

Emerging and Re-emerging Infectious Diseases, Future Challenges and Strategy

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ABSTRACT

The emerging infectious diseases and their basic causes present a threat to the stability of the nations worldwide. The factors for the emergence/re-emergence of infectious diseases are complex and interrelated. The spread of antimicrobial resistance

is another emerging global public health issue. New pathogens and antimicrobial-resistant forms of the older pathogens continue to emerge, some with the potential for a rapid and a global spread, with high morbidity and mortality and these are of public health importance.

Key Words: Emerging diseases, Re-emerging diseases, Antimicrobial resistance, Mortality, Morbidity, Public health

INTRODUCTION

There has been a worldwide explosion of infectious diseases: emerging diseases like the HIV/AIDS pandemic, or old diseases like cholera, tuberculosis, diphtheria, plague, yellow fever, dengue, or malaria. These re-emerging diseases are on the surge because of multiple factors: environmental changes, transformation of the ecosystems, the ongoing socio-economic degradation and the deterioration of the public health systems in many countries. The emerging infectious diseases and their basic causes present a threat to the stability of the nations worldwide. The factors for the emergence/re-emergence of infectious diseases are complex and interrelated [1].

In the human history, numerous infectious diseases have emerged and re-emerged. Besides many others, the so-called 'exotic' agents in particular, are a threat to our public health systems due to our limited experience in the case management and due to the lack of appropriate resources. Many of these agents are zoonotic in origin and these are transmitted from animals to man either directly or via vectors. The reservoirs are often infected subclinically or asymptotically and the distribution of the diseases basically reflects the range and the population dynamics of their reservoir hosts. As examples, emergence/re-emergence is discussed here for the diseases which are caused by filoviruses, hantaviruses, paramyxoviruses, flaviviruses and *Yersinia pestis* [Table/Fig-1]. In addition, bioterrorism has been addressed as one factor which now has to be considered in infectious disease emergence/re-emergence. The preparedness for the known and unknown infectious diseases will be a top priority for our public health systems.

The emerging communicable diseases are those for which the incidence in humans has increased in the past 2 decades or is threatening to increase in the near future. The re-emerging communicable diseases are those which are known and which reappear after a decline in their incidences. The term, 'emerging diseases', which is used interchangeably with the term, 'emerging infectious diseases', means 'the infections that newly appear in a population, or which have existed but are increasing in incidence

or geographic range' [2]. Over the past 3 decades, more than two thirds of the emerging infectious diseases have had an origin in animals [3]. These include HIV/AIDS, Ebola haemorrhagic fever and the new variant of the Creutzfeldt-Jakob disease (nvCJD). Some of these, especially HIV/AIDS and hepatitis C, have seriously affected large numbers of people worldwide [Table/Fig-2,3&4]. Others, such as Ebola, nvCJD and the influenza A (H5N1) virus which is known to cause swine flu, have posed significant threats and million of cases and thousands of deaths have been recorded worldwide [21, 22], [Table/Fig-2, 3&4]. Meanwhile, the well-known diseases which were once thought to have been conquered, such as tuberculosis, plague, cholera, Dengue fever/Dengue haemorrhagic fever, yellow fever and diphtheria are re-emerging as public health threats in many countries, after a period of decline in their incidences. The spread of antimicrobial resistance is another emerging global public health issue [4].

New pathogens and antimicrobial-resistant forms of the older pathogens continue to emerge, some with the potential for a rapid and a global spread, with high morbidity and mortality and these are of public health importance [5].

The infectious diseases have always afflicted mankind and they always will. New infectious diseases will emerge and old diseases will re-emerge as the microbes adapt to new hosts and new environments. To remain one step ahead of our pathogenic microbial foes, we must understand in detail how the pathogens interact with their hosts, and how biological, environmental, and social factors combine to allow pathogens to infect new organisms. Deciphering each step in the different processes by which microbes adapt to their new hosts, is critical to developing effective countermeasures to detect, prevent, and to treat infectious diseases.

COMMON CAUSES

Antimicrobial drug resistance, as a major factor in the emergence and the re-emergence of infectious diseases deserves special attention. Although significant reductions in the infectious disease mortality have occurred since the introduction of antimicrobials for general use in the 1940s, drug resistance has emerged because of

Group I—Pathogens Newly Recognized in the Past Two Decades	Group II—Re-emerging Pathogens	Group III—Agents with Bioterrorism Potential		
		(NIAID) Groups III		
		Category A	Category B	Category C
Acanthamebiasis Australian bat lyssavirus Babesia, atypical Bartonella henselae Ehrlichiosis Encephalitozoon cuniculi Encephalitozoon hellem Enterocytozoon bienersi Helicobacter pylori Hendra or equine morbilli virus Hepatitis C Hepatitis E Human herpesvirus 8 Human herpesvirus 6 Lyme borreliosis Parvovirus B19	Enterovirus 71 Clostridium difficile Mumps virus Streptococcus, Group A Staphylococcus aureus	Bacillus anthracis (anthrax) Clostridium botulinum toxin (botulism) Yersinia pestis (plague) Variola major (smallpox) and other related pox viruses Francisella tularensis (tularemia) Viral hemorrhagic fevers • Arenaviruses LCM, Junin virus, Machupo virus, <i>Guanarito virus</i> Lassa Fever • Bunya viruses Hantaviruses Rift Valley Fever • Flaviruses Dengue • Filoviruses Ebola Marburg	Burkholderia pseudomallei Coxiella burnetii (Q fever) Brucella species (brucellosis) Burkholderia mallei (glanders) Chlamydia psittaci (Psittacosis) Ricin toxin (from Ricinus communis) Epsilon toxin of Clostridium perfringens Staphylococcus enterotoxin B Typhus fever (Rickettsia prowazekii) <i>Food- and waterborne pathogens</i> <i>Bacterial origin</i> • Diarrheagenic E.coli • Pathogenic Vibrios • Shigella species • Salmonella • Listeria monocytogenes • Campylobacter jejuni • Yersinia enterocolitica Viruses (Caliciviruses, Hepatitis A) Protozoa Cryptosporidium parvum Cyclospora cayatanensis Giardia lamblia Entamoeba histolytica Toxoplasma Fungi Microsporidia • Additional viral encephalitides West Nile virus LaCrosse California encephalitis VEE EEE WEE Japanese Encephalitis virus Kyasanur Forest virus	<i>Emerging infectious disease threats such as Nipah virus and additional hantaviruses.</i> NIAID priority areas: Tick-borne hemorrhagic fever viruses Crimean-Congo Hemorrhagic Fever virus Tick-borne encephalitis viruses Yellow fever Multidrug-resistant TB Influenza Other Rickettsias Rabies Prions Chikungunya virus Severe acute respiratory syndrome-associated coronavirus (SARS-CoV) • <u>Antimicrobial resistance, excluding research on sexually transmitted organisms*</u> Research on mechanisms of antimicrobial resistance Studies of the emergence and/or spread of antimicrobial resistance genes within pathogen populations Studies of the emergence and/or spread of antimicrobial-resistant pathogens in human populations Research on therapeutic approaches that target resistance mechanisms Modification of existing antimicrobials to overcome emergent resistance • Antimicrobial research, as related to engineered threats and naturally occurring drug-resistant pathogens, focused on development of broad-spectrum antimicrobials • Innate immunity, defined as the study of non-adaptive immune mechanisms that recognize, and respond to, microorganisms, microbial products, and antigens • <i>Coccidioides immitis</i> (added February 2008) • <i>Coccidioides posadasii</i> (added February 2008)

[Table/Fig-1]: List of Emerging and Re-emerging Diseases

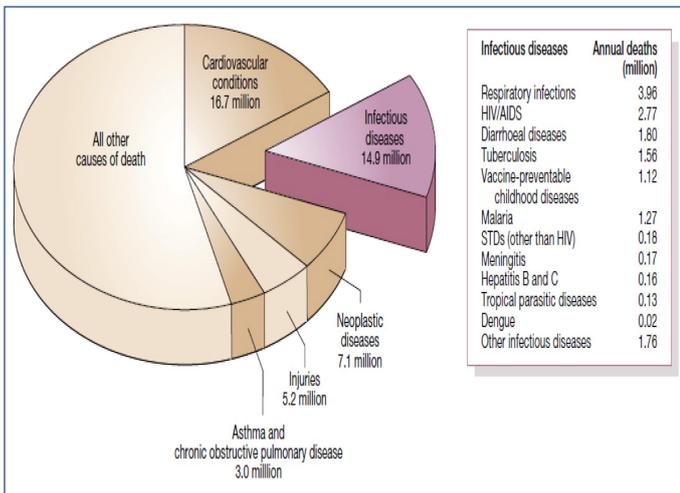
Source: National Institute of Allergy and Infectious Diseases (NIAID) [11]

their widespread use. "The drugs that once seemed to be invincible are losing their effectiveness for a wide range of community-acquired infections which include tuberculosis, gonorrhoea and pneumococcal infections and for hospital-acquired enterococcal and staphylococcal infections. The resistance to anti-viral, anti-fungal, and antiprotozoal drugs is also emerging. Drug-resistant malaria has spread to nearly all the areas of the world where malaria occurs. Point towards also have arisen over the strains of HIV which are resistant to anti-viral drugs. An aggressive public health response to these new, emerging and re-emerging infectious disease threats must be made to characterize them better and to mount an effective response for their control. The World Health Organization has outlined the following high priority areas: to strengthen the global surveillance of the infectious diseases; to establish national and international infrastructures to recognize the reports and to respond to new disease threats; to further develop applied research on the diagnosis, epidemiology, and the control of emerging infectious diseases; and to strengthen the international capacity for infectious disease prevention and control.

Only through a global concerted action will the efforts which are being made to control infectious diseases be effective. We have now entered an era where, as Nobel Laureate Dr. Joshua Lederberg has stated, "The microbe that felled one child in a distant continent yesterday can reach yours today and seed a global pandemic tomorrow" (quoted in CDC 1994). Hans Zinsser had stated this over 60 years ago [6].

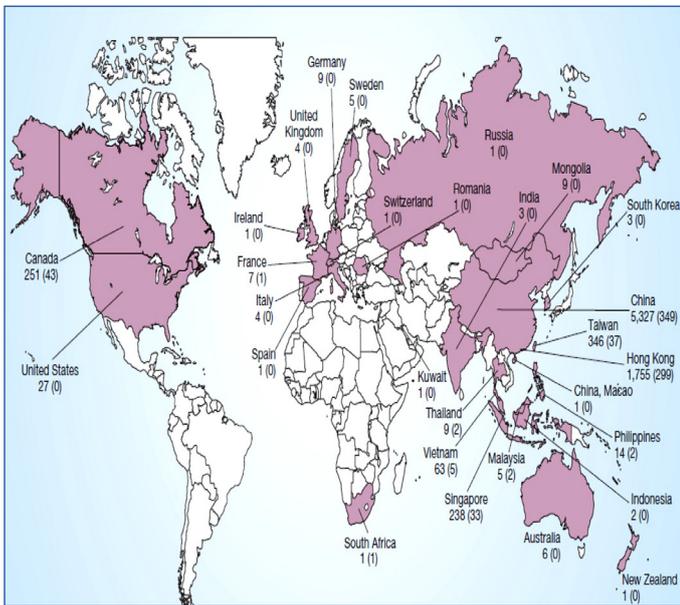
THE INTERNATIONAL HEALTH REGULATION 2005

Infectious diseases do not respect international borders. Global partnerships and the rapid sharing of data and other information enhance the preparedness and the evidence-based control strategies. The World Health Organization has a mandate of providing technical support to all the countries for health development and specific responsibilities for global health protection under the International Health Regulation (IHR) 2005. The IHR (2005) is a legally binding international instrument with the purpose of preventing, protecting against, controlling and providing a public

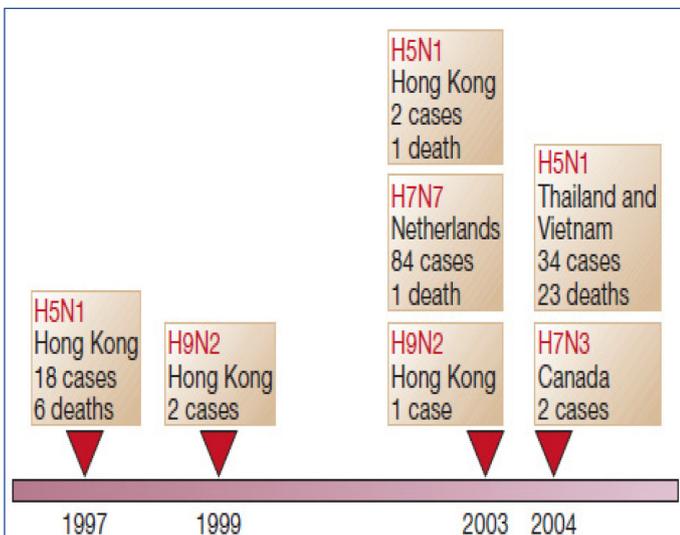


Infectious diseases	Annual deaths (million)
Respiratory infections	3.96
HIV/AIDS	2.77
Diarrhoeal diseases	1.80
Tuberculosis	1.56
Vaccine-preventable childhood diseases	1.12
Malaria	1.27
STDs (other than HIV)	0.18
Meningitis	0.17
Hepatitis B and C	0.16
Tropical parasitic diseases	0.13
Dengue	0.02
Other infectious diseases	1.76

[Table/Fig-2]: Leading causes of death worldwide. About 15 million (>25%) of 57 million annual deaths worldwide are the direct result of infectious disease [20].



[Table/Fig-3]: Probable cases of severe acute respiratory syndrome (SARS) with onset of illness from 1 November 2002 to 31 July 2003. Cases are given by country. SARS-related deaths are indicated in parentheses. A total of 8,096 cases (and 774 deaths) are presented [21].



[Table/Fig-4]: Documented human infections with avian influenza viruses, 1997–2004. Sporadic cases of mild human illness associated with avian influenza viruses were reported before 1997 [22].

health response to the international spread of diseases while avoiding unnecessary interference with the international traffic and trade. The emerging infectious diseases are real and they pose an overt threat to societies and their economies. With strong political support and a commitment to the global public goods and the effective public health systems, the challenge can be met. The advent of SARS and avian influenza underscores the importance of emerging diseases and their impact on the health and economic development. The Asia Pacific region is unfortunately, at the epicentre of such epidemics. Over 30 new infectious agents have been detected in the last 3 decades, 75% of which have originated in animals (zoonoses). New pathogens, particularly viruses, remain unpredictable and they continue to emerge and spread across the countries. Several have profoundly affected the countries and the areas in the Asia Pacific region that is home to over 3.4 billion people, or to 53% of the world’s population [7].

Dengue fever, Japanese encephalitis, Leptospirosis, Nipah virus and drug-resistant malaria are some of the diseases that have become entrenched within this region. Though several socio-economic, demographic, environmental and ecological factors facilitate the emergence and the spread of these diseases, their impact could be minimized through a well-prepared and strong public health system. To effectively respond to these diseases, a well-developed strategy and programme must be implemented through a coordinated and a pragmatic plan of action.

To meet the global challenge that the emerging disease outbreaks present, the International Health Regulation [8] provide a legal framework for an international public health response to the global spread of diseases, while avoiding unnecessary interference with the international traffic and trade. The purpose and the scope of the revised IHR are “to prevent, protect against, control and to provide a public health response to the international spread of diseases in ways that are commensurate with and are restricted to public health risks, and which avoid unnecessary interference with the international traffic and trade.” The Millennium Development Goals (MDG) [9], which is the expression of global solidarity in improving the quality of life, are also concerned with reducing the impact of the emerging diseases. The MDG addresses the issues of HIV/AIDS, TB, malaria, water and sanitation, and other development-related health determinants in the least developed countries that usually act as the trigger sites for the emerging diseases.

The factors which are responsible for the emergence and the re-emergence of infectious diseases in the developed and the developing countries are unplanned and under planned urbanization, overcrowding and rapid population growth, microbial adaptation and change, the human susceptibility to infections, the climate and weather, the changing ecosystems, the human demographics and behaviour, economic development and land use, rapid and intense international travel, poor sanitation, inadequate public health infrastructures, resistance to antibiotics, increase of humans to disease vectors, technology and industry, breakdown of the public health measures, poverty and social inequality, war and famine, lack of political will, an intent to harm, natural and man made disasters and reservoirs of infections, etc [10].

Despite the remarkable advances in medical research and treatments during the 20th century, infectious diseases remain among the leading causes of death worldwide [20] for three reasons: (a) Emergence of new infectious diseases; (b) Re-emergence of the old infectious diseases; and (c) Persistence of the intractable infectious diseases. The emerging diseases

include the outbreaks of previously unknown diseases or known diseases whose incidences in humans have significantly increased in the past two decades. The re-emerging diseases are the known diseases that have reappeared after a significant decline in their incidences. Within the past 2 decades, the innovative research and the improved diagnostic and detection methods have revealed a number of previously unknown human pathogens. Within the last decade, chronic gastric ulcers which were formerly thought to be caused by stress or diet, were found to be the result of infections which were caused by the bacterium, *Helicobacter pylori*.

New infectious diseases continue to evolve and “emerge.” Changes in the human demographics, behaviour, land use, etc., are contributing to new disease emergence by changing the transmission dynamics, to bring people into a closer and a more frequent contact with pathogens. This may involve an exposure to animals or arthropod carriers of the disease. The increasing trade of exotic animals as pets and food sources has contributed to a rise in the opportunities for the pathogens to jump from the animal reservoirs to humans. In the United States, close contact with exotic rodents was found to be the origin of the recent U.S. outbreak of monkey pox, and the use of exotic civet cats for meat in China was found to be the route by which the SARS corona virus made the transition from animals to its human hosts.

In spite of the continued discovery of new human pathogens, the old infectious disease enemies are “re-emerging.” Natural genetic variations, recombinations, and adaptations allow new strains of known pathogens to appear, to which the immune system has not been previously exposed and is therefore not primed to recognize (e.g., influenza, bird flu, swine flu, etc.). Furthermore, human behaviour plays an important role in the re-emergence of known pathogens. The increased and sometimes imprudent use of antimicrobial drugs and pesticides has led to the development of resistant pathogens, thus allowing many diseases that were formerly treatable with drugs, to make a comeback. Recently, the decreased compliance with the vaccination policy has also led to the re-emergence of diseases such as measles and pertussis, which were previously under control. The use of deadly pathogens such as smallpox or anthrax as the agents of bioterrorism, is an increasingly acknowledged threat to the civilian population. Moreover, many important infectious diseases have never been adequately controlled on either the national or the international level. The infectious diseases that have posed ongoing health problems in the developing countries are re-emerging in the United States [11].

These trends amount to produce a crisis for today and a challenge for the future [12]. The theme of the World Health Day, April 7, 1997 “Emerging infectious Diseases- Global Alert: Global Response” is of great value [13].

STRATEGY /POSSIBLE INTERVENTIONS

Re-affirming the importance of developing and implementing a biregional strategy to achieve common goals and to provide a strategic framework for strengthening the national and the regional capacity for communicable disease surveillance and response, which include the emerging infectious diseases; Recognizing that the importance of the timely and the transparent sharing of information on the public health emergencies of international concern is crucial to prevent and limit the risk of the international spread of diseases.

The development of newer techniques for surveillance [14]:

The traditional passive surveillance refers to the health authority's receipt of the reports of diseases or conditions which were submitted by physicians, laboratories, and other healthcare providers as was required by the public health legislation. However, the reportable diseases are often underreported to the health departments [15,16]. Syndromic surveillance has been defined as “an investigational approach where the health department staff, assisted by the automated data acquisition and the generation of statistical alerts, monitor the disease indicators in real-time or near real-time to detect the outbreaks of diseases earlier than would otherwise be possible with traditional surveillance” [17]. Now this is the real time to develop an electronic surveillance system, for example, the Geographic Information System (GIS) [18], or the Health Alert Network (HAN) [19] for the early notification of epidemics.

Establishment of health systems at different levels: The regional stockpiles of items such as insecticides and cholera kits and essential drugs were stockpiled, beginning right from the sub centre to the apex care level of the health system.

Pandemic surveillance for antimicrobial resistance: The surveillance of antimicrobial resistance is being strengthened through training courses and through the distribution of WHONET, a surveillance-supporting computer programme. In the western Pacific region, there are three regional antimicrobial surveillance systems – one for the general bacterial diseases (Network on Antimicrobial Resistance) and the others for gonococcal infections (Gonococcal Antimicrobial Surveillance Programme). For tuberculosis in India, the DOTS plus therapy for the treatment of multidrug resistance tuberculosis has been launched. In India, the Integrated Disease Surveillance Project (IDSP) has been launched for the surveillance, for communicable as well as non communicable diseases. Each surveillance system covers the whole region to detect antimicrobial resistance. The laboratory-based surveillance of various communicable diseases has been strengthened in many member states through technology transfer, training of the national staff, workshops which were conducted by the WHO and through the distribution of the WHO Communicable Disease Surveillance Kit.

Up gradation of the International Health Regulations: In order to ensure an effective international response for all the outbreaks of international importance, the WHO is now in the process of revising the IHR to apply a syndromic approach to the disease reporting. This will enable the outbreaks of the as yet unidentified disease syndromes to be reported globally at an earlier stage, for the appropriate international measures to be taken. Acknowledging the need to strengthen the local and the national capacity of each country and area to detect, verify, report and to respond to significant public health events, which include those which are caused by emerging diseases, in accordance with the International Health Regulations (2005) is essential.

Outbreak response: In April 2000, the WHO formalized an infrastructure, GORAN (the Global Outbreak Alert and Response Network) for responding to the heightened need for an early awareness of the outbreaks and for the preparedness to respond to them.

The procedure for the outbreak alert and response has four phases: Systematic detection, outbreak verification, real time alerts, and rapid response. For the response, the framework uses different strategies for combating the known risks and the unexpected events, and for improving both the global and the national preparedness to face them. The new forces which are at work in

an electronically interconnected world are beginning to break down the traditional reluctance of the countries to report the outbreaks due to the fear of their negative impact on trade and tourism. About 65% of the world's first news about infectious disease events now comes from informal sources, which include press reports and the internet.

The basic objectives of GORAN are, combating the international spread of outbreaks, ensuring that the appropriate technical assistance reaches the affected states rapidly and contributing to the long-term epidemic preparedness and the capacity building. In the region/ tertiary care centre, the Regional Office rapidly dispatches a Rapid Response Team (RRT) to the epidemic sites. Logistical support is also provided.

The dissemination of information: If the outbreak has been established, the accurate and timely information has to be disseminated to the member states and to the public through various media sources so that a timely and prompt action can be taken.

Administrative support and training of the staff: The outbreak control will be effective only if all the staff who are working at different levels understands the importance of their roles. As a part of the training, each health care worker and staff member should receive job category-specific instructions.

The training should be conducted before the initial assignment and a continuing education should be provided to all.

YET TO BE ACHIEVED

The speed of the notification is essential if the outbreaks of the emerging and the re-emerging diseases have to be combated effectively. In the past, the shortcomings in some countries' surveillance systems had resulted in delays in notifying the WHO and other countries about disease outbreaks. The revised International Health Regulations, 2005 will help in addressing this issue.

CONCLUSIONS

Strengthening and promoting the basic and applied research on the pathogens, hosts and the environmental factors by using the knowledge on the pathogens, hosts, and the environment interactions to enhance our ability to predict and to prevent the conditions that led to the human diseases are important. The invention of newer diagnostics, vaccines, therapies and sequencing and the post-genomics research of the emerging infectious disease agents and the animal vectors to reveal the genetic basis for the microbial/vector evolution, adaptation, and pathogenicity is the next step. Tracking better control strategies and developing the national and the international scientific expertise which is required to respond to the future health threats by supporting research and training programs are also necessary.

FUTURE

We have to give more emphasis on the surveillance, research and training, better diagnostic facilities and improved public health systems. The preparedness for emergency situations must continue to improve at both the regional and the national levels. The regional stockpiles will be periodically monitored and updated. The regional information networks on communicable diseases that link the WHO collaborating centres, international agencies, and institutions will be established by using an electronic-mail system. These networks will be linked to the global communicable diseases information system which has been coordinated by the WHO

Headquarters. The antimicrobial resistance surveillance in the region will be strengthened by increasing the number of monitoring laboratories at different locations. The regional antimicrobial resistance system for general bacterial diseases (Network on Antimicrobial Resistance) will be integrated into the global surveillance on antimicrobial resistance, like IDSP in India.

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