

## *Editorial*

### **Recent Trends in Emerging Infectious Diseases**

Infectious diseases are the world's greatest killers that present one of the most significant health and security challenges facing the global community. On April 15 and April 17, 2009, novel swine-origin influenza A (H1N1) virus (S-OIV) was identified in specimens obtained from two epidemiologically unlinked patients in the United States. The same strain of the virus was identified in Mexico, Canada, and elsewhere. Enhanced surveillance was implemented in the United States for human infection with influenza A viruses that could not be subtyped. Specimens were sent to the Centre for Disease Control and Prevention for real-time reverse-transcriptase-polymerase-chain-reaction confirmatory testing for S-OIV. The S-OIV was determined to have a unique genome composition that had not been identified previously. This virologic analysis allowed for the development of a polymerase-chain-reaction (PCR) test to determine whether, in any given person, illness with the protean manifestations of cough, fever, sore throat, diarrhea, and nausea could be confirmed as a case. Armed with this critical tool, clinicians and epidemiologists are able to make case assignments to define and track the outbreak and to determine disease severity.

WHO declared the start of the Influenza A (H1N1) pandemic on June 11, 2009. The Director-General of WHO raised the influenza pandemic alert to the highest level - Phase 6 - on the guidance and advice from an Emergency Committee established for this purpose under the International Health Regulations (IHR). As of 31 of July 2009, 168 countries and overseas territories/communities have reported at least one laboratory confirmed case of pandemic (H1N1) 09. All continents are affected by the pandemic. Total cases reported were 162380 with 1154 deaths. The declaration of a pandemic essentially means wide geographic spread and does not indicate any change in the severity of the illness. Currently the severity of the pandemic has been assessed as "moderate" globally. In vast majority of cases the virus produces mild disease. In a small proportion of people the illness can become severe and fatal.

There are important tools with which to fight this outbreak: a clear case definition, an aware health care system, and an informed public.

Swine Influenza (swine flu) is a respiratory disease of pigs caused by type A influenza that regularly cause outbreaks of influenza among pigs. Swine flu viruses do not normally infect humans, however, human infections with swine flu do occur, and cases of human-to-human spread of swine flu viruses has been documented. Laboratory testing has found the swine influenza A (H1N1) virus susceptible to the prescription antiviral drugs oseltamivir and zanamivir.

In our daily life we are surrounded by a wealth of microorganisms, the majority of which are nonharmful. Human existence would be impossible without these micro-organisms, which play critical roles in processes as diverse as photosynthesis, nitrogen fixation, production of vitamins in the human intestine and decomposition of organic matter. They are the sole, true 'recyclers' of our planet. Microorganisms are also the major driving force behind the evolution of life. Throughout evolution, human being, like all mammalian species, has maintained an intimate relationship with the microbial world. We have survived thanks to the efficient defense mechanisms we have developed against potentially dangerous microorganisms. Pathogenic microorganisms are still here because they have found ways of avoiding elimination by their host or by the microbial competition. 'Successful' pathogens have developed strategies to enter the body and reach and choose their favourite niche, while defying the powerful human immune systems.

Humans have lived with emerging and re-emerging pathogens since before the dawn of civilization. Is the situation worse now than in past decades or centuries? The answer is probably yes because there are billions more of us and some of our activities allow such infections to appear and flourish. Moreover, our mobility within and between countries is conducive to the rapid spread of microorganisms. Similar observations hold true for animals and plants, with frequent consequences for human health.

Infectious diseases are among the world's leading causes of death, and scientists from every nation perform research, share information, build laboratory capacity in poorer nations and create global surveillance networks to help prevent and control their spread.

When the incidence of such a disease in people increases over 20 years or threatens to increase, it is called an "emerging" disease, and a growing number have made watch lists and headlines in nearly every country -- highly pathogenic H5N1 avian influenza, severe acute respiratory syndrome (SARS), Ebola virus, food- and waterborne illnesses, and a range of anti-microbial-resistant bacterial diseases like multidrug-resistant and extensively drug-resistant tuberculosis (TB).

Emerging infectious diseases are diseases that have not occurred in humans before; have occurred previously but affected only small numbers of people in isolated places (AIDS and Ebola hemorrhagic fever are examples); or have occurred throughout human history but have only recently been recognized as distinct diseases due to an infectious agent (Lyme disease and gastric ulcers are examples). Re-emerging infectious diseases are diseases that once were major health problems globally or in a particular country, and then declined dramatically, but are again becoming health problems for a significant proportion of the population (malaria and tuberculosis are examples).

Emerging diseases can be new infections that arise from changes in existing organisms or known infections that spread to new geographic areas or populations. They can be previously unrecognized infections that appear when, for example, tropical forests are cleared to make way for new roads, displacing disease-carrying animals and insects. And old infections can re-emerge because of anti-microbial resistance or breakdowns in public health measures.

Most emerging infectious diseases (60.3 percent) are zoonoses, or animal diseases that can be transmitted to people.

Emerging infectious diseases (EIDs) are a significant burden on global economies and public health. Their emergence is thought to be driven largely by socio-economic, environmental and ecological factors, but no comparative study has explicitly analysed these linkages to understand global temporal and spatial patterns of EIDs. Here we analyse a database of 335 EID 'events' (origins of EIDs) between 1940 and 2004, and demonstrate non-random global patterns. EID events have risen significantly over time after controlling for reporting bias, with their peak incidence (in the 1980s) concomitant with the HIV pandemic. EID events are dominated by zoonoses (60.3% of EIDs): the majority of these (71.8%) originate in wildlife (for example, severe acute respiratory virus, Ebola virus), and are increasing significantly over time. We find that 54.3% of EID events are caused by bacteria or rickettsia, reflecting a large number of drug-resistant microbes in our database. Our results confirm that EID origins are significantly correlated with socio-economic, environmental and ecological factors, and provide a basis for identifying regions where new EIDs are most likely to originate (emerging disease 'hotspots'). They also reveal a substantial risk of wildlife zoonotic and vector-borne EIDs originating at lower latitudes where reporting effort is low. We conclude that global resources to counter disease emergence are poorly allocated, with the majority of the scientific and surveillance effort focused on countries from where the next important EID is least likely to originate.

Emergent infection is recognized as a global threat. At least 17 million die annually from infectious diseases. Of these, the South-east Asia Region accounts for almost 41 per cent, or 7 million deaths.

Factors responsible for EIDs as identified by Board on Global Health (BGH) and the Institute of Medicine (IOM), include: Microbial adaptation and change, Human Demographics and Behavior, International Travel and Commerce, Economic Development and Land Use, Technology and Industry, Breakdown of public health measures, Human susceptibility to infection, Climate and weather, Changing ecosystems, Poverty and social inequality, War and famine, Lack of political will, Intent to harm, A global political commitment is rather vague, Who will be the parties in a global social contract?, How is their will determined?, How can the liberties of individual countries be balanced against collective responsibility?, Is there collective responsibility? Must have commitment from four groups: donors, health care professionals, country authorities, and patients, and Developing world diseases don't matter to politicians here.

EIDs include Avian Flu, Swine Flu and the threat of Pandemic Influenza, E. coli O157:H7/Salmonella, Norovirus – “Not just the cruise ship virus anymore”, MDR, XDR tuberculosis, “Novel pathogens”: Bocavirus, Chikungunya virus, Community-acquired MRSA/ “Epidemic” C. difficile, Mumps, Measles, Rubella, Pertussis (Whooping Cough), Monkeypox, SARS, West Nile Virus, Anthrax, ricin and other bioterrorism agents.

Every year there are around 600 million travelers. Some will already be carrying pathogens; others will be traveling to areas in which they will suffer unintended exposure to, for them, new pathogens that, potentially, they can introduce to their communities upon their return home.

Modern civilization dates from approximately 10,000 BC. It took until 1830 for the world population to reach 1 billion persons; however, from there the world population doubled in the next 100 years and reached 6 billion 70 years after that. By the end of 21st century the world population could be between 14 and 18 billion.

In the global human population, the emergence of 335 infectious diseases between 1940 and 2004 has been reported. The emergence of these pathogens and their subsequent spread has caused an extremely significant impact on global health and economies<sup>1–3</sup>. Previous efforts to understand patterns of EID emergence have highlighted viral pathogens (especially RNA viruses) as a major threat, owing to their often high rates of nucleotide substitution, poor mutation error-correction ability and therefore higher capacity to adapt to new hosts, including humans.

The majority of pathogens involved in EID events are bacterial or rickettsial (54.3%). This group is typically represented by the emergence of drug-resistant bacterial strains. Viral or prion pathogens constitute only 25.4% of EID events. This follows our classification of each individual drug-resistant microbial strain as a separate pathogen in our database, and reflects more accurately the true significance of antimicrobial drug resistance for global health, in which different pathogen strains can cause separate significant outbreaks. In broad concurrence with previous studies on the characteristics of emerging human pathogens, we find the percentages of EID events caused by other pathogen types to be 10.7% for protozoa, 6.3% for fungi and 3.3% for helminths.

The incidence of EID events has increased since 1940, reaching a maximum in the 1980s. Increased susceptibility to infection caused the highest proportion of events during 1980–90 (25.5%), and we therefore suggest that the spike in EID events in the 1980s is due largely to the emergence of new diseases associated with the HIV/AIDS pandemic.

The majority (60.3%) of EID events are caused by zoonotic pathogens (those which have a non-human animal source), which is consistent with previous analyses of human EIDs. Furthermore, 71.8% of these zoonotic EID events were caused by pathogens with a wildlife origin—for example, the emergence of Nipah virus in Perak, Malaysia and SARS in Guangdong Province, China. The number of EID events caused by pathogens originating in wildlife has increased significantly with time, controlling for reporting effort, and they constituted 52.0% of EID events in the most recent decade (1990–2000). This supports the suggestion that zoonotic EIDs represent an increasing and very significant threat to global health. Vector-borne diseases are responsible for 22.8% of EID events in our database, and 28.8% in the last decade. Our analysis reveals a significant rise in the number of EID events they have caused over time. This rise corresponds to climate anomalies occurring during the 1990s, adding support to hypotheses that climate change may drive the emergence of diseases that have vectors sensitive to changes in environmental conditions such as rainfall, temperature and severe weather events. EID events caused by drug-resistant microbes (which represent 20.9% of the EID events in our database) have significantly increased with time, controlling for reporting effort. This is probably related to a corresponding rise in antimicrobial drug use, particularly in high-latitude developed countries.

Perhaps no human activity is as conducive to emergence of infectious diseases as warfare, a human behaviour that, measured by the number of people involved, becomes more extensive every century. The 20th century has been the bloodiest in history. There have been 150 wars in the second half of the century, resulting in more than 20 million deaths, two-thirds of them civilians. The prospects for less warfare are not good. Ethnic, religious, racial and tribal strife will be exacerbated by population growth, overcrowding and rivalries over increasingly depleted natural resources.

The economic impact of new, emerging and re-emerging infectious diseases can be enormous. The 1991 cholera epidemic in Peru cost that country an estimated \$770 million. The plague epidemic in India cost that country \$1.8 billion. BSE in the United Kingdom cost more than \$6 billion. By the year 2000, the overall costs to Thailand and India on account of AIDS have been estimated at US\$ 9 billion and 11 billion, respectively. The global cost of SARS has crossed \$30 billion. Infectious diseases like malaria and AIDS act as a massive societal brake, slowing both economic and human development.

Recent outbreaks, such as SARS in China & 32 other countries, the plague episode in India, Ebola hemorrhagic fever in Zaire, and leptospirosis in Nicaragua, depict the limited global capacity to rapidly diagnose and respond to emerging disease threats.

The goal of an optimal harmony between groups of people in society and their environment can be achieved by methods to improve host resistance of populations to environmental hazards; by effective plans to improve the safety of the environment, and by improving healthcare systems designed to increase the likelihood, efficiency and effectiveness of the first two goals (systems approach). One might view communicable diseases as an imbalance in the relationship of people and their environment which favours microbial dominance in populations. The social, economic, legal and administrative forces important for health must operate in the interest of the public.

Responding to the global threats of EID requires a coordinated global response with development of expertise in epidemiology, laboratory science, behavioural science, increased surveillance, adequate public health infrastructure, primary prevention and adequate communication.

Efforts to prevent and control problems must begin with a search for better understanding of the societal roots of disease, disability and premature death.

Extrapolation of current trends is a poor way to think about the future, particularly at times of great change. The best method seems to be to bring together a diverse group of people knowledgeable about the subject of interest, provide them with good data, and ask them to imagine a series of possible scenarios.

### Further Reading

1. Daszak, P., Cunningham, A. A. & Hyatt, A. D. Emerging infectious diseases of wildlife threats to biodiversity and human health. *Science* 287, 443–449 (2000).
2. Kate E. Jones, Nikkita G. Patel, Marc A. Levy, Adam Storeygard, Deborah Balk, John L. Gittleman & Peter Daszak. Global trends in emerging infectious diseases. *NATURE* Vol 451: 21 February 2008
3. Ferguson, N. M. et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature* 437, 209–214 (2005).
4. Morens, D. M., Folkers, G. K. & Fauci, A. S. The challenge of emerging and reemerging infectious diseases. *Nature* 430, 242–249 (2004).
5. King, D. A., Peckham, C., Waage, J. K., Brownlie, J. & Woolhouse, M. E. J. Infectious diseases: Preparing for the future. *Science* 313, 1392–1393 (2006).
6. Weiss, R. A. & McMichael, A. J. Social and environmental risk factors in the emergence of infectious diseases. *Nature Med.* 10, S70–S76 (2004).
7. Wolfe, N. D., Dunavan, C. P. & Diamond, J. Origins of major human infectious diseases. *Nature* 447, 279–283 (2007).
8. Woolhouse, M. E. J. & Gowtage-Sequeria, S. Host range and emerging and reemerging pathogens. *Emerging Infect. Dis.* 11, 1842–1847 (2005).
- 9.

**Syed Amin Tabish**  
FRCP, FRCPE, FACP, FAMS, MD  
Editor-in-Chief  
amintabish@Gmail.com