State

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Rapid livestock intensification, food chain dynamics and disease

The late twentieth and early twenty-first centuries have seen an unprecedented increase in the international supply of animal-source foods, featuring integrated production, processing and distribution chains. Intensive production is applied at a large scale, in confined feeding operations for beef cattle, dairy plants, and mass rearing units for poultry and pigs. These involve the congregation of large numbers of genetically identical animals of the same age (young) and sex, with rapid turnover and "all-in, all-out" systems. Strict bioexclusion and health protection regimes generally prevent infectious disease outbreaks, but major disease outbreaks occur occasionally, when a pathogen performs a virulence jump, escapes the vaccine used, acquires resistance to the antibiotics applied, or travels along the food supply chain (Engering, Hogerwerf and Slingenbergh, 2013). These break-out pathogens sometimes present serious veterinary public health threats.

In countries where intensive livestock production units are located amid a myriad of traditional, extensive and diversified farming systems, it is likely that a new pathogen arising in an intensive system will turn endemic. Avian influenza (AI) viruses, in particular, are evolving into a large, diverse virus gene pool, circulating in an avian host reservoir comprising both wild birds and poultry, and occasionally also infecting swine and humans. AI viruses respond to the contrasting conditions of intensive versus extensive systems, terrestrial versus aquatic poultry, and domestic versus wild avian host reservoirs. A main example is H5N1 HPAI. Risk factors associated with the spread and persistence of this virus in Asia are the rapid increase in demand for poultry products and the associated growth of poultry industries; the mixing of new and old poultry farming systems; the presence of live bird markets; contact between poultry and wild waterfowl; and poor sanitation

(Hogerwerf *et al.*, 2010). H5N1 HPAI emerged as a virulence jumper in domestic waterfowl in 1996, eventually paving the way for a panzootic of the H5N1 subclade 2.2 viruses, presumably vectored by migratory birds, in 2006 (Sims and Brown, 2008). The extent of H5N1 virus spillover from poultry to humans was found to be broadly proportional to the disease occurrence in poultry, with a few unconfirmed incidents of human-to-human transmission. In theory, a mere five mutations could make this virus transmissible by air (Herfst *et al.*, 2012). A growing number of AI viruses – including the low pathogenic avian influenza H7N9 virus first reported in late March 2013 in China – carry a molecular signature associated with human adaptation and are a significant public health concern (FAO, 2013a; Lai *et al.*, 2013; van Riel *et al.,* 2013).

The current intensive poultry production networks present a global meta-population of genetically uniform broiler hybrids and layer hens. Poultry industries are connected through input supplies, including day-old chicks, and through slaughtering, processing, distribution and marketing. The emergence, worldwide spread and persistence of virulent infectious bursal disease strains (Saif, 1998) and of viruses causing infectious bronchitis and infectious laryngo-tracheitis have arguably been facilitated by the presence of globalized poultry production chains.

Intensive pig production, with intercontinental shipments of live piglets, is believed to influence the composition of the global swine influenza gene pool. The origin of swine influenza goes back to the human influenza pandemic in 1918–1919, when influenza was observed in swine for the first time (probably transmitted from humans to pigs). Since then, this H1N1 virus has been circulating in pigs, with minor antigenic drift (Brown, 2000; Webster *et al.*, 1992). Pigs have been indicated as "mixing vessels" because they support reassortment of avian and human influenza, resulting in novel variants; several unique reassortants of avian/human/swine origin currently circulate in swine (Kobasa and Kawaoka, 2005). A new H1N1 pandemic influenza A virus (pH1N1), presumably of swine origin, emerged in March 2009 in Mexico and the United States of America and rapidly spread throughout the world, causing the first influenza pandemic of the twenty-first century (Neumann, Noda and Kawaoka, 2009; Novel Swine-Origin Influenza A [HINI] Virus Investigation Team, 2009; Trifonov *et al.*, 2009). The pH1N1 virus may have been circulating primarily in swine for more than ten years; genetic analysis revealed that this virus is derived from a triple reassortant (human/avian/swine) and a Eurasian avian-like swine H1N1 virus (Garten *et al.*, 2009; Smith *et al.*, 2009; Trifonov *et al.*, 2009). While the location of the pig-to-human virus jump remains unknown, the aetiology and emergence of this quadruple reassortant suggest a hypothesis involving intercontinental movement of live pigs.

The emergence of porcine reproductive and respiratory syndrome (PRRS) virus in pigs – also called "blue ear disease" – was first recognized in the United States of America (in 1987) and Europe (in 1990), both of which feature intensive pig industries. PRRS assumed panzootic proportions within years (reviewed in Albina, 1997; Cho and Dee, 2006). In China, a highly virulent strain of PRRS emerged in 2006, causing "porcine high fever syndrome", with high mortality in pigs of all ages (Zhou *et al.*, 2008). The epidemic affected more than 2 million pigs, of which 400 000 died (FAO-EMPRES, 2008). This PRRS variant has since become dominant in China, with half the world pig population, from where it has spread over the past three to five years to Viet Nam, Cambodia, Thailand, the Philippines and India/West Bengal.

The Q fever bacterium is an example of an aggressive disease agent emerging in intensive ruminant systems. In 2007, an acute epidemic form of Q fever (which is otherwise a low pathogenic, ubiquitous pathogen caused by the bacterium *Coxiella burnetti* and with mainly ruminant hosts) emerged in the Netherlands in dairy goats, spilling over to humans. The epidemic continued until 2010 and was brought


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under control following stamping out measures and vaccination. Reported drivers include high-density rearing of dairy goats and the proximity of humans to goat farms (Tilburg *et al.*, 2012).

Food safety hazards and antimicrobial resistance represent a twofold concern of growing importance. In recent years, outbreaks of food-borne diseases with significant impacts on health care systems and agricultural production are increasing. The common form of food poisoning results from faecal contamination of food and water. While enteric bacteria are beneficial and commonly found in the digestive tracts of humans and warm-blooded animals, including livestock, bacteria may sometimes turn harmful. Some enteric bacteria are known for their ability to exchange genetic material via mobile genetic elements such as plasmids and bacteriophages, and readily adapt to new and stressful environments. These factors are believed to contribute to the emergence of pathogenic types. This process may concern a bacterium displaying enhanced environmental survival and persistence in food systems, increased pathogenicity in human and animal hosts, and/or resistance to antimicrobials.

Antibiotics are frequently used in intensive livestock production to cure and prevent diseases or as feed additives for growth promotion. The large-scale utilization of antibiotics and chemoprophylactics drives the emergence of pathogens that have acquired resistance to these drugs (Gootz, 2010; Malim and Emerman, 2001). Genes conferring antimicrobial resistance are a natural phenomenon in bacterial communities, even in places and host reservoirs that are out of reach of human and veterinary medicine (D'Costa *et al.*, 2011). The presence of antimicrobial resistance genes in itself is therefore not new, but the widespread use of antimicrobials may enhance the circulation of these genes in microbes in food and agriculture.

A prime example of antimicrobial resistance involving livestock is methicillin-resistant *Staphylococcus aureus* (MRSA). Six months after methicillin was marketed in 1960, three methicillin-resistant isolates were reported (Grundmann *et al.*, 2006). MRSA can cause infection in pigs, several other domestic animals, and humans; there have been several cases of transmission of MRSA between cows and humans (Holmes and Zadoks, 2011). Further examples comprise the emergence in a rapidly growing number of countries of *Escherichia coli* O157:H7 infections in humans, associated with cattle feedlots; and the *E. coli* O104:H4 that emerged in Germany in 2011 via bean sprouts presumably contaminated with faecal material (Rohde *et al.*, 2011).

It would be misleading to suggest that disease emergence in livestock is specific to intensive systems. Extensive, low-input, low-output smallholder livestock systems require more animals per unit of animal-source food produced than intensive systems. Animals roaming around freely and kept at a high density tend to facilitate the circulation of pathogens, and the exchange of pathogen genetic material through coinfection by different viruses or bacteriophages. This may be illustrated by the growing dairy smallholder subsector in the Indian subcontinent, which presents both a remarkable success story and a source of infectious ruminant disease. Smallholder dairy production in the Indian subcontinent is essential to food security and the rural economy. In 2010, India and Pakistan together produced 147 million tonnes of cow/buffalo milk (FAOSTAT, 2012). Milk production increased by about 5.5 million tonnes, or 4.0 percent/year, from 2002 to 2007 (FAO, 2010). The number of dairy farms in India and Pakistan

totalled 89 million; with a combined herd size of 140 million head of cattle and buffaloes, the average number of animals per farm was therefore only 1.57, with an average yield of about 1 000 kg of milk/animal/year (for comparison, an intensive dairy farm in the United States of America may involve hundreds of lactating cows producing over 10 000 kg of milk/animal/year). Cheap feed sources compensate for the low feeding efficiency, so small-scale milk producers incur low production costs and are able to compete with large-scale, capital-intensive, high-tech dairy farming systems. At the same time, the Indian subcontinent is the world epicentre for ruminants, and high-impact ruminant diseases such as haemorrhagic septicaemia, brucellosis, sheep and goat pox, foot-and-mouth disease (FMD) and peste des petits ruminants are endemic. One of the last remaining foci of rinderpest virus detected during GREP was in Pakistan. FMD viruses circulating in Pakistan continually show up in countries to the west, assuming source-sink dynamics. Hence, the prevalence of infectious ruminant disease in the Indian subcontinent is a concern to both the local and the international livestock sectors.

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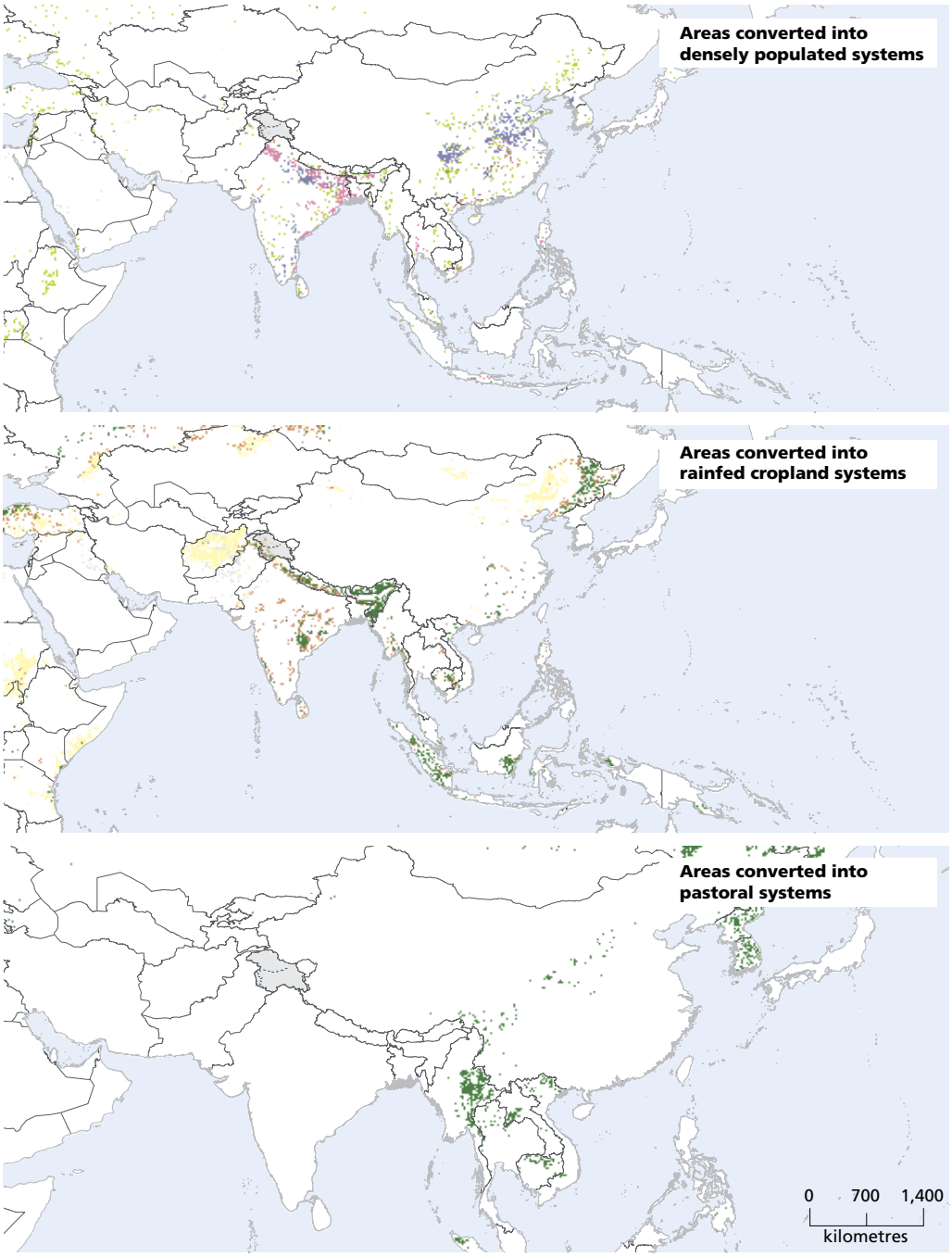
Land pressure, deforestation and disease

Animal agriculture strongly affects the state of the world's natural resource base because it requires major land and water resources, thereby reducing biodiversity and enhancing biological invasions and host species jumps by pathogens. The conversion of tropical forest to agricultural land peaked during the 1990s in Latin America, is currently at or just beyond its peak in Asia, and has still to assume its maximum proportions in Africa. The agricultural encroachment of pristine forest areas is of particular importance to public health because it increases the chance of wildlife-origin pathogens spilling over to humans (and livestock). In Asia, where land pressures are critically high, large forested areas are being converted into cropland and pastoral systems (Figure 23 and Figure 24).

Projections are that major areas classified as *remote forest systems* are being encroached on by *pastoral systems* in southeastern parts of the Russian Federation, adjacent areas of China and eastern parts of Myanmar. *Remote forest systems* in Bhutan and adjacent areas of eastern India are being replaced mainly by *rainfed cropland systems*. Rainfed cropland expansion tends to have a more destructive effect on woody vegetation than ruminant livestock encroachment does, as it entails the uprooting of trees. Rainfed cropland expansion at the cost of remote forest is of particular concern because it is expected to affect ecosystem integrity and biodiversity most severely. Agricultural expansion within *populated* forest areas, such as that occurring in the Indonesian archipelago, carries the risk of pathogen spillover from wildlife to livestock and humans.

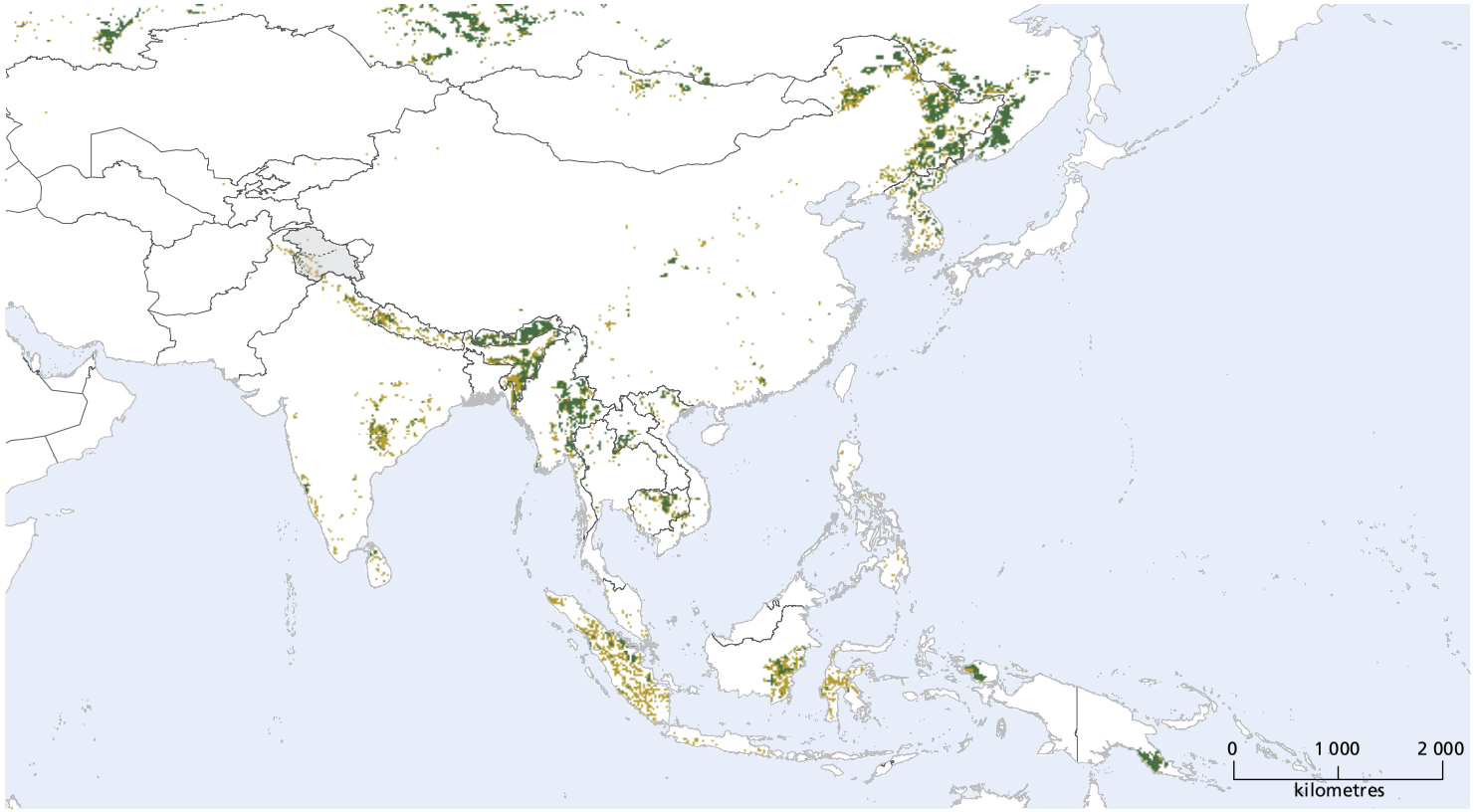
In sub-Saharan Africa, human exposure to wildlife-origin pathogens is increasing, in line with demographic growth, socio-economic changes and the build-up of agricultural land pressure. Tourism is gaining importance in the African savannah areas, which have a unique abundance of large game. Protected forest and game reserves in these areas are surrounded by a growing ruminant livestock population. As a result, pathogens may spill over from wildlife to livestock and humans, or vice versa (Murray and

23 PREDICTED LAND-USE SYSTEM CHANGES IN PARTS OF SOUTH, SOUTHEAST AND EAST ASIA (2000–2030)



Source: Adapted from Letourneau, Verburg and Stehfest, 2012.

24 PREDICTED LAND-USE SYSTEM CHANGES IN PARTS OF SOUTH, SOUTHEAST AND EAST ASIA (2000–2030): REMOTE AND POPULATED FOREST SYSTEMS CONVERTED INTO RAINFED CROPLANDS



Source: Adapted from Letourneau, Verburg and Stehfest, 2012.

Daszak, 2013). Countries in Latin America and the Caribbean also continue to report human and livestock infections originating in wildlife at the ecosystem–agriculture–human interface, involving bats, rodents and vector-borne disease complexes.

Wildlife species are a main source of microbial diversity and an important reservoir of emerging infectious disease agents. Humans may come into contact with wildlife through farming, when visiting forest and game reserves, during hunting, or because of practices related to the consumption of wild meat. Changes in wildlife ecology and behaviour can lead to disease emergence in humans and domestic animals. More than 70 percent of the infectious diseases that have emerged in humans since the 1940s could be traced back to wildlife (Jones *et al.*, 2008). Wildlife sources comprise ungulates, carnivores, rodents, monkeys, bats, birds and other, mostly mammalian, species (Woolhouse and Gowtage-Sequeria, 2005) For example, bat viruses may show up in humans where people are moving into the habitat of bats, and/or bats are moving into human environments.

Bats are reservoir hosts of several viruses that pose health risks to humans, including SARS-like corona viruses, Nipah and Hendra viruses, Ebola viruses, rabies virus and related lyssaviruses, and Menangle and Tioman viruses (Bennett, 2006; Calisher *et al.*, 2006; Turmelle and Olival, 2009). Factors that may contribute to bats being reservoir hosts include high species diversity, long life span, ability to engage in long-distance movement and dispersal, formation of large colonies facilitating intimate contact among individual bats, the use of torpor and hibernation, and factors related to host cell biology (Calisher *et al.*, 2006). Bats are found almost everywhere in the world and account for more than 20 percent of all mammal species. The emergence of bat viruses may be facilitated by liaison or intermediate hosts that play a role in amplifying viruses and bridging bat and other host species (Bennett, 2006). For example, it is likely that the SARS virus emerging in humans

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was first transmitted by bats to masked palm civets, from which it spilled over to humans in a peri-urban agricultural market in East Asia (Song *et al.*, 2005).

Deforestation was one of the probable driving forces for the emergence of Hendra virus (Plowright *et al.*, 2011). The destruction of bat habitat led to urban habituation, increased contact between flying foxes and humans/domestic animals, and decreased migration, which, in turn, led to lower immunity of bat populations and increased virus circulation (Plowright *et al.*, 2011). Hendra virus infects horses and humans, causing respiratory disease in both and encephalitis in humans (Mackenzie, 2005). The first outbreak of Hendra virus was in 1994 in northern Australia; it has since had recurrent small outbreaks and has been identified in southern coastal areas of Australia.

The emergence of Nipah virus in pigs and humans was also triggered by deforestation, directing fruit bats to nearby cultivated fruit trees (Chua, Chua and Wang, 2002). It seems likely that the virus was transmitted to pigs in the form of a food-borne infection when pigs ate partially eaten fruit dropped by flying foxes feeding on nearby mango trees. Nipah virus reportedly first emerged in Malaysia in 1998 and spread within Malaysia and to Singapore via the transport of infected pigs. Massive numbers of pigs were culled to contain the epidemic. Most human cases were adult males working in pig

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farming or pork production. In contrast, more recent outbreaks (from 2001) in Bangladesh and India involved direct transmission to humans via fruits and date palm sap contaminated with the urine of fruit bats, and through human-to-human transmission (Luby *et al.*, 2006; Sazzad *et al.*, 2013).

As mentioned above, the trigger for the emergence of SARS in humans was the consumption/handling of palm civets, which have been popular as an exotic food since the late 1980s (Shi and Hu, 2008; Wang and Eaton, 2007). The SARS coronavirus pandemic started in November 2002 in Guangdong Province, China, and within weeks had spread to 29 countries across five continents, infecting more than 8 000 people and resulting in 774 deaths. Since mid-2012, the spread of a Middle East respiratory syndrome coronavirus has been recorded within and from the Arabian Peninsula to countries in the Near East, North Africa and Western Europe (WHO, 2013). Its phylogenetic characteristics suggest that this coronavirus may be a natural bat virus. It has been speculated that the virus may have reached humans through camels as an amplifier host (Reusken *et al.*, 2013).

The encroachment of humans into the natural habitats of monkeys may result in increased pathogen spillover to humans, and eventually – given progressive exposure of humans to the "new" pathogen – generate a species jump with sustained human-to-human transmission. The human activities involved include farming near forests, deforestation and logging, hunting, and preparation and/or consumption of bushmeat. Non-human primates, such as monkeys and chimpanzees, can carry pathogens that are transmitted to humans. The phylogenetic distance between these animals and humans is small, with overlaps in immune system components and conserved cellular receptors. An important example of a pathogen that jumped from a non-human primate species to humans – via exposure to chimpanzee blood during bushmeat hunting and food preparation – is HIV-1 (Apetrei, Robertson and Marx, 2004; Chitnis, Rawls and Moore, 2000; de Sousa *et al.*, 2010). During the twentieth century, a total of three independent cross-species transmission events of Simian immunodeficiency viruses to humans apparently took place (Apetrei, Robertson and Marx, 2004; Sharp, 2002).

Mosquito-borne viruses that have used the relatedness of humans and monkeys to jump to humans encroaching into forests include dengue virus and Chikungunya virus. Dengue virus used to circulate in monkeys (Macaca and Presbytis species), with sporadic cases in humans. The fast increase in human population, urbanization and travel enabled sustained transmission in humans (Holmes and Twiddy, 2003). The Asian lineage of Chikungunya virus originally circulated between monkeys and mosquitoes, with spillover into humans, but recently evolved human–mosquito–human transmission cycles resulting in epidemics (Chevillon *et al.*, 2008). Reported drivers of Chikungunya virus epidemics in humans include human migration, settlement of mosquito vectors in urban ecosystems, and increased farming activities near forests (Chevillon *et al.*, 2008).

Rodents also carry a range of viruses and are abundant throughout the world, accounting for more than 40 percent of mammal species. Rodents occupy a wide range of habitats, reproduce at high rates, and thrive on contaminated food and water. That rodents constitute an important part of the earth's biomass is demonstrated by

estimates that they consume at least a fifth of the world's grain output (Howard and Fletcher, 2012). Contact between rodents and humans can lead to spillover of rodent viruses to humans. Hanta and Lassa viruses have emerged as major causes of zoonotic diseases. Hanta virus survives in rodent excrement, and aerosolized infectious particles in dust may infect humans (Klein and Calisher, 2007). The urbanization of areas where monkeypox virus was circulating in reservoir rodents in Africa played an important role in the emergence of monkeypox virus in humans (Parker *et al.*, 2007). Other factors leading to increased numbers of monkeypox infections may include the cessation of vaccination against smallpox, possibly in combination with increased susceptibility of humans caused by malnutrition and co-infections, increased human-to-human transmissibility, or changes in reservoir species (Parker *et al.*, 2007).