Disease appearance and evolution against a background of climate change and reduced resources

BY SOPHIE YACOUB¹, SUSY KOTIT² AND MAGDI H. YACOUB²,3,*

¹Department of Infectious Diseases, and ²National Heart and Lung Institute, Imperial College, London, UK
³Heart Science Centre, Harefield Hospital, Harefield, UK

Global health continues to face increasing challenges owing to a variety of reasons that include the almost constant changes in disease appearance and evolution. Most, but not all, of these changes affect low-income countries and are influenced by climate change. Tracking the recent and anticipated changes in the demographics and global distribution of these changes is essential for evolving effective new methods for dealing with the problems. The recent recognition by the United Nations of the importance of non-communicable diseases is a major positive step. For the sake of this paper, the following diseases were chosen: dengue and malaria, to highlight the role of climate change on vector-borne diseases. Drug-resistant tuberculosis illustrates the role of globalization and reduced resources on disease evolution. The continuing rise in cardiovascular mortality and morbidity, particularly in resource-poor countries is largely attributed to lack of preventive and therapeutic measures against such conditions as hypertension, diabetes, atherosclerosis and congenital heart disease as well as neglected diseases, of which Chagas and rheumatic heart disease will be discussed further.

Keywords: climate change; dengue; malaria; tuberculosis; rheumatic heart disease; Chagas disease

1. Introduction

Global health continues to face increasing challenges owing to a variety of reasons that include the almost constant changes in disease appearance and evolution. Most, but not all, of these changes affect low-income countries and are influenced by climate change. Tracking the recent and anticipated changes in the demographics and global distribution of these changes is essential for evolving effective new methods for dealing with the problems.

*Author for correspondence (m.yacoub@imperial.ac.uk).

One contribution of 12 to a Theo Murphy Meeting Issue ‘The sustainable planet: opportunities and challenges for science, technology and society’.
Up until recently, emphasis was put almost exclusively on infectious diseases that are responsible for a significant proportion of the problems facing global health. The recent recognition by the United Nations of the importance of non-communicable diseases, which include cancer and importantly cardiovascular disease, is a major positive step [1,2]. We here discuss changes in some of these diseases to include both communicable and non-communicable diseases in an attempt to illustrate the different issues concerned with regard to emergent diseases and changes. A list of examples of these diseases is shown in the following:

— human immunodeficiency virus and related diseases;
— severe acute respiratory syndrome;
— H1N1/H5N1 influenza;
— dengue;
— drug-resistant TB;
— ebola;
— West Nile virus;
— anthrax;
— malaria;
— Chagas disease; and
— rheumatic fever.

For the sake of this paper, the following diseases were chosen: dengue and malaria, to highlight the role of climate change on vector-borne diseases. Drug-resistant tuberculosis (TB) illustrates the role of globalization and reduced resources on disease evolution. The continuing rise in cardiovascular mortality and morbidity, particularly in resource-poor countries is largely attributed to lack of preventive and therapeutic measures against such conditions as hypertension, diabetes, atherosclerosis and congenital heart disease, as well as neglected diseases [3,4], of which Chagas and rheumatic heart disease (RHD) will be discussed further.

(a) Dengue

Dengue is the most rapidly spreading mosquito-borne disease in the world. The global burden of dengue has increased at least fourfold over the last three decades (figure 1). An estimated 50 million dengue infections now occur annually in over 100 countries, and an estimated 616 000 disability-adjusted life years per year, particularly in southeast Asia, the Americas and the western Pacific islands. About 500 000 severe dengue cases occur annually and approximately 19 000 dengue-related deaths were reported in 2002. The World Health Assembly highlighted its importance as an emerging disease in 2006, as dengue increases in new areas of the world where the public-health systems are not experienced in the prevention of the disease, or the surge capacity in clinics and hospitals is not available to deal with an often sudden increase in the number of patients, and the clinical experience is limited. In these settings, mortality and morbidity are often higher than in other regions where dengue has been endemic for decades. The World Health Organization (WHO) in 2009 reclassified the case definition of dengue clinical syndromes to make identification and management of the disease simpler [5].

Phil. Trans. R. Soc. A (2011)
There are several reasons suggested why the incidence of dengue is increasing, including climate change, globalization and importantly rapid and often poorly planned urbanization [6]. Although there is a debate over how much climate change has contributed to the spread of dengue, with the vector Aedes mosquito populations depending on rainfall, humidity and temperature, and epidemics correlating closely to annual rainfall pattern [7,8], there is a strong argument for the effects of climate change. One model predicted that climate change would increase the area of land suitable for dengue transmission to 50–60% of the world by 2085 [9]. Dengue is an urban disease with Aedes mosquitoes highly adapted to living and breeding near humans, using water-storage containers and household rubbish. In South America, the rapid urbanization of many cities with poor water and sanitation planning are being partly blamed for the huge increases in dengue that they have seen in the last two decades. Migration of rural populations to cities also provides a new reservoir of susceptible individuals.

The spread and evolution of dengue will ultimately depend on both human and climatic influences, which will need evolving new strategies to deal with each of these issues.

(b) Malaria

Malaria is the most serious vector-borne disease in the world, with more than a third of the world’s population (about 2 billion) living in malaria-endemic areas, and in 2008, there were 247 million cases of malaria and nearly 1 million deaths—mostly among children living in Africa. The determinants of its global distribution and spread need to be better defined. Of the available data, climate has been considered one of the most important factors influencing its distribution [10]. It has been postulated that through global warming, vectorial capacity of these
mosquitoes may increase in terms of abundance, distribution, biting rates, as well as other factors, which could lead to the emergence or re-emergence of malaria into new areas [3,4].

The greatest effect of climate change on malaria transmission is predicted to occur at the extreme temperature ranges at which transmission occurs, and it has been predicted that small increases in temperature at low temperatures may increase the risk of transmission substantially [11]. However, over the last decade, many of these models have shown a mismatch with predictions and actual malaria presence [12]. A model using multiple climatic variables in a two-step statistical approach to mapping malaria gave a better description of the current distribution and surprisingly predicted very little change in the overall malaria distribution, with some areas increasing their risk, while others decrease [13]. As these models only predict risk, this is often in contrast to the present situation, which in the last 50 years has seen a global malaria decline [14–16]. Climate-change data, therefore, need to be set against other factors like economic development, local and national control measures, and others including new treatment options, which reassuringly, if the present trend continues, seem to outweigh any predicted spread through climate change. However continued vigilance is essential to reduce the impact of this lethal disease.

(c) Drug-resistant tuberculosis

TB remains one of the leading causes of global morbidity and mortality, with 9.4 million new cases in 2009 and 1.3 million deaths occurring, mainly in lower income countries (http://www.who.int/tb/publications/global_report/2010/gtbr10_main.pdf). The emergence and spread of multi-drug resistant (MDR) TB and extensively drug resistant (XDR) TB are causing major concerns for TB control with almost 500,000 cases of MDR TB in 2006 [17,18] (figure 2). XDR TB, which is defined as resistance to both first-line drugs, rifampicin and isoniazid, and at least two of the second-line drugs, including a quinolone plus one of the injectables (amikacin, kanamycin or capreomycin), has now been reported from at least 58 countries, the burden being highest on the background of reduced resources [17]. South Africa has reported one of the highest incidences of XDR TB, with the human immunodeficiency virus (HIV) epidemic thought to be driving the emergence [20]. The true extent of MDR and XDR TB in Africa, however, remains unknown owing to the lack of drug susceptibility testing in the vast majority of centres. Countries of the former Soviet Union have seen some of the highest proportion of MDR rates and some of the worst resistance patterns [21]. Collapse of public-health systems, lack of national programmes for case detection and treatment, poor laboratory support for drug susceptibility testing and little political commitment have all been thought to contribute to the emergence and spread of MDR/XDR TB. This led to the Stop TB partnership being founded with the WHO in 2000, whose goal is to reduce the burden of TB by 2015 in line with the millennium development goals, through several key objectives [22]. Along with expansion of high-quality detection and treatment of TB cases, there are also separate objectives regarding management of MDR TB plus TB/HIV collaborations, and several other interventions including health-system strengthening and addressing the needs of poor and vulnerable populations [23].
Even with the constraints of reduced resources, drug-resistant TB is still manageable, when directed through dedicated programmes at a national level and in line with the Stop TB partnership goals, successful outcomes of 70 per cent have been reported, similar to those seen in resource-rich nations [24]. So the reversal of the spread of MDR and XDR TB is possible, but cannot be achieved without several key interventions of which social and economic developments will provide an important platform.

**Chagas disease**

Chagas disease caused by the protozoan parasite *Trypansoma cruzi* is another example of an emergent disease that is linked to poverty [25]. Endemic in Latin America, there is estimated to be 15 million people living with the disease and 50–200 000 new cases every year. Human disease is primarily caused by the bite of an infected triatomine bug (figure 3), whose habitat ranges from southern USA down to Argentina and Chile. Chagas disease can also be transmitted by blood products, congenitally, organ transplant, as well as via the oral route. The burden of disease in endemic areas falls on the rural poor who are most exposed to the insect vector that lives in the mud walls and thatched roofs of deprived housing.

Chagas disease is no longer a sole concern for Latin America, international spread through immigration has meant that Chagas disease is now a global health problem [26–30]. The southern states of America have experienced increases in sporadic cases of Chagas owing to the constant flow of migrants from central/south America, but also cases from autochthonous spread.

Chagas disease has spread further and has now been reported from several countries in Europe and Canada [27,28]. The cause for concern being that the local medical community is often unaware of diagnosis and management of the new disease, which leads to avoidable morbidity and mortality.
The vast majority of people with Chagas disease will be unaware they have been infected, and those that do become symptomatic do so decades after the acute infection. The acute phase, usually a benign condition of fever and lymphadenopathy occurs in childhood, resolves in greater than 90 per cent of cases to leave an indeterminate antibody positive phase. Thirty percent go on to develop a dilated cardiomyopathy or, less frequently, digestive megasymphdromes 10–30 years later [31] (figure 4). Management of Chagas disease relies on early diagnosis and treatment with anti-parasitic drugs, which have been shown to be effective in the acute and early indeterminate phase of the disease [32]. Chronic Chagas is currently managed symptomatically, but access to treatment is often limited in resource-poor settings. Chagas disease has been neglected by the scientific and pharmaceutical industries with no new drug development.
since the 1970s [33]. Successes in reducing Chagas disease incidence have been achieved through intensive insecticide spraying, rural-housing improvements and blood-donor screening [34].

Chagas disease, however, remains to be globally one of the most neglected diseases, with the consequences of ongoing transmission in endemic, resource-poor areas and international spread owing to migration largely caused by poverty.

(e) **Rheumatic heart disease**

The incidence of rheumatic fever (RF) has been estimated to be over 700 per 100 000 in the 5–20 years age group and around 10–20 million new cases every year [35–37]. Although several organs are affected during RF, the heart is the most severely damaged with heart-valve affection being the most serious complication, occurring in up to 90 per cent of patients with RF [38]. RHD is estimated to affect 15.6–19.6 million people worldwide, of which 2.4 million are children predominantly in developing countries and 233 000 to 492 000 deaths are directly attributable to RHD annually [37,39,40]. A particularly high prevalence has been reported in several resource-poor areas reaching 48 per 1000 children in Nicaragua [41], 33.2 per 1000 in Tonga [42] and 30.4 per 1000 in Mozambique [43]. Substantial increases in RF/RHD have been documented in some countries in central Asia, with the collapse of public-health systems and reduction in living standards thought to be the main contributing factors [44]. Prevalence rates in developed countries continue to decline; however, the opposite is seen in indigenous populations in these nations, particularly in Australian aboriginals [45] (figure 5).

The true global disease burden is likely to be grossly underestimated owing to a lack of echocardiographic screening that has been shown recently to be the most reliable screening tool [42,43,46,47].
A rational approach to prevention and treatment of RF and RHD requires thorough knowledge of the pathogenesis and determinants of the disease process [48]. Following specific types of streptococcal infection involves a complex process of autoimmunity. This involves both microbial and host factors [49–51]. Changes have been noted in the collagen, elastin and glycosaminoglycans distribution and localization in RHD valves, resulting in a different anatomy, histology and composition from normal valves [52,53] (figure 6).

Treatment of RF lies in early use of penicillin, and secondary prevention of RHD consists of intermittent or continuous long-term penicillin prophylaxis [54]. Determinants of the persistence of RF and RHD are believed to be poverty, overcrowding, malnutrition, low level of disease awareness in the communities, shortage of resources for providing quality care and inadequate expertise of health-care providers, potentially more virulent streptococci [55] and underlying genetic susceptibility [56].

Implementation of secondary prevention programmes in vulnerable populations and development of methods for primary prevention, such as vaccines, are therefore highly needed. However, vaccine development has been hampered by the heterogeneity of the causative streptococcus [57]. The recent recognition of an octapeptide on rheumatogenic streptococci could provide a new therapeutic target for vaccine development [49,50], and the use of glycobiology, as a novel avenue for producing effective vaccines [58]. Primary prevention combined with other prevention strategies may ultimately reduce the high prevalence of this neglected disease.

2. Conclusions

The evolution of disease owing to climate change and reduced resources continues to challenge developing and developed countries. Thorough knowledge of the factors influencing these changes is required to develop disease and population-specific strategies to impact on these important global health issues.
References


57 Medina, E. & Chhatwal, G. S. 2002 The potential for vaccine development against rheumatic fever. Indian Heart J. 54, 93–98.