

Responding to emerging diseases: reducing the risks through understanding the mechanisms of emergence

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Over the past two decades, increasing concern and attention have been directed at the potential problems and threats associated with new and emerging diseases. This has been driven by fears arising from the rapid emergence, spread and public health impact of several recent outbreaks, such as the international spread of severe acute respiratory syndrome coronavirus (SARS-CoV) (2003), the potential of avian influenza H5N1 to emerge as a highly lethal pandemic as increasing numbers of human cases are reported (2003 and continuing), and the very rapid global spread of pandemic H1N1 influenza in 2009–2010. The emergence of SARS-CoV, in particular, demonstrated the considerable economic, political and psychological effects—in addition to the impact on public health—of an unexpected epidemic of a highly infectious, previously unknown agent in a highly connected and interdependent world. These examples clearly highlight the necessity and importance of global outbreak surveillance for the early detection and response to new potential threats. They also demonstrate clearly that these emergent diseases can move rapidly between countries and continents through infected travellers so that surveillance needs to be transparent and authorities made aware of international disease events elsewhere around the globe. Some of the specific threats to the Asian Pacific region have been reviewed elsewhere.^{1–4}

So what do we mean by the term “emerging diseases,” and how do they arise? The concept, definition and factors contributing to the emergence of disease threats were encapsulated in two reports from the US Institute of Medicine that defined the major issues and described the principal causes and mechanisms leading to infectious disease emergence, as well as discussing possible strategies for recognizing and counteracting the threats.^{5,6} The most widely accepted definition describes emerging diseases as either new, previously unrecognized diseases that are appearing for the first time, or diseases which are known but which are increasing in incidence

and/or geographic range. Examples of the former include Sin Nombre virus, which first came to light in 1993 as the cause of Hantavirus pulmonary syndrome in the Four Corners area of the United States of America, and Nipah virus, which was first isolated in 1999 as a cause of acute neurological disease in peninsular Malaysia. Examples of the latter include West Nile virus, which unexpectedly jumped from the Old World to emerge in the New World in 1999, and Chikungunya virus, which, with the help of a mutation making it more able to be transmitted by *Aedes albopictus* mosquitoes, spread from island nations in the south-western Indian Ocean to India in 2005–2006, and then jumped from south-western India to emerge in Italy in 2007. These examples re-enforce the importance of the movement of pathogens through either travel or trade (see below).

Many factors or combinations of factors contribute to disease emergence. They include population movements and the effect of urbanization; changes in land use such as deforestation and irrigated agriculture; increasing globalization of food, trade and commerce; increasing international travel; and changes in human behaviour such as intravenous drug use.^{7–9} The development of new, more sensitive technologies can also provide improved detection and diagnostic procedures allowing a new dimension to pathogen discovery, thus detecting new or cryptic agents for known diseases.^{10,11} Other factors that contribute to emergence are microbial mutation and selection and genetic re-assortment that can lead to the development of new genotypes of known diseases, as we see most frequently with influenza A and also in new patterns of antibiotic resistance. Finally, and sadly, known diseases can re-emerge if public health measures are reduced or decline because of complacency or apathy of individuals, communities or policy-makers, as exemplified by reduced vaccine coverage or childhood immunization programmes, or reduced vector control, or because of civil conflict. While all these factors described above are due to human activities, natural causes may also be important in emergence, such as climate change,

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floods, drought, famine and other natural disasters, and thus should not be forgotten or discounted.

While all these factors have been implicated in disease emergence, the importance of the increase in international travel and the globalization of trade cannot be over-emphasized. This includes the movement of infectious agents between countries and continents and the transportation of vector species to establish in new habitats and ecological niches far from their origins, resulting in countries and areas becoming receptive to exotic diseases. Highly successful examples of this are the Asian tiger mosquito, *Ae. albopictus*, which has become established in one or more sites on all continents, and the spread of West Nile and Chikungunya viruses between continents. It is probable that West Nile reached the New World through the transport of an infected mosquito on an aircraft to initiate the outbreak. Chikungunya may have been transported by a similar route or through viraemic travellers to India and Italy, but its ability to cause an outbreak in Italy was due to the earlier arrival and establishment of *Ae. albopictus* mosquitoes, probably transported to their new habitat through the medium of used car tyres on board cargo vessels.

At least four different patterns of disease emergence can be distinguished:

- (1) new infectious agents as the etiological agents of known diseases, often detected because of the development of more sensitive techniques

for detection, exemplified by the first description of human herpesvirus 8, the virus associated with Kaposi's sarcoma,¹² of human coronavirus NL63,¹³ a new respiratory pathogen, and of Klassevirus 1,¹⁴ a new agent causing childhood diarrhoea;

- (2) known-agents of diseases that are increasing in incidence and/or geographic distribution, as seen with the spread of dengue, Japanese encephalitis and West Nile viruses;¹⁵
- (3) new patterns of disease epidemiology or pathogenesis due to mutation or genetic reassortment, as exemplified by the generation of new strains of avian influenza,¹⁶ and the severity of new genotypes of enterovirus 71 in the Asia-Pacific region;¹⁷ and
- (4) novel infectious agents as the cause of outbreaks/epidemics of new disease syndromes, as exemplified by SARS-CoV¹⁸ and Nipah viruses,¹⁹ neither of which had been observed previously.

Over the past two decades, approximately 75% of novel viruses have been zoonoses, with new viruses arising from ecological niches in wildlife and domestic animal populations. Indeed most of the diseases with pandemic potential fall into this category. Some examples of these are shown in **Table 1**, which also demonstrates that emerging diseases may arise anywhere in the world.

Table 1. Examples of novel, emergent zoonotic virus diseases

Year of isolation	Place of isolation	Virus	Reservoir/spillover host
1991	Venezuela	Guanarito virus ²⁰	Rodents
1992	Slovenia	Dobrava virus ²¹	Rodents
1993	United States	Sin Nombre virus ²²	Rodents (<i>Peromyscus maniculatus</i>)
1994	Brisbane, Australia	Hendra virus ²³	Fruit bats (<i>Pteropus sp.</i>)/horses*
	Sao Paulo, Brazil	Sabia virus ²⁴	Rodents
1995	Florida, USA	Black Creek Canal virus ²⁵	Rodents
1996	Ballina, Australia	Australian bat lyssavirus ²⁶	Fruit and insectivorous bats
	Argentina	Andes virus ²⁷	Rodents
1997	Hong Kong (China)	Influenza H5N1 ²⁸	Wild birds/domestic poultry*
	Menangle, Australia	Menangle virus ²⁹	Fruit bats
	Saudi Arabia	Alkhurma virus ^{30,31}	Camels and sheep†
1999	Peninsular Malaysia	Nipah virus ^{32,33}	Fruit bats/pigs*
2000	Peninsular Malaysia	Tioman virus ³⁴	Fruit bats
2002–2003	China, Hong Kong (China)	SARS coronavirus ^{35–38}	Bats/civets?*
2003–2004	Viet Nam, China	Influenza H5N1 ^{39,40}	Wild birds/domestic poultry*
2007	Melbourne, Australia	Dandenong arenavirus ⁴¹	Rodents?
	Peninsular Malaysia	Melaka virus ⁴²	Fruit bats?
	Uganda	Bundibugyo ebolavirus ⁴³	Fruit bats?/various animals (bush meat)*
2008	Lukasa, Zambia	Lujo virus ⁴⁴	Unidentified rodents
	Perak, Malaysia	Kampar virus ⁴⁵	Fruit bats?

* Spillover host; † Tick-borne

It is important to understand that although a disease may be new to us, it probably has been circulating in its own specific niche for a long time; we just haven't encountered it before. There have been many reports of zoonotic viruses described in wildlife, especially bats^{46,47} and rodents.^{48,49} In addition, many other viruses and other microbial agents have been described from wildlife in various parts of the world which have not yet been associated with human disease. Thus global surveillance for outbreaks of human diseases alone is insufficient to prepare for all eventualities, and a close watch needs to be maintained on animal diseases, in both domestic animals and wildlife. This need has given rise, in part, to the more holistic approach to surveillance, the concept of One Health,^{50,51} in which close collaboration is strongly endorsed between human and veterinary medicine through which integrated surveillance should be a major goal.

Not all countries have the epidemiological or laboratory resources, or the public health infrastructure, to respond effectively to outbreaks of infectious diseases. For those countries and areas that seek assistance in verification and/or in response and control, the World Health Organization can act, in collaboration with a broad range of partner institutions around the world, together forming the Global Outbreak Alert and Response Network (GOARN), to mount rapid assistance through the provision of expertise and specific resources.

With the advent of the new International Health Regulations (IHR) (2005), there is a strong call for accountability in reporting possible new outbreaks with a potential for international spread. The purpose of the IHR (2005) is "to prevent, to protect against, control, and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade" (Article 2).⁵² The accountability is linked to the national or local ability to detect and identify the etiology of possible risks to public health. There is a call to strengthen national capacity for surveillance and response and a requirement to alert the World Health Organization to any public health emergency of international concern. It is hoped that rapid, transparent surveillance procedures will provide an early global alert system to ensure that new outbreaks with a potential for international spread can be identified and controlled.

To ensure that countries have the core capacities to undertake effective preparedness planning, prevention, prompt detection, characterization, containment and

control of emerging infectious diseases which could threaten national, regional and global security, the Western Pacific and South-East Asia Regional Offices of the World Health Organization developed *The Asia Pacific Strategy for Emerging Diseases* (APSED) as a road map to assist countries in their core capacity building.⁵³ Considerable progress has been made towards strengthening the core capacities needed to prevent, detect and respond to threats posed by emerging diseases in both regions, and a new five-year plan has been approved to continue the building of core capacity, especially with respect to reducing the risk through strengthening surveillance and thus providing early detection and rapid response to public health emergencies.

Surveillance, early detection and rapid response are certainly the keys to reducing the risks from emerging diseases. To achieve this, there is no doubt that the IHR (2005) will provide the scope and blueprint, but the pathways will require improved surveillance through a One Health collaboration and continued core capacity-building in epidemiology, laboratory capability, and other response components through the APSED workplan. However, to achieve a high level of surveillance and an ability to respond rapidly and effectively to infectious disease threats also requires a strong political commitment by policy-makers and governments, and by a cadre of well-trained and committed health workers in relevant disciplines.

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