

Emerging and Re-emerging Infections

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Summary

An emerging infection is defined as an infection which has newly appeared in a population while a re-emerging infection is one which has existed in the past but its incidence is rapidly increasing. The reasons for the emergence and re-emergence of infections are not well understood but appear to be associated with factors that involve the pathogen, the host and the environment. These factors are often inter-related and act together in a complex manner to bring about changes in patterns of infection. Pathogens are extremely resourceful and possess mechanisms to adapt to new hosts and environments as well as to acquire new virulence traits. Host factors include herd immunity, social behaviour and demographics. Environmental factors like the climate, deforestation and new technologies have an impact on the emergence of infections. The challenge is to contain an infection when it emerges but more importantly to prevent its emergence in the first place. As the emergence of an infection is complex and multifactorial, a multidisciplinary approach is required. Health based strategies alone are insufficient. Social, economic and environmental measures and the political will to implement appropriate policies are equally important.

Key Words: Emerging infections

Introduction

An editorial published in the Medical Journal of Malaysia in March 1996 warned of emerging infections and the threat to Malaysia¹. Unfortunately such infections are now no longer just a threat as evidenced by the recent outbreak of the Nipah virus encephalitis. The emergence and reemergence of infectious diseases has become not only a national issue but of international concern as well. The world it would appear has become much more vulnerable to global spread of both new as well as old infections.

The optimism expressed by health professionals and health organisations in the 1950s and 1960s has proven unfounded. In 1951 the WHO had declared that "malaria is no longer of major importance"². In

1967 the U.S. Surgeon General remarked that it was time to close the book on infectious diseases and to divert national attention and funds to chronic diseases³.

The World Health Organisation's report for 1998 stated that of the 50 million deaths worldwide in 1997, about one-third were due to infectious and parasitic diseases⁴. Up to half of the world's 5.7 billion people are at risk of many endemic infections. Thus far from being over, the struggle to control infectious diseases has become increasingly difficult. Diseases like tuberculosis and malaria, once thought subdued are making a comeback. New infections for which there are neither vaccines nor cure are emerging in many parts of the world and the association between infectious agents and many cancers is also becoming increasingly clear.

What are Emerging or Re-emerging Infections?

An emerging infection can be defined as an infection which has newly appeared in a population. They can be:

1. An entirely novel infection - a very good example would be the Nipah virus which has never been described prior to the recent outbreak in Malaysia
2. An old infection but only newly recognised such as *Helicobacter pylori* which has only been recently identified as the cause of peptic ulcer disease. Peptic ulcer has afflicted man for centuries but its association with a bacterium was only elucidated a decade ago⁵.
3. An old pathogen which has recently acquired resistance to antimicrobial agents - there are many examples of these emerging resistant organisms. They include vancomycin resistant *Staphylococcus aureus*⁶ and extended-spectrum betalactamase (ESBL) producing gram-negative bacilli⁷.

A re-emerging infection could be defined as one which has existed in the past but its incidence is rapidly increasing. Such infections would include in Malaysia, diseases like tuberculosis and dengue fever. Table I shows the incidence of selected infections in Malaysia over the past several years.

Why do Infections Emerge?

This emergence and reemergence of infectious diseases that are occurring today could have been due in part to the complacent attitude developed by many countries towards infectious diseases following limited successes in their control achieved in the sixties and seventies.

Why infections emerge and re-emerge is still not well understood. From what little is known it would appear that the factors that impact on the emergence and reemergence of an infection are many and complex. These factors may be conveniently divided into (a) pathogen factors (b) host factors and (c) environmental factors. However these factors are often inter-related and act together in a complex manner to bring about changes in patterns of infection.

Pathogen factors

Microbes are extraordinarily resourceful entities. The success of a microbe in establishing itself as a human pathogen depends on its ability to adapt to new hosts including humans, its capacity to increase its virulence, its capacity to survive in the environment and the efficiency by which it can be propagated.

It has been shown that virulence factors can be transferred between microbes. The evidence for this is derived from the occurrence of pathogenicity islands in various bacterial species. These pathogenicity islands are

Table I
Incidence of selected infections in Malaysia
(source: Ministry of Health of Malaysia)

Infection	Year		
	1993	1995	1997
Cholera	995	2209	391
Enteric	1442	906	836
Food poisoning	1638	1438	7966
Tuberculosis	12075	11778	13539
HIV infection	2516	3546	3918
Dengue	5060	6156	18642*

*In 1998 the number of dengue cases notified rose to 27,370

blocks of genes within the chromosome that code for virulence. These genes code for a variety of virulence traits, such as the ability to acquire iron and to adhere to or enter host cells. These segments of DNA appear to have been acquired in a single step from a foreign source. The ability to acquire multiple virulence traits in one genetic event, rather than through natural selection over a period of time, provides a mechanism for sudden radical changes in bacterial pathogenicity and are likely to lead to the emergence of new infectious diseases in the future⁸.

Other factors that would also increase the threat posed by a pathogen to the human population would include arthropod borne transmission, water borne transmission, attendant borne transmission and durability in the external environment⁹. Acquisition of antibiotic resistance by the pathogen is another example of the adaptability of microbes and would obviously also contribute to their emergence¹⁰.

Host factors

Many host factors play a role in the emergence of an infection. The herd immunity in the community affects the ability of the pathogen to spread and establish itself in the community. In the sixteenth century, up to a third of the indigenous population of the West Indies and Mexico died following contact with Europeans. The Europeans had brought with them measles, influenza, mumps, smallpox and tuberculosis, infections hitherto unknown in the New World¹¹. From 1791 to 1863 approximately 80% of the indigenous populations of the Marquesas in French Polynesia died from tuberculosis, typhoid, influenza and smallpox, again infections which were newly introduced by European colonisers¹². The lack of herd immunity probably contributed to the high fatality rate among those who were infected with the Nipah virus.

Human activity both social and economic is believed to play an important role in the emergence of infections. Human activities are indeed one of the major driving forces in the emergence of an infection¹³. The lifestyles of the population will affect the spread of diseases like sexually transmitted infections. Urbanisation and overcrowding increases the spread of air-borne infections as well as water and food-borne infections. Changing

eating habits can also have a great impact on the emergence of food-borne infections. In Malaysia there has been a dramatic increase in the incidence of food-poisoning (See Table I). This could have been due in part to more people "eating out", a trend which has resulted from changes in societal roles. It is now common for both husband and wife in Malaysia to work. The mushrooming of street food enterprises coupled with poor enforcement of food hygiene regulations have also contributed to increasing food and water-borne infections.

Demographics also play an important role, in particular, the migration of people. Human migration is a potent force in the emergence and spread of infections¹⁴. Migrants may not only carry with them the microbial pathogens but also the arthropod vectors that transmit them. The migrants may also bring with them their cultural traditions and behaviour patterns which can influence their capacity to spread the disease to the indigenous populations. Their social standing and economic position often result in living conditions for migrants that are less than ideal. Overcrowded slums without potable water supply or sewage facilities contribute to the spread of many respiratory and gastrointestinal infections. The migrants also change the environment by clearing land for agricultural or building purposes. The large numbers of migrant workers in Malaysia could have contributed to the re-emergence of infections like tuberculosis and leprosy¹⁵.

Human activity also affects the environment and changes in the environment can in turn impact on the pattern of infections as will be discussed in the following section.

Environmental factors

The climate is an important environmental factor. The warm and moist conditions in the tropics favour not only the survival of microbes in the environment but also favour the propagation of vectors responsible for the transmission of these infections. The recent El Nino phenomenon has been partly blamed for the tremendous rise in the number of dengue cases in Malaysia in 1998 (See Table I). Because of the drought and the ensuing water rationing exercise, many households had to resort to storing water. This is often done in inappropriate

containers thus providing breeding opportunities for the mosquito vector. The drought probably also contributed to the increase in food poisoning cases. The lack of water at food outlets aggravated an already unsatisfactory situation.

Rapid urbanisation has also been associated with the emergence of dengue fever¹⁶. The numerous construction sites (ongoing and abandoned) in our urban areas provide ample opportunities for the breeding of the vector *Aedes aegypti*.

Ecological factors can cause emergence of an infection by placing people in contact with a natural animal reservoir or host¹³. The "new" infection though unfamiliar to man has probably existed in animals for a long period of time. By altering the ecology of the natural habitats of these animals the risk of contact between animal and people is increased. Ecological changes may also favor an increase in the population of the microbe or its natural host.

Deforestation for agricultural and other activities cause severe disruptions to our eco-systems. Deforestation for economic activity has been linked to the emergence of Hantaan virus, the cause of Korean haemorrhagic fever. The conversion of forests to rice fields led to an increase in the natural animal host, the field mouse *Apodemus agrarius* which then transmitted the infection to man.

The recently discovered Nipah virus in Malaysia is a paramyxovirus closely related to the Hendra virus discovered in Queensland, Australia in 1994¹⁷. Two outbreaks of Hendra virus involving horses and humans have so far been reported in Queensland. Fruit bats (*Pteropus sp*) are the natural hosts of the Hendra virus and horses are believed to have been infected when they ingested bat urine or placenta. Human infection appeared to have occurred through close contact with the blood and other body fluids of infected horses¹⁸. In Malaysia the Nipah virus had infected pigs which in turn transmitted the infection to man. Patients were mainly pig-farm or abattoir workers who were in close contact with the infected pigs. The natural hosts of the Nipah virus have yet to be established but it is possible that they may also be fruit bats. If this is so, contact between bat and pig must have occurred recently. It is tempting to speculate that the inter-species contact

occurred as a consequence of deforestation and other land development which had affected the natural habitat of the bats, thus forcing them to forage elsewhere for food. Whether such a theory is true remains to be proven.

New technology can also affect the way infections can spread. New methods in mass food production, processing, storage and distribution has resulted in outbreaks of food-poisoning that affect many thousands of people. An outbreak of *Salmonella* in the United States in 1994 affected over 200,000 people in several states¹⁹. This outbreak was traced to a brand of ice-cream where the premix was contaminated with *Salmonella enteritidis*. Contamination took place during transport of the premix in trailer trucks which were previously used to transport non-pasteurised liquefied eggs.

What should be done?

There are two main challenges to overcome. The first is to prevent the infection from emerging and the second to contain it should it emerge. As the reasons for emergence and re-emergence are multifactorial, the approach to prevention of emergence should be multidisciplinary involving not only health-based strategies but also social and economic solutions. It is important to recognise that the problem exists and to muster the political will to implement the appropriate policies.

Health-based strategies would include developing an efficient and effective surveillance system to monitor such emerging infections not only within but also outside the country. There should be adequate facilities for the laboratory diagnosis and treatment of unusual and highly contagious infections. Our country needs to train more infectious diseases physicians as well as microbiologists and epidemiologists. Research into emerging infections should be given priority.

These health based-based strategies must be complemented by socio-economic approaches to provide basic amenities of housing, water supply and sewage for the entire population. There has to be better control of standards for street foods and more efficient enforcement of regulations related to food hygiene.

Government and local authorities should be more conscientious about preserving the environment. Urbanisation must be planned and controlled. Development of land for agricultural and other purposes should be undertaken with caution and the health impact of such projects considered.

Conclusion

The danger of the emergence and spread of infectious diseases in Malaysia is very real. Outbreaks affecting many thousands of patients have occurred in recent years with the loss of many lives. The reasons for these outbreaks are still very poorly understood and for the

moment wholly unpredictable. Until more is known it would be prudent to be cautious. It has been said that a butterfly flapping its wings in China can result in a hurricane in the Caribbean. This is a principle of the chaos theory where it is postulated that very minor events can have very great consequences. Will the felling of a single tree result in a devastating epidemic involving many thousands of patients? It remains to be seen.

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Questions for Emerging and Re-emerging Infections:

1. Emerging infections
 - A. include only those caused by pathogens new to man
 - B. may be zoonoses
 - C. may be pathogens that have acquired new antimicrobial resistance
 - D. are predominantly caused by viruses
 - E. may be precipitated by climatic changes

2. The Hendra virus
 - A. is a paramyxovirus
 - B. natural hosts are horses
 - C. is transmitted by mosquitoes
 - D. was first discovered in Queensland, Australia
 - E. can cause fatal illness in man

3. Uncontrolled urbanisation has been implicated in the emergence of
 - A. melioidosis
 - B. dengue fever
 - C. malaria
 - D. hantaan virus infection
 - E. food and water borne infections

4. Pathogenicity islands
 - A. are foci of pathogens in the environment
 - B. are acquired as a single genetic event
 - C. are the result of mutations
 - D. code for multiple virulence factors
 - E. are located on the microbial chromosome

5. Emerging and re-emerging infections in Malaysia would include :
 - A. Coxsackie virus infection
 - B. Diphtheria
 - C. Poliomyelitis
 - D. Tuberculosis
 - E. Yaws