Surveillance and Response to Disease Emergence

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Abstract New and emerging infectious diseases affect humans, domestic animals, livestock and wildlife and can have a significant impact on health, trade and biodiversity. Of the emerging infectious diseases of humans, 75% are zoonotic, with wildlife being an increasingly important source of inter-species transmission. Recent animal health

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emergencies have highlighted the vulnerability of the livestock sector to the impact of infectious diseases and the associated risks to human health. Outbreaks resulting from wildlife trade have resulted in enormous economic losses globally. On a global level, the human health sector lags behind the animal health sector in the assessment of potential threats, although substantive differences exist among countries in the state of national preparedness planning for emerging diseases. The lack of surveillance data on emerging zoonoses from many developing countries means that the burden of human, livestock and wildlife disease is underestimated and opportunities for control interventions thereby limited. In the context of emerging zoonoses, comprehensive risk assessments are needed to identify the animal–human and animal–animal interfaces where transmission of infectious agents occurs and the feasibility of risk reduction interventions. The impact of emerging diseases can be minimised through a well-prepared and strong public health system and similar systems developed by the livestock, wildlife and food safety sectors. National animal disease emergencies, especially those that spill over to affect human health, require a whole-of-government approach for effective disease containment. As it is highly likely that zoonoses and animal diseases with the potential to affect human health will continue to emerge, surveillance and response systems for emerging zoonotic diseases will need to be strengthened and maintained at national and international levels. Applied research, linked across the human, livestock and wildlife sectors, is needed to inform preparedness planning and the development of evidence-based approaches to zoonotic disease prevention and control.

1
The Impact of Emerging Zoonoses

Emerging infectious diseases are defined as diseases that have recently increased in incidence or geographic range, recently moved into new host populations, recently been discovered or are caused by newly evolved pathogens (Lederberg et al. 1992; Smolinski et al. 2003). New and emerging infectious diseases affect humans, domestic animals, livestock and wildlife and can have a significant impact on health (WHO 2001), trade and biodiversity (Daszak et al. 2001). Of the emerging infectious diseases of humans, 75% are zoonotic, with wildlife being an increasingly important source of inter-species transmission (Daszak et al. 2001; Taylor et al. 2001; see the chapter by Cleaveland et al., this volume).

Massive global increases in demand for food of animal origin associated with population growth, income growth, urbanisation and devolution in global agriculture, is having a profound effect on health, livelihoods and environments. These factors are contributing to the exacerbation of public health and environmental problems, pressure on food production and distribution, and the illegal transport and trade in livestock, food products and people. The livestock sector represents almost half of the world's agricultural economy. Recent animal health emergencies have highlighted the vulnerability of the livestock sector to the impact of infectious diseases and the associated risks to human

health (FAO/OIE 2004). Outbreaks resulting from wildlife trade have resulted in enormous economic losses globally (Karesh et al. 2005). In addition, the world is seeing unprecedented levels of international travel that has facilitated the spread of infectious diseases. The International Civil Aviation Organization estimates that air travel among its 185 members will reach two billion passengers annually by 2005 (ICAO Circular 2005).

The management of emerging zoonoses in humans requires a public health response closely linked to control measures in livestock animals and wildlife and that takes the complex interconnections among species into full account (Wildlife Conservation Society 2005; see the chapters by Childs and Daszak et al., this volume). Considerable resources by the agricultural and animal health sectors go into modelling risk and the economic impact of crises in consumer confidence resulting from animal diseases or infected animal products (University of Sydney FAH Report 2005). On a global level, the human health sector lags behind the animal health sector in the assessment of potential threats, although substantive differences exist among countries in their national preparedness planning for emerging diseases. Until recently, little attention has been given to determining the direct and indirect costs of human disease outbreaks, including morbidity and excess mortality, health service delivery costs, public health expenditure, the psychosocial impact on affected individuals, families and communities, the economic impact on travel, tourism and the insurance industry, and loss of confidence in governments and health services.

The economic burden of emerging zoonoses often falls disproportionately on the rural sector and the poor because of their greater risk of exposure to diseases of livestock and wildlife and pre-existing urban–rural socioeconomic inequalities. The health and socioeconomic impact of zoonoses are increasingly being felt most particularly, although not exclusively, by developing countries (Seimenis 1998). The lack of surveillance data on emerging zoonoses from many developing countries means that the burden of human, livestock and wildlife disease is underestimated and opportunities for control interventions thereby limited (see the chapters by Childs, by Nel and Rupprecht, and by Stallknecht, this volume).

1.1
The AIDS Epidemic

Most of the emerging infectious diseases identified since the mid-1990s have been caused by viruses. The AIDS epidemic caused by the human immunodeficiency virus, HIV, is one of the most destructive pandemics in human history (UNAIDS 2005). Since its recognition in 1981, AIDS has killed over 25 million people and an estimated 40.3 million people were living with HIV/AIDS in 2005. HIV emerged from at least two nonhuman primate reservoirs in Africa

in the 1950s (Hahn et al. 2000). There are currently 33 nonhuman primates known to harbour their own unique simian immunodeficiency virus (SIV) strains (Kalish et al. 2005) and primate bush meat has a high prevalence of SIV (Peeters et al. 2002). In a study of 16 SIV isolates from five different primate species, 12 were able to infect human monocyte-derived macrophages, while 11 showed replication in human peripheral blood mononuclear cells, although the authors state that cell tropism does not necessarily predict virus pathogenicity in vivo (Grimm et al. 2003). Hunters in sub-Saharan Africa continue to be exposed to SIV during hunting and butchering nonhuman primates such as chimpanzees and sooty mangabeys, or by keeping wild primates as pets (Kalish et al. 2005; see the chapter by Daszak et al., this volume). Such spillover events have implications for the safety of the blood supply through the genesis of new HIV strains that are not detected by current HIV tests (Kalish et al. 2005).

More recently, Nipah virus, severe acute respiratory syndrome (SARS) and highly pathogenic avian influenza (A/H5N1) have also highlighted the importance of emerging zoonoses and their impact on health and economic development (see the chapters by Field et al., Wang and Eaton, and Webby et al., this volume).

1.2
Nipah Virus

Nipah virus, a henipavirus (Field et al. 2001), was first diagnosed in Malaysia in 1999 (Chua et al. 1999) and has caused serious disease in humans and livestock in Malaysia, Singapore (Paton et al. 1999; Tambyah et al. 2001), Bangladesh (ICDDR,B 2003, 2004a, 2004b, 2005) and India (Chadha 2006; see the chapter by Field et al., this volume). Outbreaks of Nipah virus encephalitis have been characterised by high mortality in humans. Transmission to humans is primarily through contact with infected pigs (Chua et al. 1999, 2000), although recent outbreak investigations in Bangladesh and India provide evidence for limited human-to-human transmission (WHO 2004a; Hsu et al. 2004; ICDDR,B 2004a; Chadha 2006), transmission via ingestion of food products contaminated with the saliva or urine (Enserink 2000) of Old World fruit bats (*Pteropodidae*) (WHO 2004a; ICDDR,B 2005) and/or contact transmission (WHO 2004a; ICDDR,B 2005) in environments contaminated by fruit bats. Pteropid bats are considered the natural reservoirs of Nipah virus (Eaton et al. 2006; Field et al. 2001; Chua et al. 2002). *Pteropus* species are distributed from Madagascar through the Indian subcontinent to south-eastern Asia and Australia and as far east as the Cook Islands in the Pacific (Chua et al. 2002). Serological evidence of Nipah virus infection in pteropid bats has also been found in Cambodia, although there are no reported outbreaks of Nipah encephalitis in humans (Reynes et al.

2005). Additional work remains to be done to improve our understanding of risk factors for transmission to humans and livestock, the disease ecology of Nipah virus and the geographic distribution of the reservoir species.

The cost of the outbreak to Malaysia is estimated at overUS $500 million. Over one million pigs were destroyed for outbreak control (US $97 million), control activities cost US $136 million, 36,000 jobs were lost, and there were 257 cases of encephalitis including 105 deaths (Nor and Ong 2000; FAO/APHCA 2002).

Four outbreaks of Nipah virus have occurred in the same region of Bangladesh from 2001 to 2005, all occurring between January and April but each attributed to different exposure factors (Hsu et al. 2004; WHO 2004a; ICDDR,B 2003 2004a 2004b 2005). Genotyping virus from the Bangladesh outbreaks have showed a 95% homology with isolates from the Malaysian outbreak in 1999. In outbreaks in the Meherpur district (2001) and Faridpur district (2004), direct contact with the secretions of ill patients is thought to have played a role in transmission of the disease (Hsu et al. 2004; ICDDR,B 2004b; WHO 2004a). In the outbreak in Naogaon district (2003), cases were associated with exposure to a herd of pigs (ICDDR,B 2004a). In Goalanda, Rajbari district, nine of the 12 Nipah cases were boys under 19 years who climbed trees where fruit bats fed overnight (WHO 2004a). Contamination is thought to have occurred while eating the same fruits, although whether infection was a result of ingestion or contact transmission was not determined. In January 2005, 12 cases of Nipah virus were reported in Basail Upazila, Tangail District, of whom 11 died (92%) (ICDDR,B 2005). The only significant exposure associated with illness was drinking raw date palm juice, which is consumed within a few hours of collection. Date palm juice potentially contaminated with the saliva and/or urine of *Pteropus giganteus*, the species of fruit bat widely distributed throughout Bangladesh, is considered the most likely source of transmission.

1.3
Severe Acute Respiratory Syndrome

Severe acute respiratory syndrome caused by the SARS coronavirus (SARS-CoV) emerged in the Guangdong province of the People's Republic of China in November 2002 (see the chapter by Wang and Eaton, this volume). The Himalayan masked palm civet (*Paguma larvata*) is considered the source of infection in humans (Chinese SARS Molecular Epidemiology Consortium 2004; Guan et al. 2003; Kan et al. 2005). One reservoir of SARS-like coronaviruses closely related to those responsible for the SARS outbreak is now known to be cave-dwelling bats in the genus *Rhinolophus* (Chinese horseshoe bats) (Li et al. 2005). These viruses, termed SARS-like coronaviruses, display greater genetic variation than SARS-CoV isolated from humans or from civets. The SARS epidemic demonstrated

that even in well-resourced countries, the initial response to SARS was hindered by inadequate disease surveillance systems, poor communication and information sharing, and insufficient public health capacity. Unprecedented levels of international travel and trade enabled the rapid spread of SARS within and between continents. In global terms, SARS was a small epidemic resulting in just over 8,000 cases and 774 deaths (WHO 2004b). However, SARS severely challenged the capacity of curative and preventive health services, including the ability of public health services in unaffected countries to investigate suspected cases of SARS. The epidemic temporarily reduced consumer confidence in Asia, costing Asian economies US $11–18 billiion and resulting in estimated losses of 0.5%–2% of total output according to official macroeconomic data, and economic impact studies from international financial institutions, industry associations, and public policy research institutions (US General Accounting Office 2004). SARS had significant, but temporary, negative effects on a variety of economic activities, especially travel and tourism even in unaffected countries. Tourism fell by 9.7% in the Asia Pacific region as a direct result of SARS (Department of Tourism, Industry and Resources 2004).

1.4
Highly Pathogenic Avian Influenza

Human cases of A/H5N1 avian influenza were first reported in Hong Kong in 1997, when it infected 18 people with six deaths (Tam 2002). The World Organization for Animal Health (OIE) received the first report of its re-emergence on 12 December 2003 from the Republic of Korea. The disease spread rapidly within South-East Asia (Cambodia, China, Indonesia, Japan, the Lao People's Democratic Republic, Malaysia, the Republic of Korea, Thailand and Viet Nam), had infected domestic poultry flocks and wild birds in Russia, Kazakhstan and Mongolia by July 2005, and Romania, Croatia and Turkey by October 2005, confirming the westward spread of the virus (FAO 2005; see the chapter by Webby et al., this volume). Evidence shows that the A/H5N1 virus is now enzootic in many parts of Asia and is spreading rapidly in Europe. One estimate of the direct costs to the agricultural sector in Cambodia, Thailand and Viet Nam is of the order of US $560 million (McLeod 2005). Genetic analyses of isolates from Mongolia, Kazakhstan, Romania, Russia and Turkey show a close genetic relationship to wild bird isolates from the Qinghai Lake outbreak, China. Outbreaks of A/H5N1 have recurred despite aggressive control measures, including the culling of millions of poultry since December 2003. At the time of writing in January 2006, human cases with an overall fatality rate around 50% have been reported in Cambodia, China, Indonesia, Thailand, Turkey and Viet Nam (see the chapter by Webby et al., this volume).

A/H5N1 avian influenza has also proven highly pathogenic to wading birds and a number of terrestrial mammals. In 2004, concurrent with outbreaks of avian influenza in poultry, a total of 147 of 441 tigers (*Panthera tigris*) and two leopards (*P. pardus*) kept in the zoo in Suphanburi, Thailand, died after an acute respiratory illness with high fever or were euthanised to prevent possible spread to other zoo animals. The aetiological agent was subsequently confirmed as A/H5N1 avian influenza. The animals had been fed raw chicken carcasses that were contaminated with the A/H5N1 virus (Keawcharoen et al. 2004). Cases occurring 12 days after the tigers were last fed raw poultry were attributed to tiger-to-tiger transmission (Thanawonghuwech et al. 2005). During the outbreak, there were also anecdotal reports of fatal A/H5N1 virus infection in domestic cats, previously thought to be resistant to influenza A infections (ProMed mail 2004). When cats ($n = 3$) were experimentally infected with A/H5N1 virus isolated from a fatal human case in Vietnam (A/Vietnam/1194/04), they exhibited respiratory symptoms, diffuse alveolar damage and excreted virus at 3 days post-infection (Kuiken et al. 2004; see the chapter by Webby et al., this volume). Three control cats inoculated with a human A/H3N2 virus isolate from a human (A/Netherlands/18/94) showed no evidence of infection or disease. The study also demonstrated that cats could be infected with A/H5N1 virus both by horizontal transmission and by feeding on virus-infected birds (Kuiken et al. 2004). There is considerable concern that other carnivores may also be susceptible to infection through eating infected poultry or infected wild birds.

Almost all human infections can be linked to contact with infected poultry, but instances of inefficient human-to-human transmission may have occurred in several family clusters in Vietnam (Tran et al. 2004), and possibly in Thailand (Ungchusak et al. 2005) and Indonesia (WHO 2007). The risk of further human cases continues, as do opportunities for a human-adapted pandemic strain to emerge following a recombination event. Kuiken et al. concluded that cats might also enable the adaptation of A/H5N1 to mammals, thereby increasing the risk of a human influenza pandemic (Kuiken et al. 2004). More recently, concerns have been raised that inappropriate vaccination of poultry to control the disease may lead to asymptomatic transmission among birds and spread of the virus between farms from poor biosecurity during vaccination campaigns (Parry 2005).

These scenarios highlight the importance of controlling avian influenza in livestock as far as possible to prevent human infections, and the need for strong collaboration between the animal and human health sectors. The United Nations Food and Agriculture Organization (FAO)/OIE regional animal laboratory network will be closely linked to the World Health Organization (WHO) Global Influenza Programme (WHO 2004c) to allow rapid

sharing of virus samples and assessment of changes in A/H5N1 strains circulating in animal populations suggestive of increasing resistance to antiviral drugs or which may diminish the effectiveness of the human prototype H5 vaccines currently under development.

Although there is considerable epidemiological uncertainty about the extent of an influenza pandemic, it is expected to be more damaging in human health, social and economic development terms than previous public health emergencies. The Asian Development Bank has modelled the economic impact on Asia of a relatively mild influenza pandemic of 1 year's duration and with an attack rate of 20% and a case fatality ratio of 0.5%. The scenario is far less severe than the pandemic of 1918 but probably more severe than the pandemics of 1957 and 1968. The model puts the potential cost to the region at between US $99.2 billion and $282.7 billion in lost consumption, trade and investment, with an additional $14.2 billion lost through staff incapacity and death (Bloom et al. 2005).

1.5
Transmissible Spongiform Encephalopathies

The transmissible spongiform encephalopathies (TSEs) are a group of fatal neurodegenerative diseases of humans and other mammalian species (WHO 2003a). Although the pathogenesis of TSEs is incompletely understood, most researchers believe the aetiological agent is a prion, the misfolded form of a normal cellular protein designated PrP^{Sc}, that acquires infectivity. TSEs are genetically determined, sporadic or acquired from exposure to TSE-contaminated materials. The accumulation of PrP^{Sc} in the brain is a hallmark of most forms of TSE.

Scrapie of sheep and goats and bovine spongiform encephalopathy (BSE) are serious livestock diseases that have resulted in significant losses to livestock producers through death or destruction of affected animal populations. Both are subject to eradication programs (Ramasamy 2004) in affected countries and import restrictions in unaffected countries.

Scrapie has been known to infect sheep for at least 250 years (WHO 2003a) and is not transmissible to humans. Its infective nature was first described in 1935 following transmission studies in sheep that involved the intraocular inoculation of a healthy ewe with infected sheep spinal cord tissue. Disease surveillance, herd depopulation and selective breeding programs were proving successful control measures until recently. There is a well-established association between sheep prion protein genotype and the risk of death from scrapie (Baylis et al. 2004). Certain genotypes are associated with susceptibility to the disease and others with resistance. The intensified surveillance of scrapie in the European

Union, together with the improvement of PrP^{Sc} detection techniques, has led to the discovery of a growing number of atypical scrapie cases. In 2002, researchers in Germany, Portugal and France identified a variant form of scrapie that appears to infect sheep of the genotype ARR/ARR purposefully bred in Europe as a lineage resistant to scrapie (LeDur et al. 2005; Roden et al. 2006). The prion proteins of the variant form accumulate in different parts of the brain, have different biochemical properties and produce a spectrum of disease that differs slightly from traditional scrapie. Inoculation of transgenic mice expressing ovine PrP with material from three sheep homozygous for the resistant PrP(ARR) allele efficiently transmitted the disease to the mice. These observations suggest that a previously unrecognised infectious TSE agent infects sheep flocks (LeDur et al. 2005) and may have important implications in terms of scrapie control and public health.

The appearance of BSE resulted in an explosive epidemic of fatal encephalopathy in cattle herds in Britain. BSE has been causally linked to variant Creutzfeldt-Jakob disease (vCJD) in humans (Bruce et al. 1997; Collinge et al. 1997). BSE has had profound effects on the livestock industry, animal and human food safety, the international requirements for import risk assessments and certification of freedom of disease. The history of BSE is a cautionary tale of the unanticipated and unintended impact of new technologies and production practices introduced by the livestock industry on human and wildlife health. BSE also highlights the various economic, social and political costs and impacts resulting from disease prevention and large-scale control strategies.

BSE was first reported in British cattle in November 1986, and by September 2005 183,850 confirmed cases had been reported to the OIE (OIE 2005a). Mathematical modelling indicates that the epidemic began in the mid-1970s and that approximately one million cattle must have been infected and entered the food supply. Current evidence supports the hypothesis that BSE originated from the recycling of cattle infected with a scrapie-like agent derived from either sheep or cattle in feed containing rendered meat and bonemeal. Changes to the rendering process from the 1970s to the early 1980s appear to have reduced the inactivation of PrP^{Sc} and enabled propagation of the agent. BSE became a notifiable disease in the UK in June 1988, and soon afterwards, a ban on the feeding of ruminant-derived protein to ruminants became mandatory. The ban was extended to specified high-risk bovine offals (SBOs) for human consumption in November 1989 based on the infectivity of tissues of scrapie-infected sheep, and in September 1990 SBOs were prohibited for use in feed for all animals and birds in the UK. The BSE epidemic in Britain peaked at the end of 1992 when 37,280 incident cases were detected and then declined rapidly, although a small number of cases continued to occur (Enserink 2005; OIE 2005a). In 2004, 343 cases were reported in Britain and just over 150 in 2005. BSE in animals

born after the ruminant feed ban have been attributed to exposure to contaminated feed after the ban, maternal transmission or other unidentified routes of transmission. In October 2004, French researchers confirmed a TSE in a goat slaughtered in 2002 that could not be distinguished from BSE on the mouse bioassay which takes 2 years to complete (Europa 2004). One additional goat tested positive of 140,000 goats examined from April 2002 to January 2005.

Because of the global export of cattle and cattle-derived products, BSE has since been reported on a smaller scale from all 25 EU countries with the exception of Sweden (Grist 2005), and in Israel (Nitzan-Kaluski and Leventhal 2003), Japan (Yamakawa et al. 2003) and most recently from Canada (Coulthart et al. 2003) and the United States (Larkin 2002). In some of these countries, BSE-affected cattle were detected even after a probabilistic risk assessment integrating release, exposure and consequence assessments indicated a negligible probability that BSE was introduced and established (Morley et al. 2003). Materials potentially contaminated with the BSE agent had been distributed around the world through the trade in live cattle and cattle by-products before export bans and import risk assessments were put into place. These products include a range of high-risk materials, some masked by trading patterns that have included processing and re-exportation of hazardous products. The occurrence of BSE in cattle in Europe and elsewhere raised new concerns about the precautions needed to ensure the safety of the international trade of cattle and cattle products. Many countries still have no monitoring systems or insensitive surveillance in place for BSE and may not have the financial and response capacity to eliminate BSE should cases occur. From 2001 to 2004, abattoir-based testing of asymptomatic cattle for BSE in European Union countries cost €1.6 million per BSE case detected, with an overall cost of approximately €1.6 billion (Enserink 2005).

In March 1996, ten cases of a newly recognised variant of Creutzfeldt-Jakob disease (CJD), the most commonly recognised form of human TSE, were reported in the United Kingdom. The new form was designated variant-CJD. Consumption of BSE-infected beef products, particularly mechanically recovered meat, is the most likely route of transmission in humans. These cases were temporally and geographically linked to outbreaks of BSE, making an aetiological link highly likely. Several different PrP^{Sc} types in humans have been identified, each associated with a different clinical phenotype of CJD. Strain-typing experiments have shown that the vCJD agent is different from that causing sporadic CJD but similar to the BSE agent. Humans that are homozygous (methionine/methionine) at codon 129 are more susceptible to both variant and sporadic CJD. All but one of the cases of vCJD to date has been homozygous at codon 129; the single heterozygous (methionine/valine) case was infected via a blood transfusion and demonstrated for the first time that codon 129-heterozygous individuals are susceptible to vCJD infection

(Peden et al. 2004). Speculation continues on whether cases of vCJD with very long incubation periods will occur among individuals heterozygous or homozygous (valine/valine) at codon 129 who were exposed to high-risk beef products before the bans.

Since 2003, two cases of vCJD in the UK were attributed to infections via the transfusion of red cells from donors who later died of vCJD (Peden et al. 2004; Llewelyn et al. 2004). A substantial body of animal data have also demonstrated that TSEs can be transmitted through blood (Ironside and Head 2003), even when the donor is in the subclinical phase of disease (Houston et al. 2000). Epidemiological studies of lymphoreticular system tissues have shown a low, but measurable, carrier state in vCJD. PrP^{Sc} has been found in appendix, spleen, tonsil and lymph nodes of patients with vCJD, and in this regard differs to other human TSEs (Hill et al. 1999). TSEs are highly resistant to the sterilisation and equipment reprocessing techniques that readily destroy bacterial and viral pathogens and have radically changed the practice of infection control during surgical and invasive diagnostic procedures. The widespread distribution of PrP^{Sc} throughout the lymphoid and central nervous systems raises concerns about the risk of transmission through surgical and ophthalmological procedures (Dunstan and Alpers 2005). The appearance of vCJD has also challenged the safety of the blood supply and organ donation. Changes in surgical practices, such as the use of disposable equipment for common procedures and the need to destroy or quarantine expensive equipment that would previously have been reprocessed for use, have resulted in considerable costs to health care systems around the world.

From 1986 to 2003, 37 cases of TSEs occurred in 37 zoo animals involving 12 species, including the ungulate species *Tragelaphus strepsiceros* (greater kudu) and wild-captive *Felidae* (cheetah, tiger and lion). In 1990, the first case of feline spongiform encephalopathy in a domestic cat was reported in the UK, with 91 reports by September 2001. Exposure to uncooked infected bovine materials is assumed to be the source of transmission in the felids. The ongoing risk of interspecies transmission of TSEs needs careful assessment (Ramasamy 2004) in view of the experimental evidence that tissues from subclinically infected animals (Race and Chesebro 1998) can be infectious to other species.

Historically TSEs have only affected wildlife in small numbers. Transmissible mink encephalopathy is associated with exposure through feed contaminated with a TSE agent (Williams and Miller 2003). Chronic wasting disease (CWD) of mule deer and elk, first discovered in Wyoming and Colorado in the 1980s, has been spreading across the United States and Canada, raising concerns about the risk of transmission to free-ranging cervids that may lead to losses in biodiversity (Daszak et al. 2001) and that threatens the viability of game farming industries (Williams and Miller 2003). CWD is thought to be spread orally, either through direct contact among animals or via environmental contamination.

Current TSE risk assessments (Grist 2005) acknowledge the importance of generic uncertainties in the following areas: the prevalence levels of TSE-infected individuals in animal and human populations; whether a threshold dose of prions is required to initiate infection; whether ingested prions accumulate in an individual over time; the dose of prions required to overcome the species barrier for interspecies transmission to occur; the nature of prion transportation and longevity in the environment; and whether genetic heterozygosity will lead to a second wave of vCJD of very long incubation periods. These and other unanswered questions raise concerns that the lifting or loosening of BSE control measures and reductions in research funding recently announced by the European Union is premature, and that long-term vigilance is required to prevent a resurgence of disease and to monitor the effects of emerging TSE variants (Enserink 2005).

1.6
Wildlife Zoonoses

Emerging infectious diseases of wildlife such as Ebola virus and West Nile virus, which have resulted in spillover events to humans and livestock, are a threat to animal welfare and biodiversity (Daszak et al. 2001; Pourrut et al. 2005; see the chapter by Daszak et al., this volume). Others, such as chronic wasting disease in elk and deer, may result in transmission to humans through the consumption of game meats. The outbreak of monkeypox in pet owners and handlers (including a veterinarian) in the USA in 2003, highlighted the importance of wildlife species in zoonotic disease and the extent of the international trade in wildlife species (Guarner et al. 2004; CDC 2003). The source of the outbreak was traced to the legal importation of exotic rodent reservoirs of monkeypox from Ghana in West Africa (see the chapter by Regnery and Damon, this volume). Native pet prairie dogs housed near some of these rodents in a distributor's premises became infected, and the subsequent multi-state distribution and sale of the prairie dogs resulted in human infections.

2
Minimising the Impact of Emerging Zoonoses

Preparedness planning for disease emergence usually involves some form of risk assessment to assess the likelihood of infection and disease, and the impact on susceptible populations. In the context of emerging zoonoses, comprehensive risk assessments are needed to identify the animal–human and animal–animal interfaces where transmission of infectious agents occurs and risk reduction interventions are feasible (see the chapter by Cleaveland et al., this volume).

As wildlife is important in the epidemiology of many, if not most, zoonoses, wildlife should be taken into account in the risk analysis framework (Kruse et al. 2004). Health risk assessments for emerging zoonotic diseases should be undertaken whenever possible in the context of developmental projects that have ecological impacts and are likely to bring people into greater contact with wildlife (see the chapter by Daszak et al., this volume).

Assessing the risk of spillover events (Daszak et al. 2000) among species requires an understanding of the behaviour and ecology of emerging pathogens and the complex interactions between the agent, its natural reservoir(s), the behaviour of humans or animals susceptible to infection, and the ecosystems in which they interact. It is becoming increasingly apparent that bats are the reservoirs for a number of pathogenic viruses (Calisher et al. 2006; Field et al. 2004; see the chapter by Field et al., this volume), including rabies (Warrell and Warrell 2004; see the chapter by Nel and Rupprecht, this volume), the Australian bat lyssavirus (Fraser et al. 1996; Field et al. 1999, 2004; Gould et al. 2002; Warrell and Warrell 2004), henipaviruses (Eaton et al. 2006), SARS-like coronaviruses (Li et al. 2005), and Ebola virus (Leroy et al. 2005; see the chapter by Gonzalez et al., this volume), and are considered candidate reservoirs for Marburg virus (Leroy et al. 2005; see the chapter by Gonzalez et al., this volume). Other taxa may also prove to have co-evolved with a variety of viruses pathogenic for humans and animals (Peterson et al. 2004). For some emerging zoonoses, limited knowledge of these relationships, especially for wildlife diseases, makes the risk assessment of spillover particularly difficult (Polley 2005), thereby also limiting our ability to design interventions that will reduce opportunities for interspecies transmission.

Data to inform risk assessments, especially in less developed countries, are often lacking or unreliable, and some risk models have therefore extrapolated the results obtained from data collected in developed countries (FAO 2004). Accordingly, differences between countries and regions in the risk parameters used to develop the model need to be considered in designing and implementing surveillance and diagnostic systems for emerging diseases and risk reduction strategies. Some of these data are routinely collected or arise from research conducted in the human health, agriculture and wildlife sectors. In some countries, national livestock databases designed to increase the safety and traceability of livestock products are potentially valuable sources of data and are being used to strengthen veterinary epidemiology and economic analysis (James 2005). Livestock data which can be used for epidemiological purposes include movement records, animal health program data, quality assurance schemes, production records and breeding records.

Insufficient work has gone into collating and triangulating data from these various sources to build an integrated and dynamic picture of the evolution of emerging zoonoses. The potential applications of integrated human, livestock

and wildlife data include developing a better understanding of the descriptive epidemiology of emerging zoonoses, improved risk and decision analysis, and mathematical models to inform policy development and disease control management in all sectors. Using cartographic and geostatistical methods during epidemiological investigations can provide real-time quantitative data for identifying and tracking the geospatial spread of infectious diseases (Lai et al. 2004).

3
Mechanisms for Surveillance and Response to Emerging Zoonoses

Factors that drive disease emergence in human, livestock and wildlife populations are increasingly the result of human activity, and include changes to global ecology and climate, land use, animal husbandry and food production practices, air travel and the globalisation of trade (see the chapter by Childs et al., this volume). The impact of emerging diseases can be minimised through a well-prepared and strong public health system and similar systems developed by the livestock, wildlife and food safety sectors. To respond to emerging zoonoses effectively, preparedness plans, early warning systems and response capacity must be strengthened and implemented in a coordinated way across all sectors.

To meet the global challenge that emerging disease outbreaks present, the International Health Regulations (IHR) (WHO 2005a; Merianos and Peiris 2005) provide a legal framework for the international public health response to control cross-boundary infectious diseases. The purpose and scope of the revised IHR "are to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with, and restricted to, public health risks and which avoid unnecessary interference with international traffic and trade." The IHR (2005) explicitly recognise the need for intersectoral and multidisciplinary cooperation in managing risks of potential international public health importance. The IHR include a decision algorithm to assist countries in determining whether an outbreak or other unusual disease event may constitute a threat to international public health. National health authorities are required to report to the World Health Organization in the event of the following: smallpox, wild type poliovirus, human influenza (new subtype) and SARS; any event of potential international public health concern; and known epidemic-prone diseases that have the potential to spread internationally or threaten trade (e.g. cholera, plague, viral haemorrhagic fevers and West Nile fever).

In 2000, the WHO Department of Communicable Diseases Surveillance and Response in Geneva, Switzerland, initiated the formation of the Global Outbreak Alert and Response Network (GOARN) (WHO 2000), which provides the operational and technical response arm for the control of global outbreaks. Since April 2000, GOARN has played a key role in providing support to outbreak investigations in countries seeking assistance. Technical cooperation includes the provision of multidisciplinary field teams to assist in outbreak investigation and control, laboratory diagnosis and verification, clinical case management, and the delivery of vaccines and other therapeutic agents, equipment and logistics. Recent GOARN responses to diseases of zoonotic origin include multiple outbreaks of SARS and highly pathogenic avian influenza (A/H5N1) in humans, Ebola and Marburg haemorrhagic fevers, Nipah virus disease, plague and Rift Valley fever.

In response to the profound effects of emerging zoonoses such as Nipah virus, SARS and human cases of influenza A/H5N1 in the Asia Pacific Region, countries of the region in collaboration with the WHO South-East Asia and Western Pacific Regional Offices have adopted the *Asia Pacific Strategy for Emerging Diseases* (WHO 2005b). The Strategy aims to minimise the health, economic and social impact of emerging diseases through a targeted program of capacity building for public health surveillance and outbreak response in accordance with the core requirements of the IHR. Similar strategies are being implemented through a variety of public health networks in other WHO regions. Reducing the risk of diseases acquired from animals is a key objective of the Asia Pacific Strategy, which describes a broad, multinational, and multisectoral approach over the medium to long term. Success in the prevention and control of emerging zoonoses will require close collaboration between local and national health, agriculture, wildlife and food safety authorities in parallel with risk reduction activities involving international organisations such as WHO, FAO and OIE.

The quality of pathogen surveillance in animals varies greatly among countries and typically does not include wildlife (Kuiken et al. 2005; see the chapters by Childs et al. and by Stallknecht, this volume). The Terrestrial Animal Health Code (2005) (OIE 2005b) aims to assure the sanitary safety of international trade in terrestrial animals and their products through health measures to be used by national veterinary authorities to avoid the transfer of agents pathogenic for animals or humans, while avoiding unjustified sanitary barriers. The Terrestrial Code states that "countries shall make available to other countries, through the OIE, whatever information is necessary to minimise the spread of important animal diseases and to assist in achieving better worldwide control of these diseases". The Terrestrial Code lists procedures for the international reporting of diseases, ethical rules for international trade, certification and animal welfare, the principles of import risk analysis, and the organisation of

import and export procedures. There are a large number of notifiable animal diseases under international surveillance: anthrax, bovine spongiform encephalopathy, bovine tuberculosis, brucellosis, Crimean Congo haemorrhagic fever, highly pathogenic avian influenza, hydatid disease, Japanese encephalitis, leptospirosis, Nipah virus encephalitis, Q fever, Rift Valley fever, *Salmonella enteritidis* and *S. typhimurium* in poultry, screwworm, trichinellosis, tularaemia, and West Nile fever have the potential to cause human disease. National disease control requirements under the Terrestrial Code identify the need for a formal and ongoing system for detecting and investigating outbreaks of disease, procedures for the rapid collection and transport of clinical specimens, laboratory investigation guidelines for diagnostic quality assurance and a system for recording, managing and analysing diagnostic and surveillance data. In addition, the Terrestrial Code makes recommendations for the standardised monitoring of antimicrobials used in animal husbandry to evaluate usage patterns by animal species, antimicrobial class, potency and type of use in order to evaluate antimicrobial use and detect the emergence of resistance. Antimicrobial resistance may also have implications for antimicrobial efficacy in human health and in wildlife.

Agricultural pests and diseases may spread across borders or be introduced through travel, trade and the illegal trafficking of animals. Infectious agents can cause disease control emergencies, especially in developing countries with limited response capacity, and may result in major economic losses. On occasion, extensive emergency operations with international assistance become necessary particularly if detection and response are delayed. In 1994, the FAO established an Emergency Prevention System (EMPRES) for Transboundary Animal and Plant Pests and Diseases (FAO 2005) in order to minimise the risk of such emergencies developing. EMPRES has four main components – early warning, early reaction, co-ordination and applied research – and all are integral to preparedness planning for emerging infectious diseases.

All countries should participate in regional, and where possible, global surveillance and diagnostic networks for human, livestock and wildlife health, and enable the sharing of information to characterise risk, prevent disease spread, and enhance control efforts. To be most effective, preparedness planning for emerging zoonoses requires a whole-of-government approach, clear command, control and coordination structures across the health, agriculture and wildlife sectors, and appropriate funding of the human health and veterinary services for their disease alert and response operations. Opportunities for shared training and involvement in multi-sectoral outbreak simulations should be identified to test operational communications, networking and partnerships, and to identify gaps in preparedness across the various sectors.

Countries should define the criteria (trigger points) for declaring a national animal disease emergency and initiating whole-of-government action. The

availability of human, material and financial resources, including technical expertise and surge capacity, should be assessed as part of preparedness planning for emerging diseases and linkages formed with regional and global networks, such as a the Global Outbreak Alert and Response Network, that can provide emergency support to affected countries. Relevant local trigger points for alert and response should be defined as part of emergency preparedness planning by all human and veterinary health services.

4
Elements of Early Warning and Response Systems for Emerging Zoonoses

Early warning and response systems for emerging zoonoses require effective cross-jurisdictional, intersectoral and interdisciplinary collaboration. Early warning systems have been implemented at sub-national, national, regional and global levels. Networking, and linking individuals and agencies, will be key factors in building and sustaining surveillance and response capacity against existing and emerging disease threats. These activities can also provide the support needed in the areas where key capacities, such as diagnostics, do not currently exist or are under-resourced and require development.

Areas of expertise considered critical to improve detection, monitoring and investigation of emerging infections include field epidemiology, clinical and veterinary sciences, laboratory diagnostics, field ecology (mammalogy and entomology), behavioural science, medical anthropology, risk communication, social mobilisation (behaviour change communication) and other related disciplines.

4.1
Early Warning Systems

Early warning systems are based predominantly on epidemiological surveillance in the form of event-based and case-based activities. Event-based surveillance is purposely designed to detect unusual or unexpected disease events such as disease clusters or unexplained deaths (Merianos and Peiris 2005; WHO 2005a; see the chapter by Childs, this volume). Case-based surveillance provides information on individual cases of disease. Both lead to improved awareness and knowledge of the distribution of disease or infection and, depending on the completeness and quality of the data collected, might permit forecasting the evolution of an outbreak. Development, strengthening and implementation of early warning and response functions within integrated national disease surveillance systems are critical steps in building the core capacities for surveillance and response under the IHR (2005). Similar

guidance is provided to detect, investigate and control outbreaks of disease in domestic animals, livestock (OIE 2005b; FAO 2005) and wildlife.

Mortality surveillance—the investigation of unusual mortality—should be an integral part of early warning systems for public health, domestic animals, livestock and wildlife. Wild bird mortality has provided early indications of highly pathogenic avian influenza infection (Sturm-Ramirez et al. 2004; Liu et al. 2005) and West Nile virus (McLean et al. 2002). West Nile virus occurs over a broad geographic range and in diverse vertebrate hosts and vector species. Until recently, there were few reports of deaths in wild birds and a small number of cases of equine encephalitis. Mortality in domestic birds was first reported in Israel in 1997 (Banet-Noach et al. 2003), and encephalitis was reported in horses in Italy in 1998 (Cantile et al. 2000) and France in 2000 (Murque et al. 2001). In 1999, West Nile virus caused an outbreak of encephalitis in humans in the New York area concurrent with cases of equine encephalitis and deaths in crows and other native and exotic bird species. A mortality surveillance system for the rapid detection of West Nile virus was implemented as an integrated response between wildlife health and public health agencies (McLean et al. 2002). The death of nonhuman primates has been associated with outbreaks of Ebola haemorrhagic fever (Rouquet et al. 2005). Wild animal outbreaks began before each of the five human Ebola outbreaks in the forest zone between Gabon and Republic of Congo. All human Ebola virus outbreaks from 2001 to 2003 in that area resulted from handling infected wild animal carcasses. Through the establishment of an animal mortality monitoring network, health authorities were twice alerted to the imminent risk of a human Ebola outbreak weeks before they occurred (Rouquet et al. 2005).

Supporting effective surveillance are the routine clinical, laboratory and epidemiological information systems that can provide valuable baseline data and are often the sources of data that help identify and track unusual disease events. Such data sources include outpatient, hospital-based and public health and animal health records, hospital mortality data, the laboratory accession system used for specimen tracking, and data on the use of pharmaceuticals. Routinely collected data can support surveillance activities and may be the only ongoing data for general mortality surveillance in the veterinary field.

4.2
Risk-Based Surveillance

Targeted surveillance of high-risk settings and populations can provide cost-effective early warning of infection. Risk settings include farms, slaughter-houses, livestock and wildlife markets, hospitals, laboratories, international

borders and hubs for international travel and trade. High-risk occupations include health care workers, laboratory staff, veterinarians, primary producers, cullers, stock transporters and chicken catchers, abattoir workers, hunters, and distributors of animals, especially wildlife. Serological surveillance of high-risk populations, including baseline serology for occupation risk groups, health monitoring, and methods for identifying disease in vaccinated animals (such as monitoring unvaccinated sentinel animals and laboratory investigations that can discriminate vaccinated from infected animals), can provide important information on background rates of infection and disease, the size and distribution of susceptible and immune populations and species, and the effectiveness of control measures such as immunisation. Molecular epidemiology, especially when combined with human networking and animal movement data, allows tracing of disease transmission pathways and the identification of pathogen maintenance cycles (James 2005). The ability to differentiate vaccine-induced and wild antigens and antibodies has profound implications for epidemiological surveillance and disease control policy.

Major hubs of wildlife trade provide practical surveillance and control opportunities, especially if there is a supportive regulatory framework in place (Karesh et al. 2005). Air travel statistics have been used to model the importance of international travel hubs in the spread of epidemic-prone diseases in humans (Bauch et al. 2005; see the chapter by Daszak et al., this volume).

The effectiveness of existing local and national human and animal disease surveillance systems to detect known and novel zoonoses should be routinely evaluated to identify gaps and weaknesses. Astute clinicians and veterinarians are often the first to detect unusual disease events and are an integral part of the surveillance system for emerging diseases. Building awareness, knowledge and skills of clinicians in both sectors about emerging zoonoses will improve their early detection.

Effective wildlife surveillance is often limited by funding constraints, which necessitates optimisation of study design, sampling methodology and diagnostic methods; these are potential areas of applied research.

4.3
Improving Pathogen Identification

Laboratory diagnosis is an essential component of disease surveillance, both for the routine confirmation of diseases and for rapid determination of the aetiological agent during outbreaks (WHO 2005a). Laboratory surveillance systems are particularly useful for the detection of rare zoonotic infections that have spilled over into humans, domestic animals or livestock.

Laboratory assistance on-site to support outbreak investigations has proven very useful in emerging disease outbreaks. The use of new technologies for field use, such as rapid diagnostic tests, robust and portable nucleic acid-based technologies and multi-pathogen microarrays for the detection of known pathogens and their virulence factors (Burton et al. 2005; Sergeev et al. 2004) have greatly reduced the time taken to arrive at a definitive diagnosis during outbreaks.

There is an urgent need to strengthen linkages between national clinical and veterinary reference laboratories with regional and international laboratory networks that support verification and quality assurance and can provide diagnostic services for emerging and dangerous pathogens when necessary. These networks can also collaborate in the development of rapid diagnostic tests, including point of care tests, for surveillance purposes and test their performance under field conditions.

The WHO has been active in strengthening global laboratory networks to ensure that all countries have access to technical expertise for pathogen identification, reference and verification in humans, internal and international quality assurance, logistical assistance in the form of equipment, supplies and transport, and access to appropriate levels of biocontainment. Diagnostic and molecular biological capacity of OIE/FAO Reference Laboratories and Collaborating Centres are also being strengthened, and technology transfer is provided to National Agricultural Research Systems through the established system of networks of national and regional laboratories (FAO/OIE 2004).

4.4
Improving Information Management for the Early Detection of Emerging Diseases

Effective surveillance for emerging zoonoses requires the exchange of information among public health authorities, veterinary services and the wildlife sector. Timely analysis of surveillance data are needed to identify, track and manage threats to public health, the livestock industry and to wildlife, and to support evidence-based interventions for control. Information management should include systems to support the alert and event confirmation functions of early warning systems. All sectors should aim to improve or develop information systems for epidemic intelligence, verification status, laboratory investigations and field operations. Wherever possible, these systems should be integrated so that critical information for decision making is readily available. In addition, mechanisms and communication technologies that facilitate the rapid exchange of epidemic intelligence across the health, livestock and wildlife sectors as required should be implemented and tested

as part of emergency preparedness. Because information of zoonotic disease occurrence in animals is important to public health officials, WHO, FAO and OIE developed GLEWS, the Global Early Warning and Response System for Major Animal Diseases, including Zoonoses, to combine information from each organization so that outbreaks can be detected earlier and the coordination of response to emerging zoonoses improved (WHO/FAO/OIE 2004).

5
Control Measures

5.1
General and Threat-Specific Control Measures

Decreasing contact among species through community education, legislation and regulation or direct intervention is considered a practical approach to reducing the risk of emerging zoonoses (Karesh et al. 2005; see the chapter by Real and Biek, this volume). Following an outbreak of A/H5N1 in Hong Kong in 1997 that resulted in 18 cases and six deaths, control measures aimed at reducing exposure of humans to potential H5-infected poultry were instituted and included culling of all poultry in Hong Kong, the segregation of waterfowl and chickens, the introduction of import control measures for chickens and waterfowl and central slaughtering of waterfowl (Tam 2002). Following illness caused by influenza A/H9N2 (G1) strain in two children in Hong Kong in 1999, closing down retail poultry markets for 1 day per month and subsequent exclusion of quail from live bird markets reduced the rate of A/H9N2 avian influenza virus (especially the G1 strain) in market birds (Kung et al. 2003).

In addition to health monitoring for occupational exposure to dangerous pathogens, evidence-based protective measures for high-risk groups, such as vaccination and the use of personal protective equipment, should be applied wherever possible. However, in some situations the groups at highest risk of animal-to-human transmission of infectious diseases are poorly defined and may require specific prevention interventions that are culturally and socially acceptable. A/H5N1 infections in women and children exposed to infected poultry through activities such as slaughtering, defeathering and/or handling sick or dead birds is an important example.

Activities to prevent and control zoonotic diseases must also recognise the local cultural and economic factors that influence the patterns of human–animal and animal–animal interactions, and the ecological changes associated with land usage and animal husbandry practices that increase the frequency and intensity of human exposure to animal reservoirs of disease.

5.2
Improving Pathogen Containment in Laboratories and Biosafety in the Field

"Laboratory biosafety" describes the containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins or their accidental release (WHO 2004d). "Laboratory biosecurity" describes the institutional and personal security measures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens and toxins (WHO 2004a). Effective biosafety systems depend on well-formulated laboratory policies, optimal work practices, appropriate containment equipment and inventory controls, personnel risk assessments and effective management. Managing risks in the laboratory is dependent on both biosafety and biosecurity.

Breaches in laboratory biosafety and biosecurity have resulted in individual cases or outbreaks of disease caused by dangerous pathogens (Heymann et al. 2004). The three laboratory-associated outbreaks of SARS after transmission had ceased in July 2003 are a salient lesson. These incidents were attributed to breaches in laboratory biosafety and resulted in one or more cases of SARS: Singapore (WHO 2003b; Report of the Review Panel on New SARS Case and Biosafety; Lim et al. 2004), Taipei (WHO 2003c) and Beijing (WHO 2004e, 2004f). Fortunately only one of these incidents resulted in secondary transmission outside of the laboratory. The last incident was a cluster of nine cases, one of whom died, in three generations of transmission affecting family and hospital contacts of a laboratory worker.

All countries have an ongoing responsibility to develop, implement and monitor national standards to protect specimens, pathogens and toxins from accidental release or misuse. Biosafety also includes the measures put in place to protect laboratory staff and others involved in the diagnostic chain: appropriate training, health monitoring, the use of appropriate personal protective equipment, procedures for the investigation of spills and other incidents, and the laboratory equipment and engineering of the physical environment needed to reduce risks. The US Office of Health and Safety has developed a security plan based on facility risk assessments (Richmond and Nesby-O'Dell 2002). According to that plan, the key elements of laboratory security are systematic site reviews of physical security, data security, employee security, access controls to laboratory and animal areas, procedures for agent inventory and accountability; controls on shipping or transfer and receiving of select agents, incident and injury policies and emergency response plans, and a mechanism to investigate and address breaches in security. Preventive measures such as the immunisation of staff against vaccine-preventable diseases, and protocols for post-exposure prophylaxis where applicable, should also be written into laboratory management plans.

The responsibility for biosafety and biosecurity begins at the point of collection of clinical specimens, whether in a clinical setting, for research purposes or as part of a field investigation. New or poorly characterised infectious diseases such as emerging zoonoses pose particular difficulties for biosafety risk assessments. When knowledge of the pathogenic agent is insufficient to perform an appropriate risk assessment, for example, with clinical specimens or epidemiological samples collected in the field, a precautionary approach should be adopted during specimen manipulation. Standard precautions, especially handwashing, should always be followed and barrier protection used (gloves, gowns, eye protection) when handling clinical specimens. When dealing with poorly understood pathogens, additional (transmission-based) precautions and the use of special protective equipment, such as high-efficiency respirators, are recommended.

Decisions about the level of biocontainment required should consider available epidemiological data (morbidity and mortality data, suspected route of transmission, other outbreak investigation data) and the geographical origin of the specimen. Both human health laboratories and animal facilities are designated according to a risk assessment and the risk group of the microorganisms under investigation, as Biosafety Level (BSL) 1, 2, 3 or 4 (WHO 2004d). At Biosafety Level 3, manipulation of all potentially infectious material must be conducted within a biological safety cabinet or other primary containment device. The maximum containment laboratory – Biosafety Level 4 – is designed for work with dangerous pathogens. The WHO Laboratory Biosafety Manual recommends that any activities which require virus culture or manipulation involving the growth or concentration of a pathogen should be carried out in a BSL3 facility while routine diagnostic procedures (such as serology, haematology and biochemistry) or the manipulation of inactivated agents can be conducted under BSL2 conditions. Aerosol-generating procedures must be carried within a class 2 biological safety cabinet within a BSL3 laboratory and the operator should follow strict transmission-based precautions, including the use of appropriate personal protective equipment.

Concerns have been raised that there is a lack of standardisation in biosafety policy, practice and monitoring of the current levels of biocontainment within and between countries (Mackenzie and Olowokure, in press). Differences in requirements exist between animal and human laboratory biocontainment requirements within the United States, and between the US, British, Australian, European, Canadian and WHO guidelines (Mackenzie and Olowokure, in press). Accreditation of laboratories does not occur in many developing countries that handle dangerous pathogens. A set of international standards would assist in assuring conformity with good operating procedures

and standards of biosafety and biosecurity. International standards are also required for quality assurance, building engineering, laboratory management, staff training, health monitoring of laboratory staff, and incident investigation and management in the event of accidental breakage, spills and other potentially hazardous events (Mackenzie and Olowokure in press).

6
Applied Research

Global efforts are underway to develop a comprehensive research agenda on the determinants of inter-species transmission of disease for policy development and evidence-based prevention and control activities. Key areas of research include:

- The environmental, ecological and climatic factors which facilitate the emergence, maintenance and transmission of zoonoses, including deforestation, developmental projects, global warming, urban ecology, the dynamics of inter-species transmission of infectious diseases between wild and domestic animals and between animals and humans.

- The evolutionary changes of pathogenic infectious agents that result in increased infectivity, virulence or transmissibility and mechanisms of pathogen dispersal.

- The human, livestock and wildlife host factors that facilitate the emergence of infections and their spread and the protective factors resulting in resistance to disease, including genetic analysis.

- New diagnostic tools and surveillance technologies that can support rapid and accurate diagnosis under field conditions. Technologies that have proven particularly useful in the study of emerging zoonoses include remote sensing and global information systems.

- Improved mathematical models of transmission dynamics to improve our ability to predict future disease outbreaks.

- Improved case management and the development of new vaccines and other therapeutic modalities for the treatment and prevention of emerging zoonoses.

- The social inequalities and behavioural factors that influence the distribution of emerging diseases, their course and the populations that are most affected.

- The impact of disease control strategies on affected populations, including the costs, benefits, incentives and disincentives of participation in control measures in order to frame effective interventions.

- The effectiveness of intervention methods used by public health, agriculture and wildlife sectors to prevent, mitigate and control emerging zoonotic diseases, and the risks and benefits for other sectors.

- Economic evaluation of historical outbreaks and modelling of future outbreaks of zoonotic disease.

- Development of more powerful study designs and sampling methodologies, and diagnostic methods, to optimise wildlife surveillance.

7
Conclusions

As it is highly likely that zoonoses and animal diseases with the potential to affect human health will continue to emerge, surveillance for zoonotic diseases will need to be strengthened and maintained at national and international levels. Surveillance, laboratory capability, knowledge, skills and technology transfer, and communications along with adequate funding for all these aspects are key elements when developing capacity to detect and respond to emerging diseases. Applied research is another critical component that is often under-funded, with evident funding shortfalls in the wildlife sector.

Viral zoonoses are the most common diseases to have emerged in the last four decades. Recognition of the importance of wildlife as a reservoir of zoonoses is increasing, although in most countries, the resources provided to wildlife research and conservation management remain limited. An expanded research agenda in the factors leading to disease emergence integrated across the human health, livestock and wildlife sectors is needed to inform risk assessments and preparedness planning for the prevention and control of zoonoses. Cost-effective prevention, investigation and control strategies necessitate an interdisciplinary and multi-sectoral approach within countries and internationally.

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