Infections at the Animal/Human Interface: Shifting the Paradigm from Emergency Response to Prevention at Source

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Abstract The majority of emerging infectious diseases have their source in animals, and emergence occurs at the human/animal interface, when infections in animals breech the species barrier to infect humans, the population in which they are often first identified. The response is frequently characterized by a series of emergency activities to contain and manage the infection in human populations, and at the same time to identify the source of the infection in nature. If infection is found to have a source in animals, and if animals cause a continuous threat of human infection, culling is often recommended with severe economic impact. Currently, efforts are being undertaken for closer interaction at the animal/human interface through joint surveillance and risk assessment between the animal and human medicine sectors, and research is underway in geographic areas where emergence at the animal/human interface has occurred in the past. The goal of this research is to identify infectious organisms in tropical and other wild animals, to genetically sequence these organisms, and to attempt to predict which organisms have the potential to emerge in human populations. It may be more cost-effective to learn from past emergence events, and to shift the paradigm from disease surveillance, detection, and response in humans; to prevention of emergence at the source by understanding and mitigating the factors, or determinants, that influence animal infection. These determinants are clearly understood from the study of previous emergence events and include human-induced changes in natural

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environments, urban areas, and agricultural systems; raising and processing animal-based foods; and the roles of global trade, migration, and climate change. Better understanding of these factors learned from epidemiological investigation of past and present emergence events, and modeling and study of the cost-effectiveness of interventions that could result in their mitigation, could provide evidence necessary to better address the political and economic barriers to prevention of infections in animals. Such economically convincing arguments for change and mitigation are required because of the basic difference in animal health—driven by the need for profit; and human health—driven by the need to save lives.

Contents

1 Infections at the Animal/Human Interface

Severe Acute Respiratory Syndrome (SARS) was the first major emerging infection identified during the twenty-first century (Parashar and Anderson 2004). A close examination of the outbreak—its origins, the human sickness and death it caused, the national and international responses that occurred, and the effect these responses had on Asian economies—provides a clear lesson of the importance of emerging infections at the animal/human interface, and underscores the reasons that emerging infections must be rapidly detected, assessed, and managed. But understanding and mitigating the factors that align to cause emergence could move this current paradigm of detection, assessment, and response further upstream, to prevention of emergence at its source.

Severe Acute Respiratory Syndrome (SARS) was first detected as a severe atypical pneumonia in the Guangdong Province of China (Heymann and Rodier 2004a). It soon became a burden in hospitals where many patients required respiratory support, and broad-spectrum antibiotics had no effect. As is common with emerging infections, particularly when they present with symptoms common to other known infections, unsuspecting hospital workers became infected. They in turn inadvertently infected family members, and infection then spread to the communities in which they lived (Heymann and Rodier 2004b).

One of these health workers—a medical doctor—travelled to Hong Kong where he stayed in a hotel on the same floor as both Chinese and international guests. Some of these hotel guests became infected. Hypotheses of how they were infected ranged from transmission by aerosols—generated by the infected doctor by cough, sneeze, or vomit—in the corridors or through the hotel ventilation system to shared closed environment such as sharing the same lift (Chan-Yeung and Xu 2003). Some of the infected hotel guests travelled while still in the incubation period, and as illness developed and became serious they were admitted to hospital in Hong Kong, Singapore, Canada, and Vietnam. Hospitalized, they too became the source of infection for hospital workers who in turn served as unintentional amplifiers of transmission to their families and communities.

Molecular and epidemiological investigation suggested that the infection of the index case—never identified—was an onetime event (Walker et al. 2012; Xu et al. 2004). As more information became available, it was further hypothesized that this initial infection was due to close contact with an infected animal, possibly a civet cat, in one of the province's many live (wet) animal markets (Woo et al. 2006). The animal host was thought to have been a carrier of a coronavirus that mutated while replicating, either in the animal or an infected human, in such a way as to cause severe human illness (Wang and Eaton 2007).

The world's interconnectivity through air transport facilitated the international spread of SARS. Precautionary travel advisories were made by the World Health Organization (WHO) recommending that people avoid unnecessary travel to countries where outbreaks were occurring, and by July 2003, just over 7 months after the SARS coronavirus was thought to have emerged, human to human transmission had been interrupted and the outbreak was declared over (Heymann 2006).

SARS resulted in 8,422 probable infections and 916 (11 %) deaths (Chan-Yeung and Xu 2003). The economic impact of the outbreak on GDP was estimated at US$30–100 billion from decreased commerce, travel, and tourism (Keogh-Brown and Smith 2008). Unlike HIV, which is thought to have emerged during the late nineteenth or early twentieth century, the SARS coronavirus did not become endemic, and economic recovery was rapid.

SARS and other emerging infections share a common theme: infection is often first detected in human populations in which an emergency containment response occurs, most times before the source of infection is understood. Initial recommendations for control are thus based on what evidence is available from the current outbreak or previous outbreaks caused by similar organisms. They are of necessity precautionary, and often severe. And as for SARS, the burden and response can cause a wide-ranging negative impact to economies.

If it were possible to identify infectious agents carried by wild and domestic animals and to predict if, when and where they would emerge in humans, and if these animals could then be somehow removed from contact with humans or cleared of infection, human sickness and death could be prevented and economies protected. Studies are underway to identify and characterize infectious organisms in wild animals in geographic sites where emerging infections are known to have occurred in the past (Grace et al. 2012; Jones et al. 2008; UC Davis: Vet Medicine 2009). Though it is possible through these studies to understand the variety of infectious agents carried by wild animals, prediction of which organisms will emerge in human populations using genetic sequence or other information will likely be very challenging and as yet is not possible (Biek and Real 2010).

Moving further upstream, investigation of individual emergence events can identify the risk factors, or determinants, that align to cause the putative breaches in the animal/human species barrier. If these risk factors could in some way be mitigated, the risk of future emergence could be decreased. The current paradigm of emergency response, and the concurrent attempts at prediction and prevention, could then be shifted further upstream.

2 Shifting the Paradigm

In the case of SARS, there was a flurry of field research activity in the Guangdong Province during and just after the outbreak, but over time funding decreased and research slowed. Among the research that was completed was a study of workers in some of the province's wet markets that suggested that up to 22 % (12/55) had antibody evidence of a coronavirus infection related to the SARS coronavirus, but that none had a history of severe respiratory symptoms such as were occurring in persons with SARS (Parry 2003). Further field research might have helped to better understand the risk factors for emergence, but it was not conducted, and the epidemiology remains unclear.

Risk factors for emergence, in addition to being a market worker as suggested by the completed study, might also include being a hunter of wild animals, being a restaurant worker who kills and or butchers/prepares wild animal meat for consumption, or being a member of a household who buys live or recently killed wild game meat from a wet market (Weiss and McMichael 2004; Wolfe et al. 2007).

Even though evidence is available from just one epidemiological study of SARS, a series of actions outside the human and animal health sectors could be useful in preventing a future outbreak in the Guangdong Province from another emerging pathogen (Daszak et al. 2012; Wood et al. 2012). These include education of all those who come into contact with wild game (and domestic animals) about how to protect themselves against infection; regulation with enforcement of wet markets and eating establishments that does not drive these activities underground, but rather ensures safe animal handling; and regulation and enforcement of trade between hunters and markets, and between markets and those who purchase. Other activities might be research to determine whether wild animals (e.g. civet cats) could be raised commercially under conditions that prevent their infection and risk to humans—or further downstream, more effective education of health workers about infection control. This latter activity would ensure that if other actions such as those above fail to prevent emergence, amplification of transmission of emergent organisms could be prevented.

Risk factors for emergence events caused by a more broad range of organisms might occur in sectors such as plant agriculture, community planning, water, and sanitation. Human migratory dynamics, land-use approaches, and the influence of climate and manipulation of natural ecosystems can also amplify known risks, and create novel emergence pathways (Patz et al. 2008).

Mitigation of the risk factors for emergence thus requires a focussed and collaborative effort across multiple disciplines—a one health approach, as defined by the American Veterinary Medical Association (2008) (American Veterinary Medical Association 2012). Emergence may occur among humans living and working in small rural farming communities carved out of tropical rain forests, savannah, mountains, and desert that are in close proximity to wild animals, or to domestic animals they tend that have been in close proximity to wild animals. Outbreaks of Nipah and Ebola Reston Virus infection in pigs raised in unprotected environments in Malaysia and the Philippines, respectively, are an example, and both outbreaks spilled over into human populations (Luby et al. 2009; Miranda and Miranda 2011).

Emergence may occur in larger urban communities where human contact with animals is limited to a few farm animals in close proximity to households, to domestic pets, or to rodents and other animals that have adapted to the urban environment (Alirol et al. 2011). Animals come in contact with humans or other animals as they range (e.g. cows and chickens in parts of Asia) or browse (e.g. urban foxes and rodents) (Bradley and Altizer 2007). The continued high rate of contact between humans and poultry in both smaller backyard farms and larger market system farms continues to permit repeated human exposure to the H5N1 influenza A virus that is endemic in poultry stock. Children and adults are thought to have been infected by contact with living chickens in backyards, and adults have been shown to become infected at some point during the process of raising or slaughtering/butchering chickens (Kerkhove et al. 2011).

Risk factors of emergence in these settings are lacking or inadequate community planning, lack of understanding by populations about risks associated with animal contact, failure to adopt and adhere to safe farming and slaughter/food processing and preparation practices, and failure to maintain sanitation and water infrastructure. Mitigation across all these sectors would require empowering communities to develop a safer living environment through urban planning, developing and maintaining robust water and sanitation infrastructure, controlling rodent and other animal populations in both peri-urban and urban areas, ensuring safe animal husbandry, and providing understanding of risks through community-based education (Fobil et al. 2012).

Risk factors for emergence also occur all along the food chain. Growing demand for animal-based food has led to the ever more complex food chains that involve live animal processing and trade networks (Schlundt et al. 2004). Prevention of infectious disease emergence through the food chain and agricultural system requires understanding of the risks at each step along the pathway from the farm to the fork. If infectious agents pass through the food chain and enter foods, their impact can be minimized at the final intervention point, where animal-derived foods can be prepared carefully in the factory, restaurant, and household either by cooking or other means to remove or mitigate the risk of infection. Others must be controlled earlier—during the period animals are being raised, during slaughter, and during transport (Collins and Wall 2004).

Climate change also appears to be a factor in emergence of human infection. Rainfall associated with ENSO (El Niño/*Southern Oscillation*) in East Africa, for example, has contributed to frequent outbreaks of Rift Valley fever as a result of flooding that increases breeding sites of the mosquito vector (Anyamba et al. 2009). The frequency of leptospira transmission from rodents to humans has been shown to increase during events in Latin America, Bangladesh, and India following heavy rains and flooding (Lau et al. 2010). Lassa fever has also emerged after severe drought in Sierra Leone, when rodents carrying the Lassa virus were forced to move closer to humans so that they could survive on agricultural products in cultivated fields or storage facilities, contaminating human food supplies (Bonner et al. 2007).

Risk factors related to climate change are multiple, and in addition to more robust civil engineering projects to prevent flooding and channel water for irrigation, better rodent and wild animal control is required, as is continued participation in the negotiation of the International Climate Control Treaty (Tol et al. 2007).

Finally, overuse of antibiotics in livestock animals is thought to be a risk factor for the emergence of antimicrobial-resistant bacteria in animals. Though there is still much debate within the scientific community as to the contribution of antibiotics in farming systems to the rise of antibiotic resistance, the implications on emerging antibiotic resistance in human populations is even less well understood (Barton 2000). But there is general consensus that farming systems are likely to contribute to the flow of antibiotic residues and resistant microbes in the wider ecosystem and in humans by runoff into water used or consumed by humans, especially in economically poor settings where farming communities exist alongside densely populated human environments with poor sanitation/sewage systems (Abraham 2011; Segura et al. 2009). Clearly, cross-sector action is required to mitigate these risks using the example of the connection between antimicrobial resistance in both animal and human sectors provides a key lesson for ensuring interdisciplinary planning is incorporated when designing zoonotic control strategies.

3 The Opportunity

There is an opportunity to learn from past emergence events, and from those that are presently occurring or will occur in the future. Application of what has been learned can help shift the paradigm from detection, assessment, and response to prevention at the source. But solid evidence must be available or obtained, assessed for risk, and used. There is a great amount of scientific knowledge about the risk factors of emergence and their mitigation already available from previous investigation and risk assessment. Much more can be obtained from in-depth study

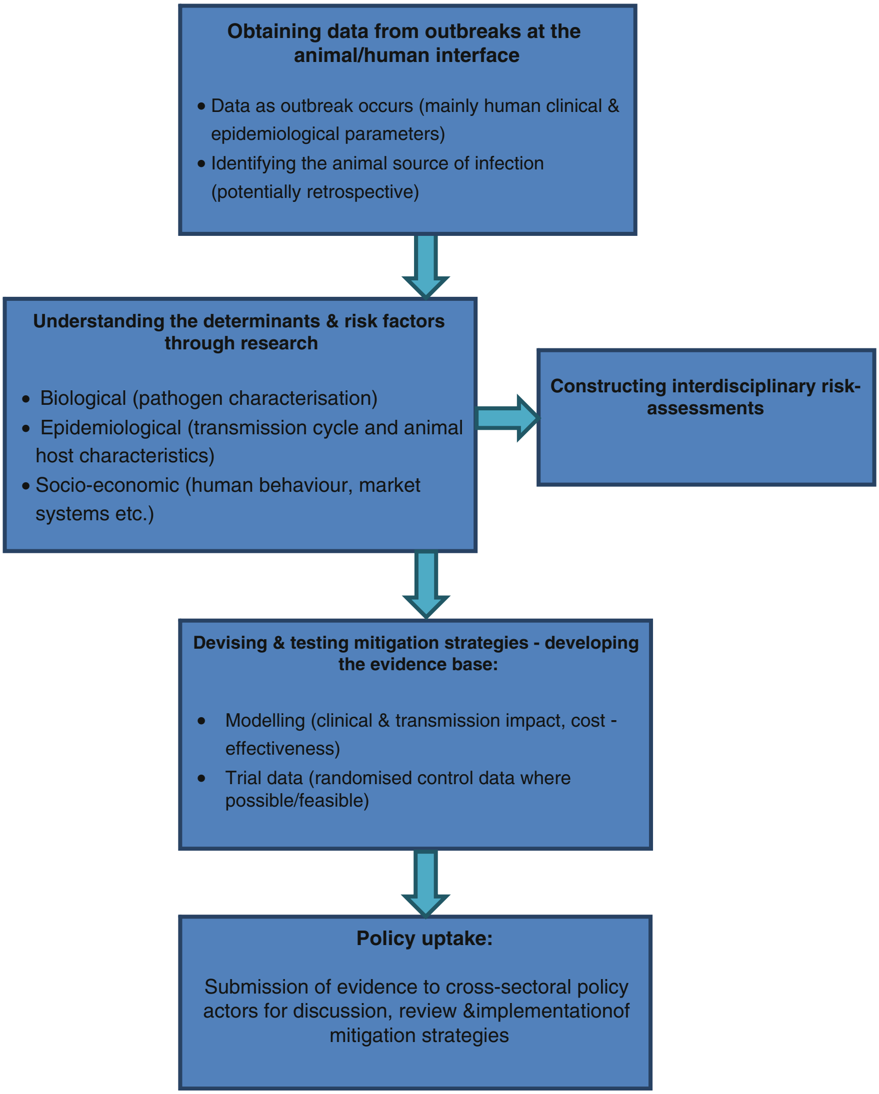

Fig. 1 Transforming evidence at the animal/human interface into policy, a simple flow chart

of each emergence event as it occurs. Research must also take into account human behavior, and ensure that populations most at risk clearly understand the measures required to reduce or protect behavior that is high risk. Many emergence events occur in well-defined geographical areas involving the poorest communities, so designing interventions and strategies that are cost-effective and sustainable will be imperative.

Many of the measures required to shift the paradigm will encounter political barriers, especially when commercial benefits are at stake, and these barriers will need to be broken down by using clear and easy to understand evidence from cost-effectiveness and of a variety of risk mitigation strategies (Fig. 1). By working together at the animal/human interface using a one health approach, emergence events in the future can be decreased, and lives and economies saved.

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