

Emerging zoonotic epidemics in the interconnected global community

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The rate at which epidemics of zoonotic disease in humans have surfaced over the past 25 years has shaken – some would say shattered – the assumption that zoonotic diseases are under control, says Paul Gibbs. In this review he analyses the global factors that have led to the increased emergence of zoonotic diseases, sketches several recent epidemics (and where relevant, their relationship to bioterrorism), discusses the lessons learned, and concludes by outlining an agenda for action

CHANGING LANDSCAPE OF INFECTIOUS DISEASE AT THE BEGINNING OF THE 21ST CENTURY

● This article is based on the Wooldridge Memorial Lecture given by Professor Gibbs at this year's BVA Congress, held at the Royal Society of Medicine from September 30 to October 1. While it attempts to be global in scope, the perspective inevitably draws upon the experience of the author in living both in the UK and the USA, strengthened by visits to many of the countries from which the diseases discussed in the review have emerged

In contrast with today, the period during the 'cold war' was characterised by few concerns over epidemic diseases. In the late 1960s, the Surgeon General of the USA, William H. Stewart, said that '... it was time to close the book on infectious diseases and pay more attention to chronic ailments such as cancer and heart disease.' Who was to doubt the Surgeon General? Smallpox was all but eradicated using a vaccine little changed from the one developed by Edward Jenner in the 1790s. Other diseases, such as measles in children and rinderpest in cattle, were also succumbing to vaccination campaigns. A measure of that success came towards the end of the 1970s, when the world rejoiced that smallpox had become the

first disease to be eradicated from the human species.

Such halcyon days from the 1960s to the early 1980s are now only a memory. The turn of this century has brought with it a succession of disasters, both natural and man-made. We now live in a closely interconnected global community; a global society that has survived the 'cold war' only to be plunged into a 'war on terrorism'. The emergence of Al Qaeda, the wars in Afghanistan and Iraq – and natural disasters such as the tsunami in Asia, the earthquake in Pakistan, and the hurricanes along the USA's Gulf Coast – have overshadowed the large number of naturally occurring emerging diseases and epidemics that we have faced around the world in recent years. Amid all the disasters, perhaps we have failed to see the warning signs of possibly even bigger epidemics ahead.

Laurie Garrett expressed her concern over newly emerging diseases in a

'world out of balance' as early as 1994 in 'The Coming Plague' (Garrett 1994). Avian influenza is one such threat today; a reminder to society of the potential of disease to wreck communities and nations. It was noted that the earthquake that led to the Asian tsunami in 2004 literally rocked the earth's rotation for a millisecond. In the 21st century, emerging zoonotic diseases have the potential – a possibility more than a probability – to devastate the global human population, the effect of which could be to 'rock' the earth for a century or more.

Today, it has been estimated that 75 per cent of emerging diseases are zoonotic.

Emerging diseases caused by viruses lead the charge of those that have shown their global reach since 1999 (Table 1). It is estimated that the rash of emerging or re-emerging livestock disease outbreaks around the world since the mid-1990s, including bovine spongiform encephalopathy (BSE), foot-and-mouth disease (FMD) and avian influenza, has cost the world's economies over US \$80 billion (Karesh and others 2005).

EMERGENCE OF BIOTERRORISM AS A GLOBAL THREAT

The attacks on the World Trade Center in New York and the Pentagon in Washington in September 2001 were followed quickly that October by the release of weapons-grade anthrax spores in the Capitol buildings. With the arrival of actual bioterrorism, not just the threat of it, at the heart of the US Government, a sea change has occurred in the way in which the USA and many other countries must view infectious diseases. A new dimension has been added to our concern. The natural biology, environmental stability and availability of disease agents, and the ease with which they can be obtained, make several prime candidates (Table 1) as potential instruments of bioterrorism. Remember: (a) bioterrorism is not biowarfare, and extensive epidemics are not a prerequisite for creating great public anxiety; (b) while it is an old adage, it is still true that the only significant difference between a naturally occurring epidemic and one that has arisen through bioterrorism is motive; and (c)

At the start of his lecture, Professor Gibbs drew attention to a portrait of Edward Jenner that hangs on the walls of the Royal Society of Medicine. Jenner's observation that the zoonotic character of cowpox could be used to protect against smallpox was, he suggested, 'arguably the most important observation in the history of infectious disease'. In honour of Jenner's scientific approach and the role of the cow in protecting mankind from smallpox, Louis Pasteur named the process of inoculation 'vaccination' (from vacca, Latin for cow) – appropriate recognition for the 'one medicine' for human and veterinary disease, as practised by Jenner and Pasteur



Portrait: Royal Society of Medicine

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TABLE 1: Simple analysis of the relative importance and epidemic potential of several emerging diseases*

Priority diseases	Animal health impact	Zoonotic potential	Significant bioterrorism potential	Concerns
West Nile encephalitis	+++	+++	No	Will it spread in Europe? What of the future in South America?
Foot-and-mouth disease (FMD) [†]	++++	+/-	Yes	When and how might FMD reappear in Europe or the USA?
Severe acute respiratory syndrome (SARS)	-	+++	Yes	When might this sleeping dragon of Asia re-awake?
Monkeypox	+	++	Yes	Could it be smallpox next?
Bovine spongiform encephalopathy	+++	++	Yes	A diminishing epidemic in both cattle and humans?
Bluetongue	+++	-	No	Is global warming aiding spread of the virus into Europe?
Avian influenza H5 and H7 serotypes	++++	++++ [‡]	Yes	Truly the enemy at the gate of the Western World?
Unknown agent created through biotechnology for use as a bioterrorist weapon	++++	++++	Yes	Technically feasible. The USSR reportedly developed a smallpox/Ebola recombinant virus

* For brevity, several emerging diseases are not mentioned. The most important is AIDS, the causal virus of which is HIV. HIV is believed to have its origins in primates in West Africa and thus should also be considered a zoonotic disease. The table also omits several zoonotic viral diseases, such as Ebola and Nipah virus, which have remained largely localised in Africa and Australasia, respectively, but have the potential for pandemic spread

[†] While FMD rarely causes human infection, the draconian 'stamping out' strategies to control disease can cause anxiety and grief of public health significance

[‡] Only if adaptation to humans and effective transmission occurs

there is always a possibility that bioterrorism could arise through a novel recombinant virus created purely for the purpose of bioterrorism. Were an attack to occur with a novel agent, the efficiency of the first response would be critical to nip the epidemic in the bud. Looking for the unknown enemy over the horizon has always been difficult!

FACTORS PROMOTING INCREASED NUMBERS OF EPIDEMICS IN THE 21ST CENTURY

There are myriad interconnected factors influencing the increasing rate at which diseases have emerged in recent years, including:

- Extensive global trading and tourism patterns of the late 20th century (pathogens as hitchhikers);
- Speed of mass transportation (less than disease incubation time, so infected people can travel undetected);
- Exposure to new pathogens through ecosystem disruption (human population pressures; exposure to wildlife);
- Intensification and monoculture in farming (potentially leading to viral amplification);
- Technical sophistication in food processing, masking its true origins (individuals cannot exercise innate protective responses); and
- Evolutionary pressures through overpopulation and change in tropism (intensive agriculture).

Often we do not truly understand the unique combination of factors that

promotes an epidemic of human disease. However, a dispassionate analyst quickly recognises the ever increasing population of one species, man, and the success of this species in the 21st century in colonising virtually the entire land surface; gaining the ability to travel quickly around the world and in large numbers; and establishing a complex network of global trading. These are important factors in explaining the increasing rate of zoonoses in the 21st century.

With so many infectious agents arguably still waiting to be discovered, defining the probability that a specific disease will emerge is impossible. What is evident is that the ever increasing human population brings the species into greater contact with animals, and greater global connectivity provides rapid dissemination of infectious diseases from the initial focus. Whereas in previous centuries a disease focus might have died out through failing to establish a chain of transmission, now it has the opportunity to rapidly recruit susceptible hosts on a global stage. To draw an analogy, there is now so much available tinder on the forest floor that the flickering early flame can rapidly be fanned into a forest fire.

In support of this thesis, consider the following:

- The human population of Earth took until 1800 to reach one billion; by 2000 it had exceeded six billion;
- In 1800, the time taken to circumnavigate the globe by sailing ship was approximately one year. Today, no two cities served by commercial aircraft are more than 24 hours apart;

- Annually, the world's airlines carry a total approaching two billion passengers. At any one moment, about half a million people worldwide are flying in commercial aircraft (Select Committee on Science and Technology 2000);

- In 2003, there were 200 million passenger departures/arrivals at British airports; and

- In lieu of precise trade data, Billy Karesh of the Wildlife Conservation Organization in New York conservatively estimates that in east and south-east Asia, tens of millions of wild animals are shipped each year regionally and from around the world, for food or use in traditional medicine (Karesh and others 2005). Live turtles are even shipped to the markets of China from Florida.

CASE STUDIES OF RECENT EPIDEMICS AND THE LESSONS LEARNED

The following overview of epidemics, from 1999 to 2005, focuses on the USA. It illustrates many of the points raised earlier. By and large, the reactions of the government and citizens of the USA reflect those of any country. Table 2 gives the timeline and the reaction within the USA to the events.

1999: West Nile encephalitis in North America

When West Nile virus was confirmed as a cause of encephalitis in humans in New York in 1999, the pernicious effect of the Surgeon General's remarks in the 1960s, and the consequent extent of the neglect of public health in the USA, were

Cattle carcasses burning on a farm in Gloucestershire during the 2001 foot-and-mouth disease outbreak. Such images, widely disseminated by the media, horrified the public, and had an impact on animal disease control policies that extended well beyond the UK



Photograph: Barry Batchelor/PA/Empics

finally realised. West Nile virus had never been recorded previously in the Western Hemisphere, and no one had ever considered that it could be introduced.

St Louis encephalitis (SLE) virus, a virus related to West Nile virus and endemic to the USA, was initially diagnosed as the cause of the epidemic, until an astute veterinarian at the Bronx zoo noticed that several native birds were dying. Since SLE virus is not recognised as pathogenic for indigenous birds in the USA, the observation quickly led to the correct identification of the virus. The delays, first in recognising that an epidemic of human encephalitis was underway in New York (cases were occurring in several boroughs and were not initially recognised as linked), and, secondly, in identifying the causal virus, contributed to problems in implementing aggressive attempts to control the mosquito vectors and, as a result, the virus successfully overwintered. Each subsequent year the virus spread geographically, and by 2004 the virus had spread widely across the contiguous states of the USA, several provinces of Canada, and south to the Caribbean and Mexico. By 2004, over 15,000 horses were known to have died of West Nile encephalitis in the USA. In

2003 and 2004 alone, there were over 12,000 confirmed cases of West Nile infections in humans, with 362 deaths.

Molecular analyses of West Nile viruses from many different geographical sites around the world indicated that it might have been introduced from Israel. The precise origin and method by which the virus arrived in the USA are unknown. It is most likely that an infected mosquito arrived on a flight from the Middle East. In contrast with aircraft arriving in Australia, the cabin spaces of intercontinental flights entering the USA are not routinely sprayed with insecticide before entering the USA.

2001: Foot-and-mouth disease in Europe

It may seem surprising to see FMD discussed in this review. While FMD virus can cause human disease, this is only rarely reported, even during extensive epidemics in domestic livestock. When FMD occurs in a country that is normally free of disease and that does not vaccinate its livestock, a 'runaway' epidemic can ensue. To control the epidemic, a draconian 'stamping out' policy is usually imposed. This is what happened in the UK and the Netherlands in 2001. The psychologi-

cal impact (sometimes even leading to suicide) of seeing one's herd slaughtered makes this a disease of public health importance beyond zoonotic infection.

The stamping out of FMD in Europe in 2001 was carried out in the daily spotlight of the world's television cameras. Many evenings in the USA, it was the lead story for the prime-time news. 'FMD' even made it as one of the top 10 new words for CNN in 2001. The extent of the slaughter in the UK, necessary to create the 'firebreaks' around infected farms, was horrific to most viewers. For those in government in the USA, this reaction illustrated the power of the media to lead public opinion, sensitised them to the genuine anguish of society over animal welfare and stamping out policies, and illustrated the logistical complexity of disease control and carcase disposal. The controversies that arose through the use of extensive slaughter to control the epidemic and how, in turn, the concerns of society are being translated into a radical change in policy within the European Union (EU) for the control of FMD and other exotic animal diseases, have been noted with keen interest by countries outside the EU.

Before the terrorist attacks on the World Trade Center and the Pentagon and the intentional release of anthrax spores in Washington DC in the autumn of 2001, the risk that food production would be targeted by bioterrorists was of concern only to those who had intimate knowledge of animal and plant pathogens. While there is no evidence to believe that the epidemic of FMD in the UK, and its subsequent extension to continental Europe, was caused by bioterrorism, the extent of the epidemic indicated to many in the USA that FMD could be a very powerful bioterrorist weapon in causing widespread disease in livestock and economic disruption for the targeted country. Further, while the public's health remains the first priority of the nation, the importance of protecting the food supplies has not been ignored. The US government, in common with others, takes the threat of a bioterrorist attack using FMD very seriously. For example, the research centre for FMD on Plum Island, formerly in the Department of Agriculture, now has a new administrative home in the Department of Homeland Security, and information on the stockpile of FMD vaccines is now restricted.

The epidemic of FMD in Europe in 2001 provided important lessons in the control of highly infectious animal diseases in large populations, and the expectations of modern society in industrialised nations. ►

TABLE 2: Timeline of epidemic zoonoses of the 21st century from the perspective of the USA

Year	Event	Comment from USA perspective
1999-ongoing	West Nile virus arrives in New York	The poor state of preparedness of national public health services in the USA is realised
2001	Foot-and-mouth disease hits UK 9-11 attack on the World Trade Center	Reality check! Is the USA equally unprepared? War on terrorism begins
2003	Anthrax bioterrorism hits Washington DC SARS pandemic Monkeypox in the Mid West	The nation feels vulnerable Canada is hit hard, but the USA is lucky Could it have been a bioterrorist attack using smallpox? Do we truly import wildlife from Africa with no import restrictions or health checks?
2004	BSE H5N1 avian influenza explodes in Asia	Did we say we would never get it? Some human cases and deaths. Fear of pandemic human influenza rises
2005	H5N1 avian influenza spreads to more countries in Asia and then to Europe	Virus adapts to village poultry, ducks and wild birds. More human cases. Fear of human pandemic increases as migratory birds spread the virus to Europe

2003: Severe acute respiratory syndrome

In an average winter, significant human mortality is associated with influenza. Death is seen mostly in the elderly from complications such as pneumonia (in the USA, there are approximately 30,000 influenza-related deaths each year). The winter of 2002/03 in the Northern Hemisphere was relatively quiet for influenza, but a respiratory disease, now known as severe acute respiratory syndrome (SARS) emerged, causing human deaths in several countries around the world. While the disease, which is now known to be caused by a novel coronavirus, did not cause a major epidemic, either in the UK or the USA, it had a significant impact in Asia and in localised areas worldwide. The World Health Organization (WHO) declared the epidemic over in mid-July. A total of 916 people died, mostly in China. In North America, the Canadian city of Toronto became the focus of attention as SARS spread within several hospitals, causing 41 deaths. At one time, travellers were advised by the WHO to avoid travelling to Toronto. Quarantine for the control of human disease fell into disuse in the latter half of the 20th century, but was re-introduced on a limited scale to control SARS. It was largely voluntary quarantine, but governments quickly reviewed their legislative authority to impose mandatory quarantines on their citizens.

The origin of the virus appears to have been Guangdong Province in China, but only when the disease appeared in Hong Kong was this emerging disease recognised. Hong Kong is a major airport hub for Asia, and international travellers in the incubatory phase of the disease are believed to have disseminated the virus widely from Hong Kong. The causative virus was quickly recognised as a novel coronavirus using traditional and molecular diagnostic techniques. Unlike many coronaviruses, SARS virus replicates with cytopathic effect in Vero cells, thus simplifying study.

Since so many coronaviruses are capable of causing disease in domestic animals, the possibility that the SARS virus could have originated in wild animals was quickly investigated. Wild animals are still widely used in traditional Chinese cuisine and sold caged in markets. Coronaviruses that appear to be very closely related to SARS virus have been isolated from masked palm civets (*Paguma larvata*) and raccoon dogs (*Nyctereutes procyonoides*) sampled in Chinese markets. The true reservoir of the virus has recently been identified as the Chinese horseshoe bat (*Rhinolophus sinicus*) (Lau and others 2005).

A US National Intelligence Council report stated that, even though SARS has



Photograph: Vincent Yu/AP/Empics

Life goes on . . . a wedding in Hong Kong during the SARS outbreak in 2003

infected and killed far fewer people than other common infectious diseases such as influenza, malaria, tuberculosis, and HIV/AIDS, it has had a disproportionately large economic and political impact. This is because it spread in areas with broad international commercial links and received intense media attention as a mysterious new illness that seemed able to go anywhere and hit anyone. As the first infectious disease to emerge as a new cause of human illness in the 21st century, SARS underscores the growing importance of health issues in a globalised world (US National Intelligence Council 2003).

2003: Monkeypox infects humans in the USA

The SARS epidemic illustrated the importance of wildlife as a source of zoonotic viruses, and the extent of the international trade in wildlife species for food and traditional medicine. An outbreak of a pustular pox disease, that was similar to very mild cases of smallpox, in pet owners and handlers (including a veterinarian) in the USA in early summer of 2003, raised alarm and also pointed to the importance of wildlife species in zoonotic disease.

The disease was quickly diagnosed as monkeypox, an uncommon disease usually restricted to West and Central Africa. The disease was first recorded in the 1950s in monkeys, hence its name. Subsequently, the virus was recognised in the 1970s as a cause of a disseminated pustular skin disease in humans similar to smallpox (but less severe) in the same geographical areas as the affected monkeys. The causal virus is an orthopox virus closely related to smallpox, vaccinia and cowpox viruses. Epidemiological studies of monkeypox have now established that rodents are the reservoir of the virus and that the disease in monkeys and humans is incidental. The specific role of any particular species as

a reservoir has not been established. While the virus can be transmitted from monkeys to humans, and indeed from one human to another, a continuous chain of transmission is not established.

Following the use of anthrax for terrorism in October 2001, the public in the USA had been warned that smallpox could be used with far greater effect than anthrax. The risk of a terrorist using smallpox virus has been taken seriously; many first responders and medical staff throughout the USA have been vaccinated. Considering the clinical similarity between early cases of smallpox and monkeypox, reports of disease in humans early in May 2003 understandably caused alarm. Could this be smallpox? Such fears were relatively quickly dismissed once the virus had been characterised. However, the porous nature of the nation's borders to the introduction of the virus and the ease with which it was spread were both alarming features of the outbreak. At the time, there were no restrictions on the importation of wild rodents from West Africa.

The source of the outbreak was traced to a legal importation of approximately 800 small mammals from Ghana in West Africa to Texas in April 2003. The consignment contained 762 African rodents, including rope squirrels (*Funisciurus* species), tree squirrels (*Heliosciurus* species), Gambian giant rats (*Cricetomys* species), brushtail porcupines (*Atherurus* species), dormice (*Graphiurus* species) and striped mice (*Hybomys* species). The imported rodents were then distributed to several states. Native pet prairie dogs (*Cynomys* species) housed near some of these rodents in a distributor's premises in Illinois became infected, and it was the subsequent distribution, exhibition and sale of the prairie dogs that spread the virus to people.

Black H'mong women pursue traditional crafts in north-west Vietnam. As in other parts of Asia, much of the rural population of Vietnam live in close contact with their livestock (chickens, ducks, water buffaloes and pigs)



Photograph: Paul Gibbs
lance evidence to indicate that BSE is not extensive in the cattle population, has failed to convince Asian buyers to open their markets to American beef and the cattle industry is currently losing an estimated US \$10 billion per annum in export sales.

The history of BSE and the biological and ecological enigmas posed by prion-associated diseases have highlighted the need to study the transmissible spongiform encephalopathies (TSEs) in greater detail. Since the 1970s, the USA has also had to contend with the problem of chronic wasting disease (CWD) of deer. This disease, which occurs both in free-living deer and farmed deer over a wide area in both the USA and Canada, does not appear to cause disease in humans, but there is an abiding concern that CWD could also be a public health issue. The control of CWD is a priority within the USA and Canada for wildlife and regulatory officials.

A quote from MacKenzie (2004) – 'It started out as a British disease, but the UK exported it and then its trading partners spread it even further afield. Now no country can be sure it has kept BSE out. Mad cows have gone global' – is arresting. Fortunately, the global epidemic of BSE is, in the opinion of many, now over. Because of the prolonged incubation period, and the stable nature of prions, we can expect to see occasional cases of BSE and possibly vCJD occurring in countries around the world for many years. However, prevention of the cycling and amplification of prion materials through the supplementation of cattle feed with meat and bone meal has been identified as the focal point for preventing BSE epidemics, and such supplementation is now proscribed in most countries of the world. But if BSE can occur spontaneously, as many believe is possible through gene mutation, increased surveillance may detect occasional cases in old animals even in the presence of effective feed bans. While extensive human exposure to prion material, as occurred in the UK in the late 1980s and early 1990s, is unlikely to occur, vigilance is needed. The use of prions for bioterrorism should not be ignored.

2004 and 2005: Avian influenza (H5N1) in south-east Asia

While it is unlikely that another epidemic akin to that of vCJD in the UK, of a TSE arising from an animal source, will ever occur in humans, this cannot be said for highly pathogenic avian influenza. The threat of mutation of the avian influenza (H5N1) virus that is causing disease in south-east Asia (and now Europe), so that it can be successfully be transmitted between humans, is of great concern. Although by the mid-

The Centers for Disease Control (CDC) reported that the illness in prairie dogs was reported to include fever, cough, conjunctivitis and lymphadenopathy, followed by a nodular rash. Some prairie dogs died, whereas others apparently recovered. CDC laboratory testing of some animals from the original shipment of rodents from West Africa confirmed the presence of monkeypox virus in one Gambian rat, three dormice and two rope squirrels. The Gambian giant rat, believed to be the index case in the USA, apparently experienced a much milder illness than that observed in prairie dogs, with no respiratory signs and limited skin lesions.

A total of 71 cases of monkeypox in humans was reported. The CDC commented that while infection in humans may be acquired through the respiratory system, most of the human cases in this outbreak appeared to have acquired infection through the skin. The route of transmission in animals is less clear. The virus might have been transmitted by aerosol, through skin abrasions, or through the ingestion of infected animal tissues.

To prevent the introduction of further infected rodents into the USA, and to control the distribution of potentially infected prairie dogs, the federal government banned, in mid-June, the interstate movement, sale, exhibition and release into the environment of prairie dogs, and those species of West African rodents already in the USA as listed above. The order also banned the importation of all rodents from West Africa. The outbreak illustrated that historically there has been little oversight of international trade in pet animals and wildlife species in the USA, and also that there is no single agency with jurisdiction.

2003: BSE in the USA

The first recognition in the USA in December 2003 of BSE, or mad cow disease as it is most commonly called in the popular press, in a cow previously imported into the USA from Canada, was unexpected. Because of the complexity of cattle marketing in North America, the historical reluctance of the cattle industry to support a robust animal identification scheme, and the subsequent confirmation of a second case in a cow born in Texas, the USA has joined the list of those countries considered infected with BSE.

BSE was first identified in the UK in 1986 and recognised to be caused by a prion. The extensive epidemic of BSE in the UK is believed to have been associated with cattle feed supplemented with meat and bone meal infected with prions. However, it was not until 1996 that an association was made between BSE and a newly recognised encephalopathy affecting young people that became known as variant Creutzfeldt-Jacob disease (vCJD). The assumption is that vCJD is acquired through eating infected beef. Since that time, cases of BSE have been recognised in cattle born in most countries of Europe, Japan and Canada. The incubation period for all prion diseases is long and partly determined by the genotype of the individual, thus the extent of the epidemic of vCJD cannot be predicted (so far, there have been approximately 158 cases in the UK). The earlier estimates of many thousands of young people developing this fatal disease appear to have been wrong; nevertheless, the public fear of vCJD, once BSE is discovered in a country, has invariably had an enormous economic impact extending far beyond the beef industry. The economic impact of BSE has been and continues to be enormous in the UK, but the USA, despite surveil-

dle of November 2005 only 130 confirmed cases of avian influenza virus infections of humans had been reported in people in Asia since December 2003, the mortality rate has been very high, with 67 deaths (WHO 2005). No convincing evidence exists to suggest that mutation of the virus to allow human-to-human infection has occurred, but the ecology and current virus load in the poultry of south-east Asia significantly elevate the risk of this occurring. If the H5N1 virus were to mutate to permit efficient transmission between humans, and if it were to retain the ability to cause a mortality rate similar to that of the current infections, the ensuing pandemic could be horrific. The Spanish influenza pandemic of 1918, which is believed to have killed approximately 50 million people, had an overall mortality rate of approximately 2 per cent; the current mortality rate of H5N1 avian influenza virus in humans is around 50 per cent.

Since the first identification of H5N1 as a human pathogen in Hong Kong in 1997, the virus has widely established itself in the chicken, and more recently the duck, populations of the rice growing areas of south-east Asia. The 'nomadic' ducks of the villages are clinically normal reservoirs of infection. Earlier in 2005, it was estimated that as many as 10 per cent of the ducks in the Red River delta of north Vietnam were shedding infectious virus (T. Van Dung, personal communication). The ducks often scavenge with the village chickens and pigs, which both may amplify the virus. The ducks, chickens and in some areas possibly the pigs as well, are an enormous source of potential infection for the villagers who unknowingly expose themselves by close contact, when killing and preparing poultry for meals, and specifically when ingesting uncooked duck blood on festive occasions. The veterinary authorities in countries such as Vietnam have encouraged the villagers to reduce the duck herds, but the ducks are valuable to the economy of the village as gleaners of fallen rice after harvesting and for control of the snail and insect populations in the rice fields.

The recent movement of H5N1 virus into Europe with infected migratory and imported wild birds is of great concern to Europe's poultry industry. The migration patterns of the wild birds also extend to Africa; thus H5N1 may, in the waning months of 2005, have the potential to be a pandemic avian pathogen. Amid the intense focus on the risk of pandemic human influenza, it is often overlooked by the media that the virus can cause very high mortality rates in domestic poultry and possibly selected species of wild birds. Certainly,

TABLE 3: Lessons learned from epidemics of the 21st century

Year	Event	Lessons learned/actions initiated by event
1999	West Nile virus arrives in New York	Greater coordination of public health services, improved research and diagnostics
2001	Foot-and-mouth disease hits UK	Worldwide, biosecurity is seen as important and the food supply of nations is seen as vulnerable to bioterrorism. The power of the media to direct public opinion to question disease control policies is realised
	9/11 and anthrax bioterrorism in the USA	Preparedness for bioterrorism accelerates. The USA 'declares war' on terrorism
2003	SARS pandemic	Global surveillance and international cooperation needs improvement. There is increasing awareness of the importance of wildlife in zoonoses
	Monkeypox in the USA	Problems of jurisdiction and the need for concerted action in regulating international trade in wildlife
	BSE in the USA	Awareness of international sensitivity and trade. The interface of complex biology and complex trade
2004/05	H5N1 avian influenza explodes in Asia	All of the above. Need for financial support for developing countries. The importance of international agencies such as the World Health Organization and the Food and Agricultural Organization of the United Nations

there is a risk in Europe that the virus may cause clinical disease in people in close contact with wild birds and poultry, and further that the feared mutation to allow the virus to be transmitted between people could occur in Europe. However, because of the high infection rates (that is, virus load) in the poultry populations of south-east Asia, and the intimacy of the relationship between people and birds in the region, it is more probable that Europeans will be affected by a pandemic human influenza strain that arrives with an infected international human traveller on a commercial flight from Asia, rather than from a mutation occurring in a virus that has arrived in a migratory bird.

Virologists and epidemiologists have been following the deepening problem of H5N1 in Asia since 1997, and have repeatedly warned of the emerging risk of a pandemic of human influenza. To their credit, the countries of the region have wrestled with the problem and invested heavily to control the disease in their poultry, but most are developing countries and lacking resources. Until recently, there has been little concerted financial support from the international community in support of these programmes. The presence of H5N1 in south-east Asia has never been just a regional problem; it has merited attention as a global threat since 1997. In-depth studies are needed to investigate the epidemiology of the disease in Asia. It is not necessarily the same in each country. Socioeconomic analyses are needed to optimise disease control programmes in the communities. Let us hope history does not record that earlier international intervention in south-east Asia might have prevented a catastrophic pandemic of influenza.

The Spanish influenza epidemic of 1918, the reference point for our concern that a pandemic is possible with

H5N1, is now believed to have been caused by a virus that mutated from an avian host to infect humans. Relative to the emergence of H5N1 in Asia, it is appropriate to note a parallel emergence of influenza virus in dogs (Crawford and others 2005). In 2004 and again in 2005, epidemics of canine influenza occurred across the USA. The virus has maintained itself by dog-to-dog transmission and now appears to be endemic. Similar in character to the Spanish influenza in humans in 1918 and cases of H5N1 infections in humans in south-east Asia, some affected dogs die acutely of a haemorrhagic pneumonia. This was the first time that an influenza epidemic had ever been recorded in dogs. The causal virus has been identified as H3N8 and by molecular analysis is closely related to equine influenza virus. The origin of the virus remains unexplained, but the example illustrates the promiscuous nature of influenza virus to 'jump species' and further justifies the concern over the potential of the H5N1 strain of avian influenza to initiate pandemic influenza in humans.

WHAT HAVE WE LEARNED AND HOW ARE WE RESPONDING?

A summary of the lessons learned from each of the epidemics mentioned above is presented in Table 3. It is beyond the scope of this review to discuss them in detail, but the following are examples of political and scientific action in the UK and USA.

- Creation of the Department of Environment, Food and Rural Affairs in the UK during the FMD epidemic.
- Creation of the Department of Homeland Security in the USA shortly after the 9/11 and anthrax attacks.
- Presidential Directive HSPD-9 on

Defense of the USA's Agriculture and Food against terrorist attacks, major disasters and other emergencies in the USA.

- Coordination of laboratory networks across the USA;
- Creation of State Agricultural Response Teams (SART);
- Identification of select agents in conjunction with the CDC; and
- US funding for research on emerging diseases structured to come largely from bioterrorism preparedness.

However, notwithstanding the current drive to address both emerging zoonotic diseases and bioterrorism, the Trust for America's Health and the US National Academies are critical of the ability of the USA to respond to animal-borne epidemics, as detailed below. Other nations can probably identify a similar list.

- The USA lacks a national programme to prevent and control diseases that impact humans, animals and our food.
- There is no coordinated effort or single agency with a 'command and control' responsibility.
- There is a lack of effective communications with the public about these diseases and their impact.
- Disease surveillance systems are not linked.
- Funding to combat bioterrorism has not adequately supported efforts to counter zoonotic disease threats, especially from the animal health perspective and infrastructure.
- There is a fragmentation of jurisdictions, authorities, statutes and research; for example, there are 200 different government offices and programmes responding to five zoonotic diseases.
- Animal and public health are separated by culture and organisation

So how did this situation arise? Certainly, for reasons mentioned at the start of this review, neglect of the public health services and regulatory veterinary medicine had begun in the late 1960s, with consequent intellectual impoverishment in the disciplines of infectious disease and epidemiology. This situation was accelerated in the 1980s by the leaders of the UK and USA. Margaret Thatcher and Ronald Reagan were the architects of the downfall of communism and the end of the 'cold war'; for this they should be applauded. They also championed reduced taxation, and cut government expenditure in the hope that they could reduce bureaucracy and improve efficiency. With regard to the USA, as a consequence:

- Individual states have shouldered

greater responsibility, but have had problems due to the unfunded mandates;

- Public and animal health services were drastically reduced in the 1980s and 1990s;
- There has been inadequate support for developing countries to promote public and animal health; and
- The UN (and its agencies) has become a 'whipping boy' for inefficiency.

AGENDA FOR ACTION

Because of the myriad interconnected factors that promote the emergence of diseases, many of the actions needed for the control and prevention of emerging diseases and zoonoses are multidisciplinary and far wider than simple veterinary responsibility. Several represent an agenda for social reform: human population control; sustainable development; balanced farming, with farmers as stewards of the land; greater commitment to and support of international agencies; coordination of emergency response at the global level; economic support to the developing world; and improved communications with the public. In response, the public has a responsibility in meeting the challenge of emerging diseases and zoonoses by becoming informed and engaged in seeking relevant social reform.

At the veterinary level, we must promote cross-disciplinary science; address 'ecology more than economy'; recognise the importance of wildlife as reservoirs of infection; improve vaccines and diagnostic tests; train and consult field epidemiologists as well as molecular scientists and modellers; improve and coordinate surveillance of disease at the global level; and improve communication with the public on the importance of disease control.

Whether we are involved in clinical practice, research, regulatory medicine, academia or industry, our role as veterinarians and allied professionals, in meeting the challenge of emerging diseases and zoonoses, is to inform and educate at all levels, wherever and whenever we can. We also need to recognise the power of nature, whether it takes the form of epidemics, hurricanes or earthquakes, and be ready to respond. The early events of the 21st century have taught us that we must try harder.

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