

EDITORIAL

Emerging viral diseases: some comments from a regional perspective

Over the past few years, increasing concern and attention have been directed at the problems and issues associated with new and emerging diseases. These were first raised at a conference on emerging viruses held in May 1989 and cosponsored jointly by the Rockefeller University, the National Institute of Allergy and Infectious Diseases and the Fogarty International Center. The concept, definitions and concerns associated with disease emergence were subsequently encapsulated in the Institute of Medicine's 1992 report, *Emerging Infections: Microbial Threats to Health in the United States* (1), which 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. This report has engendered widespread discussion among scientists, policy makers and health administrators throughout the world, and has provoked responses from the US Centers for Disease Control and Prevention (CDC) (2), from the World Health Organization through the establishment of the unit for Emerging and other Communicable Diseases Surveillance and Control (EMC), and from many other government and nongovernment organizations. Common to all these reports is the very clear message that the threats from new and emerging diseases are global: infectious diseases are not confined by countries or national borders, nor by ethnicity or colour. Moreover, international collaboration and cooperation in surveillance and monitoring, and a free and rapid information exchange, are essential components in our efforts to reduce any threats that emerging diseases might present.

Emerging diseases can be defined as either new, previously unrecognized diseases which have appeared for the first time, or diseases which are known but which are increasing in incidence and/or geographic range (1, 3-5). Some diseases are described as re-emerging, and this encompasses diseases which had

previously been controlled by immunization or chemotherapy, but which are rapidly increasing again through reduced vaccine coverage, or through gaining resistance to antibiotics. Diseases have, of course, emerged throughout history as various plagues of humans, animals or plants, and new infections continue to emerge every year (6). Although a disease may be new to us, it has probably been circulating in its own specific niche for a long time; we just haven't encountered it before. A change in our activities or perhaps in certain environmental conditions either allows a new disease to spill over from the obscurity of its own niche to infect a new population, or provides the conditions conducive for a disease to increase in incidence or geographic spread. Re-emerging diseases, however, are frequently the result of complacency or apathy by individuals, communities or policy makers, leading to reduced vaccine coverage (particularly childhood immunization programs) or the breakdown in cold chain conditions, or the result of over-prescribing and/or over-use of drugs and antibiotics (especially in agriculture) leading to microbial resistance.

Many factors or combinations of factors can contribute to the emergence or re-emergence of diseases. Some of these include:

- International travel and commerce
- Population movements, particularly increased urbanization leading to overcrowding
- Changes in land use, including deforestation and increase in irrigated agriculture
- Water entrapment and dam building
- Changes in human behaviour, such as sexual behaviour and intravenous drug use
- Globalization of food supplies
- New technologies, including new diagnostic procedures, new medical advances such as organ transplantation,

- new methods for food processing, etc
- Microbial mutation and selection, genetic reassortment and recombination, etc
- Breakdown in public health measures, civil conflict
- Natural causes such as floods, drought, famine and climate change.

It is not difficult to provide examples for many of these factors (1). Thus international travel and commerce has allowed diseases such as pandemic influenza, cholera and dengue to spread rapidly from one country to another, or from one continent to another. Urbanization has been, and continues to be, a major factor in the emergence of dengue and dengue haemorrhagic fever. Changes in land use, particularly increased irrigated agriculture, has been a major factor in the spread of Japanese encephalitis in Asia, often associated with deforestation as countries seek to extend and expand their agricultural land. Closely linked to irrigation is the building of dams, which has been a factor in the increased incidence of Rift Valley fever and possibly other vector-borne diseases. Changes in human behaviour have been important in the emergence of human immunodeficiency and hepatitis C viruses. Globalization of food supplies has resulted in various epidemics from imported foods, such as cyclospora contaminating berry fruits from Guatemala imported into the United States. New technologies in disease diagnosis and in molecular biology have been responsible for the emergence of a large number of new microorganisms, including *Helicobacter pylori*, human herpes viruses 6, 7 and 8, recent members of the hepatitis alphabet, and a plethora of new papillomaviruses, while new food processing methods have given rise to bovine spongiform encephalopathy (or mad cow disease). Finally, new diseases have emerged and re-emerged following mutation (or recombination) and selection of microorganisms to antibiotic resistance or to increased pathogenicity, such as multidrug-resistant tuberculosis, *Streptococcus pyogenes* causing various forms of invasive disease, and the emergence of *Escherichia coli* O157:H7 as the cause of haemorrhagic colitis and haemolytic uraemic syndrome. The re-emergence of diseases due to the breakdown of public health services include the vaccine-preventable diseases such as measles, pertussis

and rubella; while sadly these are often the result of public apathy, they may also be the result of a breakdown of the infrastructures necessary for the delivery of public health, such as the maintenance of an adequate cold chain. The importance of the latter has become crucial as we head towards the total eradication of polio.

The purpose of this editorial is to briefly comment on some of the emerging viral diseases in our region, especially zoonotic viruses. Some of these viruses have been discussed elsewhere as they pertain to emergence in Australia and New Zealand (7), and it should be noted that a number of non-zoonotic emerging viruses are common to most other countries although differences may occur in their incidence and epidemiological patterns. Table 1 lists a few of the most recent emerging viral diseases worldwide, both newly recognized viruses and viruses which are increasing in incidence and/or geographic range. There are at least four different patterns of emergence, three of which can be distinguished from the viruses shown in Table 1; these are:

- 1 new viruses causing previously unrecognized diseases, as exemplified by the New World hantaviruses as aetiological agents of hantavirus pulmonary syndrome, and by equine morbillivirus in Australia;
- 2 new viruses as the aetiological agents of known diseases, as demonstrated by hepatitis C with non-A non-B hepatitis, and human herpesvirus 6 with roseola infantum; and
- 3 known viruses and their diseases that are increasing in incidence and geographic range, such as Japanese encephalitis and dengue viruses.

The list does not include re-emerging virus diseases, which comprise the fourth pattern of emergence. These are principally vaccine-preventable virus diseases, the most important in our region being measles and rubella. Measles has been responsible for outbreaks in a number of regional countries over the past 5 years, and increased incidences of rubella and congenital rubella syndrome have been reported from New Zealand and Australia

TABLE 1

RECENT EXAMPLES OF EMERGING AND RE-EMERGING VIRUSES

Year	Virus	Reference
1997	Australian pig paramyxovirus (Menangle virus)	8
	Japanese encephalitis virus (PNG)	S. Flew et al., unpublished work, cited in 9
	Influenza H5N1 (Hong Kong)	10,11
1996	Australian bat lyssavirus	12
	Hepatitis G	13
1995	Japanese encephalitis virus (Torres Strait)	14
1994	Human herpesvirus 8	15
	Equine morbillivirus (Australia)	16
	Sabia virus (Brazilian haemorrhagic fever)	17
1993	Sin Nombre virus (hantavirus pulmonary syndrome)	18
1991	Guanarito virus (Venezuelan haemorrhagic fever)	19
1990	Human herpesvirus 7	20
	Hepatitis E	21
1989	Hepatitis C	22
1988	Human herpesvirus 6 (with roseola subitum)	23
1986	Human herpesvirus 6 (first isolation of the virus)	24

(reviewed in 7).

It is interesting to note that the first pattern of emergence described above is usually the result of unexplained epidemic activity. That is, a cluster of similar and/or associated cases occur for which no known aetiological agent can be recognized. Subsequent diagnostic and epidemiological detective work then leads to evidence of a new, previously unrecognized infectious agent. Both of the examples given above fit this description: Sin Nombre virus, the first aetiological agent of hantavirus pulmonary disease to be recognized, was detected following a cluster of cases of fatal respiratory disease on an Indian reservation in the Four Corners region of the United States (where Colorado, New Mexico, Utah and Arizona abut) in 1993 (18,25) with additional related viruses described subsequently from North and South America (reviewed in 26); and equine morbillivirus was isolated during an epidemic of severe respiratory disease in 21 thoroughbred race horses and two humans in Brisbane in 1994, also with significant mortality (16,27). Both viruses were shown to be zoonotic diseases, the former with deer mice (*Peromyscus maniculatus*) as the natural or reservoir host (18) and the latter with fruit bats

(flying foxes, *Pteropus* sp.) as the reservoir hosts (28). While there has been no evidence of hantaviruses in either Papua New Guinea or Australia, antibodies to equine morbillivirus have been found in all four major species of fruit bats in Australia and two species of fruit bats in Papua New Guinea (29).

Novel viruses can also be discovered by serendipity – sometimes during surveillance and monitoring activities for other viruses. An example of this was the first isolation of Australian bat lyssavirus from a fruit bat displaying neurological signs in 1996 and which was submitted for autopsy examination as a possible equine morbillivirus infection (12). Australian bat lyssavirus is antigenically closely related to classical rabies virus and is now known to be widely distributed in fruit bats and in at least one species of insectivorous bat, from Victoria through New South Wales and Queensland to the Northern Territory (reviewed in 7). There has been no evidence of this virus yet in Papua New Guinea.

None of these novel viruses had been recognized previously although they had almost certainly been circulating in their

respective niches for many hundreds of years and causing sporadic cases of disease in humans and/or animals. It is certain that many other viruses are circulating in specific niches which have yet to be detected, either because they have not been associated with disease, or because humans have not entered, interfered with or investigated their niches. An example of the type of niche which may be important as a potential ecological site for disease emergence and which should encourage close and continuous monitoring by public health authorities is that of deforestation, either for timber or, as is often the case when agricultural expansion is contemplated, clear felling. Such incursions into virgin forest potentially open up previously cryptic niches and put timber workers at risk of encountering novel disease agents. Subsequent clinical disease may then be rapidly and easily transmitted to local communities.

The best example of the third pattern described above, and one that has recently become very relevant to Papua New Guinea and Australia, is Japanese encephalitis (JE) virus. This virus suddenly emerged in our region in 1995, causing a small outbreak in the Torres Strait, with three clinical cases from Badu Island, two of which were fatal (14). This emergence was unexpected and occurred 3000 kilometres from the nearest focus of JE activity in Bali. Subsequent studies have shown that JE virus has been present in Western Province since at least 1989, and that Western Province was probably the source of the virus which spread into the northern and central islands of the Torres Strait (30). This has since been confirmed through the isolation of JE virus from *Culex annulirostris* mosquitoes trapped at Lake Murray, Western Province, with the same signature nucleotide sequences as the strains isolated in 1995 from Badu Island (C. Johansen, S. Ritchie, R. Paru, M. Bockarie and J. Mackenzie, unpublished results). From extensive serological results, JE appears to be increasing in incidence in Western Province and spreading into adjacent parts of Gulf and Southern Highlands Provinces (31). Three human cases from near Kiunga, one of which was fatal, have been recognized clinically and confirmed by laboratory tests (S. Flew, J. Oakley, C. Johansen, D. Phillips, R. Hall and J.

Mackenzie, unpublished results). We have no idea how long JE virus has been in Western Province or how it reached there. It is probable, however, that sporadic cases of infection have occurred previously, since even if the patients had reached a clinic or local hospital such cases would have been diagnosed as cerebral malaria because of the nonavailability of laboratory facilities. JE virus is recognized by the World Health Organization to be a major threat because of its propensity to spread and colonize new areas, and because of its high incidence of fatal infections and of infections resulting in severe, life-long sequelae.

Japanese encephalitis virus and equine morbillivirus are examples of emerging viruses common to both Papua New Guinea and Australia, and it is probable that Australian bat lyssavirus will also prove to be common to both countries. However, they represent only three of a number of emerging viruses common to both countries. As mentioned above, most non-zoonotic emerging viral diseases occur worldwide (7), whereas zoonotic and vector-borne viral diseases tend often to be more restricted to specific regions. An exception to this is dengue, which is considered to be an emerging virus because of its propensity to spread and to frequently be re-introduced into countries throughout the tropical and subtropical areas of the world. Dengue is relatively common in coastal cities and towns of Papua New Guinea (32), and it is probable that either all four dengue types are endemic to Papua New Guinea or are frequently re-introduced. There is good circumstantial evidence to suggest that dengue type 2 virus moved from Papua New Guinea through the Torres Strait into northern mainland Australia in 1997 to initiate epidemic activity, probably through the movement of viraemic people (33). Indeed epidemic dengue in northern Australia is always the result of re-introductions through the movement of viraemic tourists or returning residents who had been infected overseas (34,35).

Emerging diseases of livestock and wild animals are also of concern for a number of reasons, including their potential as zoonotic infections of humans, and the importance of the former in food production and international

trade, and of the latter in wildlife conservation. Examples of emerging diseases in livestock animals are bovine spongiform encephalopathy ('mad cow' disease) in British cattle (reviewed in 36) and the recent isolation of a paramyxovirus causing fetal death and fetal malformations in domestic pigs in New South Wales (8); it is interesting to note that both of these are also zoonoses. Examples of emerging diseases in wildlife are kangaroo blindness caused by an Australian orbivirus closely related to Wallal virus (37; P. D. Kirkland, personal communication) and the mass mortalities of seals caused by a canine distemper-like virus, phocid distemper virus (38). Emerging and re-emerging animal diseases in Australia have recently been the subject of a detailed review (39).

It is virtually impossible for us to predict the future emergence of new viral diseases; all we can be sure of is that new viruses will be discovered, and that undoubtedly some will be zoonotic. Many of these will be of local or regional importance rather than global, but there is always the potential for a new, previously unrecognized viral disease to emerge as a worldwide pandemic with a high morbidity and/or mortality. Indeed this was the fear when human infections occurred with the avian influenza A H5N1 virus strain in Hong Kong in 1997 (10,11). Thus there is a need for global surveillance and monitoring networks, and for a number of strategically located laboratories with rapid diagnostic facilities. Such networks are in the process of being established through the World Health Organization and the United States Centers for Disease Control and Prevention (CDC). It is essential that all countries participate and collaborate fully and openly; infectious diseases do not recognize national boundaries, and with the speed of air travel an infection in one continent yesterday can be a case of clinical disease in another country tomorrow, and an epidemic of tens or hundreds of cases next week. This is our global village.

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