

Eco-social processes influencing infectious disease emergence and spread

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SUMMARY

The complexity and connectedness of eco-social processes have major influence on the emergence and spread of infectious diseases amongst humans and animals. The disciplinary nature of most research activity has made it difficult to improve our understanding of interactions and feedback loops within the relevant systems. Influenced by the One Health approach, increasing efforts have recently been made to address this knowledge gap. Disease emergence and spread is strongly influenced by host density and contact structures, pathogen characteristics and pathogen population and molecular evolutionary dynamics in different host species, and host response to infection. All these mechanisms are strongly influenced by eco-social processes, such as globalization and urbanization, which lead to changes in global ecosystem dynamics, including patterns of mobility, human population density and contact structures, and food production and consumption. An improved understanding of epidemiological and eco-social processes, including their interdependence, will be essential to be able to manage diseases in these circumstances. The interfaces between wild animals, domestic animals and humans need to be examined to identify the main risk pathways and put in place appropriate mitigation. Some recent examples of emerging infectious disease are described to illustrate eco-social processes that are influencing disease emergence and spread.

Key words: infectious disease, emergence, social-ecology, one health, epidemiology, human health, animal health, ecosystem health.

INTRODUCTION

Over the last few decades there has been an apparent increase in the number of emerging infectious diseases of humans and animals (Jones *et al.* 2008; Morse *et al.* 2012). It is important to understand the causes of this increase so that we can, ideally, prevent or reduce the rate of emergence of new pathogens, or be able to predict, rapidly detect and control future emerging diseases in order to minimize their impact on humanity (Morse *et al.* 2012). However, the causes are likely to be part of a complex of interacting biological and social factors, operating at multiple scales from local to global (Wilcox and Colwell, 2005) and therefore inter- and trans-disciplinary research is required that informs effective policy and action (Coker *et al.* 2011).

CONTEXT

We are living in a time of rapid global change, the so-called anthropocene epoch. Humans have been modifying their environment since pre-historic times,

but it is in the last 300 years that there has been an exponential increase in human population and exploitation of natural resources leading to anthropogenic changes to the global ecosystem (Crutzen, 2002; Zalasiewicz *et al.* 2011). A number of foresight groups are attempting to understand change and explore what might happen in future decades, for example the UK government, the European Environment Agency, and the Australian Commonwealth Scientific and Industrial Research Organisation (Foresight, 2011; EEA, 2015; Hajkowicz, 2015). They identify a number of global megatrends, which are described as large-scale, high impact, often interdependent, social, economic, political, environmental or technological factors that are likely to determine the trajectory of change over the coming decades. Some of these megatrends are likely to influence future disease emergence, such as; increasing human population, urbanization, globalization, increasing mobility and connectedness, inequality, increasing consumption, habitat destruction, biodiversity loss and climate change.

The global human population reached 7.3 billion in 2015 and is projected to increase to 9.7 billion by 2050 and 11.2 billion by 2100, with most of the increase in Africa and Asia (UN, 2015). While the number of people living in rural areas is expected

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to plateau or decrease slightly by 2050, the number of people in urban areas is expected to increase from 3.9 billion in 2015 (54% of global population) to 6.3 billion in 2050 (66% of global population) with most of this increase in Africa and Asia (UN, 2014). Expanding land use for human habitat has caused a reduction in global forest cover. Hansen *et al.* (2013) used satellite data to map global forest loss and show that between 2000 and 2012 there was a net loss of 1.5 million km², and rate of loss was increasing in tropical areas. Transport networks have expanded and are more efficient, so that most people live within a few hours travel time from a city. The growing human population is increasing global demand for food, and agriculture is becoming more intensive to meet this demand. As some parts of society become better off there is increasing demand for animal products, which is largely being met through increasing intensive livestock production, especially in China and Southeast Asia. With projected increasing economic development across Asia, Africa and South America this trend is likely to continue, unless there is a shift in consumption patterns or methods of production.

With an increasing number of people living in urban areas, fewer people engaged in primary food production, and the lifting of international trade barriers, there has been a transition from local to international food value chains (Rushton *et al.* 2007), resulting in a complex global food trade network with a core group of countries that are highly connected to most other countries and account for a high proportion of total trade (Ercsey-Ravasz *et al.* 2012). This high connectivity allows many countries to have access to almost any food item at any time of year, but increases the risk of spread of contaminants, pathogens or vectors with poor traceability. Recent examples have been the European horsemeat in 'beef' products scandal in 2013 (Anon, 2014) and the European *Escherichia coli* O104:H4 outbreak in 2011 (Appel *et al.* 2012).

DISEASE EMERGENCE AND SPREAD

An emerging disease can be defined as a new disease caused by a previously unknown pathogen or changes in a known pathogen, or an existing disease that is spreading to a new geographical area or population (<http://wwwnc.cdc.gov/eid/page/background-goals>). In the past two decades, there have been several important epidemics and pandemics caused by the emergence of previously unrecognized pathogens; Nipah virus, SARS, Schmallenberg and MERS-CoV. For some pathogens there is evidence that changes in the interface between wild animals, domestic animals and humans provided the opportunity for spillover of infection from wild animals. Subsequent spread was then determined by the ability of the pathogen to transmit amongst domestic

animals and/or humans, or, in the case of vector-borne disease, suitable environmental conditions. This was facilitated in several cases by intensification of livestock production resulting in amplification of transmission within domestic animals and spillover of infection into humans (Jones *et al.* 2013).

Emergence of previously unknown pathogens

Nipah virus was first detected in 1998 in Malaysia, when an outbreak of encephalitis occurred in humans (Chua *et al.* 2000). Almost all cases had been in contact with pigs, some of which had respiratory signs (Chua *et al.* 2000; Epstein *et al.* 2006), and the reservoir host was found to be *Pteropus* sp. fruit bats (Mohd Yob *et al.* 2001; Chua *et al.* 2002; Epstein *et al.* 2006). Based on retrospective investigations, Epstein *et al.* (2006) and Daszak *et al.* (2006) propose that the emergence of Nipah virus in this ecosystem was driven by the establishment of a large intensive pig farm combined with fruit trees in a forest area in Northern Malaysia, within foraging range of two roosts of Nipah virus-infected fruit bats. The bats were attracted to the fruit trees on the farm, providing an opportunity for virus spillover to the pigs. Nipah virus was highly infectious in pigs and spread rapidly via live pig transport movements through the commercial pig population in the south of Malaysia that had been increasing in size and density in response to pork demand from other countries in the region (Pulliam *et al.* 2012). The pigs acted as an amplifier host for in-contact humans. The outbreak was controlled by mass culling of pigs in the outbreak area and neighbouring areas (Chua *et al.* 2000), restrictions on planting fruit trees close to pig units (Pulliam *et al.* 2012), and there have been no further outbreaks of Nipah virus in Malaysia. Nipah virus was then detected in Bangladesh in 2001, and has since caused annual seasonal clusters of human encephalitis with limited human-to-human transmission (Field, 2009). In this area, it appears that there is no amplifying host and humans acquire infection by drinking bat-contaminated date palm sap (Daszak *et al.* 2006; Epstein *et al.* 2006). There is serological evidence that Nipah virus occurs throughout the range of pteropid bats, from Madagascar to Southeast Asia and Oceania (Reynes *et al.* 2005; Sendow *et al.* 2006; Epstein *et al.* 2006, 2008; Iehlé *et al.* 2007; Wacharapluesadee *et al.* 2010), and also infects other types of fruit bats in West Africa (Hayman *et al.* 2008; Drexler *et al.* 2009). With the current trend of agricultural intensification in all these areas, it is possible that pigs or another amplifying host could be brought into contact with an infected fruit bat population, leading to new Nipah virus disease epidemics.

Severe acute respiratory syndrome (SARS) first emerged in 2002 in China. The earliest known

human cases were associated with contact with captive wildlife, and it is believed that wild animals such as masked palm civets and racoon dogs were infected with SARS coronavirus or its ancestor, by spillover from infected horseshoe bats (*Rhinolophus* sp.), either in the wild or in live animal markets (Li *et al.* 2005). Humans then became infected through close contact in the markets, followed by human-to-human transmission that rapidly spread the virus to 27 countries in all continents through international travel (Heymann, 2004), causing about 8000 cases with 10% mortality (http://www.who.int/csr/sars/country/table2004_04_21/en/).

Schmallenberg virus (SBV) is a vector-borne virus affecting cattle, sheep and goats that was first detected in Germany and the Netherlands in 2011 (Hoffmann *et al.* 2012; Veldhuis *et al.* 2013). Deep sequencing identified a previously unknown Orthobunyavirus (Hoffmann *et al.* 2012; Wernike *et al.* 2014). Orthobunyaviruses are arthropod-borne and occur in Africa, Asia and Oceania, but had not previously been detected in Europe (Hoffmann *et al.* 2012). SBV rapidly spread across Europe during 2012 and by 2014 almost all European countries had been infected (EFSA, 2014). SBV infection can cause transient fever, diarrhoea and reduced milk production in cattle, and it has a teratogenic effect that causes mummified foetuses, stillbirths or severe congenital malformations in lambs and calves (Wernike *et al.* 2014). Vector competence assays have indicated that *Culicoides* species are likely to be able to transmit SBV (Veronesi *et al.* 2013; Balenghien *et al.* 2014), and SBV RNA has been detected in several countries in field-trapped *Culicoides* spp. including *C. obsoletus*, *C. scoticus*, *C. chiopterus* and *C. dewulfi*, which are commonly found on livestock farms (De Regge *et al.* 2012; Rasmussen *et al.* 2012; Elbers *et al.* 2013; Goffredo *et al.* 2013). The origin of *Schmallenberg virus* is so far unknown. Based on retrospective testing of archived samples there is no evidence of SBV infection in northern Europe prior to 2011 (Garigliany *et al.* 2012; Gerhauser *et al.* 2014) so it is likely to have been first introduced during early 2011 (Beer *et al.* 2013). SBV antibodies have been detected in sera collected from livestock in Turkey in 2006 (Azkur *et al.* 2013), which raises the possibility that SBV is circulating in an unknown endemic area outside Europe, and could have entered through introduction of infected *Culicoides* or infected animals (Tarlinton *et al.* 2012). Once introduced, infection spread rapidly across Europe, most likely by wind-borne spread of *Culicoides* (Beer *et al.* 2013), but other vectors or movement of infected livestock or wild animals could have played a role. SBV antibodies have been detected in a variety of wild species including red and roe deer (Linden *et al.* 2012; Laloy *et al.* 2014) and wild boar (Desmecht *et al.* 2013). Beer *et al.* (2013)

observe that SBV emerged in the same area as BTV-8, BTV-6 and BTV-11 a few years earlier, which may indicate that this part of Europe is at high risk for introduction of vector-borne diseases due to the combination of several factors; a high number of large international airports and ports, high human density creating high demand for importation of fresh produce from around the world, high cattle and sheep density, and the presence of competent vectors, *Culicoides* spp.

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first identified in 2012 in Saudi Arabia in a human patient with severe pneumonia and acute respiratory distress (Zaki *et al.* 2012). Since that date 1733 cases have been confirmed in 27 countries, of which 36% have died (<http://www.who.int/emergencies/mers-cov/en/> accessed 15/6/2016). All cases have occurred or originated in the Arabian Peninsula and Middle East, or are secondary to those cases. Disease investigations and serological studies conducted in the Middle East have provided strong evidence that dromedary camels are a host species and a source of human infection (Alagaili *et al.* 2014; Haagmans *et al.* 2014; Memish *et al.* 2014; Meyer *et al.* 2014; Reusken *et al.* 2014a). Antibody prevalence is also high in camels in many parts of Africa, but so far there has been no evidence of human MERS cases in Africa (Chu *et al.* 2014; Corman *et al.* 2014; Muller *et al.* 2014; Reusken *et al.* 2014b). Most MERS cases are secondary, mainly family or workplace contacts or nosocomial infections (WHO, 2013), but transmission is not sustained except where inadequate infection control is practiced (Hemida *et al.* 2015). The possibility that bats are a reservoir or bridge host has been explored and closely related betacoronaviruses have been detected in insectivorous bats in South Africa, Europe and China (Annan *et al.* 2013; Ithete *et al.* 2013; Yang *et al.* 2014). It is possible that the ancestor of MERS-CoV came from a bat, and then spilled over into camels and then to humans. Alternatively, bats might be a maintenance host with spillover into both camels and humans. The emergence of MERS from camels in the Arabian Peninsula could be explained by changes over the last few decades in camel-keeping. The camel population is estimated to have increased about ten times since the 1960s, and traditional extensive camel production is being replaced by semi-intensive and intensive sedentary production situated close to urban areas to supply demands for milk, meat and other camel products (Gossner *et al.* 2014; Hemida *et al.* 2015). Most of the camels traded in the Middle East are being imported from the Greater Horn of Africa (Corman *et al.* 2014; Muller *et al.* 2014).

Avian influenza is a pathogen that is constantly evolving through genetic drift and re-assortment, producing strains with variations in transmissibility

and pathogenicity in different hosts. The emergence and persistence of highly pathogenic avian influenza virus (HPAIV) H5N1 in Asia and Egypt provides an example of the challenge presented by complex eco-social systems. HPAIV H5N1 first emerged in China in 1996, and spread through South–East and parts of South Asia, becoming endemic in several countries. There have been sporadic introductions to Africa and Europe, but H5N1 has only become endemic in Egypt demonstrating the importance of the local ecosocial system in virus persistence (Pfeiffer *et al.* 2013). Wild water bird movements and poultry trade are the main mechanisms for long-distance spread, whereas local spread is influenced by the characteristics of the local poultry production and marketing system (Pfeiffer *et al.* 2011). In south-east Asia, small and medium-sized poultry producers appear to play a key role in maintenance of HPAIV H5N1. They keep chickens together with domestic water birds, and, through live bird trade networks, are connected with other consumers and other producers, in some cases across international borders. The poultry density and intensity of trade varies over space and time, depending on the demand for poultry meat and meat prices. This production system has contact with wild water bird populations, fighting cock networks, as well as large-scale industrial poultry production, all of which play a role in the spread of infection. Increasing demand from urban consumers has resulted in intensification of this live poultry trade, providing an environment that supports virus maintenance and the continuing emergence of new HPAIV H5N1 clades and variants of avian influenza (Pfeiffer *et al.* 2013). The recent emergence of avian influenza A (H7N9) in China provides an example of how these systems are able to generate new viruses, and in this case the absence of clinical disease in poultry meant that it was only recognized through fatalities in humans (Horby, 2013). In contrast the most recent human flu pandemic in 2009–2010 was caused by a virus of swine origin, influenza A (H1N1) that spread rapidly across the world through human-to-human transmission facilitated by our increasing global connectedness (Girard *et al.* 2010).

Diseases with extended geographical range

A number of existing diseases have expanded their geographical range, facilitated by trade networks of live animals and their products, and human movement (Hui, 2006; Karesh *et al.* 2012). *Bluetongue virus* is a vector-borne disease of domestic and wild ruminants transmitted by *Culicoides* midges, with 24 serotypes occurring widely across Africa, Asia and America. Apart from sporadic incursions to Spain and Portugal, Europe used to be free of bluetongue virus, but since 1998 at least five serotypes (BTV-1, -2, -4, -9 and -16) have been introduced

into Southern Europe from Africa and Asia and become endemic due to the northern expansion of the main vector *Culicoides imicola* associated with climate change, and the vector competence of indigenous European *Culicoides* sp. (Wilson and Mellor, 2009). In 2006, bluetongue occurred for the first time in Northern Europe. The serotype was identified as BTV-8, similar to strains found in sub-Saharan Africa, and it was transmitted by indigenous *Culicoides* sp. (Wilson and Mellor, 2009). It caused a large epidemic in domestic ruminants and then overwintered to re-emerge in 2007 and 2008. The initial route of introduction is unknown but could have been via movement of infected animals, animal products, or vectors introduced with imported goods or on ships or planes, with subsequent spread facilitated by unusually warm autumn temperatures that were suitable for vector survival and over-wintering (Saegerman *et al.* 2008; Wilson and Mellor, 2009). In the same area of Northern Europe, BTV-6 was detected in 2008 and BTV-11 in 2009, as well as *Schmallenberg virus* in 2011, indicating an apparent high-risk area for vector-borne livestock disease introduction (Beer *et al.* 2013).

West Nile virus is a mosquito-borne flavivirus with a sylvatic cycle in birds, which occurs in Africa, Europe, Asia and Australasia. It causes a febrile disease in horses and humans as well as infecting rodents and other small mammals, all of which are dead-end hosts. In 1999, it was introduced to New York, most likely by the transportation of an infected mosquito, bird or human, where it found a competent vector, *Culex pipiens*, and a large population of susceptible wild birds. This resulted in an epidemic in wild birds and humans, and the disease spread rapidly throughout the USA, to Canada, Central and South America via infected migratory and resident birds, dispersing mosquitoes, and human-assisted mosquito movements on trains, trucks and airplanes (Daszak *et al.* 2001; Marra *et al.* 2004; Pfeiffer and Dobler, 2010). Another mosquito-borne flavivirus, Zika, has also recently greatly extended its range. Previously, sporadic cases had occurred in Africa and Asia, but since 2007 it has caused a number of outbreaks in Pacific island countries, and in 2015 appeared for the first time on the American continent in Brazil, rapidly spreading across South and Central America. Zika is transmitted by various *Aedes* species; mainly *Aedes aegypti* in Asia and South America. Further spread of Zika into North America is expected due to air travel, international trade and the presence of competent mosquito vectors (Plourde and Bloch, 2016).

Ebola virus disease (EVD) was first detected in 1976 when outbreaks occurred in the Democratic Republic of Congo and South Sudan, causing severe disease with a high case fatality (Feldmann and Geisbert, 2011). The causative agents were identified as Filoviridae, a family of viruses that

includes Marburg virus and five species of Ebola virus; Sudan, Zaire, Bundibugyo, Cote d'Ivoire and Reston Ebolaviruses (Feldmann and Geisbert, 2011; Pigott *et al.* 2014). To date there have been 24 outbreaks in humans, all in equatorial Africa (Maganga *et al.* 2014; Pigott *et al.* 2014), although it is likely, based on serological evidence, that cases are underreported and some are asymptomatic (Groseth *et al.* 2007). For some of the outbreaks the source of index human cases has been identified as close contact with gorillas, chimpanzees, duikers or bats (Formenty *et al.* 1999; Leroy *et al.* 2004, 2009; Feldmann and Geisbert, 2011). Secondary cases are usually in-contact family members, health-care workers, or nosocomial infections (Pigott *et al.* 2014). The natural reservoir of Ebola virus has not yet been confirmed, but there is increasing evidence that bats could be a reservoir host for Zaire Ebolavirus (Leroy *et al.* 2005, 2009; Pourrut *et al.* 2009).

In March 2014, there were cases of a high mortality haemorrhagic fever in Southeast Guinea, which was diagnosed as Ebola virus disease due to Zaire Ebolavirus, the first outbreak in West Africa. Investigation showed that the likely index case was a child who died in December 2013 (Baize *et al.* 2014) and the source of infection was possibly fruit or insectivorous bats (Saez *et al.* 2015). In the time between the index case and outbreak diagnosis, the virus infected the child's family and healthcare workers, and then relatives and contacts of these secondary cases in other villages and the local hospital, from where it spread to other prefectures. By the time of diagnosis there were multiple chains of transmission over a wide area (Baize *et al.* 2014) and into neighbouring Liberia and Sierra Leone. It subsequently spread to urban areas including the capital cities of all three countries (Gire *et al.* 2014; Wallace *et al.* 2014; Gostin and Friedman, 2015). By the end of 2015 there had been 28 637 confirmed, probable and suspected cases of which 40% have died (WHO, 2016). The largest previous outbreaks have had no more than 500 cases.

Serological and molecular evidence indicated that this virus had been present in the region for at least 10 years, and there had probably been previous undiagnosed spillovers (Dudas and Rambaut, 2014; Schoepp *et al.* 2014). The outbreak area is a mosaic of farmland, savannah, bush and forest, maintained by human activity for several centuries (Wallace *et al.* 2014; Huff and Winnebah, 2015). Both fruit and insectivorous bats are common, and fruit bats are traditionally hunted and eaten (Bausch and Schwarz, 2014; Saez *et al.* 2015). The main recent land use change in the region has been large land leases for intensive agriculture, which have led to habitat fragmentation and decreased biodiversity, affecting bat migratory and feeding patterns (Wallace *et al.* 2014; Huff and Winnebah, 2015). If

bats are a reservoir for Ebola virus, then the possibility of spillover into humans has been there for many years, but recent land use changes may have increased the risk (Huff and Winnebah, 2015).

It is likely that a combination of factors led to the unprecedented size of the outbreak. Liberia and Sierra Leone are both recovering from recent conflict, and Guinea has a history of poor governance leading to distrust of government and authorities (Bausch and Schwarz, 2014; Piot, 2014; Gostin and Friedman, 2015). Lack of investment in health services post-conflict (Heymann *et al.* 2015) meant that health services were understaffed and poorly equipped with limited community-based services so communication and surveillance were weak. Together with no previous experience of Ebola these factors contributed to the delayed diagnosis of Ebola, and nosocomial infections that amplified the outbreak (Baize *et al.* 2014; Wallace *et al.* 2014; Gostin and Friedman, 2015; Huff and Winnebah, 2015). The delayed diagnosis was compounded by a slow and inefficient national and international response (Piot, 2014; Wallace *et al.* 2014), and an initial top-down authoritarian approach to control that did not take into account local culture and institutions, led to non-compliance with control measures (Gostin and Friedman, 2015). Infection therefore spread rapidly across the three countries and into high density urban and peri-urban populations (Pigott *et al.* 2014; Gostin and Friedman, 2015). The area in Guinea where the epidemic started is a rural area populated by a number of small marginalized ethnic groups, an area of underdevelopment that has also hosted refugees from the neighbouring countries (Bausch and Schwarz, 2014; Wallace *et al.* 2014). There is a lack of trust in western medicine, so top-down messages about Ebola virus disease were not believed, and some traditional funeral practices led to spread of infection (Piot, 2014; Gostin and Friedman, 2015). All these factors were exacerbated by increasing human population, urbanization, increasing connectivity, and high rates of poverty in all three countries (Bausch and Schwarz, 2014; Pigott *et al.* 2014; Piot, 2014). Several authors have highlighted the role played by informal urban and peri-urban settlements in Ebola transmission. These overcrowded settlements have poor water, sanitation, health services and other infrastructure, and conventional approaches to infectious disease control such as isolation and quarantine are very difficult to implement (Snyder *et al.* 2014; Waldman, 2015).

Plasmodium knowlesi provides an excellent recent example of how eco-social processes have led to the emergence of a parasitic disease. This protozoan parasite causes malaria in humans and was first observed in the blood of long-tailed macaques in 1927 and soon afterwards experimental infection was demonstrated in humans (Antinori *et al.* 2013).

The first natural human infection was reported in the 1960s in an American working in the forests of peninsular Malaysia but no other human cases were detected (Chin *et al.* 1965; Singh and Daneshvar, 2013). Then in 2004, Singh and colleagues reported on a large number of naturally acquired *P. knowlesi* infections in humans in Sarawak, Malaysian Borneo (Singh *et al.* 2004), and since then *P. knowlesi* cases have been identified elsewhere in Malaysia and across Southeast Asia (Singh and Daneshvar, 2013). Over 50% of microscopically confirmed malaria cases in Malaysia are due to *P. knowlesi* (Yusof *et al.* 2014) and there is evidence for an increasing incidence of *P. knowlesi* in Sabah, Malaysian Borneo (William *et al.* 2013, 2014). Although heightened awareness of *P. knowlesi* and improved diagnostic techniques have likely contributed to the rise in *P. knowlesi* reporting, the fact that *P. knowlesi* infections have risen relative to other malaria species suggest that there is a real increase in *P. knowlesi* cases. This has public health significance as *P. knowlesi* can cause serious morbidity and death (Cox-Singh *et al.* 2008).

The geographic range of the *P. knowlesi* parasite is limited by the distribution of the vectors (mosquitoes in the *Anopheles leucosphyrus* group) and the two main reservoir hosts, long-tailed and pig-tailed macaques (*Macaca fascicularis* and *Macaca nemestrina*) (Moyes *et al.* 2014). To date there is no evidence of sustained human-to-human transmission of *P. knowlesi* and humans appear to be infected when they spend time on farms or in forested areas close to macaques (Imai *et al.* 2014; Vythilingam *et al.* 2014). Forests are shrinking across southeast Asia (Hansen *et al.* 2013) and it has been postulated that deforestation and the accompanying environmental changes are one of the major drivers for emergence of *P. knowlesi* as such changes can lead to increased spatial overlap between humans, macaques and vectors (William *et al.* 2013). A recent study investigating the relationship between landscape factors and spatial distribution of *P. knowlesi* in Sabah revealed that numbers of *P. knowlesi* cases at the village level were associated with forest cover and historical forest loss in the surrounding areas (Fornace *et al.* 2016), thus supporting the hypothesis that deforestation is a key driver for *P. knowlesi* transmission in this location. This is backed up by predictions of the geographical distribution of macaque reservoir hosts and *P. knowlesi* vectors, which indicated that long-tailed macaques and vectors of the Leucosphyrus Complex were likely to be found in areas of disturbed forest, which could bring them into contact with humans (Moyes *et al.* 2016). Changes in vector behaviour or species as a result of deforestation and vector control may also play a role in *P. knowlesi* emergence but further research is needed to confirm this.

Apart from *P. knowlesi*, there are numerous other *Plasmodium* species which infect non-human

primates. An analysis of the likelihood of natural zoonotic transmission of these other 'monkey malarials' was published in 2009 (Baird, 2009), and predicted that *P. cynomolgi* transmission to humans was highly likely and indeed the first case of naturally acquired *P. cynomolgi* infection was reported in 2014 (Ta *et al.* 2014). As deforestation and non-human primate habitat degradation is continuing in many parts of the world, it is to be expected that there will be increasing reports of zoonotic transmission of primate malarials in the future.

Chagas disease is a chronic condition caused by the protozoan parasite *Trypanosoma cruzi* and is endemic to Latin America (Rassi *et al.* 2010). Chagas is primarily a vector-borne disease transmitted by blood-sucking triatomine bugs. However, transmission can also occur by blood transfusion or organ donation, from mother to infant and through consumption of *T. cruzi*-contaminated food and drink (Rassi *et al.* 2010). Over the past 30 years substantial progress has been made in control of Chagas disease in Latin America through implementation of national and international programmes with a large focus on vector control (Dias, 2007).

Despite the general decrease in Chagas disease across Latin America, there have been reports of disease emergence in certain locations within this region. For example, human Chagas cases are on the increase in the Amazon region of Brazil. In this area *T. cruzi* infection is endemic in a variety of wild animals and transmitted by sylvatic triatomine bugs (Coura *et al.* 2002). It is generally considered an anthrozoosis, acquired when humans enter the forest to hunt, collect plants or as tourists or when sylvatic triatomine bugs invade human dwellings, attracted by light (Coura and Junqueira, 2012). However, there have been disease outbreaks caused by consumption of contaminated food and drink (Coura *et al.* 2002). Various human activities are increasing the risk that Chagas disease will become endemic in the Amazon region. Firstly, there is uncontrolled deforestation in the region, which is driving the adaptation of sylvatic triatomine bugs to human dwellings, due to the reduction in numbers of wild mammals, their natural food source (Dias *et al.* 2002; Coura and Junqueira, 2012). In addition, Vaz and colleagues demonstrated that *T. cruzi* seroprevalence in small wild mammals in fragmented forest environments was higher than in continuous forest, likely due to low diversity of small mammals and increased abundance of marsupials, which could favour transmission to humans (Vaz *et al.* 2007). Secondly, there is increasing migration of humans and domestic animals from Chagas endemic areas into the Amazon region, due to improved roads, hydroelectric power and oil and gas exploration (Coura and Junqueira, 2012), which could lead to importation of different *T. cruzi* strains and domestic triatomines. In other

areas of Latin America, for example in the foothills of the Colombian–Venezuelan plain, increased cultivation of African oil palm is providing an excellent habitat for the *T. cruzi* vector *Rhodnius prolixus*, which can then rapidly re-infest houses after insecticide spraying (Guhl *et al.* 2009). The movement of infected people from rural to urban areas and increased urbanization, often with poor quality housing where vectors can thrive, has led to emergence of Chagas in urban areas of Latin America (Delgado *et al.* 2013; Pinazo and Gascon, 2015).

In recent years, there has also been an emergence of Chagas disease in historically non-endemic regions, mainly driven by migration of people from Latin America to other parts of the world (Bonney, 2014). It is estimated that there are approximately 300 000 infected people in the USA and 80 000 in Europe (Coura and Vinas, 2010). It can take between 10 and 30 years from initial infection to clinical presentation, so many infected individuals are unaware of their infection status, meaning that there is a risk of transmission of *T. cruzi* via blood transfusion or organ donation in non-endemic countries (Angheben *et al.* 2015). Although triatomine bugs are found in the USA, very few autochthonous Chagas cases have been reported. However, climate change and lack of physician awareness about the disease mean that there is potential for emergence of Chagas as an endemic disease in this country (Lambert *et al.* 2008).

ECO-SOCIAL SYSTEMS AND DISEASE EMERGENCE – ECOHEALTH OR ONE HEALTH

As the above examples demonstrate, the eco-social system changes that have occurred particularly over the last 20 years have created an environment in which pathogens can emerge and spread very quickly around the world, and it is predicted that there will continue to be significant change over the next few decades, and the rate of change is likely to accelerate, unless there is a major global paradigm shift towards sustainability. Efforts to understand and mitigate the risk of disease emergence need to acknowledge the complexity of this global system, requiring an inter-disciplinary approach bringing together social, medical and natural scientists as advocated by One Health and Ecohealth approaches (Wood *et al.* 2012; Zinsstag, 2012).

The widely used risk analysis approach to disease management, synthesizes scientific evidence to assess risk, from which decision-makers can develop appropriate risk management activities. The emphasis in risk analysis tends to be on biomedical science, rather than socio-economic drivers of disease risk, but it is now clear that effective management of the disease threats associated with eco-social system changes requires a systems approach (Pfeiffer, 2014). Coker *et al.* (2011) presented a conceptual framework

for such an approach within a One Health context, emphasizing the importance of the institutional and the wider societal context in which disease occurs. Different stakeholders are likely to have different and sometimes contradictory goals in relation to risk of disease emergence, so an inter-disciplinary approach is necessary to be able to explore the wider system context and provide evidence to support policy change for improved human, animal and ecosystem health and wellbeing (Wood *et al.* 2012). Wilcox and Colwell (2005) use an eco-social approach, combining concepts and theory of population, community and systems ecology, to develop a theoretical framework for global zoonotic disease emergence that integrates anthropogenic and biological processes from molecular and cellular level to global scales.

CONCLUSION

Eco-social processes have increasingly influenced the human–animal–environment interface in the past few decades, leading to increasing risk of disease emergence and spread, and this trend is likely to continue in the near future unless there is a major paradigm shift towards sustainable management of our world. To mitigate the impact of disease we need to embrace systems-thinking and inter-disciplinary approaches, not just integrating human and animal health, but also environmental and social science, to be able to adequately take into account the societal context in which disease occurs and is managed.

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