J.Natn.Sci.Foundation Sri Lanka 2008 **36** Special issue: 127-133

Emerging infectious diseases

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Submitted: 29 August 2008

Abstract: Emerging infections diseases (EIDs) cause a significant burden on the global economies and are a major public health problem in many countries. The incidence of EID has increased dramatically in recent years, mainly due to zoonotic infections.

Sri Lanka has also been significantly affected by EIDs such as dengue, chikungunya and antibiotic resistant bacterial infections. Diseases such as leptospirosis, which have been present for many decades in Sri Lanka are now causing significant public health problems and have been associated with very high mortality. In addition, infections due to the avian influenza A (H5N1) strain, Severe Acute Respiratory Syndrome (SARS) virus and the Nipah virus are some of the pathogens which have a potential of causing severe epidemics in Sri Lanka in the future.

As it is beyond the scope of this review to discuss all the current EIDs, it will mainly concentrate on EIDs that have recently caused major public health problems in Sri Lanka and also those that have a possibility of causing major epidemics.

Keywords: Chikungunya, containment, dengue, emerging infectious diseases.

INTRODUCTION

Infectious diseases have been a major threat to humans since historical times. Pandemics that occurred due to the plague and influenza have wiped out entire villages and caused more deaths and morbidity than the two World Wars combined[1]. Although advances in science in the last decade have had a significant impact on prevention of the occurrence of major pandemics, the world population is still under significant threat from many emerging and re-emerging infectious diseases. Emerging infectious diseases (EIDs) cause a significant burden on the global economies and are a major public health problem in many countries.

Many of the infections defined as EIDs are pathogens from newly emerged strains, drug resistant bacterial strains(multi drug resistance tubercle bacillus), those that have entered the human population recently (Human Immunodeficiency Virus or HIV, Severe Acute Respiratory Syndrome or SARS virus), or are due to RNA viruses (dengue, chickungunya), which have become more capable in overcoming host defenses or adapting to a new host due to the higher mutation rates in their genomes[2]. The incidence of EIDs has increased dramatically in recent years. Although this increase could be attributed to better identification of disease causing pathogens and better reporting, it has been shown that unfortunately, a significant rise in EIDs has actually occurred[3]. The rise in EIDs is thought to be due to many factors such as environment changes, rapid and unplanned urbanization, new agricultural practices, changes in population density, antibiotic usage and increased contact with wild animals [2, 4]. Furthermore, congested working and living environments and greater international travel also increase the spread of infections within the world [3]. As a consequence of these activities the majority (60.3%) of EIDs today are caused by zoonotic infections [2], probably due to the progressive destruction of the natural habitats of many wild animals and thereby increasing contact between them and humans. In fact 71.8% of these zoonotic pathogens (SARS, Nipah virus, Ebola, chikungunya) have had their original reservoirs in wild animals[2]. Vector borne diseases such as dengue,

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chikungunya etc., also constitute a major portion (29%) of EIDs.

As it is beyond the scope of this review to discuss all the current EIDs, it will mainly concentrate on EIDs that have recently caused major public health problems in Sri Lanka, and also those that have a possibility of causing major epidemics (SARS, avian influenza) in Sri Lanka in the future. EIDs that have come into prominence in Sri Lanka include leptospirosis, dengue fever (DF), HIV infection, cutaneous leishmaniasis (and more recently, visceral leishmaniasis), typhus, chikungunya and antibiotic-resistant bacterial infections.

Dengue viral infections

During the 19th century, dengue was considered a sporadic disease, causing epidemics at long intervals. However, dramatic changes in this pattern has occurred and currently, dengue ranks as the most important mosquito-borne viral disease in the world. In the past fifty years, its incidence has increased 30-fold with significant outbreaks occurring in five of six WHO regions, with the European region being the only exception [5].

Although dengue infections have been endemic in South Asia for over a century, it rarely caused significant disease outbreaks until the 1980s. However, its epidemiology has dramatically changed over the past two decades, and it is now one of the leading causes of hospitalization and death among children[6]. Sri Lanka and India have been affected by epidemics of Dengue Hemorrhagic Fever (DHF) for nearly 2 decades. Bhutan, which had been free of epidemics of DHF experienced its first outbreak in 2004 [7]. Currently, in the South Asian region only Nepal and Afghanistan are free of cases of DHF possibly due to geographic and climatic factors, such as high mountain areas in Nepal and little rainfall in Afghanistan, leading to poor vector densities.

The rapid increase in dengue viral activity in India and Sri Lanka from 1999 to 2003 suggests its potential to cause more severe epidemics in the future [8]. The rise in the incidence of dengue infections in the rural areas further adds to this threat [9, 10]. Therefore, unless vector densities are reduced, dengue infections may overtake other infectious diseases as the number one killer in many countries in South Asia.

The economic burden of dengue infections has not been formally assessed in any of these countries. However, dengue infections are likely to cause adverse impacts on the economy judging by the data available from other countries (approximately US $61 per family in Thailand)[11]. In Thailand, the annual economic burden of DHF on the country was estimated to range between US$ 31.5 and 51.5 million, depending on epidemic activity[6]. However, the true economic impact is likely to be much higher as the lost work and productivity, absence from school, lost tourism and social disruption have not been taken into account when computing these figures. Therefore, if the incidence of dengue infections escalates as predicted by some authorities, it would be a major economic burden to the poorest economies in the world.

Dengue viral infections in Sri Lanka

Dengue viral infections have been endemic in Sri Lanka since the mid 1960s, which was when the first cases of DF/DHF were reported [12, 13]. Although the Sri Lankan population had been exposed to the virus for decades severe forms of dengue infection (DHF) were rare, except for the 2 epidemics that occurred in 1965 (26 cases and 6 deaths) and 1972 (27 cases) [12-14]. DEN-1 and DEN-2 serotypes were isolated from the outbreaks in 1965-1966[14]. The first large scale outbreak of DHF occurred in 1989 with 206 clinically diagnosed cases of dengue and 20 deaths (case fatality rate 9.8%), and in 1990 with 1080 cases and 60 deaths [15]. Although some believe that the emergence of DHF in Sri Lanka in 1989 coincided with the appearance of a new DEN-3, subtype III variant [16], others have disagreed and shown that the virus strains identified prior to the DHF epidemics and thereafter were similar [14]. Therefore, at present it is unclear whether the emergence of a new variant of DEN-3 is the sole cause of the emergence of the current epidemiological pattern of dengue infections.

Since 1989, the number of cases of DF/DHF has markedly risen with each epidemic, and in 2004, 15457 cases with 88 deaths were seen [17]. Figure 1 shows the number of DHF cases and deaths since 1989 in Sri Lanka. The occurrence of the massive epidemic in year 2004 is thought to be due to yet another change in the predominant circulating virus serotype (from DEN-2 to DEN-3) [18, 19]. DEN-3 was also the cause of the epidemics that occurred in India and other countries of the region during this period [20].

In 2002, DF/DHF ranked as the third commonest notifiable disease in Sri Lanka (first and second were malaria and tuberculosis[21,22] (*personal communication*, H. Tissera). In the Colombo district, 27.5% of children had evidence of infection at 6 years of age, and this figure rose to 45% at 17 years of age [23]. In recent years deaths due to dengue infections have been greater than those due to malaria, with dengue becoming the number one killer mosquito borne infection in Sri Lanka [21]. The

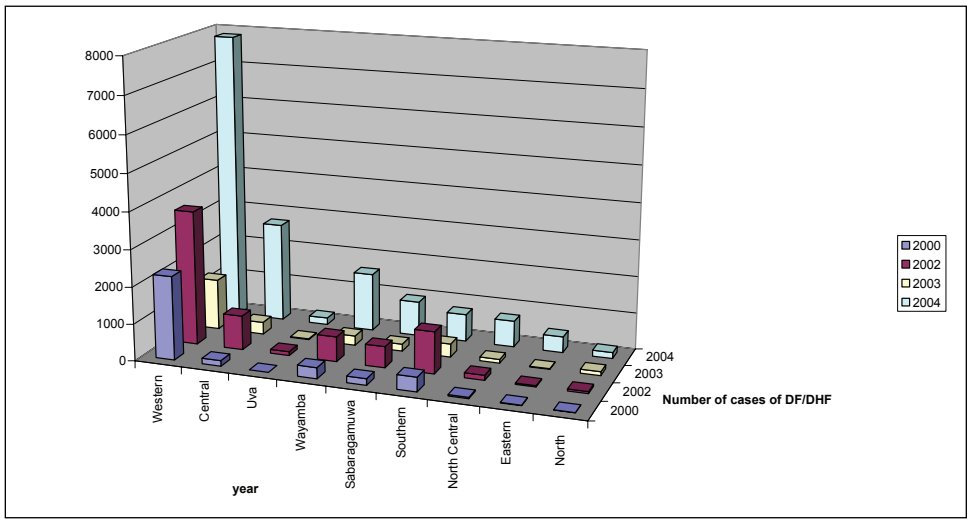

Figure 1: The number of cases of DF/DHF in all provinces in Sri Lanka in recent years

highest case fatality rate (3.3 – 5.2%) is seen in children between the ages of 1 – 4 years. Fortunately, in recent years case fatality rates have been lower (between 0.6% and 2.2%), possibly due to better disease management. However, as seen in India[24] and several other countries, more cases of DF/DHF have occurred among adults since 2001(*personal communication*, H. Tissera).

Future trends :

Dengue was initially an 'urban' disease, where epidemics mainly occurred in densely populated urban settings. However, in both Sri Lanka, and India this pattern appears to have changed with the disease now spreading to rural areas as well [25]. Although vector densities are generally much higher in urban areas when compared to rural areas, vector densities in rural areas are now seen to be quite high[10,26]. Therefore, the potential 'threat' of major dengue outbreaks in rural areas is present. In Sri Lanka, although the highest incidence is seen in the Western Province (44.9% in 2007), there has now been a dramatic increase in the incidence in all provinces. This has been more marked in the North Central Province (11.8% in 2007 vs 4.8% in 2004),Wayamba Province (15.9% in 2007 vs 10.2% in 2004) and Sabaragamuwa Province(12.2% in 2007 vs 6% in 2004 (*personal communication*, H. Tissera). Therefore, there is a potential threat of more severe dengue epidemics occurring throughout the country in the future.

Chikungunya: the evolving pandemic

Although chikungunya has caused sporadic epidemics in many developing countries during the last 3 decades[27], it only received global attention when it first struck a developed country, La Réunion Island in 2005 to 2006, which is governed by the French government[28]. During this epidemic 40% of the entire population in the island were affected[27]. This current pandemic caused by chikungunya virus was thought to originate in Kenya in 2004, from where it spread to Madagascar, parts of Europe and also to the Indian subcontinent[28]. So far, 1.36 million suspected cases have been reported in India alone and an estimated 6369 deaths have occurred. However, it is beleived that the actual figures may be many times larger due to gross under-reporting[29]. Although sporadic outbreaks of chikungunya had occurred in India previously, the recent epidemic was the largest ever reported, and is thought to be due to an African virus strain rather than the Asian strain which was previously circulating [29]. The currently circulating chikungunya virus strain is thought to be more virulent than the previous strains due to certain point mutations in the virus[29].

Chikungunya is an arboviral infection caused by a virus belonging to the Alphavirus family. It can be transmitted effectively by both *Aedes aegyptii* and *Aedes albopictus* types of mosquitoes[27, 30]. It was first isolated in 1953 from Tanzania[27, 30]. Until recently it was thought to cause a benign clinical illness characterized by fever, rash and joint pains[30]. However, recent research and documentation of clinical features have shown that it is not a benign virus as previously thought, but can give rise to incapacitating joint pain and inflammation lasting for weeks to months, meningoencephalitis and fulminant hepatitis, which can also be transmitted from mother to baby and can sometimes be fatal [28-30].

Chikungunya in Sri Lanka :

Although the first outbreak of chikungunya occurred in Sri Lanka in 1965, the first major epidemic occurred in

2006. During the 2006 to 2007 time period 37,000 cases of chikungunya like illness were reported in Sri Lanka mainly from the Western and North Western Province[31]. The most affected districts were Puttalam, Kalmunai, Colombo, Jaffna, Mannar, Batticoloa and Trincomalee. However, it is likely that the actual number was much higher due to under-reporting of chikungunya cases in Sri Lanka. Following these epidemics, surveillance activities on Chikungunya fever were initiated in all sentinel hospitals by regional epidemiologists motivating the clinicians to entertain high suspicion cases of this illness. As this is a relatively 'new' disease in Sri Lanka, and also due to lack of laboratory facilities to identify and correctly distinguish patients with chikungunya from other similar viral infections, data regarding the true incidence of this disease in Sri Lanka are scarce.

Cutaneous leishmaniasis in Sri Lanka

The first locally acquired case of cutaneous leishmaniasis was reported from Ambalantota in 1992 [32]. Most of the early cases were soldiers who appeared to have acquired it while on combat duty in the north and east of the country, but a more widespread distribution and a wider involvement of civilian cases have since been recognized. Studies to determine the local pathogenic strains [33] and vector species are underway.

Typhus

Typhus has become increasingly recognized since the turn of the century, especially from the southern, central and north-western provinces. On-going studies[34] are helping to define the pathogenic species and vectors.

Antibiotic resistance

Antibiotic resistance has been reported from Sri Lanka involving *Staphylococcus aureus* (including methicillin resistance and vancomycin intermediate sensitivity), *Streptococcus pneumoniae* (including penicillin resistance), typhoid fever (including fluoroquinolone intermediate resistance) and tuberculosis (including multi-drug resistant tuberculosis).

The situation with regard to anti-retroviral therapy in HIV infection is not known, but the options available are limited and facilities to monitor drug resistance (which is virtually invariable after some time) remain inadequate. Fortunately, drug resistance is still not a problem in malaria and leprosy; combination therapy had been practiced for leprosy since the 1980s, and a recent policy decision was taken to adopt artimisinin-containing combination therapy (ACT) for malaria too, hopefully further forestalling the emergence of drug resistance.

EIDs that could be a possible threat to Sri Lanka

Infections due to avian influenza A (H5N1) strain, SARS and the Nipah virus are some of the pathogens which have a potential of causing severe epidemics in Sri Lanka in the future.

Avian influenza A (H5NI) infections

Infection due to influenza H5N1 virus was first described in a poultry farm in Hong Kong in 1997 [35]. The infection is most frequently seen among wild birds and domestic poultry. Although human-to-human spread does occur, it is believed that the virus is relatively inefficient in such form of transmission. Despite these limitations, 240 cases of avian influenza have been reported in humans since 2003, with 140 deaths. Approximately 20% of adults who contract this infection are thought to develop respiratory failure and the mortality rate in children who develop bird flu is reported to be 50% [35]. Therefore, although the virus has a limited capacity of spread from human to human, it appears to be a deadly virus due to the associated high mortality. Furthermore, one of the deadliest influenza epidemics that occurred in 1918, killing more than 20 million people worldwide is now thought to be an avian influenza virus strain that had adapted to cause infection in humans [36]. This caused much concern among the scientific community in the world, because if the current avian influenza H5N1 strain adapts itself to spread readily among humans, the consequences could be devastating.

Nipah viral infections

Nipah viral infections were first identified when it caused an outbreak of encephalitis in Malaysia and Singapore in 1998 to 1999 [37]. During this period, 276 cases with 105 deaths occurred in these countries, mainly among those who were involved in pig farming activities. This virus subsequently spread to the West Bengal area of India in 2001 [38] and to Bangladesh. So far several epidemics have occurred in Bangladesh from 2001 to 2005 [39].

The Nipah virus belongs to the family *paramyxoviridae*, and fruit bats are thought to be its natural reservoir. Humans are thought to be infected by secondary hosts such as pigs and horses, by being exposed to products contaminated by infected bats and also by human to human transmission [37,39]. It causes encephalitis which has a fatality rate of 38-75% [38]. Epidemiological data from Bangladesh suggest that epidemics of encephalitis due to the Nipah virus are a seasonal event that occurs due to human-fruit bat interaction [39]. Although Sri Lanka has been free from any such cases so far, the close proximity of the countries which experience regular

Nipah virus epidemics, should alert us to the possibility of future outbreaks in Sri Lanka.

SARS:

SARS was the first major pandemic caused by a coronavirus, which affected 30 countries and resulted in 8,096 cases and 774 deaths [40]. The source of the pandemic which originated from the Guangdong province in China is thought to be from animals such as civets, raccoon dogs and bats, as viruses similar to the SARS-CoV virus was subsequently isolated from these animals [40]. In this epidemic, person to person transmission mainly occurred in the hospital environment through nebulizers, intubation, bronchoscopy or resuscitation on patients with SARS [41]. A unique form of airborne transmission by this virus is thought to be responsible for the rapid spread and also the high incidence among health care workers [42]. Although the global SARS pandemic has been successfully contained, there is still a potential risk of the same virus or similar viruses re-emerging and causing outbreaks, and therefore preparing for such situations is of utmost importance.

Preparing for emerging infectious diseases

The world was taken by surprise by the SARS pandemic, which showed that lack of prior preparation for handling such epidemics can have a serious impact on public health and the economy of a country[3]. The importance of being prepared for EIDs was best illustrated in this pandemic, where the majority of SARS outbreaks occurred in hospitals, and 21% of those involved were health care workers [43]. During the SARS epidemic in 2003, the disease spread rapidly from Hong Kong, to Toronto in a matter of days. However, the spread of SARS in Hong Kong, and subsequent morbidity and mortality were markedly higher when compared to Toronto. Retrospective studies have shown that this difference was in fact due to differences in the preparedness of health care systems in these countries to handle such disease situations.

Many lessons were learnt from this pandemic such as the fact that early recognition of cases, proper isolation and prevention of disease spread were crucial in controlling such epidemics[35]. Therefore, the importance of training healthcare workers in early identification of EIDs and in the appropriate use of infection control measures such as the proper use of personal protective equipment, personal hygiene and environmental measures cannot be overemphasized. Although, Sri Lanka was spared of the SARS epidemic and so far also from avian influenza H5N1 infection, the preparedness and ability of the Sri Lankan health care system to handle such epidemics is questionable.

Preparing hospital staff for dealing with EIDs :

Although Sri Lanka has one of the best health care systems in Asia, as evident by the very low infant and maternal mortality rates, high vaccine coverage rates and life expectancy, hospital waste management and waste disposal methods and infection control methods are far from satisfactory. For instance, it was revealed that 92% of hospital labourers in a tertiary care hospital was unaware of the need for collecting sharps into sharp bins and 42.9% was unaware that HIV and Hepatitis B infections could be contracted through needle stick injuries [44]. Furthermore, it was also revealed that waste disposal methods were unsatisfactory, the provision of self protective clothing was inadequate or non existent and waste storage facilities in hospitals were far from what has been recommended as safe[44]. Therefore, as the threat from EIDs in the world and in Sri Lanka is on the rise, it is vital to educate and train all health care personnel on proper infection control and waste disposal methods.

Laboratory preparation for handling EIDs :

Laboratories play a crucial role in the early identification and containment of epidemics due to EIDs[45]. Laboratories are needed for active disease surveillance of infectious diseases, to determine changes in the pathogens which may enhance their virulence leading to larger outbreaks, to identify new and re-emerging pathogens responsible for disease outbreaks and those that cause unusual disease manifestations[46]. Therefore, the development of both diagnostic and research laboratories in the country are needed in order to prepare for any threats due to possible 'new' EIDs, or to control and prevent any disease outbreaks[45] that can occur due to currently existing infectious diseases in Sri Lanka. While developing the laboratory facilities in Sri Lanka, it is also important to train properly all levels of technical staff regarding proper infection control measures in order to prevent laboratory acquired disease outbreaks. Unfortunately, most laboratories in the Asia-Pacific region lack national bio-safety programmes[46], and Sri Lanka is no exception.

The World Health Organization (WHO), in its recently formulated action plan, which is known as the 'Asia Pacific Strategy for Emerging Infectious Diseases' highlights the importance of the development of diagnostic and research laboratories, proper training of staff in following meticulous infection control measures, and also establishing close collaboration between national and regional laboratories[46]. In addition, laboratories play a vital role in the surveillance of antimicrobial resistance, and could assist the prevention of the spread of multi drug resistant organisms by formulating a national action plan for proper antibiotic use.

Containment and prevention of epidemics due to EIDs at a national level:

Epidemics and pandemics occur when they are least expected, and if such massive epidemics do occur, hospitals and all health care facilities should be adequately equipped to treat such patients, while limiting the spread of infection to others and also ensuring measures to contain the epidemic as soon as possible and reduce the number of cases as far as possible. The importance of close collaboration and efficient communication among all health care institutions in disease outbreaks cannot be overemphasized[3]. Formulating a national plan which is agreeable to all health care institutions, laboratories and health care workers is crucial in order to prevent and contain any outbreaks due to EIDs that may occur in Sri Lanka in the future. However, it is evident that EIDs are on the increase globally [2, 46]. Therefore, it is important to identify the factors that are responsible for this increase, which may include environmental consideration, ecological and climatic factors along with host factors, inappropriate use of antibiotics, population behaviour and breakdown of public health services due to civil disturbances and displacement of populations [46], and initiate effective preventive control measures in time.

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