

Emergence and Spread of Infectious Diseases

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Abstract

Most pathogens causing diseases in humans are derived from animals including both wildlife and domestic animals, and the majority of emerging infectious diseases in particular have originated from wildlife. Since there are diverse species of animals yet unidentified globally, including viruses and bacteria, it seems inevitable that emergence of new infectious diseases will continue if human activities that change or destroy wildlife habitats are not stopped. It seems impossible, however, to stop such human activities, since exploitation of resources is prerequisite to providing sufficient food, housing and clothing to the 6.7 billion people living on the earth. Furthermore, international movement of wildlife also facilitates the emergence of new infectious diseases. The only thing we can do to reduce the threat of emerging infectious diseases is to detect them and respond as quickly as possible so that we can prevent further spread of the diseases to humans and establishment of the pathogens in human populations.

Key words: emerging infection, wildlife, zoonoses

1. Introduction

In 1995, the Centers for Disease Control and Prevention (CDC) started publishing a new scientific periodical, *Emerging Infectious Diseases*, in response to increased awareness of potential threats posed by emerging and re-emerging infections. Since then we have witnessed the emergence of West Nile fever in North America, Hendra and Nipah virus infections and severe acute respiratory syndrome (SARS) in Southeast Asia, monkeypox in the United States and so on. The H5N1 subtype of the influenza A virus now epizootic around the world is regarded as a potential candidate for an influenza virus which could cause a global pandemic. It was previously shown that approximately three fourths of emerging diseases were zoonotic (Taylor *et al.*, 2001; Woolhouse & Gowtage-Sequeria, 2005). In this review article, therefore, I will provide an overview of the emergence and spread of new infectious diseases from the perspective of zoonoses.

2. Emerging Infectious Diseases

Diseases newly appearing or newly recognized, diseases that are new to particular regions and already known diseases, the incidence of which has been increasing recently, are regarded as emerging infectious diseases. Nearly one infectious disease per eight months has emerged since 1980 (Institute of Medicine, 2003). The Institute of Medicine published reports in 1992 and

2003 which pointed out thirteen key factors involved in the emergence and spread of new infectious diseases (Institute of Medicine, 1992; Institute of Medicine, 2003). Woolhouse and Gowtage-Sequeria (2005) ranked these factors and the top ten are listed below.

Rank*	Factors
1	Changes in land use or agricultural practices
2	Changes in human demographics and society
3	Poor population health (<i>e.g.</i> , HIV, malnutrition)
4	Hospitals and medical procedures
5	Pathogen evolution (<i>e.g.</i> , antimicrobial drug resistance, increased virulence)
6	Contamination of food sources or water supplies
7	International travel
8	Failure of public health programs
9	International trade
10	Climate change

* Ranked by the number of associated pathogen species (most to least).

From Woolhouse, M.E.J. and S. Gowtage-Sequeria (2005)

As is obvious from the list, the major drivers are anthropogenic interventions in ecosystems. Human activities accelerate the emergence of infectious diseases. To support the unprecedentedly increasing human population of the globe, it is inevitable that humans will continue to disturb ecosystems to obtain precious resources through rain forest clearing, road and dam building, agricultural irrigation and other activities.

3. Most Emerging Diseases are Caused by Zoonotic Pathogens

According to Woolhouse and Gowtage-Sequeria (2005), about 73% of emerging infectious diseases are zoonoses—diseases or infections naturally transmissible between vertebrate animals and humans (WHO/FAO, 1959). Moreover, even many diseases now considered contagious only to humans are thought to be derived from pathogens in animals domesticated several thousand years ago or from wild non-human primates (Wolfe *et al.*, 2007). Human encroachment on the habitat of wild animals harboring microbes will increase opportunities for encounters between wild animals and humans. If contact, whether direct or indirect, occurs after the encounter, subsequent spillover of microbes from animals to humans may follow. It is also possible that pathogens from wildlife might be transmitted to humans via domestic animals. According to Taylor *et al.* (2001), approximately 70% of zoonotic pathogens are not transmitted among humans after successful spillover. If the basic reproductive ratio (R_0) of the pathogen is greater than 1, the infection will continue to spread until all susceptible individuals are dead or immune. Pathogens showing R_0 of greater than 1, therefore, have the potential to emerge among the human population. On the other hand pathogens with R_0 of less than 1 will not spread among humans. It is, however, possible that pathogens with R_0 of less than 1 could emerge if the primary spillover from wild animals to humans occurs very frequently. For instance more than ten million people receive post-exposure prophylaxis against rabies every year. Although rabies is not an emerging disease, the rabies virus casts a great burden on humans even though the virus cannot spread from human to human. Microbes perpetuating in their ecological niche will do nothing to humans unless humans encroach on areas where the microbes are lurking in natural reservoirs.

4. Several Examples of Recently Emerging Infectious Diseases

Since this issue of the Global Environmental Research is devoted and confined to influenza and West Nile fever, characteristics of some other zoonotic diseases which have recently emerged are discussed in this article.

4.1 Nipah virus infection

In 1998, a previously unknown encephalitis struck pig farmers in Malaysia (Chua *et al.*, 1999). Since respiratory and neurological disease in pigs preceded the human cases, over one million pigs were slaughtered to contain the disease in humans. A virus resembling the measles virus was isolated from a patient. It was found that the virus was closely related to but distinct from the Hendra virus, which also emerged in 1994 in Australia (Murray *et al.*, 1995). The new virus was named after the place where the patient was found, Nipah. Together

with the Hendra virus, the Nipah virus was assigned to a new genus *Henipavirus*. Epidemiological investigations were conducted to look for the natural reservoir of the Nipah virus and it was eventually found that fruit bats of the genus *Pteropus* were the natural reservoir of the Nipah virus (Yob *et al.*, 2001; Chua *et al.*, 2002). Habitat loss and hunting are believed to force those animals to approach areas where humans and domestic animals live, resulting in cross-species transmission of viruses from the bats to new hosts. Moreover, in Bangladesh, infections were reported to have been caused by consumption of fruit or palm sap contaminated with the saliva of infected bats (Luby *et al.*, 2006). Human-to-human infection was reported in Bangladesh, though apparently it occurred inefficiently. Although there is no specific animal species that is responsible for the emergence of new infectious diseases (Woolhouse & Gowtage-Sequeria, 2005), bats are receiving much attention because they have been implicated as a cause of recent emergences of deadly pathogens (Wong *et al.*, 2007) such as the Ebola virus, Marburg virus and severe acute respiratory syndrome (SARS) corona virus.

4.2 Acquired immunodeficiency syndrome (AIDS)

If we stick to the definition of zoonoses proposed by the World Health Organization (WHO), the human immunodeficiency virus (HIV) is not zoonotic, since the virus can no longer spread to animals under natural conditions. However, the evidence is accumulating that HIV-1 was derived from the simian immunodeficiency virus of chimpanzees in central Africa (Hahn *et al.*, 2000; Keele *et al.*, 2006). Bush meat hunting and consequent exposure of people to the organs or blood of animals are thought to be the major drivers promoting a spillover of simian viruses to humans. Human behavior such as intravenous drug injection and homosexuality contributed to adaptation of the virus to human beings and its establishment as a new human-specific pathogen. According to UNAIDS, the Joint United Nations Programme on HIV/AIDS, the estimated number of people infected with HIV is more than 33 million, whereas more than 2.5 million people are newly infected and 2.1 million people die of AIDS every year (UNAIDS, 2007). It would be therefore prudent to consider AIDS one of the most devastating zoonotic diseases in human history.

4.3 Ebola hemorrhagic fever

At this moment, there is an ongoing outbreak of Ebola hemorrhagic fever in Uganda. As of December 7, 2007, 93 people were suspected of being infected with the virus, 22 of whom died. More than 300 people were under observation (WHO, 2007). The Ebola virus belongs to the family Filoviridae and was first identified in 1976 (Johnson *et al.*, 1977). The Ebola virus infects not only humans but other non-human primates such as chimpanzees and gorillas. Since non-human primates are highly susceptible to the virus and die quickly after infection, scientists believe that creatures other than

non-human primates might be the natural reservoir of the Ebola virus. The subsequent search for the reservoir animals has been hampered by the great diversity of fauna and flora in African rain forests. Recent studies, however, have suggested that three species of fruit bats are potential hosts for the Ebola virus (Leroy *et al.*, 2005). Non-human primates as well as forest duikers are speculated to be incidental hosts from which the Ebola virus is eventually transmitted to humans. Humans become infected with Ebola virus by direct contact with dead animals. Hunting animals for bush meat, especially hunting weakened animals, may increase the potential risk of acquiring the infection.

4.4 SARS

In 2003, a previously unknown virus was identified in patients suffering from severe pulmonary distress in Hong Kong. The prominent feature of the virus causing SARS was that it could be readily transmitted among humans after its spillover to the human population. The virus, SARS coronavirus (Drosten *et al.*, 2003; Ksiazek *et al.*, 2003; Rota *et al.*, 2003), was first thought to be derived from Himalayan palm civets raised for sale in wet markets in the southern part of China (Peiris *et al.*, 2004). Wet markets are notorious for the intermingling of diverse species of animals. Wet markets are also implicated in the evolution of highly pathogenic avian influenza viruses (HPAIV). Subsequent studies, however, showed that it was unlikely that palm civets were the natural reservoir of the SARS coronavirus. Intensive investigations revealed that many corona viruses of different lineages occur among different species of bats. Furthermore, the presence of a coronavirus closely related to the SARS coronavirus was discovered when Chinese horseshoe bats were investigated (Li *et al.*, 2005). It was thus speculated that a certain corona virus harbored by an unidentified species of bat first gained access to wildlife yet to be identified and then to other species of wild animals, eventually reaching humans via animals captured and sold at wet markets.

4.5 Monkeypox

The monkeypox virus was first isolated from captive non-human primates but monkeys are not the natural reservoir of this virus. Although monkeypox is zoonotic, several cycles of transmission among humans are known to have occurred. It is not well understood how the virus is maintained in the environment, although the virus is enzootic to geographically limited places like West Africa and the Congo basin. However, in 2003, the virus suddenly appeared in the United States. Seventy two people who had been keeping prairie dogs as pets were confirmed or suspected to be infected with the virus. Epidemiological investigation conducted afterwards indicated that Gambian rats imported from Ghana were the culprits (Regnery *et al.*, 2007). It was then revealed that African dormice kept together with those rats had been redirected to Japan. It was fortunate that the animals could be traced and recovered and that they

tested negative for the presence of monkeypox virus infection.

5. Driving Forces of Emergence

As already discussed in the preceding sections, not only spillover but also later spread of the infectious agents among humans can be accelerated by biological, environmental or sociological factors. Outbreaks of Nipah and Hendra viruses were attributable to changes in agricultural practices that resulted in close contact between bats and domestic animals. Bushmeat hunting was implicated in the emergence of AIDS and Ebola hemorrhagic fever. In Central Africa, more than one billion kilograms of wild animal meats are consumed annually. The number of animals killed each year for foods is estimated to be around 580 million in Central Africa, whereas 6.4 to 15.8 million vertebrates are estimated to be consumed in the Amazon Basin every year (Karesh *et al.*, 2005; Fevre *et al.*, 2006; Chomel *et al.*, 2007). Furthermore, live animals, including wildlife are sold in wet markets in various geographic areas around the globe, including the United States. Since different species of animals intermingle within the premises, wet markets provide microbes great opportunities to find new host species in which they can thrive. Wet markets have played essential roles in the emergence of the SARS coronavirus and HPAIV. In addition, international trade in wildlife is estimated to bring six billion US dollars to the industry. Introduction of the monkeypox virus and possibly the West Nile virus was due to legal as well as illegal importation of wildlife into the US. It is estimated that more than 40,000 non-human primates, four million live avian species, and 640,000 live reptiles are traded every year. Humans are thus estimated to be exposed to wildlife greater than several billion times a year. Direct and indirect contact between humans and wildlife may increase the probability of spillover of wildlife pathogens to humans. After spillover, human behavioral changes have accelerated the global spread of AIDS and establishment of AIDS as a human-only disease, whereas rapid movement of people contributed to the worldwide spread of the SARS coronavirus. International trade in live domestic animals like chickens and cows has promoted the dissemination of HPAIV and bovine spongiform encephalopathy, respectively.

6. Detection and Response

The global human population is growing exponentially and is expected to reach seven billion in the year 2015, indicating that human encroachment into wildlife habitats will never cease. The number of known species is estimated to be no more than 12.8% of the total species that actually live on the earth. We have recognized only 0.4 and 1% of bacteria and viruses (Watson *et al.*, 1995), respectively, suggesting that human activities such as further development of tropical rain forests will

result in encounters of humans with unknown species harboring unknown microbes. It seems possible that humans will experience quite a few infectious disease emergences in the future. When domestic animals are responsible for the emergence of new infectious diseases, culling of animals is a prerequisite for prevention of the spread of the disease. It is, however, impossible to take a similar approach as far as wildlife is concerned. Although at least 200 million domestic birds have died or been culled to prevent the spread of HPAIV since 2003, culling of wild birds, now thought to be partly involved in dissemination of the virus, is not recommended by international organizations such as the WHO and FAO. The most important measure to counter emerging infectious diseases is enhanced surveillance that enables us to conduct early detection of clusters of infected people as early as possible. Establishment of sound response mechanisms is also important. The International Health Regulations issued by the WHO in 2005 and enacted in 2007 are expected to enhance such abilities globally. Furthermore expanded surveillance targeting wildlife will be also needed to detect new infectious diseases that may cause pandemics in humans.

7. Conclusion

The explosion of the human population on the earth makes it easier for microbes to find new hosts, whereby some of them undergo evolutionary processes to adapt to humans. Since human population growth shows no signs of ceasing and since human activities disturbing ecosystems will never end, it seems inevitable that pathogens lurking in wildlife will emerge as human pathogens in the near future. Detection of emerging infectious diseases through vigilant surveillance and prompt response is mandatory to fight against the continuing threat of emerging infectious diseases.

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(Received 31 January 2008, Accepted 27 June 2008)