Canada, and the north central region of the United States [9]. In these areas, *E multilocularis* is maintained in a sylvatic cycle that involves foxes and small rodents as the definitive and intermediate hosts, respectively. While other wild canids and domestic dogs and cats can serve as alternate definitive hosts, infected humans are an aberrant or intermediate host [10]. Once ingested by humans, the egg releases an oncosphere that finds its way from the duodenum to visceral tissues, usually the liver, where the metacestode stage develops as multiple infiltrating hydatid cysts of slow but constant growth and expansion [11]. The infection is so aggressive that the lesion was initially thought to be a neoplasm. It was Rudolf Virchow, the father of modern pathology and also the first person to use the term "zoonosis," who correctly identified the disorder as an infectious process.

Because clinical signs usually develop 5 to 15 years post–initial infection when tissue invasion is extensive, often the only treatment possible is radical surgery with concurrent long-term antiparasitic treatment [11]. In many instances more drastic measures, such as liver transplantation, are the only alternatives. These treatments represent a considerable cost burden to patients and countries where the disease is endemic.

The range of *E multilocularis* is currently expanding to areas where it was not previously reported, and this expansion is apparently due to the

translocation of the definitive host. In Europe, the increasing fox population, in part the result of successful rabies control programs, has resulted in animals invading urban centers. These urban centers provide not only abundant small rodent intermediate hosts, but also alternative definitive hosts such as the domestic dog and cat.

As the range of *E multilocularis* increases, incidence of human disease is carefully monitored. In Alaska, there is considerable evidence of the disease among Eskimos. Children are most likely to be infected, presumably because of play habits and increased oral exposure, with the disease appearing as they become young adults [10,12]. In some areas, seroprevalence among the human population is increasing, although a specific rise in clinical cases has not yet been seen. It is unknown whether this seroprevalence is due to immunity or to an early stage of infection, before cyst development [13,14]. More extensive epidemiologic investigations are warranted.

Control of alveolar hydatid disease is problematic. Focal geographic eradication of the cestode has been reported on the small Japanese island of Rebun by eliminating dogs and foxes on the entire island. This method is impractical in larger geographic areas because of ecological, ethical, and humane considerations [15]. It has been proposed that control of *E multilocularis* could be better achieved by broad ecological study of the region in question and implementation of education programs. These educational programs can focus on the modification of specific high-risk behaviors, the periodic administration of anthelmintics to companion pets, and baiting methods with anthelmintics for the wild reservoir [16]. Education appears to be an economically feasible control measure in small urban areas, where it has shown promising results in decreasing *E multilocularis* environmental contamination [17].

Over 100 years have passed since Rudolf Virchow cast a spotlight on alveolar echinococcosis by clarifying the infectious nature of the process. The lethality of the disease, the economics of treatment options, and the spread into nonendemic and often urban areas are all considerable causes for modern concern.

Emerging zoonotic disease—occurrence in a new species

It is well known that 75% of all emerging infectious diseases of humans occur as a result of an animal pathogen's moving into a human host. A less-recognized possibility is that of an infectious agent in one animal species moving into a second animal species to create an emerging disease of animals. What is the total number of potential pathogens currently present in animals? How many are capable of moving from animals to humans, or from one animal species to another?

A recent paper by Dr. Sarah Cleaveland et al [18] catalogs and categorizes all known pathogens of humans, domestic livestock, and

domestic carnivores based on their ability to move from one species to another. Surprisingly, of the 1415 known pathogens of humans, 61.6% have an animal origin. A total of 616 pathogens were documented for domestic livestock, with 77.3% considered ''multiple species'' (ie, capable of infecting more than one type of animal). For domestic carnivores the total was 374 pathogens, with 90% classified as ''multiple species.'' So it is apparent that there is considerable promiscuity among animal pathogens. As unusual species are grouped together, swapping of flora can easily occur.

Cleaveland makes no efforts to catalog the number of agents found in wildlife—understandably so. The list would be not only enormous but also notably incomplete, because we lack detailed knowledge about existing diseases of so many wild species of animals. In this light, it is notable that many of the emerging human and animal diseases we have dealt with in recent years have come from wildlife. This is a largely unexplored arena, with many more pathogens yet to emerge. The following two examples demonstrate how a pathogen moving from one animal species to another can have a very significant subsequent impact on public health.

Monkeypox

Monkeypox made headlines in the spring of 2003 as an African disease that sneaked into the Midwestern United States through the exotic pet trade and generated dozens of human infections in four different states. Contrary to popular belief, this was not the first incursion of the virus into the United States. During the late 1950s and 1960s, six outbreaks of monkeypox were reported among captive nonhuman primates in research facilities throughout the United States [19,20]. In four of these cases, the origin of the incriminated monkeys was not Africa but India and Southeast Asia. However, subsequent serologic surveys in wild populations in South Asia failed to identify this area as a possible niche of the virus. It is probable that these animals were exposed at some point during their transportation or quarantine process. Traceback investigations on the remaining two outbreaks were not reported, and human infections did not occur on any occasion—perhaps because vaccinia immunization provides good cross-protection against monkeypox, and smallpox vaccination was very active during those years.

The monkeypox virus belongs to the Orthopox genus in the family Poxviridae and was originally isolated in 1958 from a sick cynomolgus monkey at the Statens Seruminstitut in Copenhagen, Denmark. The term monkeypox may be something of a misnomer, because this virus is more frequently associated with small rodents than with primates [21]. Since the first human report in 1970, in what is today the Democratic Republic of Congo (DRC), numerous reintroductions to the human population have occurred, mostly in central and western Africa, including a large outbreak from 1996 to 1997 in the DRC involving more than 400 individuals [22,23].

A unifying factor in all human monkeypox clusters is the close interaction of humans with wildlife. During African outbreaks, humans were exposed either during seasonal hunting activities or when they were forced to retreat deeper into the rain forest during civil turmoil [24,25]. Index cases in these outbreaks are usually associated with exposure to rodents rather than monkeys. Close and continuous human/wildlife interaction is needed to maintain monkeypox in a human population; human-to-human transmission alone will not sustain the virus among humans. Nevertheless, if the herd immunity of a population is low, person-to-person transmission and repeated introductions of the virus from the wild reservoir can lead to more and larger clusters of human monkeypox. Several serologic and epidemiologic studies implicate squirrels and the Gambian giant rat as the key players in the circulation of the virus in nature [26,27].

The introduction of monkeypox to humans in the central United States during the 2003 outbreak provides a good example of cross-species and cross-continental trafficking of infectious agents. The monkeypox virus, a specifically African entity, was quiescently exported from its home continent in one of its customary hosts, a Gambian giant rat, and jumped ship, as it were, into a previously unexplored and proximate microbial niche, prairie dogs that had been housed with the exported Gambian rats. The virus flourished in this new and foreign microbial habitat, creating an acute and emerging disease problem for this North American species of rodent. It was not long before an emerging disease of prairie dogs became a significant public health crisis.

In the spring and early summer of 2003, there were 35 confirmed human cases of monkeypox, scattered across four Midwestern states. All of these individuals were infected by direct or indirect contact with infected prairie dogs [23,26]. An unexpected finding was the relatively mild clinical presentation of the disease when compared with outbreaks in Africa.

Traceback investigation revealed that prairie dogs, source of the human infection, became infected at an animal distributor facility in Illinois when they were housed together with infected Gambian giant rats and dormice imported from Accra, Ghana [26]. Out of 200 prairie dogs that were estimated to have been exposed to the infected African animals in this facility, 93 were traced forward. The remaining 107 animals either died or were sold in informal transactions without sufficient record-keeping to allow traceability.

With no knowledge of the fate of more than 100 potentially exposed prairie dogs, not to mention the unknown number of African rodents in various collections throughout the United States, we cannot predict the future of monkeypox in the Western Hemisphere. Its impact on native wildlife populations of rodents and its potential establishment as an enzootic disease in the United States are worrisome.

Ebola

Since its emergence in 1976, the Ebola virus has become a "sleeping giant" in western and central Africa. Following its first documented emergence, Ebola has re-emerged to be recognized on at least 18 more occasions, mostly in the African continent. Each new outbreak tends to generate screaming media attention, perhaps because of the gruesome and rapid clinical course of the disease or, more likely, because of previous highlighting of the disease in best selling books and motion pictures. In fact, Ebola has become a kind of poster child for the whole field of emerging disease. In terms of human morbidity and mortality, Ebola is a bit actor in the overall drama of emerging diseases, but its occurrence and documented recurrences have generated considerable public consciousness-raising and have increased funding levels for infectious diseases overall and emerging diseases in particular.

Studies in Africa have determined that monkeys and apes are important players in the transmission of the virus to humans [28]. In fact, most outbreaks in humans have been preceded by primate die-offs or traced back to contact with dead primate carcasses. Close exposure to these ape carcasses and consumption of bushmeat from these primates are targeted as possible conduits of infection to the human population. In addition, carcasses of duikers found near dead apes were also positive for Ebola virus, indicating not only a broader host range but also the possibility of additional sources of bushmeat for human infection. However, neither primates nor duikers are considered the natural host, because the virus is highly lethal in these animals [28,29].

The reservoir of Ebola remains anonymous. Many sampling surveys have been performed but provide only limited information regarding the wild reservoir [30,31]. More encouraging information has been obtained from experimental infections of possible wild candidates, such as the fruit bat. In these experiments, bats were capable of sustaining and allowing viral replication with negligible clinical signs [32]. Recently, an ecologic niche modeling study has suggested several characteristic features of this unknown reservoir. The study establishes the reservoir distribution in the evergreen broadleaf forest, mainly in the Congo Basin [33]. In addition, climate variability may play a role in filovirus transmission and might be useful as a predicting factor, as rainfall has proved to be a factor in "triggering" the emergence of Ebola hemorrhagic fever.

It is clear that an ecological approach to pathogen transmission can benefit our understanding of emerging diseases, and Ebola hemorrhagic fever exemplifies this principle. The limited genetic variation between isolates of Ebola subtype Zaire isolated 20 years apart suggests that ecological rather than genetic factors play a central role in the initiation of outbreaks [34].

Elucidation of the ecology of Ebola virus and definitive identification of its natural reservoir are pivotal for the development of prevention programs.

Such prevention programs will benefit not only the human population but also the declining endangered monkey and ape population in the region [28,35]. In the meantime, human disturbances of pristine ecosystems along with the unsafe practices of the bushmeat trade will provide ideal settings for Ebola re-emergence.

Emerging zoonotic disease—brand new agent

Perhaps the most frightening and unpredictable category of emerging disease is that of those that are caused by a previously unknown virus or bacterium. Of course, the agents are not really brand new, only new to our knowledge. Recent years have seen such agents emerge in disastrous ways to affect human populations. Although the new disease usually makes screaming headlines at the moment when large numbers of humans become infected, in fact, in many instances the "new" agent has surfaced just previously as an emerging disease in an animal population. It is this proximate source that extends to infect humans.

Nipah virus

Nipah virus is a recently discovered member of the Paramyxovirus family that was quiescent in its ecologic niche for countless years until anthropogenic factors allowed it to replicate in an environment that engendered extensive human exposure. An outbreak of disease in pigs preceded the human clinical disease. The illness in swine was originally attributed to classical swine fever infection, but it soon became apparent that a novel infectious agent was responsible. Extensive replication in bronchiolar epithelium coupled with an exertional cough ensured that the infected pigs were spewing prolific amounts of virus into the environment. In humans, Nipah virus infection presents clinically as an acute febrile encephalitis. Nipah virus was first isolated from the cerebrospinal fluid of a patient from the Sungai Nipah village in Malaysia [36], 6 months after its emergence in late September 1998. Close similarities of the new virus to another recently discovered paramyxovirus, Hendra virus, prompted virologists to create a new genus, Henipavirus, to include both entities. In Malaysia, the Nipah virus outbreak came to an end after the establishment of strict control measures and the culling of over a million pigs [37]. The outbreak extended to Singapore, where it was halted by ceasing the importation of pigs from Malaysia. At the end of this episode, a total of 283 human cases of viral encephalitis with 109 deaths were reported, for a fatality rate close to 40% [38].

Because fruit bats had been identified as the natural reservoir for Hendra virus, several ecological surveys were undertaken to investigate the possibility that Nipah virus also had originated from fruit bats. Early studies

were able to detect antibody titers against Nipah virus in five species of fruit bats [39], and eventually the virus was isolated from the urine of an Island flying fox and from a partially eaten fruit regurgitated from one of these bats [40]. These findings implicated bats of the *Pteropus* species as the natural reservoir for Nipah virus. The critical link with the human population was made when the virus moved from fruit bats to swine. The susceptibility of swine and the marked respiratory involvement created an outbreak situation, with resulting spread to humans and a major public health crisis. The proposed chain of events that enabled this interaction began around 1997 when extensive slash-and-burn deforestation produced a haze that extended all over Southeast Asia [41]. This deforestation and haze, aggravated by an El Niño Southern Oscillation drought, decreased the already scarce quantities of fruiting forest in the region. Impelled by these anthropogenic factors, *Pteropus* bats invaded areas of fruit cultivation, like the index farms, that were also used as piggeries.

Nipah virus elicits major public health concerns because of its high mortality rate, ability to infect a wide range of hosts, and broad geographic distribution of the reservoir host. This concern is accentuated by its negative economic impact and its official listing as a critical biologic agent for public health preparedness. During the 1998 outbreak, it was demonstrated that in addition to pigs various domestic animals could serve as hosts, namely dogs, cats, and horses [42]. Also, rodents have recently been experimentally and productively infected [43]. This wide availability of potential hosts, along with the globally limited but regionally widely distributed reservoir, represents a potential threat of emergence beyond Southeast Asian boundaries. Approximately 60 species of *Pteropus* bats have been identified, and all are distributed in a range that extends from the islands of Mauritius, Madagascar, Pemba, and Comoro, along the sub-Himalayan region of Pakistan and India, through Southeast Asia, the Philippines, Indonesia, New Guinea, and the southwest Pacific islands as far east as the Cook Islands and Australia. Although the distance these animals will travel, and thus their disease-carrying capacity, is debatable, it is recognized that the overlapping distribution of three species of flying foxes is all that is required to form a continuous link between the east coast of Australia and Pakistan [44]. This important ecological aspect must be taken into consideration during epidemiologic investigations of future emergences outside Malaysia, such as the outbreak recently (February 26, 2004) reported in Bangladesh [45].

Severe acute respiratory syndrome

Two years after welcoming a new millennium, humanity experienced severe acute respiratory syndrome (SARS), the first pandemic of the twenty-first century. This event catalyzed global public health emergency responses in a way no previous disease had. The outbreak in humans began in

November 2002, as atypical pneumonia appeared first in the southern Chinese province of Guangdong and subsequently spread to nine countries, including the United States [46]. All told, there were approximately 8435 human cases and 789 deaths in 33 countries around the world [47]. A novel coronavirus (SARS-CoV) was eventually identified as the culprit in SARS [48].

Despite extremely rapid and sophisticated molecular characterizations, the source of the SARS virus remains speculative. The SARS-CoV proteins share little similarity with the proteins of any of the three major existing serogroups of coronaviruses. Various coronaviruses are well recognized for causing disease in animals—specifically, infectious bronchitis in chickens, infectious peritonitis in cats, and diarrhea in piglets and calves. However, the SARS-CoV had very little in common with any of these well-studied pathogens. There is, however, mounting evidence to suggest that SARS-CoV has a zoonotic origin. A promising lead arose when a SARS-CoV–like virus was isolated from Himalayan palm civets found in the Guangdong live-animal market, and a subsequent serosurvey study demonstrated viral titers among asymptomatic animal traders in Guangdong, suggesting previous infection with a SARS-CoV–like virus [49,50].

Speculation about a genetic reassortment of an animal coronavirus with further adaptation to the human host is presently being evaluated. Certainly, a wild animal market could provide the ideal setting for such reshuffling of genes among different wild animals and eventually humans.

Evidence indicates that the introduction of SARS-CoV to humans was a fairly recent event [51]. Epidemiologic studies have shown that at least 2 months before the outbreak the virus was circulating in the capital of Guangdong, Guangzhou, a city noted for its ''wet markets'' where wild game trade for human consumption is very popular. Food handlers made up more than one third of the initial cases. Only half of the cases could be attributed to contact with SARS patients, suggesting transmission from an unknown reservoir [52].

The SARS pandemic catalyzed public health systems worldwide, and the economic costs were staggering. Despite the most intensive epidemiologic investigations and emergency response ever mounted against an infectious disease, the source of the agent remains elusive, making it extremely difficult to predict when and where the next resurgence may occur.

Summary

Wild game meat, livestock trading, pocket pets, and Arctic tapeworms—decades ago, who would have envisioned that these disparate entities would be threaded together in a great haiku of public health problems? Emerging diseases have created a new kaleidoscopic lens through which we view the world. These emerging diseases will not only continue to emerge but will

probably do so at an ever-increasing rate. As was articulated in a recent National Academies of Science report, myriad factors in our interconnected global village are creating the microbial equivalent of a "perfect storm" [53]. However, unlike a major climatic event, where various meteorologic forces converge to produce a tempest, this microbial perfect storm will not subside. There will be no calm after the epidemic; rather, the forces combining to create the perfect storm will continue to collide, and the storm itself will be a recurring event.

Watching the steady stream of new and emerging diseases, one is reminded of the carnival game "Whack-a-mole." In this game, the participant is given a rubber mallet and tasked with defeating each mole that pops out of a series of holes. The satisfaction derived from neutralizing one mole is immediately replaced with the drive to beat back the next. The operator must act quickly to eradicate each new surfacing mole. Perhaps today we need an entirely different strategy. Rather than responding to each new crisis as it arises (ie, each new mole that emerges), we need to address the underlying factors in disease emergence seriously and expeditiously. Instead of focusing on the next big health crisis, we need to conduct thoughtful and thorough studies of the ecology and overall species susceptibility of disease.

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