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Whence Comes the Phoenix?

Emerging and reemerging pathogens are like weeds because both are adaptable exploiters of unstable environments. Andrew Dobson

Infectious diseases account for more than one-quarter of all deaths worldwide. There seems to be the frequent emergence of new infectious diseases.

The evolving nature of infectious diseases poses challenges. There are practical challenges, such as developing diagnostics, treatments, and vaccines, and of designing effective surveillance and intervention strategies. There are intellectual challenges, including understanding the complex and multifaceted causes of the emergence and spread of new pathogens and the reemergence of those previously thought to be in decline.

Humans are affected by a diversity of pathogens. A recent review found 1,407 currently recognized species of human pathogen. A species count, however, only provides a simple measure of pathogen diversity. Medically important variation, e.g., in traits such as virulence factors, immunogenicity, and drug resistance, occurs within species as well as between them. Individual species manifest a wide variety of life cycles, transmission routes, pathogenicities, and epidemiologies.

Emerging and reemerging infectious diseases are defined by the CDC as "diseases of infectious origin whose incidence in humans has increased within the past two decades or threatens to increase in the near future." More than 175 of the 1407 species cause diseases that are regarded as falling into this category.

Many human pathogens are commensals that do not ordinarily cause disease; many others are distributed in the wider environment such as water or soil; some infect host species other than humans. Almost 60% of human pathogens, however, are zoonotic. A small minority of these are mainly passed from humans to animals rather than the other way around. An animal reservoir is an important feature of human pathogenic species biology. The most striking feature of such animal reservoirs is their diversity. We share our pathogens with ungulates, carnivores, rodents, primates, other kinds of mammals such as bats, as well as with birds. Many of the reservoirs are domestic animals, but just as many are wildlife species. These patterns apply to the whole range of pathogens from viruses to helminths.

Emerging and reemerging zoonoses are not associated with any particular animal reservoirs but they are associated with pathogens that can infect several different kinds of hosts. Some pathogens that are not now regarded as zoonotic, such as HIV-1, were animal-acquired .

When a pathogen of one host species first invades a new one, it is called a "species jump". Successful species jumps require both the opportunity and capacity to infect new host species. Opportunity depends on the pathogen contacting the new host, perhaps through changes in the ecology or the behavior of either of the host species. The capacity to infect reflects whether the pathogen is compatible with its new host. But the pathogen still needs to overcome the "species barrier," generally meaning it cannot establish an infection unless the new host species is exposed to a higher dose than was required to infect its original host.

Those pathogens that already have a broad host range seem more likely to be successful at jumping into new host species than do pathogens with narrow host ranges. The determinants of host range are poorly understood. One key factor, at least for viral pathogens, appears to be their use of cell receptors that are phylogenetically conserved across a range of host species. The ability to infect a host species is merely the first step.

Invading a new host species also depends on the ability to transmit between individual hosts within a species. Many emerging pathogens have so far had limited transmissibility between humans, Only if a primary infection generates more than one secondary infection can a novel pathogen successfully invade a new host population.

Small changes in infection or transmission rates can lead to large changes in the potential for pathogen emergence. Such change can be the result of changes in the demography or behavior of the host population, changes in susceptibility of the host population due to decreased immunocompetence, or changes to the pathogen itself. The recently confirmed cluster of influenza A H5N1 virus cases in Indonesia in 2006 from one individual with person-to-person spread to 7 additional family members was alarming. The virus was also changing as it spread from one person to another.

Changes to a pathogen can prove critical. Each infection provides an opportunity for the pathogen to adapt to its new host. The likelihood of adaptation occurring is sensitive to the number of infections, the extent of genetic change required to affect susceptibility and transmissibility, and to the genetic lability of the pathogen. The importance of this last factor may help explain why so many recent species jumps involve RNA viruses, which have mutation rates several orders of magnitude higher than other kinds of pathogen, as is the case of HIV.

We are only beginning to understand the biological basis for pathogen adaptation to a new host. Changes affecting only a small number of amino acids in the viral proteins that determine cell receptor specificity may be all that is required for such viruses to gain a foothold in a new host species. Perhaps the most striking recent example of successful adaptation to humans is simian immunodeficiency virus. This pathogen, having entered the human population, rapidly evolved to become HIV-1. The possibility of adaptation similarly underlies current concerns about influenza A H5N1 virus causing an influenza pandemic.

Another example of present concern is a report from the Republic of Congo where at least 60 people have been affected by an outbreak of monkeypox. It has been theorized that monkeypox may well have the ability to change in the human host to take on characteristics sufficiently similar to smallpox to become a pandemic scourge.

Monkeypox virus infection has been identified as an emerging zoonotic disease. It is maintained in a large number of rodent and nonhuman primate species in Africa. Reported monkeypox virus infections of humans have escalated during the past three decades, as have outbreaks with human-to-human transmission. This increase is likely due to numerous factors, such as enhanced surveillance efforts, environmental degradation and human urbanization of areas where monkeypox virus is maintained in its animal reservoirs and, consequently, serve as a nidus for human infection.

As a zoonotic agent, monkeypox virus is far less sensitive to eradication measures since it is maintained in wild-animal populations. With the emergence of HIV in Sub-Saharan Africa and an increased frequency of human monkeypox virus infections, especially in immunocompromised individuals, monkeypox virus may evolve, maintain itself independently in human populations, and gain enhanced virulence.

Factors that drive pathogen emergence and reemergence include those relating to the hosts, those relating to pathogens, and those relating to the environment. Human factors include population growth, urbanization, population health and hospitalization, travel, and migration patterns. Pathogen factors include capacities to adapt to humans and to acquire virulence factors and antibiotic resistance as well as failures of disease control programs. Environmental factors include land use, agricultural practices, production and supply of food and water, trade in animals or animal products, and climate change.

The diversity of these drivers is immediately apparent, and is often associated with human activity. Changes in the way humans interact with their environment, and particularly with animal populations both domestic and wild, can provide new opportunities for pathogens. Recognition may provide approaches to halt some of them.