Introduction

Livestock infectious diseases and zoonoses

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Infectious diseases of livestock are a major threat to global animal health and welfare and their effective control is crucial for agronomic health, for safeguarding and securing national and international food supplies and for alleviating rural poverty in developing countries. Some devastating livestock diseases are endemic in many parts of the world and threats from old and new pathogens continue to emerge, with changes to global climate, agricultural practices and demography presenting conditions that are especially favourable for the spread of arthropod-borne diseases into new geographical areas. Zoonotic infections that are transmissible either directly or indirectly between animals and humans are on the increase and pose significant additional threats to human health and the current pandemic status of new influenza A (H1N1) is a topical example of the challenge presented by zoonotic viruses. In this article, we provide a brief overview of some of the issues relating to infectious diseases of livestock, which will be discussed in more detail in the papers that follow.

Keywords: emerging infectious diseases; livestock and zoonotic pathogens; vector-borne diseases; global impact; food security

1. INTRODUCTION AND FOOD SECURITY

At the beginning of the twenty-first century, the world is faced with a changing landscape of infectious diseases that affect man and animals, and that pose significant threats to health and welfare and to the international food security agenda. Livestock diseases that have devastating outcomes on animal health and that impact on national and international trade remain endemic in many parts of the world. Threats from old and new pathogens continue to emerge, fuelled by changes in the environment (climate, hydrology, disruption of ecosystems, etc.), in agriculture and food production (intensive systems of husbandry, farming monoculture, food processing, etc.) and in the demography and connectivity of the modern ‘global’ village (population growth, urbanization, international trading, world tourism and rapid transportation, etc.; Gibbs 2005). The spread of new influenza A (H1N1) is illustrative: between February 2009 when the first cases of an influenza-like illness in people were reported in the Gulf coast state of Veracruz, Mexico, and 24 June 2009, it had spread to 91 countries with 55,867 cases reported (see http://www.who.int for daily updates).

The global human population is expected to increase from approximately 6.5 billion in 2008 to approximately 9.2 billion by 2050 (UNDP 2008), with around one billion of this increase occurring in Africa. Population growth on such a scale poses enormous challenges for food production in general, as an increased demand for 50 per cent more food is expected by 2030, and for livestock in particular, especially in developing countries where material increases in household incomes and accompanying urbanization drives demand for meat and dairy products (Delgado et al. 1999; Jones & Thornton 2009). The first year in which more than half the people on Earth (approx. 3.3 billion) inhabited urban areas was 2008, and by 2030, this number is expected to increase to approximately five billion, with the vast majority of urban growth occurring in Africa and Asia (UNFPA 2008). Alongside these unprecedented changes in the size and location of human populations and the demands for food, the impacts of environmental change are likely to be detrimental to agricultural production (Fresco 2009). These factors will therefore drive a requirement for a systematic application of science through the entire food chain in order that all food-producing sectors adapt to changing temperatures, nutrient and water conditions and exposure to harmful pathogens. The opportunities for scientific innovation are tremendous in number and scope and must be exploited if the world’s population is to have enough to eat in the decades ahead. Control of livestock pathogens will continue to be a highly important component of efficient food production and become associated more overtly with the food security agenda.

The world cattle population is estimated currently to be approximately 1.3 billion head, with 30 per cent in Asia, 20 per cent in South America, 15 per cent in Africa, 14 per cent in North/Central America and 10 per cent in Europe (http://cattletoday.info). Estimates of the global number of smaller livestock vary considerably from source to source, but it is

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generally accepted that there are approximately one billion pigs, approximately two billion small ruminants and more than 50 billion poultry reared annually for food production. Methods of farm production are tremendously varied and bring with them their own particular risks in terms of the introduction and transmission of infectious diseases. At one extreme is the very low-intensity subsistence livestock farming, particularly of poultry, sheep and goats, that operates in the poorest of the world’s rural households and that is critical to sustaining local food supplies, alleviating poverty through income generation and for nutritional status. These animals are often kept under scavenging conditions with little attention to disease control, housing or feed supplementation, suffer a high burden of endemic disease and are likely to be in close contact with other livestock species and humans, and potentially in contact with a variety of non-domestic animals. The impact of epidemic diseases on the livelihoods of these poor farmers, particularly if there is high mortality or the imposition of animal movement restrictions or culling, is severe (http://smallstock.info). In this issue, Perry & Grace (2009) consider in detail the impacts that livestock diseases, and control of these, can have on developing and promoting national and international policies that are pro-poor and that will reduce rural poverty. At the other end of the farming spectrum are the highly organized and intensive sectors of the poultry industry where the rapid growth rates of birds reared in stocking densities of up to 50,000 birds in a single shed give the most efficient feed-to-meat conversions of any farm system and provide cheap, high-quality products for the consumer. This intensity of husbandry can only be done by controlling many infectious diseases that would otherwise inflict severe losses or even prevent intensive poultry production completely, by the administration of vaccines at the start of the rearing period. For the poultry sector, the emergence of a new pathogen, or a new variant of an old pathogen has the potential to spread rapidly and devastate national flocks, as has happened on several occasions with strains of highly pathogenic avian influenza (Alexander 2000, 2007; Velkers et al. 2006). Indeed, some outbreaks of highly pathogenic avian influenza have resulted in the destruction of entire national flocks of poultry and complete restocking has been required from an international breeding company before poultry production could be resumed. Such vulnerability illustrates the importance of infectious livestock diseases within the context of global food security.

Some of the pathogens considered in this series of reviews present an actual or real risk to a serious shortage of food in many parts of the world. Within Europe, the recent incursions of bluetongue virus (BTV) and subsequent outbreaks of disease have provided a reminder that livestock can quickly become exposed to the ravages of a new disease that takes hold because of changing conditions. Across Northern Europe, BTV has become a very recent new threat to sheep and cattle and in 2008 the mortality rates of infected sheep were high (more than 10% in some countries). Only the introduction by the UK of a national plan for vaccination against BT in 2008 prevented establishment and spread of the disease, and the high susceptibility of most European breeds of sheep to BTV means that vaccination must continue. While the gradual northward spread of BTV from Northern Africa and the south Mediterranean regions had been observed for several years (Mellor et al. 2008), the abrupt introduction of BTV-8 in Northern Europe was unexpected and a further reminder that livestock diseases can appear rapidly and without apparent warning (Wilson & Mellor 2009). Bovine spongiform encephalopathy in the UK in the 1980s is arguably the best exemplar of a new and highly significant disease of livestock emerging as a consequence of change, in this case to feeding practices, with a profound impact on food supplies and security and public confidence.

## 2. EMERGING AND RE-EMERGING DISEASES

Increases in the emergence or re-emergence of animal and human infectious diseases have been evident in many parts of the world for several years (Weiss & McMichael 2004; Gibbs 2005; Woolhouse et al. 2005). Over 1600 human pathogens are now described, an average of three new diseases is reported approximately every 2 years, and a new infecting organism is published every week (http://www.gideononline.com). Some emerging diseases such as Lyme borreliosis, cat-scratch fever (bartonellosis), fifth disease (parvovirus B19), legionellosis and cryptosporidiosis are actually much older, but the causative agents were recognized only relatively recently; similarly, several presumed non-infectious conditions such as peptic ulcer, Kaposi sarcoma and cervical cancer are now known to have infectious aetiologies. Nevertheless, there is no doubting the emergence of many genuinely new diseases and, whereas 60 per cent of all known infectious agents are zoonotic (Taylor et al. 2001; Jones et al. 2008), it is estimated that approximately 75 per cent of ‘new’ human pathogens reported in the past 25 years have originated in animals and the risk of zoonoses is predicted to continue to increase (King et al. 2006). RNA viruses pose particularly high zoonotic risks because they can emerge and spread rapidly and a recent statistical analysis of 146 viruses of livestock indicates that the ability of a virus to replicate in the cytoplasm (without nuclear entry) is the strongest single predictor of cross-species transmission and the ability to infect humans (Pulliam & Dushoff 2009).

Against the background of zoonoses accounting for around 60 per cent of new disease introductions (Taylor et al. 2001; Jones et al. 2008; Jones & Thornton 2009), the ‘megacities’ of the world provide an obvious focus of attention as they typically constitute melting-pot environments for the mixing of human and animal infectious diseases and their potential rapid spread, both locally and internationally. In 2000, there were 18 megacities with populations in excess of 10 million inhabitants, by 2025 Asia alone is expected to have at least 10 megacities and by 2030 over two billion people in the world will be living in slums associated with cities (http://en.wikipedia.org/wiki/Megacity). Mexico City, with a

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population of around 23 million people, was the focus of the early phase of the 2009 spread of influenza A/H1N1, and Ma et al. (2009) in this issue describe the emergence of zoonoses in the context of China, where it is forecast that cities will contain a total population of 800 million people by 2020. The emergence of the severe acute respiratory syndrome (SARS) virus and its rapid international spread provides another recent example of the transmission of a new disease from a megacity. Fortunately, the outbreak of SARS was ‘owned’ by the countries involved subsequently and a series of fast-acting global campaigns by medical practitioners and others proved adequate to stop the disease from becoming established. However, many diseases, including livestock diseases, are regarded as seemingly intractable problems and if the affected areas of the world straddle political or economic boundaries, especially involving countries in different national, regional and economic groupings, a lack of ownership of the disease may more typically define the need for containment and control.

The rate of introduction of vector-borne pathogens to previously ‘free’ areas of the world is increasing (Jones et al. 2008). It is estimated that almost half of the world’s population is infected by vector-borne pathogens (http://sedac.ciesin.columbia.edu) with the greatest impact on developing countries within tropical and subtropical areas. The impacts of climate change and global warming are becoming more obvious and the survival and spread of BTV into Northern Europe provides a disturbing example of how an ‘exotic’ vector-borne livestock pathogen can quickly become established within new geographical regions to present new and significant risks to livestock production. Since the arrival of BTV-8 in The Netherlands in 2006, bluetongue (BT) has spread widely throughout Northern Europe with around 57 000 holdings in Europe affected by BTV in 2007 (with tens of thousands of animals killed) and around 33 000 holdings were affected in 2008. Significantly during the past 3 years, more serotypes have been introduced very recently within Northern Europe (including BTV-1, BTV-11 and BTV-16) and, with BTV-1 circulating, it is now clear that ongoing and sustained vaccination campaigns will be necessary for several years if the disease of BT is not to cause further welfare problems and high rates of mortality in sheep.

Other livestock diseases are also moving geographically and include African Swine Fever (ASF), the cause of a very serious haemorrhagic fever of pigs, which leads to mortality rates close to 100 per cent. Rather typically for diseases that are now emerging as serious pathogens on a potentially far larger scale than hitherto (and somewhat neglected for scientific study), there is no vaccine against ASF virus (ASFV) and control and has to rely on other approaches, such as slaughter of infected herds. ASF had been previously confined mainly to sub-Saharan Africa, with continued spread to previously uninfected countries on that continent, but the introduction of ASFV into Georgia in 2007 and its subsequent spread from the Caucasus has introduced a new risk to pig production in Europe. In this issue, Costard et al. (2009) review the mechanisms by which ASFV is maintained within wildlife and domestic pig populations, how it can be transmitted, the broader risks for global spread of ASFV and how disease might be mitigated. Wild boars have the potential to distribute ASFV widely and they are also known as reservoirs for a number of other important diseases and their growing importance in transmission of zoonotic diseases is the specific theme of Meng et al. (2009) in this issue. The roles of wildlife in transmission are being identified with increasing clarity and for avian influenza wild waterfowl have been shown to be capable of widely distributing the virus. Iqbal et al. (2009) in this issue set the scene for their work on investigating whether different avian influenza viruses show variation in the degree of diversity from the consensus sequence of the virus as they replicated in different hosts by broadly reviewing the maintenance of highly pathogenic H5N1 viruses in different avian host species. They note the prevalence of the virus in waterfowl such as ducks and swans, but also a variety of other wild bird species, including sparrows, crows, magpies and birds of prey.

Other wildlife seen as increasingly important in the transmission of zoonotic pathogens includes the fruit bat, which is known to be a reservoir of internationally important zoonotic pathogens such as Hendra virus and Nipah virus. Greater risks to human health from wildlife pathogens appear to be inevitable as a consequence of increasing human contact with wildlife through greater access to, and disturbance of, wildlife habitats. Deforestation and the taking of land for livestock farming can lead to the habitats of wildlife being disturbed, and the spread of Nipah virus to pigs (and thence to humans) in 1998 in Malaysia is associated with the movement of fruit bats from their forest environment to cultivated orchards and pig farms, driven by fruiting failure of forest trees during El Nino-related drought as more land was sought for farming (Chua et al. 2002; Looi & Chua 2007).

In general, much less is known about infectious agents of wildlife, livestock and even companion animals than of humans, and there are several examples where enzootic viruses of animals (SARS coronavirus, hantaviruses, Ebola and Marburg viruses, Nipah virus, Hendra virus and human immunodeficiency viruses) were completely unknown until they switched hosts to cause disease in humans (Parrish et al. 2008). However, emerging infectious diseases (EIDs) and zoonoses are not solely due to viruses and a recent detailed study of 335 EID events in man and animals between 1940 and 2004 concluded that more than 50 per cent were due to bacteria or rickettsia, more than 10 per cent to protozoa, 6 per cent to fungi and 3 per cent to helminths (Jones et al. 2008). A major concern is that vector-borne diseases have increased dramatically over the last decade adding support to hypotheses that climate change drives emergence of diseases where arthropod vectors are sensitive to environmental changes. Tropical areas have seen the highest increases in EIDs, and while those caused by zoonoses emanating from wildlife are correlated with wildlife biodiversity, those caused by emergence of new drug resistant strains are correlated with...

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agronomic factors such as antibiotic use and population density. In the spring of 2009, a new influenza A (H1N1) virus emerged and spread rapidly throughout the world, and was declared a pandemic by the World Health Organisation on 11 June. Epidemiological data indicate that the outbreak in humans started in mid-February in Veracruz, Mexico (Fraser et al. 2009), the virus is related to swine influenza A (H1N1) viruses recently circulating in pigs in North America and in Europe/Asia and carries a mixture of genes from viruses circulating in these two geographical regions (Garten et al. 2009; Trifonov et al. 2009). Six gene segments are most similar to those of swine H1N2 influenza A viruses isolated from North America in the late 1990s, whereas two gene segments are related to those of Eurasian strains of the early 1990s. Evolutionary phylogenetic analysis suggests that it is likely that initial transmission to humans occurred several months before recognition of the outbreak and that it is possible that reassortment of swine lineages to generate the direct precursor of the pandemic strain may have occurred years ago (Smith et al. 2009). However, the virus has not been previously detected in any animal or human populations and definitive scientific evidence to support its origin directly in pigs is not yet confirmed (Irvine & Brown 2009). It has been established experimentally that the virus can infect and transmit between pigs (Brookes et al. 2009), and it is highly probable that natural transmissions between humans and pigs will become a feature of the pandemic, although a complete picture of the potential host species range of these viruses has not yet emerged and many questions relating to disease severity in susceptible hosts, transmission dynamics within and between hosts and probable risks of selection for increased virulence due to zoonotic transmission remain to be determined.

Maudlin et al. (2009) in this issue make the point that, unlike newly emerging zoonoses that attract the attention of the developed world, many endemic zoonoses are neglected by comparison and this ‘in turn artificially downgrades their importance in the eyes of administrators and funding agencies’. This is a problem familiar to most scientists working on endemic livestock pathogens per se and presents many risks to the broader relevant scientific activity, not least the prospect that important basic and underpinning research data, tools and reagents are not in place. A good example of endemic zoonoses that continues to cause divergent clinical disease is toxoplasmosis, caused by the ubiquitous apicomplexan protozoan Toxoplasma gondii, which has high prevalence in many parts of the world associated with consumption of tissue cysts in undercooked meat, or exposure to oocysts derived from cat faeces (Sibley et al. 2009, this issue). As well as causing congenital infections with severe clinical sequelae, T. gondii establishes chronic, persistent infection in humans with a lifelong risk of reactivation, often associated with immunosuppression. Ocular toxoplasmosis is on the increase in immunocompetent people throughout the world, with an estimated incidence of 2 per cent in the USA (up to five million patients) and a much higher incidence in southern Brasil (Holland 2003) where it has been shown recently that clinical disease is associated with the emergence of newly described divergent parasite genotypes (Khan et al. 2006).

The changing incidence of pathogens and patterns of diseases over time requires the scientific community to review, develop and use different sets of skills. For example, climate change and the increasing spread of vector-borne diseases has driven a need for more entomologists and vector biologists and the re-emergence of helminth infections globally will, as Robinson & Dalton (2009) note in this issue, increase the need for basic laboratory research on zoonotic helminths. As the diseases change, so will the professional skills set required.

3. PAST SUCCESSES AND FUTURE PROSPECTS
Infectious diseases are remarkably difficult to eliminate and only smallpox virus has formally been eradicated. However, a highly significant veterinary achievement is the expectation that, by 2010, the disease rinderpest (the cause of cattle plague) will also have been eliminated from the planet. This prospect was facilitated by the launch in 1994 of a Global Rinderpest Eradication Programme (GREP) both to consolidate gains in rinderpest control and to move towards disease eradication. While the biology of the virus was permissive to control by vaccination, the GREP was ultimately successful because it implemented a highly effective international coordination mechanism to promote the initiative, confirm freedom from rinderpest in affected areas and to deliver technical guidance and the means to achieve the goals. Thus, the expected eradication of rinderpest represents a triumph for a holistic approach to control, which integrates vaccination, robust diagnostic practices and, crucially, the political wills of many countries.

Unfortunately, for the prospects of further eradication successes, most pathogens are characterized by phenotypes presenting different antigenic forms that are stable with time (antigenic diversity) or that show antigenic variation during the course of infection. The presence of multiple serotypes or variants of a pathogen is a major hurdle for long-term control by vaccination and it seems that more complete successes such as the eradication of smallpox virus and rinderpest virus are aspirational rather than realistic. However, good progress continues to be made on the control of several important livestock pathogens and mechanisms are now in place to bring together the critical scientific expertise and political will to succeed. For example, to provide tools to endemically affected countries to help with control of foot and mouth disease (FMD) virus and to improve methods to better manage and reduce risk of outbreaks in FMD-free countries, a Global Foot-and-Mouth Disease Research Alliance (GFRA) was established in 2003 to bring together the relevant animal health research organizations worldwide. Thus, the GFRA is aligned conceptually to the GREP and is spearheading work to understand more about key issues of the biology of FMD virus, such as predictions of the virulence and spread of FMD virus under different circumstances, immunological

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mechanisms of protection against disease and virus replication and how to generate longer-lasting protective immunity after vaccination, the drivers of virus evolution and ways to improve vaccine stability and generate protection to multiple serotypes. Initiatives such as GFRA will help to share the burden of controlling burdensome diseases because, as Paton et al. (2009) point out for FMD in this issue, if the potential for disease control becomes too large for individual nations to tackle, responsibility for control may be seen to belong to a third party. This type of political dimension is clearly a significant factor in the prospects of better control of some very important diseases and any inertia in implementing plans at national government levels will make it easier for pathogens to persist and spread further.

The ability to control livestock diseases effectively is sometimes problematic because of the ‘carrier state’ in which a pathogen persists in the host for extended periods. Stevens et al. (2009) in this issue report that the bacterium Salmonella enterica may develop a carrier state in the host after primary challenge and such carriers typically excrete high levels of bacteria during recovery from enteric or systemic disease, often in the absence of clinical signs. In some cases, the carrier state may exist for the lifetime of the host, for example, with bacterial species such as S. enterica serovar Dublin.

FMD is also characterized by a carrier state in which FMD virus locates rapidly to, and is maintained in, the light zone of germinal centres (Juleff et al. 2009) and it remains a fundamental problem to be overcome before more effective control measures can be put in place. The tropism of pathogens and why some organisms translocate from one site of development to another remains generally poorly understood. Stevens et al. (2009), this issue, report an emerging theme among pathogens associated with enteric fevers, such as S. enterica serovar Typhi, Brucella spp. and enteropathogenic Versinia spp.; they use ‘stealth strategies’ to evade detection by the innate immune system of the host and thus any control by the host at the level of mucosal surfaces.

In summary, considerable challenges are presented by livestock and zoonotic pathogens to the health and well being of animals and man. For some critically important diseases, the first line of defence will be the deployment of state-of-the-art approaches to diagnosis and surveillance to provide a network of global intelligence on their spread and an assessment of risk presented. Combined with this, the delivery of effective vaccine strategies for the control of major pathogens of livestock will be especially testing and a continuum of new and better vaccines able to deliver more long-lasting and durable protective immunity and to be effective against multiple strains or variants will be essential.

REFERENCES


Chua, K. B., Chua, B. H. & Wang, C. W. 2002 Anthro-" 


