Zoonoses (Project 1)
Wildlife/domestic livestock interactions

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Contents

1. Executive summary 3

2. Methodology 11

3. Importance of zoonoses and the livestock-wildlife interface 15

4. Mapping zoonoses at the livestock-wildlife interface 26

5. Disease transmission routes and the relative importance of the wildlife-livestock route 33

6. Pathogens of wildlife capable of recombining with analogous organisms in domestic livestock 41

7. Risk factors for disease transmission from wild or domestic animals to people and between wildlife and domestic livestock 51

8. Drivers influencing the interaction between wildlife and livestock and the implications for zoonoses transmission 58

9. Historical changes in transmission, factors which foster novel transmission routes and hosts, and wild animal candidates for future disease transmission 68

10. Key factors influencing the risk of the transfer of infections between livestock and wildlife in developing countries: production and socio-economic factors 88

11. Management of zoonoses at the livestock-wildlife interface 95

References 111

Annex 1. Assumptions around DALY calculations 126

1. Executive summary

The objective of this study was to synthesise the best available scientific knowledge about zoonotic disease transmission through livestock and wildlife interaction (direct or indirect), with emphasis on risk factors, drivers and trajectories of transmission, as well as promising interventions for controlling important zoonoses, based on managing the interaction between domestic livestock and wildlife.

A multi-disciplinary team from the International Livestock Research Institute, Kenya, and the Royal Veterinary College, United Kingdom, with expertise in zoonoses, epidemiology, socio-economics, and wildlife, undertook the review. A database of important zoonoses was compiled and used to develop a list of priority zoonoses with a livestock-wildlife interface for developing countries. Spatial relationships between important zoonoses and land use and human population density were explored. A systematic review was carried out focussing on: disease transmission routes, risk factors for disease transmission, drivers of wildlife-livestock interactions, pathogens of wildlife capable of recombining with organisms in livestock, wildlife species that are potential sources of zoonotic pathogens, production and socio-economic factors influencing the risk of transmission, and risk management and control interventions. The main findings are summarized in this executive summary.

Zoonoses can be broadly defined as diseases that are naturally transmissible between animals and people. Zoonoses are of concern for two main reasons; the health and economic burdens caused by zoonoses long known to cause disease in animals and people that persist in vulnerable groups, and the potential for emerging zoonoses to give rise to novel disease outbreaks. **The burden of persisting zoonoses is mainly borne by poor people in developing countries, whilst emerging zoonoses are of more concern to the rich in developed countries with larger economies and fewer other infectious disease problems.**

As zoonoses are by definition transmissible between animals and humans, it is not surprising that most are also transmissible between wildlife and domestic animals. Transmission depends upon contact (direct or indirect) between livestock, domestic animals and people and transmission opportunities are subject to various, sometimes opposing drivers. **The unprecedentedly large human population and the associated increases in demand for land, food (and use of natural resources is the root cause of increased transmission opportunities**. However, developed countries have high animal and human populations but zoonoses are of low health significance suggesting the high level of zoonoses in developing countries is not due to absolute population size but other factors. These could include the speed of increase in human and animal populations driving a livestock revolution[2] with rapid yet poorly-regulated changes in livestock-keeping systems, and massive intensification in parallel with continued high levels of livestock ownership and close contact between humans and livestock. However, **the origin, distribution and impact of emerging zoonoses is less skewed towards poor countries** than is the case for persisting zoonoses**.**

[2] The Livestock Revolution is the rapid, demand driven increase in livestock production and trade in developing countries.

Three important proximal drivers of increased zoonoses transmission and extension of the livestock-wildlife interface are **rapidly increasing livestock trade, agricultural expansion with incursion into new areas, and cultural consumption practices** (especially consumption of bush meat in Africa and Asian for buying from wet-markets selling live domestic animals and wildlife in Asia). In developed countries, recreation and conservation can lead to locally increased risk but the associated disease burden is not important in comparison to other causes of sickness and death.

Agriculture intensification is not always a risk amplifier but the rapid and poorly regulated intensification associated with the livestock revolution in developing countries, is. While increasing the numbers of livestock kept will of itself increase risk, the effects of intensification are less clear. High livestock numbers, high stocking densities, poor husbandry, and inappropriate use of antibiotics associated with intensification in developing countries all favour disease transmission and emergence. However, reductions in the proportion of the population keeping livestock, improvements in biosecurity that are easier to implement and regulate on large farms, and better surveillance and disease control are characteristics of agriculture intensification in developed countries and are risk mitigating. On the other hand, the **increasing genetic homogeneity** of livestock associated with intensification (monoculture) in both developed and developing countries is probably an important factor in spread and amplification of disease.

For both persisting and emerging zoonoses, it appears that a broad range of pathogens can be acquired from a many different hosts under a wide range of contexts, which may or may not involve a wildlife-livestock interface. It is especially difficult to make predictions about the few and unusual emerging pathogens that go on to have massive impact. Mad cow disease in Britain's advanced well-regulated dairy sector, SARS[3] with links to wildlife in Asia's busy wet-markets, avian influenza in intensive and little-understood production systems in China, and Rift Valley Fever emerging in low density, traditional livestock systems in Africa have few common features, although all four diseases have a livestock-wildlife interface. The difficulty of generalising from small numbers of cases means that **predicting high impact zoonoses is challenging**. Nonetheless, some 'hot-spots' in terms of geographic areas and 'ones to watch' in terms of pathogens and hosts can be tentatively identified and these should be subject to higher surveillance along with evaluation of the costs and benefits of this risk targeting.

In developed countries, management of persisting and emerging zoonoses has been relatively successful (although often expensive). **Successful control is less likely where wildlife have a substantial role in transmission**. Elimination of wildlife populations is generally not a feasible control strategy; reducing wildlife numbers can be useful but small-scale and short-term programs are generally ineffective and may be harmful; physical separation of livestock and wildlife is difficult, expensive and can have unwanted side-effects. In poor countries, management has been much less successful. However, the historically recent, massive, unplanned reduction in wildlife populations especially in African and South America has affected zoonoses prevalence, positively or negatively depending on the context and temporal scale (ecosystem incursion often increases risk in the short term, while decreasing in the long term). **The major deficit in current management of zoonoses**

[3] Severe acute respiratory syndrome is a respiratory disease in humans which is caused by the SARS coronavirus

with a livestock-wildlife interface is that programmes are not based on adequate epidemiological or socio-economic understanding.

In the next section we set out the key messages identified by experts in this study along with their strength of supporting evidence, and identify the associated evidence gaps and the possible contribution of research. The questions are those set out in the review terms of reference.

What is the extent of the problem of zoonoses, the context and the relative importance of the wildlife/domestic livestock transmission route?

- Zoonoses are absolutely and relatively more important in low-income countries compared to high-income countries (evidence strong - Chapter 3). In low-income countries, infectious diseases are responsible for nearly 40% of the burden of human sickness and death, and one fifth of this is attributable to zoonoses or diseases recently emerged from animals, with recently emerged disease (mainly AIDS[4]) about twice as important as zoonoses (evidence medium -Chapter 3). In high-income countries, infectious diseases are much less important (4% of total burden). While diseases emerging recently from animals and food-borne zoonoses are an important part of this small burden, other zoonoses have minor impacts (Evidence strong - Chapter 3). Many of these zoonoses, in both rich and poor countries, have a livestock-wildlife interface.
- The total impact of zoonoses with a livestock-wildlife interface, goes far beyond human sickness and death and includes multiple other burdens, such as: monetary cost of illness; cost to livestock sector; opportunity cost to economies; negative social and psychological impacts; and, negative impacts on wildlife and ecosystems (Evidence strong - Chapter 3).
- The Global Burden of Disease assessment led by the World Health Organisation (WHO) suggests food-borne zoonoses, human African trypanosomosis and leishmaniasis are the most important zoonoses globally – all have a livestock/wildlife interface (evidence medium -Chapter 3).
- Published expert opinion considers brucellosis, human African trypanosomosis and tuberculosis to be the most important zoonoses – all have a livestock/wildlife interface (Evidence weak - Chapter 3).
- In the study conducted for this report, we identified 292 important zoonoses from the literature: 82% of these had a wildlife reservoir, 74% had a domestic animal reservoir and 60% had both a wildlife and a domestic animal reservoir (Evidence medium - Chapter 3).

Key evidence gaps:

- There is a lack of systematic surveillance data for zoonoses in general, and for zoonoses with a livestock-wildlife interface in particular. Studies are needed to determine presence, prevalence, impacts and risk factors.
- There is lack of evidence on the multiple burdens of zoonotic disease and measuring the burdens and mapping the occurrence of zoonotic disease is a first step for prioritization and rational management in resource-scarce contexts. Many important zoonoses are missing from the WHO Global Disease Burden which is now the lead metric for guiding human health interventions; in addition complementary metrics are needed to capture economic, social and environmental burdens of disease.

[4] Acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS) is a disease of the human immune system caused by the human immunodeficiency virus (HIV)

- There is a lack of evidence on the application of innovations to surveillance, modelling and geo-spatial mapping with potential to improve assessment and hence management.

Possible research contributions

- Cross-sectional studies to map presence and prevalence of important zoonoses.
- Burden of disease (DALYs) estimates for neglected and hitherto un-measured zoonoses.
- Metrics that capture the other impacts of zoonoses (multiple burdens of disease).
- Frameworks for prioritisation for investment in zoonoses (research and development).
- Novel rapid and low-cost diagnostics suitable for field-use.
- Surveillance systems that use innovative approaches e.g. risk-based, participatory, mobile phone, HealthMap, molecular, etc.
- Surveillance systems that improve links between human, livestock and wildlife disease data.
- Better linking of surveillance to action.
- Rigorous impact assessments of different surveillance models including according to established frameworks e.g. CDC.
- Prioritisation of research on wildlife origin zoonosis and key species presence/prevalence to determine risk.

Which wildlife species have been implicated in the transfer of disease from livestock to humans and what are the key factors that influence the risk of transmission?

- Many different wildlife species are implicated as hosts for the important zoonoses identified by our study (n=292). Of the hosts (663) listed in our database, 51% were domesticated animals and 36% were wild animals, with the remainder being un-specified or likely to include both domestic and wild species (e.g. hosts listed as 'birds' or 'herbivores') (Evidence weak - Chapter 3).
- There are few studies on risk factors for transmission from wild and/or domestic animals to people and between wildlife and domestic livestock in the literature, and studies are biased towards certain species and orders (evidence strong - Chapter 7).
- Consumption of bush-meat represents one of the more salient ways in which humans come in close contact with wildlife and their pathogens. It is an important source of zoonotic transmission from wildlife (Evidence medium - Chapter 5).
- Environmental contamination with pathogens by livestock and/or wildlife is another major transmission route (evidence medium - Chapter 5).
- Agro-ecosystem change, especially forest fragmentation and edge effects, can increase pathogen flows between people, livestock and wild animals, and increase disease risk (Evidence strong - Chapters 5, 7 and 8).
- Agro-ecosystem change can also decrease disease risk, and a shift from wildlife to domestic animal hosts can select for decreased pathogenicity (Evidence medium - Chapter 7).
- Socio-economic determinants of health can be more powerful determinants of risk than biological factors (Evidence moderate - Chapter 7).

Whether there are other wildlife species that could become key candidates for transfer of disease in the future and why?

- Viruses are more likely to be emerging than other types of pathogen. A wide host range is associated with pathogen emergence (Evidence medium - Chapter 9).

- Data on multispecies pathogen transmission and adaptation of viruses is limited to a few families, mostly RNA viruses: notably coronaviruses, lentiviruses, flaviviruses, paramyxoviruses and avian influenza viruses (Evidence strong - Chapter 6).
- The putative original hosts for these viruses are: bats (3 viruses), primates (2 viruses) and cats, cattle, horses, birds and rabbits (1 virus each). However, there are many other potential candidate pathogens and hosts, that have not been properly evaluated. (Evidence medium - Chapter 6).
- While many organisms have the potential to infect many species, the key to changes in disease transfer is contact rates and host opportunities (often anthropogenically driven) (Evidence medium - Chapter 6).
- Bats have recently been the source of a number of emerging zoonotic diseases, some of which have involved domestic animals in transmission and amplification. Encroachment of humans and livestock into bat habitat and disturbance of bat populations due to hunting and habitat destruction, as well as bat behaviour and demography is increasing the likelihood of pathogen spill-over and future disease emergence. (Evidence medium - Chapter 9).

Key evidence gaps

- Many zoonoses have multiple transmission routes and multiple host reservoirs that are poorly understood; assessing the importance of different transmission routes and the roles of hosts in specific contexts is a pre-requisite for effective and efficient control.
- Lack of understanding of the human behavioural determinants of livestock and wildlife interaction and exposure through, for example, hunting, harvesting, consumption, recreation, and agricultural intensification.
- Lack of evidence on putative transmission hotspots, including; livestock markets; urban and peri-urban wildlife and farming; fragments and edges; wildlife conservation areas and buffer zones; wildlife value chains; as well as dynamic hotspots caused by natural disasters and conflict.

Possible research contributions

- Reviews of existing evidence on attribution, transmission routes and epidemiology.
- Conventional and molecular epidemiology to map pathogen flows, especially in suspected hotspots (static and dynamic).
- Wildlife surveys to detect pathogens and host ranges, focusing on the species and pathogens that show greatest potential for zoonotic transmission and emergence (peri-domestic species, rodents, bats, viruses).
- Transmission experiments to understand infectivity and host ranges.
- Case control and risk factor studies to investigate links between human illness and livestock, wildlife, food, water and other factors including socio-economic, to inform disease management.
- Human behavioural and socio-economic studies to understand the institutional environment within which people make decisions and the underlying anthropogenic drivers of disease transmission.
- Modelling (multi-dimensional, interdisciplinary) to better understand disease dynamics.
- Application of value chain analysis to wildlife, food and product systems.
- Survey of peri-domestic attributes that are important to bringing wildlife in contact with people and livestock and assessment of risks.

What are the main drivers (global and generic within regions) changing the degree of interaction between wildlife and domestic livestock and what are the key characteristics (e.g. geographic, political, economic, demographic, gender etc) which they affect in influencing the risk of transmission?

- The growth in human population and consumption is driving widespread environmental change (urbanisation, agricultural expansion and intensification, and wildlife habitat change), which has led to zoonotic disease emergence and re-emergence. However there have been few studies, (and fewer in developing countries), that quantify or identify causal links for this probable association. (Evidence medium - Chapters 5, 6, 8, 10).
- Changing land use and agricultural expansion disrupts wildlife habitats and brings humans and their livestock into closer proximity to wildlife resulting in changes in host-pathogen dynamics and increased risk of spillover. (Evidence strong - Chapters 5, 6, 8, 10).
- Livestock production intensification increases the population and density of livestock and increases the likelihood of livestock becoming an amplifying host, or source of environmental contamination. (Evidence medium - Chapters 8, 10).
- Livestock and wildlife movements, marketing and trade increase the risk of local and international movement of pathogens and spillover to humans. (Evidence strong - Chapters 5, 8, 10).
- Wildlife management for conservation or recreational hunting can increase the population size and density resulting in higher disease prevalence in wildlife and increased risk of spill over to livestock. (Evidence medium - Chapters 5, 8).
- Disease emergence is influenced by human behaviour including decisions driven by lack of information and rule-breaking behaviour. (Evidence medium - Chapter 10).
- Climate change is predicted to affect the geographical distribution and population densities of wildlife species, which will interact with many other factors to have variable effects on disease dynamics. (Evidence weak - Chapters 8, 9).
- Other commonly cited factors that influence emergence or re-emergence with varying degrees of evidence are detailed in Chapter 9; these include: deterioration of public health services, human migrants (often associated with war and conflict or disaster), urbanization, natural disasters, globalization, water management projects, use of fertilizers, deforestation, loss of biodiversity and extreme climatic effects. (Evidence weak to medium – Chapter 9).
- It is the context in which potential pathogens exist and evolve that matters most to disease emergence and not molecular mechanisms, which have always existed and are primed to take advantage of opportunities as they are presented (Chapter 6).

Key evidence gaps

- More studies of contextual aspects of the wildlife-livestock interface are needed, and on drivers within species (susceptibilities) for pathogen evolution and amplification.
- Work is needed on understanding more specifically how the changing biomass of humans and domestic animals and biodiversity decline will affect pathogen emergence and evolution.
- There is limited understanding of rapidly changing institutional environments where people from rural and urban areas and national and international groups are mixing, and rule systems and their associated enforcement (household, community, private, legal) are constantly being

modified with pockets of activities that are poorly monitored, allowing for rule breaking behaviour.

Possible research contributions

- Frequency and likelihood of pathogen flow across species under different contexts.
- Key ecological changes which drive pathogen emergence and transmission.
- Specific research into mechanisms of amplification and persistence.
- Longitudinal studies to understand changes in dynamics over time.
- Research into natural disease and infection processes in biodiverse animal communities and how these systems select for and maintain low pathogenicity microbial communities.
- Foresight or modelling to understand possible trajectories of disease dynamics in the face of anthropogenic drivers such as climate change and demography.
- Developing ways of quantifying the anthropogenic drivers of changes in disease dynamics.
- Ground-truthing assumptions around impacts of drivers on emergence.
- Development of methods for assessing rule and enforcement structures across food and product systems

What are the possible interventions (and associated governance structure) that could limit the interaction of key wildlife species with domestic livestock and the potential economic and social impacts (at both state and household level) of those interventions?

a) What is the evidence regarding intervention methods that reduce contact between wildlife and livestock?

- Risk factors are context specific, and the effectiveness of an intervention strategy will vary with context. Interventions based on risk are more effective and efficient than conventional management. (Evidence moderate - Chapter 7).
- Elimination of wildlife populations as a means to reduce contact is not desirable and in any case probably not feasible (Evidence moderate - Chapter 11). Reducing wildlife population can reduce risk to livestock, but small-scale and short-term control is ineffective and can even spread disease (Evidence strong - Chapter 11).
- Separation of livestock from wildlife by fencing generally reduces risks of disease transfer but the loss of heterogeneity in the landscape increases risk of stochastic disease events through loss of endemism and immunity. Few barriers are impermeable. Environmental, social and economic costs of fencing are high and unacceptable in countries with strong wildlife economies and with migrating wildlife. (Evidence strong - Chapter 11).
- Innovations may radically improve control even in poor countries. (Evidence weak).

b) Associated governance structures

- Both top-down and community-based programs have had little long-term success in tackling epidemiologically complex disease at the human-livestock-wildlife interface in developing countries (Evidence medium).
- Integrated and One Health approaches lead to better control (Evidence weak/medium).
- Pro-poor development is one of the most effective ways of reducing zoonoses (Evidence strong).

Key evidence gaps

- Current assessment and management is, for the most part, not based on good surveillance or risk data. Risk-based management offers a great opportunity for improving management of zoonoses. This involves basing management on context-specific epidemiology and risk factors.
- People's reaction to the presence of disease is inadequately understood making it difficult to tailor interventions that create synergies for household and community actions.
- The costs, benefits and broader impacts of zoonoses management are imperfectly understood as well as the incentives needed for sustainable control.
- Adapting innovations: promising technological, organizational and social innovations exist but need to be better adapted to developing country contexts.

Possible research contributions

- Systematic reviews to identify interventions for which credible evidence exists.
- Identifying risk factors to guide zoonoses management in specific contexts.
- Developing integrated intervention packages to target risk factors, incorporating technological, social and economic innovations.
- Randomised controlled trials of intervention packages assessing efficacy, appropriateness, equity, sustainability and impacts of interventions.
- Development of a database on local and community responses to disease presence.
- Comparing successful and failed interventions in order to develop guidelines for policy and practice.
- Economic and social experiments to better understand incentives around disease control and sustainability.
- One-Health methods for linking different types of interventions.
- Socio-ecological approaches to determining optimal control methods based on reducing risk and increasing resilience.
- Research into novel control technologies and approaches such as vaccines, population control, disease resistance, biosecurity, husbandry and ecosystem-based interventions.
- Modelling of different control options (epidemiology, ecology, economics).

Note: The strength of evidence supporting the various statements is assigned by experts responsible for the review using criteria set out in the methodology.

2. Methodology

Overview

A multi-disciplinary team from the International Livestock Research Institute, Kenya, and the Royal Veterinary College, United Kingdom, with expertise in zoonoses, epidemiology, socio-economics, and wildlife, undertook the review. A database of important zoonoses was compiled and used to develop a list of priority zoonoses with a livestock-wildlife interface for developing countries. Collaboration with HealthMap and AU-IBAR permitted initial exploration of spatial relations between zoonoses of importance, land use and human population density. A systematic review was carried out in line with the scope set out in the Terms of Reference.

Identification of zoonoses with a wildlife livestock interface

We considered that zoonoses appearing in standard textbooks could be classified as 'important'. This is an important point of departure from other studies that include all zoonotic pathogens, even those that are extremely rare. One of our hypotheses was that important zoonoses might have different characteristics in terms of type and host. Three standard textbooks were used to identify these zoonoses of importance (PAHO, 2003, Goldsmid, 2005, MVM, 2008). Information was extracted from the text and entered into an Excel database. Initially 343 diseases were identified, which reduced to 292 diseases after removing duplicates and standardising names. The disease name, the specific causative agent, type of agent (bacteria, virus, protozoa, helminth, fungus, arthropod, other), region (developing, developed), reservoirs (wildlife, domestic), and hosts were recorded for each disease.

From the database of 292 important zoonoses, the research team selected 61 zoonoses that both had a livestock-wildlife interface and were important in developing countries. Additional information was added to the database on the mode(s) of transmission for each disease and the involvement of large mammals.

Mapping of zoonoses

We investigated the use of web-based mapping and geo-referenced maps for mapping diseases and relating the spatial distribution of disease to human demography, environment (land cover) and wildlife distribution. One web-based disease mapping system that we explored was HealthMap (www.healthmap.org), which is an automated system that gathers information for disease outbreak monitoring and real-time surveillance of emerging public health threats from non-traditional sources such as online news outlets and expert discussion forums, as well as government websites (Major, 2008). HealthMap was developed as a freely accessible and automated system that monitors information on emerging diseases in real time. It currently gathers reports from 14 sources, including Google News, which summarises information from more than 20,000 different websites. It uses search criteria that include disease names, symptoms and keywords. The system collects an average of 300 reports per day, most of which (85%) come from news media sources (Major, 2008).

Out of the list of diseases, disease syndromes or types of disease for which HealthMap had data we requested data for Africa on 15 zoonotic diseases or disease syndromes or types that were mainly zoonotic for the period of January 2006 to April 2011. The diseases and syndromes were anthrax, avian influenza, botulism, bovine tuberculosis, brucellosis, *Clostridium difficile* infection,

Cryptosporidium, diarrhoea, dysentery, foodborne illness, gastroenteritis, leptospirosis, salmonella, trichinosis, and waterborne illness. HealthMap provided data on disease outbreak by disease type, global positioning system (GPS) coordinates and source of information.

We generated maps of individual zoonotic diseases and species richness for all 15 zoonotic diseases. The species richness map was derived by adding diseases outbreaks in an area of one by one degree grid. These maps were overlaid with human population maps and we derived statistics from the number of people that were within the area of diseases outbreaks. Next we overlaid with protected areas to find how many outbreaks occurred inside and outside protected areas. The human population data was sourced from ILRI and data on the protected areas from WDPA (WDPA, 2010).

Evaluation of the HealthMap database indicates that a number of diseases did not have full coverage for the period used in this study, which may be because HealthMap relies on reported disease outbreak information from the print media (Major, 2008). Between October 2006 to July 2007 a wide variety of pathogens were detected with information on 141 unique infectious disease categories that was based on data sourced from Google News feed alone (Major, 2008). The pathogens most reported were avian influenza (877 reports), *Escherichia coli* (733), and *Salmonella spp.* (479). Over the study period reports of outbreaks of infectious disease occurred in 174 countries, with the greatest number from the United States (4351 reports), the United Kingdom (1018), Canada (880), and China (737). However, there was an under-reporting of disease for developing countries. The information shows a clear bias to countries with more media outlets, more developed public health resources and greater availability of electronic communication (Major, 2008). Major (2008) reports that the research group at HealthMap is now developing ways to improve coverage for Africa and South America, which have the highest risk and burden of emerging infectious diseases. The project intends to monitor other internet sources, such as blogs, discussion sites, and listservs to increase its capacity to capture more diseases and also extends its coverage.

A second source of data was the African Union Interafrican Bureau of Animal Resource (AU-IBAR) Animal Resource Information System (ARIS), which has recently been upgraded to capture and transfer animal disease data in real time (AU-IBAR, 2010). This information is sourced from the monthly reports of the national veterinary services of AU member states. The number of national monthly reports has increased from 10 in 2000 to 47 in 2009 and the quality of spatial information has also improved with the use of GPS (AU-IBAR, 2010). We extracted a dataset of anthrax outbreaks recorded in 2009 to examine how the geo-coded data could be modelled in a global information system (GIS) platform. It was not specified which species of livestock or wildlife were affected. We conducted an explanatory analysis to explore the association between the spatial distribution of anthrax and human population density, land cover, and species richness of wildlife (mammals, ungulates, primates and carnivores). The land cover map was derived from the GLC2000 (Fritz et al., 2004), the human population density from the ILRI GIS database and the wildlife species richness from the African Mammalian Databank (Boitani et al., 1999). The mammalian species richness was derived as a proxy for wildlife host species richness (Jones et al., 2008). The species richness maps were generated from geographical range distribution maps for terrestrial mammalian species found in Africa (Boitani et al., 1999). Species richness was calculated as the number of species in an area. We also generated species richness maps for ungulates, carnivores and primates and related them to anthrax outbreaks.

Systematic review

The systematic review was the main part of the study and followed a standard approach, comprising the following activities:

- Thematic areas within the scope of the TOR were identified, and team members were assigned to different themes
- A set of search criteria was developed for each theme
- relevant literature databases were identified
- A search for papers was conducted for each theme
- The paper titles were screened by research assistants for relevance to the theme and the abstracts were obtained for suitable papers
- The abstracts were blind reviewed for relevance to the them by at least two team members and abstracts selected by two or more people were retained
- Full papers were retrieved for the selected abstracts and read by at least one team member: the quality of each paper was evaluated and the key findings from each paper was recorded using a standard template
- For each theme, the findings from the selected papers were collated and presented as a chapter in this report

Seven themes were identified by the team and team members were assigned to each theme based on their expertise:

- Disease transmission routes and relative importance of the livestock-wildlife route (leader Silvia Alonso supported by Delia Grace and others).
- Pathogens of wildlife capable of recombining with analogous organisms in domestic livestock (leader Richard Kock supported by Declan McKeever and others).
- Risk factors for disease transmission from wild/domestic animals to people and between wildlife and domestic livestock (leader Delia Grace supported by Silvia Alonso and others).
- Drivers influencing interaction between wildlife/livestock and the implications for zoonoses transmission (leaders Dirk Pfeiffer, Bryony Jones supported by Richard Kock, Mohammed Said and others).
- Historical changes in transmission, factors which foster novel transmission routes and hosts, and wild animal candidates for future disease transmission (leaders Dirk Pfeiffer, Bryony Jones supported by Richard Kock and others).
- Production and socio-economic factors influencing the risk of transmission between wildlife and domestic livestock and from wildlife/livestock to people (leader Jonathan Rushton supported by Richard Kock, Jemimah Njuki, Mohamed Said and others).
- Risk management and control interventions and their success or failure with emphasis on interventions based on managing interaction between hosts (wildlife/livestock/humans) (leader Delia Grace supported by Silvia Alonso and others).

To identify papers relevant to each theme, the team generated a list of search criteria for each theme. Two forms of searches were done, general and disease specific, for papers published in the past 5 years using PUBMED and CABDIRECT databases (African Journal On line was used initially but was later abandoned because it yielded very few hits). For disease specific searches, team members identified important zoonoses related to each theme and the disease name was added to the search

terms used for the general searches Every effort was made to obtain the papers that were selected for full paper review, although this was not possible in every case.

The paper reviewers assessed the strength of evidence for each paper based on the following criteria: credibility of researchers; adequacy of study design (original studies); thoroughness of review (review papers); possible bias; populations covered; overall importance. Systematic reviews usually involve setting strict criteria on quality of evidence to screen for highly credible original studies; however, in this review when strict criteria were applied insufficient or no studies were obtained. Using less strict criteria, review articles and discussion papers were included, and additional papers obtained from reference lists of selected papers or known to the team members but not obtained through the systematic search were also obtained. This large and fuzzy literature on the review topic, meant writers relied extensively on their own knowledge and expertise.

Table 2.1. Summary of papers reviewed during the systematic review

Theme	No. papers selected as relevant based on title	No. papers selected based on abstract review	No. papers that were relevant based on full text review	Number of additional papers used	Total number of papers contributing to theme chapter
Disease transmission routes and relative importance of the wildlife-livestock route	98	28 (of which 8 original studies)	11	5	16
Pathogens of wildlife capable of recombining with analogous organisms in livestock	171	30	30	36	66 (of which 45 original studies)
Risk factors for disease transmission from wild/domestic animals to people and between wildlife and livestock	153	13	4	8	12
Drivers influencing interaction between wildlife and livestock and the implications for zoonoses transmission	124	30	15	27	42 (of which 19 original studies)
Historical changes in transmission, factors which foster novel transmission routes and hosts, and wild animal candidates for future disease transmission	182	86	43	37	80 (28 original studies)
Production and socio-economic factors influencing risk of transmission between wildlife and livestock and from wildlife/livestock to people	?				33
Risk management and control interventions and their success or failure with emphasis on interventions based on managing interactions between hosts.	94	24	22	7	29
Total number of papers (some papers were relevant to more than one chapter)					239

3. Importance of zoonoses and the livestock-wildlife interface

The first part of this paper discusses some of the concepts around understanding zoonoses and what is meant by a livestock-wildlife interface; we go on to summarise evidence on the importance of zoonoses (with reference to the livestock-wildlife interface) in terms of human health impacts and other societal concerns; the third part presents a systematic approach to identifying and prioritising zoonoses with a livestock-wildlife interface of relevance to developing countries and discusses the characteristics of these diseases.

Summary of main messages

- There is no clear consensus or definition of what constitutes zoonoses at the livestock-wildlife interface. In this systematic review, we refer to zoonoses, or diseases common to animals and humans, the epidemiology of which involves domesticated and non-domesticated animals (including fish).
- In low-income countries, infectious diseases are responsible for nearly 40% of the burden of human sickness and death. One fifth of this (or 8% of the total disease burden) is attributable to zoonoses or diseases recently emerged from animals (7% and 13% respectively). Evidence: medium.
- In high-income countries, infectious diseases are much less important (4% of total burden); diseases emerging recently from animals and food-borne zoonoses are an important part of this small burden, but other zoonoses have minor impacts. Evidence: strong.
- Zoonoses are absolutely and relatively more important in low-income countries compared to high-income countries. Evidence: strong.
- As well as human health impacts, zoonoses with a livestock-wildlife interface are responsible for multiple burdens including: cost of illness; cost to livestock sector; cost to economies; negative social and psychological impacts; and negative impacts on wildlife and ecosystems. Evidence: strong.
- The Global Burden of Disease assessment led by the World Health Organisation suggests food-borne zoonoses, human African trypanosomosis and leishmaniasis to be the most important zoonoses globally; all have a livestock-wildlife interface. Evidence: medium.
- Published expert opinion considers brucellosis, human African trypanosomosis and tuberculosis to be the most important zoonoses; all have a livestock-wildlife interface. Evidence: weak.
- We identified 292 important zoonoses from the literature: 82% of these had a wildlife reservoir, 74% had a domestic animal reservoir and 60% had both a wildlife and a domestic animal reservoir. Evidence: medium.

3.1 What are zoonoses and what is a livestock-wildlife interface?

Zoonoses are usually defined as diseases and infections that are naturally transmitted between vertebrate animals and people (WHO, 1959). A landmark paper showed that the majority of human diseases (61%) are shared with animals (Taylor et al., 2001). However, this summary statistic goes only part way to understanding diseases at the interface of humans, animals and the environment. The difficulty of attribution makes it difficult to unambiguously describe diseases as zoonoses at the livestock-wildlife interface: many diseases have multiple causes, some of which are zoonoses; many pathogens have multiple transmission pathways (some of which are zoonoses) and in most cases the

relative importance of zoonotic pathways is not known; some diseases that are classified as zoonoses are probably better thought of as communicable diseases common to animals and people; and the categories of livestock and wildlife are artificial and not always helpful. Moreover, hosts, pathogens and transmission paths are not fixed but are constantly evolving. Lastly, the disease-centric model of pathogen and host which has long dominated medical thinking, is giving way to a perspective that includes health issues at infra-pathogen scale (transmission of drug resistance between bacteria by plasmids) and supra-host scale (ecosystem services for health provision). Some of these issues are discussed in greater depth in Box 3.1. The commonly encountered model of wildlife as reservoirs of disease only captures some of the complexity of interactions at the livestock-wildlife interface. Table 3.2 gives a typology of zoonoses at the wildlife-livestock interface.

For the purposes of this systematic review, zoonoses at the livestock-wildlife interface, are defined as: diseases that are common to animals and humans, the epidemiology of which involves domesticated and non-domesticated animals.

Box 3.1 Conceptual issues around identifying zoonoses at the livestock-wildlife interface

Attribution: Diseases may be caused by multiple pathogens, some of which are zoonotic
Tuberculosis is one of the most serious diseases of people. The majority of cases are due to *Mycobacterium tuberculosis*, transmitted almost entirely by human-to-human transmission. (*M. tuberculosis* is a reverse zoonoses and there are documented cases of animals being infected by people, but this is unlikely to play an important role in transmission.) However, a proportion of human tuberculosis cases are caused by *M. bovis* the cause of cattle tuberculosis. In developed countries where cattle tuberculosis is well controlled this proportion is very low (around 0.1-1% of cases), but before milk pasteurization *M. bovis* was an important cause of human tuberculosis, especially intestinal tuberculosis in children. There are few studies of zoonotic tuberculosis in developing countries and poor communities; those that exist have shown proportions of human tuberculosis due to *M. bovis* of up to 45% in some populations (Rodwell et al., 2008), although from 5-20% is more typical (Cosivi et al., 1998).

Table 3.1.Human diseases caused by multiple pathogens

	Examples of zoonotic species	Examples of non-zoonotic species	Proportion of disease due to zoonotic pathogens
Tuberculosis	*Mycobacterium bovis*	*M. tuberculosis*	10% (<1% to >20%)
Leishmaniasis	*L major*; most other species	*L. tropica; L donvani*	Unclear, perhaps 75%
Lymphatic filiariasis	*B malayi, B timori*	*Wuchereria bancrofti*	10%
Shistosomiasis	*S. japonicum*	*S. mansoni,* *S. haematobium*	10%
Malaria	*P. knowlesi* and others	*P. falciparum* and others	Very small

Attribution: Pathogens may have multiple transmission cycles some of which are zoonotic and others not
Many arboviruses have a sylvatic cycle, whilst some also have an urban cycle and an intermediate cycle.

- Sylvatic cycle (sometimes known as the jungle cycle): the virus cycles between an arthropod and a non-human mammalian host. Humans are usually dead-end hosts that are infected by the arthropod.
- Intermediate cycle: occurring in agro-ecosystems with both human and non-human mammalian hosts.
- Urban cycle: the virus cycles between humans and an arthropod species.

In the case of dengue, a high burden disease, almost all transmission is urban (human to human or

anthroponotic) and many people would not consider it to be a zoonoses. However, the existence of a sylvatic cycle means that it is by definition a zoonoses, and may have implications for persistence and resurgence of disease, as diseases with a sylvatic cycle are more difficult to control.

Many diseases are transmissible through different sets of hosts. For example, dairy cattle are a major reservoir for *Escherichia coli* O257:H7, but once a person is infected (typically through milk, meat or vegetables contaminated with cattle faeces) then person-to-person transmission is also possible. There is generally little information on the importance of different transmission routes, which makes control difficult.

Attribution: Common source communicable diseases

Zoonoses are often conceptualised in terms of diseases with reservoirs of infections in animals. For many zoonoses, the reservoir is the environment and humans, wildlife and livestock may all be affected. These are sometimes referred to as 'communicable diseases common to humans and animals' and are not always considered as zoonoses. Tetanus spores are present ubiquitously in the environment as well as the intestines of animals and humans. While human infection from an animal bite is possible, or from application of cow dung to the umbilicus, much of the high burden of human tetanus is from the environment and not directly from animals.

Attribution: Arbitrary distinction between livestock and wildlife

There are many different classifications of the animals with which humans share ecosystems. Livestock, domestic animals, peri-domestic animals, food animals, work animals, companion animals, feral, pest, and wildlife overlap and vary by context. Depending on the context dogs may be food animals, work animals (guard dogs), companions, or feral. Niche livestock such as guinea-pigs, rabbits, pigeons and giant snails are important in some areas and often harbour specific diseases and zoonoses. Wildlife are increasingly being domesticated (deer, elk) or managed. In some contexts feral livestock (pigs, camels, goats) occupy similar niches to wildlife.

Transmission pathways are not static but shift according to evolutionary pressure

A shift from wildlife-to-wildlife, to wildlife-to-domestic animal, to domestic animal-to-human (zoonotic), to human-to-human (anthroponotic transmission) would be an expected evolutionary response of pathogens to increased transmission opportunities. Numerous investigators believe that visceral leishmaniasis was originally an infection that circulated among wild animals (canids and perhaps rodents), and that later, domestic dogs were included in its cycle; eventually, the disease became an infection transmitted between humans without the intervention of an animal reservoir, as is the case of kala-azar in India. This is also the pattern for human influenza pandemics. Influenza viruses circulate in wild birds, some viruses then evolve to be able to affect domestic birds and pigs, then to viruses that occasionally affect people, and then to viruses that are highly contagious between people.

Animals conditioning agro-ecosystems in ways that foster or reduce disease

Animals may alter ecosystems in ways that increase and decrease the risk of disease in people. Some examples are:

- histoplasmosis, a disease of humans, dogs, cats, cattle, sheep, horses, and many wild mammals. The fungus causing the disease grows in soil enriched with avian or bat faeces; birds themselves are not susceptible to the disease, but their faeces play a central role in creating a reservoir for the disease.
- *Clostridium tetani* is a normal inhabitant of the intestines of horses and domestic ruminants and ruminant faeces contributes to contamination of soil with tetanus spores, especially where animal manure is used as fertiliser.
- *C. difficile,* a common cause of infectious diarrhoea in hospitalised humans, is part of the microfauna of domestic animals. Use of cephalosporins in animals is increasing the risk of resistant strains entering the food chain and environment, potentially leading to an increase of cases in the community rather than the current nosocomial incidence.
- HPAI H5N1 is associated with specific agro-ecological conditions that are present in South East Asia, China and Egypt. The role of back-yard poultry and domestic ducks in wetland systems contributing to the persistence of infection and wild bird reservoirs is suggested from available literature, but equivalent study of the contribution of intensive poultry production systems has been resisted by the industry and widespread vaccination has reduced surveillance and epidemiological investigation.

Table 3.2 Different epidemiological patterns for zoonoses with a livestock-wildlife interface

Patterns	Definition	Example
People in the parasite development cycles	Humans are final, intermediate or aberrant hosts for diseases with multi-host life cycles	Humans are final host and aberrant hosts for pig tapeworm
Wildlife reservoir for livestock and human infection	Infection circulates in wildlife making eradication from livestock difficult and hence posing risk to humans	Brucellosis in bison; tuberculosis in badgers
Diseases in ecosystems	Diseases exist in sylvatic (wildlife only), domestic (domestic animals) or urban (human only) cycles, specific to ecosystems, that may connect	dengue (sylvatic and urban); trichinella
Communicable diseases common to humans and animals	Livestock, wildlife and humans are susceptible to a disease that is common in the environment but animals are not involved in transmission to humans	Many fungal diseases
Animals as transporters facilitating pathogen spread	Animals allow spread of disease by transporting pathogens in fleas or ticks	Dogs and animals transport fleas with bubonic plague
Animals conditioning ecosystems to better support pathogens	Wildlife or livestock contaminate environment with pathogens or create conditions that foster pathogen growth	Ruminant guts and faeces are reservoirs for anthrax and botulism Pigeon and bat faeces are reservoirs for histoplasmosis
Agriculture as a risk factor for zoonoses	Agriculture increases risk by providing hosts or environmental conditions for pathogens	Food-borne zoonoses Emerging pathogens such as *C. difficile* and avian influenza
Reverse zoonoses	Wildlife or domestic animals are at risk from human diseases but do not play a role in transmission or spread	Human tuberculosis in dogs Measles in monkeys

4.2 Importance of zoonoses at the livestock-wildlife interface

4.2.1 Importance to human health

4.2.1.1 Contribution to Global Health Burden

The unit of Disability Adjusted Live Year (DALY) has revolutionised assessment and prioritisation of human health burden (Mathers et al., 2002). Introduced by the Global Burden of Disease study in the early 1990s, DALYs are the present value of future years lost due to premature death or being alive with poor health. The Global Burden of Disease (GBD) provides a comprehensive and comparable assessment of mortality and loss of health due to over 150 diseases, injuries and risk factors for all regions of the world. Of 33 diseases listed in the section covering infectious disease

and respiratory infections, one third are zoonoses or have a zoonotic component, and all of these have a wildlife interface.

There are three problems with using the GBD to assess the importance of zoonoses. Firstly, several zoonoses with considerable burdens are not included in the GBD assessment. For example rabies is estimated to cost 1.7 million DALYs per year in Africa and Asia alone but is not considered as a named disease or illness (Maudlin et al., 2009). Other important zoonoses with a wildlife interface and large burdens that are not included are cystic echinococcosis, cysticercosis, leptospirosis and brucellosis. Secondly, zoonoses (especially in poor countries) are systematically under-reported relative to other diseases (Schelling et al., 2007, Maudlin et al., 2009) and, as the GBD report is based on national information on levels of mortality and cause, this bias is reflected in the GBD. The third problem is one of attribution. The GBD is, as the name suggests, organised around diseases and not pathogens or transmission pathways. For example, diarrhoeal diseases, amongst the highest causes of morbidity and mortality in poor countries, comprise one category. Although the majority of important diarrhoeal pathogens are zoonotic (Schlundt et al., 2004) and many of these have a wildlife interface, it is not currently possible to identify the zoonotic component from GBD figures. A promising initiative is underway to attribute food-borne disease to pathogen level (Kuchenmüller et al., 2009) which will assist in better understanding of the zoonotic burden.

Despite these caveats, DALYs represent a universally agreed way of assessing the burden of disease to human health and a logical approach to at least roughly estimating the health burden of zoonoses at the livestock-wildlife interface. We apply this to the assessment of zoonoses with a livestock-wildlife interface in Table 3.3 (details of the calculations are provided in Annex 1).

Table 3.3 Burden of zoonoses in terms of death and disability

	High income countries		**Low income countries**	
	Total DALY	**% Total**	**Total DALY**	**% Total**
All causes of sickness and death	122,092,000	100%	827,668,844	100%
Infectious and respiratory causes	4,128,000	3.4%	319,905,538	38.7%
Zoonoses and diseases recently emerged from animals	768,770	0.6%	64,951,636	7.8%
Diseases recently emerged from animals	631,600	0.5%	44,727,571	5.4%
Zoonoses	140,770	0.12%	22,084,983	2.7%
Zoonotic food-borne disease	131,400	0.11%	17,762,144	2.1%

The most important zoonoses in low-income countries in order of declining burden are: zoonotic food-borne disease, human African trypanosomosis, zoonotic leishmaniasis, zoonotic lymphatic filiariasis, Japanese encephalitis, zoonotic schistosomiasis and zoonotic tuberculosis.

In high income countries, zoonoses and diseases recently emerged from animals constitute 18.6% of the burden of infectious and respiratory disease but only 0.6% of the total burden: most of this burden is due to HIV/AIDS. Zoonoses make up just 3.4% of the total burden of infectious and respiratory disease and nearly all of this is due to zoonotic food-borne disease.

In low-income countries, the total disease burden is much higher than in high-income countries and the share of infectious and respiratory diseases more than ten-fold higher. Zoonoses and diseases recently emerged from animals constitute 20.3% of the infectious and respiratory disease burden; zoonoses are relatively more important than in high-income countries, making up 6.9% of the infectious and respiratory disease burden whereas in high-income countries they constitute 3.4% of the infectious and respiratory disease burden. Moreover, while the proportion of infectious and respiratory disease is 13 times higher in low-income countries than high-income countries, the proportion of zoonoses is 23 times higher. This supports the common perception that zoonotic diseases are relatively more important in low-income countries.

3.2.1.2 Expert opinion

The only systematic global prioritisation of zoonoses with a pro-poor, development perspective was carried out by ILRI in 2002 (Perry et al., 2002). In this study, brucellosis, which is not included in the GBD, was considered to be by far the most important zoonosis, followed by trypanosomosis and tuberculosis (Figure 3.1).

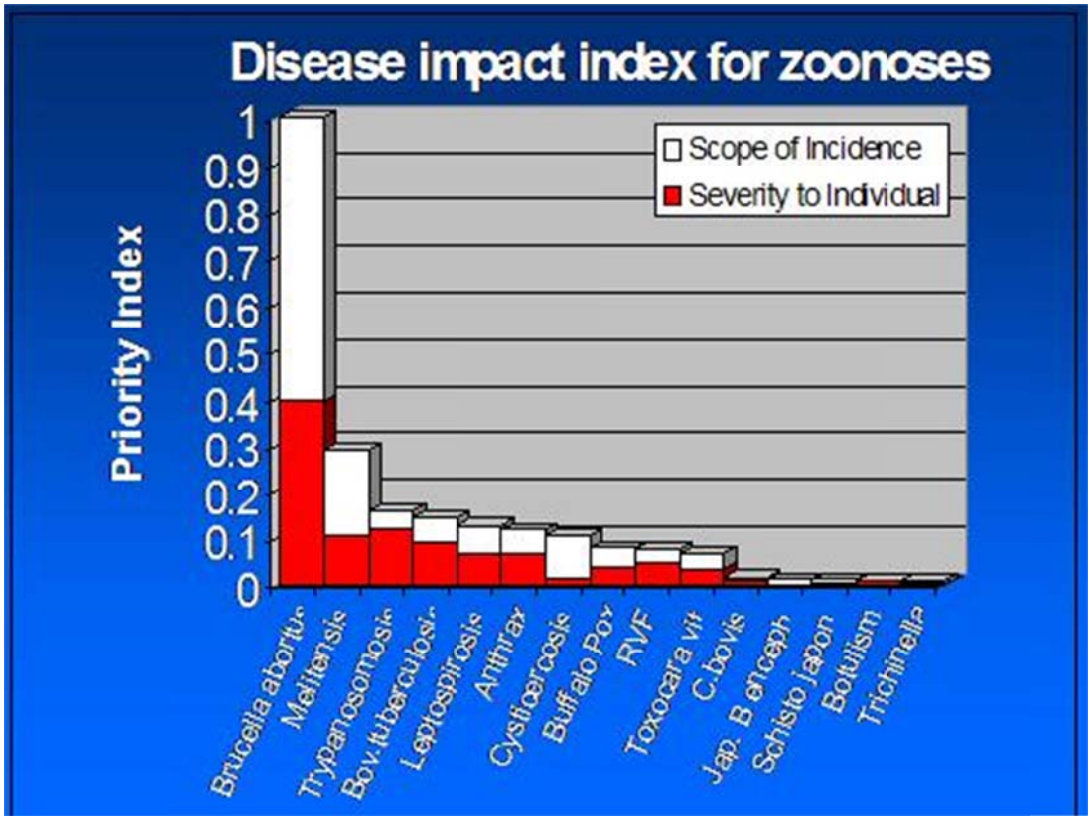
Diseases were ranked in order of those with the greatest importance to the livelihoods of the poor in each livestock production system in their region. The diseases were then ranked by the identification and quantification of their impacts on the poor. Then, three major impacts of each disease or syndrome were identified and scored. These were socio-economic impacts (primarily production losses and control costs incurred by the poor), zoonotic impacts and national impacts (a combination of marketing impacts on the poor with public sector expenditure on disease control). A weighting was applied to the scores for each disease relating to the importance of different impacts on the poor (for example, socio-economic impact was given a weighting of 85% and national impact, 15%). Zoonotic diseases were ranked separately due to the difficulty of measuring the monetary value of human health impacts.

Six different sets of rankings of animal diseases by experts and farmers, without a specific focus on zoonoses, are summarised in Perry and Grace (Perry and Grace, 2009). The authors note a striking lack of consensus between the lists; however, brucellosis, tuberculosis and human African trypanosomosis appear on several lists.

We found only one systematic comparative study of the direct costs of animal diseases at national level (Great Britain) (Bennett and Ijpelaar, 2005). Part of the study looked at the costs and health impacts of ten zoonoses; enterotoxigenic *E. coli*, salmonellosis, fascioliasis, leptospirosis (*L. hardjo*), pasteurellosis, salmonellosis and tuberculosis in cattle; psittacosis (enzootic abortion), orf and toxoplasmosis in sheep; *Streptococcus suis* Type II meningitis in swine; and salmonellosis in poultry. Salmonellosis related to poultry had by far the highest human health costs together with the highest human welfare impact score. This was followed by salmonellosis related to cattle and *E. coli* O157

related to cattle. The most important diseases are food-borne, related to agricultural intensification, and with limited wildlife interface in their epidemiology.

Figure 3.1 Expert derived rating of the importance of zoonoses in terms of pro-poor development
From Perry et al., 2002.



3.2.2 Importance to economies, livelihoods and ecosystems

DALYs by definition only measure the disutility to the individual of being ill. They do not capture the medical costs of illness to the individual or society. Individual costs of illness could include transport costs and purchase of medication. Societal costs could include the provision of health care infrastructure. Indirect costs include loss of production as a result of illness and costs of averting behaviour such as boiling milk or buying mosquito nets. In developing countries with limited resources, both the direct and indirect costs of illness cannot be ignored and the focus on life years rather than the economic prosperity that would allow life years to be valued more highly, has been questioned (Deaton et al., 2010).

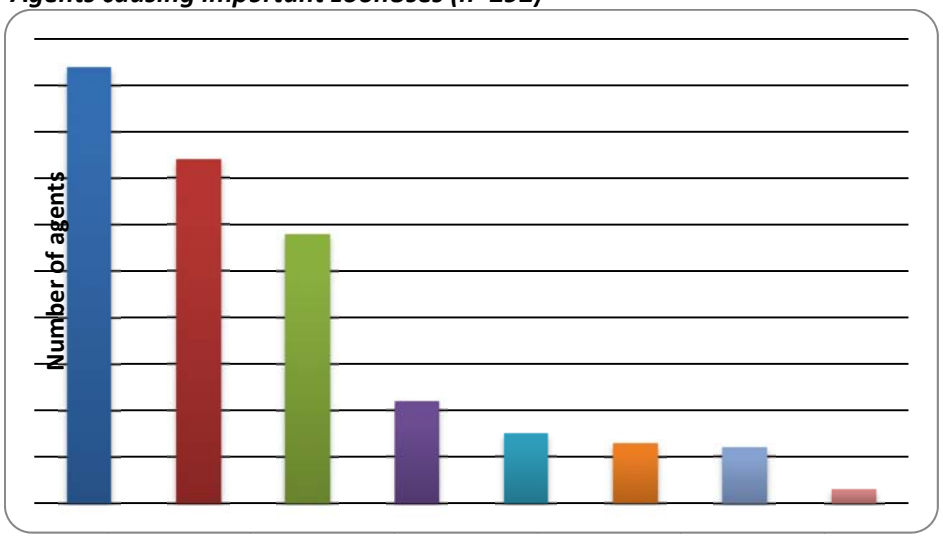
Many of these zoonoses also have large impacts on the livestock sector and national economies, especially diseases which cause morbidity and mortality in animals such as brucellosis, leptospirosis, and anthrax. Emerging diseases, such as SARS, avian influenza or BSE, have very high costs due to their impact on the global economy. This impact has been better characterised and estimates vary from millions to trillions of dollars. Zoonoses also have importance to conservation .

Although studies have been carried out for individual diseases (and some are cited in Chapter 11), there is no equivalent of the DALY that allows us to globally assess and compare the costs of zoonoses with a livestock-wildlife interface.

3.3 Zoonoses of importance to developing countries with a wildlife-livestock interface

We identified 292 important zoonoses (zoonotic diseases) by combining and screening a number of data sources (see Chapter 2 for methodology). Our study, like others, did not show a major discrepancy between developed and developing countries in terms of the number of zoonoses reported to be present – 75% of zoonoses were present in developing countries, 75% in developed countries and 56% in both. Disease detection and reporting is much better in developed countries, so this apparent absence of difference may reflect an increased risk for poor countries. We found that 82% of the zoonoses had wildlife reservoirs or affected wildlife, 74% had livestock reservoirs and 60% had both. Just over 30% of the important zoonoses were caused by helminths, 25% by viruses and 20% by bacteria (Figure 3.2). Of those hosts (663) listed in our database of 292 important zoonoses, domestic and peri-domestic (pest) species predominated; 51% were domestic (cattle, sheep, goats, camel, equines, dogs, cats, pigs and poultry) and 12% were rodents. Wild animals constituted 36% of the database and the remainder were unknown or potentially included both. Amongst wildlife hosts, rodents were the most common followed by primates.

Figure 3.2: Agents causing important zoonoses (n=292)



These findings differ from the landmark studies of Taylor et al. (2001) and Cleaveland et al. (2001), who considered all zoonoses (not just important zoonosis) and used pathogens as the unit of analysis rather than diseases as these studies, in that we found carnivores and ungulates to be relatively more important and viruses less important (Cleaveland et al., 2001, Taylor et al., 2001). This is higher representation of livestock than reported in other studies, which is probably the result of our focus on 'important' zoonotic diseases rather than all zoonotic pathogens. However, livestock are subject to closer observation and better than wildlife, which would result in over-representation of livestock associated zoonoses in scientific literature.

Important zoonoses identified by research team

Experts identified 61 diseases at the livestock-wildlife interface in developing countries considered important because of actual or potential negative impacts on people, domestic animals, wildlife and ecosystems. While most were confirmed zoonoses, some were considered important because of possible or potential (though not proven) zoonotic transmission or because understanding the disease had implications for zoonoses at the livestock-wildlife interface. Among these diseases, viruses predominated as the causative agent, followed by bacteria then protozoa and helminths. Nearly half of these diseases had multiple transmission routes (39%). Amongst those with only one transmission route, 16 were vector borne, 11 were transmitted by direct exposure, 8 were food-borne and one was transmitted by aerosol.

Table 3.4 Important zoonoses at the livestock-wildlife interface in developing countries

Disease Name	Causative Agent	Type of agent
Acariasis (mange)	Sarcoptes spp , Cheyletiella spp, Dermanyssus spp, Ornithonyssus spp	Arthropod
Myiasis	Hypoderma bovis	Arthropod
Anthrax	Bacillus anthracis	Bacteria
Botulism	Clostridium botulinum	Bacteria
Bovine tuberculosis	Mycobacterium bovis	Bacteria
Brucellosis	Brucella abortus	Bacteria
Campylobacter enteritis	Campylobacter jejuni, C. coli	Bacteria
Haemolytic uraemic syndrome	Escherichia coli (0157:H7)	Bacteria
Johne's Disease	Mycobacterium avium subspp pseudotuberculosis	Bacteria
Leptospirosis	Leptospira interrogans	Bacteria
Lyme disease	Borrelia burgdorferi	Bacteria
Plague	Yersinia pestis	Bacteria
Relapsing fever	Borrelia recurrentis	Bacteria
Salmonellosis	Salmonellae enterica	Bacteria
Tuberculosis	Mycobacterium tuberculosis	Bacteria
Tularemia	Francisella tularensis sub sp turalensis	Bacteria
Actinomycosis	Actinomyces israelii	Fungal
Cryptococcosis	Cryptococcus neoformans	Fungal
Clonorchiasis	Clonorchis sinensis (Chinese liver fluke)	Helminth
Cutaneous larva migrans	Ancylostoma braziliense, A. caninum, Uncinaria stenocephala	Helminth
Alveolar echinococcosis	Echinococcus multilocularis	Helminth

Cystic echinococcosis	Echinococcus granulosus	Helminth
Fascioliasis	Fasciola gigantica	Helminth
Schistosomiasis japonica	Schistosoma japonicum	Helminth
Intestinal schistosomiasis	Schistosoma mansoni	Helminth
Trichinellosis	Trichinella spiralis	Helminth
Amebiasis	Entamoeba histolytica	Protozoa
Babesiosis	Babesia canis, B. microti, B. divergens, B. bovis, B. equi	Protozoa
Cryptosporidiosis	Cryptosporidium parvum	Protozoa
Giardiasis	Giardia lamblia	Protozoa
Leishmaniasis	Leishmania donovani, other spp	Protozoa
Malaria of nonhuman primates	At least 20 species of Plasmodium	Protozoa
Toxoplasmosis	Toxoplasma gondii	Protozoa
Trypanosomiasis (African sleeping sickness)	Trypanosoma brucei, T. brucei rhodesiense, T. brucei gambiense	Protozoa
Anaplasmosis	Anaplasma phagocytophilum	Rickettsia
Q fever (Query fever)	Coxiella burnetii	Rickettsia
Chikungunya	Alphavirus	Virus
Cowpox	Cowpox virus	Virus
Crimean Congo Haemorrhagic Fever	Nairovirus	Virus
Dengue fever	Dengue fever virus	Virus
Ebola haemorrhagic fever	Ebola viruses	Virus
Foot-and-mouth disease	Foot-and-mouth disease virus (aphthovirus types A, O, C, SAT 1, SAT 2, SAT 3 and Asia)	Virus
Hantaviral diseases	Hanta virus	Virus
Hemorrhagic fever with renal syndrome	Hantaan virus, Dobrava virus, Puumala virus, Seoul virus	Virus
Hendra virus infection	Hendra virus (paramyxovirus)	Virus
Hepatitis E	Hepatitis E virus	Virus
Influenza type A (swine/avian/Hong Kong flu)	Influenza virus (myxovirus)	Virus
Japanese B encephalitis	Japanese encephalitis virus (flavivirus)	Virus
Lassa fever	Lassa virus (arenavirus)	Virus

Marburg HF	Filovirus	Virus
Monkey pox	Flavivirus	Virus
Newcastle disease	Newcastle disease virus (paramyxovirus)	Virus
Nipah virus infection	Nipah virus	Virus
Orf (contagious ecthyma)	Poxvirus	Virus
Rabies	Rhabdovirus	Virus
Rift Valley fever	Phlebovirus	Virus
Rota virus	Rota virus	Virus
Severe acute respiratory syndrome (SARS)	Coronavirus	Virus
Tick borne encephalitis	Flavivirus	Virus
West Nile fever	West Nile virus (Flavivirus)	Virus
Yellow fever	Flavivirus	Virus

Our expert-based disease selection broadly supports the literature cited in confirming the importance of viruses and multi-host pathogens as most problematic agents and bats, carnivores and domestic herbivores as most problematic hosts.

4. Mapping zoonoses at the livestock-wildlife interface

Introduction

Epidemiologists have traditionally used maps when analyzing associations between locations, environment and diseases (Clarke et al., 1996). Ostfeld et al., (2005) points out that maps have been used for two distinct purposes in epidemiology. The first involves retrospective analyses of spatiotemporally dynamic epidemics to understand what factors govern the spatial pattern and rate of spread of diseases. The second major use of maps in epidemiology is to characterize spatial variation in contemporaneous (static) ecological risk of infection and potential causes of that variation and that spatial data on disease incidence can be used to extrapolate the risk of exposure from current distributions to new geographical areas. The ability to make maps interactively has increased the potential for many users to use the information. Coupled with increasing analytical functionality of Geographical Information System (GIS) that ranges from visual to exploratory and modelling, the uses of GIS in epidemiology has increased significantly (Pfeiffer and Hugh-Jones, 2002, Ostfeld et al., 2005).

The output generated by GIS in map format has the particular advantage of showing implicit representation of spatial dependence relationships in an intuitive manner. The technology is becoming an essential component of modern diseases surveillance systems (Pfeiffer and Hugh-Jones, 2002, Jones et al., 2008). The opportunities for epidemiological investigation have increased with web-based mapping tools, use of Global Positioning System (GPS) in mapping disease outbreaks and increased precision and frequency of collecting the information.

Results

Using HealthMap data, Figure 4.1a shows the spatial distribution of 15 zoonotic diseases or groups of diseases in relation to human population density. The outbreaks occurred in both low and high human population density areas (Figure 4.1b). Major cities had outbreaks of zoonotic disease. The high density reported cases included Cairo and Al-Giza in Egypt where avian influenza outbreaks were reported, and in West Africa avian influenza was reported in Kano. Also food-borne illness was reported in Safaga and El Manial in Egypt. These areas have population densities of more than 10,000 people per km^2. Examples of other big towns with population densitities of less than 10,000 people per km^2 that reported outbreaks of disease included Kampala (outbreaks of dysentery, diarrhoea and botulism), and Cocody, Abidjan (outbreak of avian influenza).

This type of spatial analysis provides us with potential information on risks of diseases to a population. As these disease databases become more populated with information, it will strengthen the basis for modelling and also provide insights on what type of threats these diseases can have on human populations.

The next step of the analysis was to derive a hotspot map on the 15 zoonotic diseases, which is shown in Figure 4.1c.. As indicated in the map the hotspots were located in Egypt along the Nile, central and western Kenya, central Uganda, Zimbabwe, and north western South Africa. The analysis indicates that West Africa is also an area with a high number of zoonotic disease reports. The

countries include Nigeria, Togo, Benin, Cote d'Ivoire, Gambia, Guinea and Senegal. In other countries such as Morocco, Algeria, Ethiopia, Namibia, Angola, Zambia and Madagascar we observe pockets of areas of high zoonotic disease reports. Another level of analysis is to find out what are the drivers of these diseases, which is not addressed in this project.

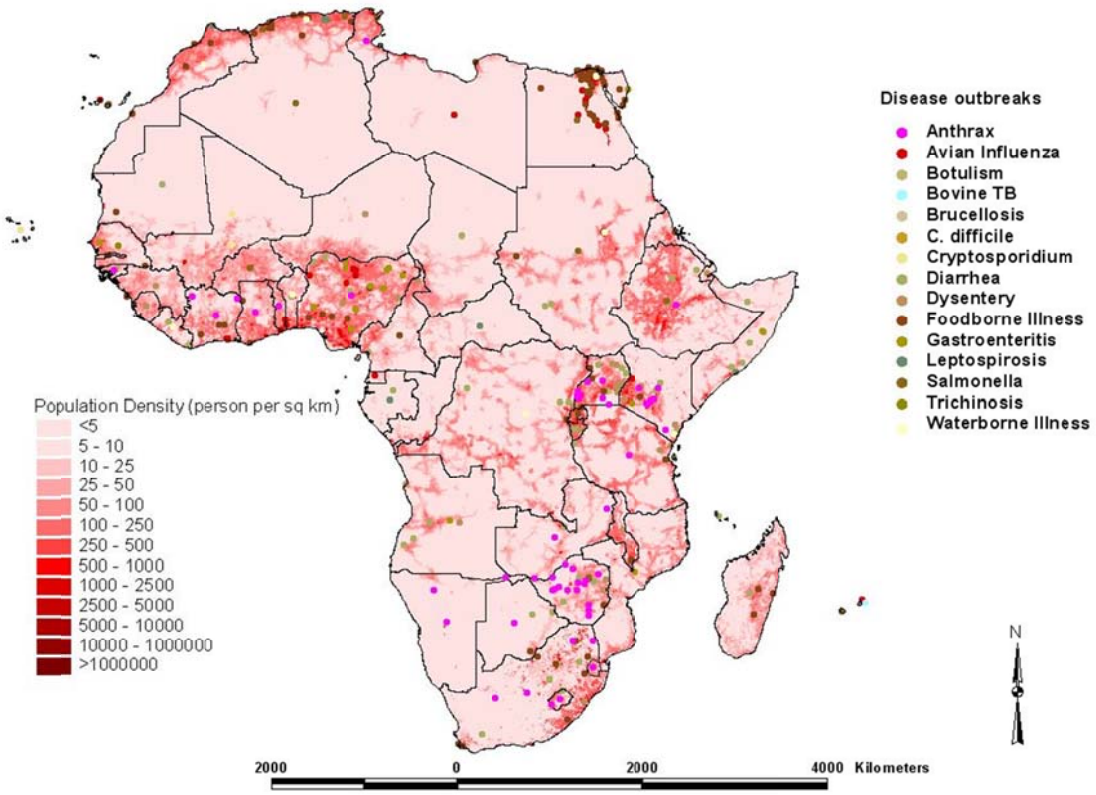


Figure 4.1a Spatial mapping of 15 zoonotic disease outbreaks in relation to human population, Jan 2006 to April 2011

The dots represent outbreaks, with a different colour for each of the 15 disease types.

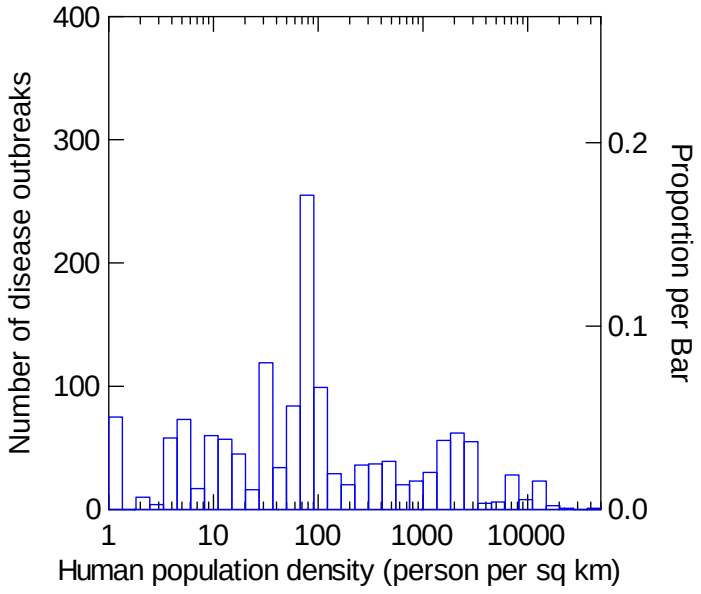


Figure 4.1b Disease outbreaks in relation to human population density, Jan 2006 to April 2011

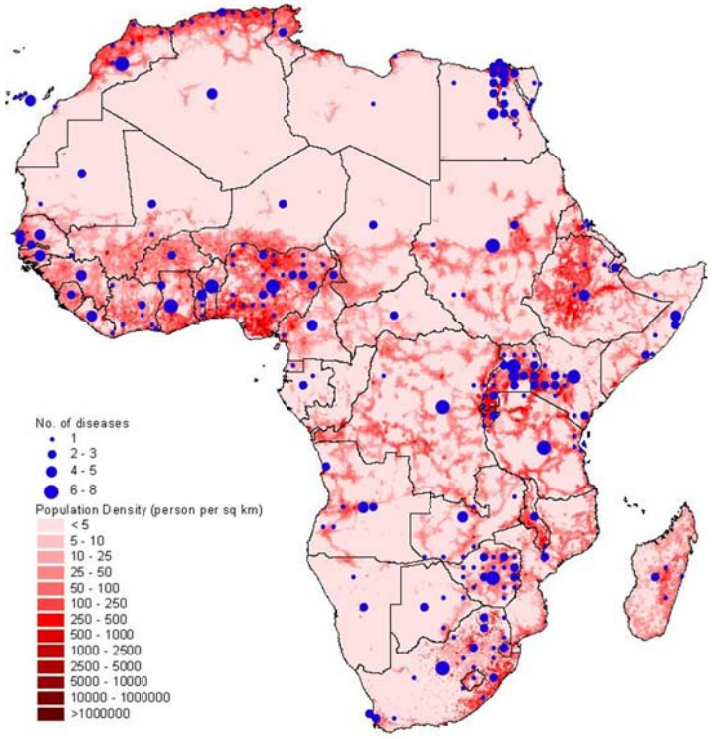


Figure 4.1c Hotspots of zoonotic diseases in Africa.
The map was derived from zoonotic diseases outbreaks. Circles represent one degree grid cells, and the area of the circle is proportional to the number of diseases in the cell.

The diseases varied across the continent and we listed some of disease outbreaks in some of the hotspots. In Egypt there were outbreaks of avian influenza, food-borne illness, and dysentery. In Nigeria the outbreaks were gastroenteritis, food-borne illness, diarrhoea, avian influenza and anthrax. In South Africa it was food-borne illness, dysentery, diarrhoea, *Cryptosporidium* and avian influenza. In Zimbabwe the outbreaks reported were diarrhoea, dysentery, anthrax, gastroenteritis, food-borne illness and avian influenza. Uganda had similar disease outbreaks as reported in Zimbabwe. In Kenya the diseases recorded were diarrhoea, avian influenza, dysentery, salmonella, anthrax and food-borne illness.

The next level of analysis focused on anthrax using 2009 AU-IBAR data. Anthrax is caused by the gram-positive sporulating bacterium *Bacillus anthracis*, which primarily affects herbivorous livestock and wildlife species, but also poses a serious public health risk in many parts of the world (Lembo et al., 2011). Figure 4.2a shows the outbreaks of anthrax in relation to human population density. Fifty per cent of the outbreaks were reported in low human population density areas (less than 50 persons per km^2). About 35% of the outbreaks were located in areas of between 50 and 200 persons per km^2. Fifteen per cent of outbreaks were reported in areas where the population densities were great than 200 persons per km^2. The high incidence in areas of low human population density is that most of the outbreaks occurred in natural vegetation that is less inhabited by people. Spatial analysis on the relationship between anthrax outbreaks and land cover shows that outbreaks in 2009 occurred in dense vegetation mostly in woodlands and shrublands (Figure 4.3a and 4.3b) compared to other land cover.

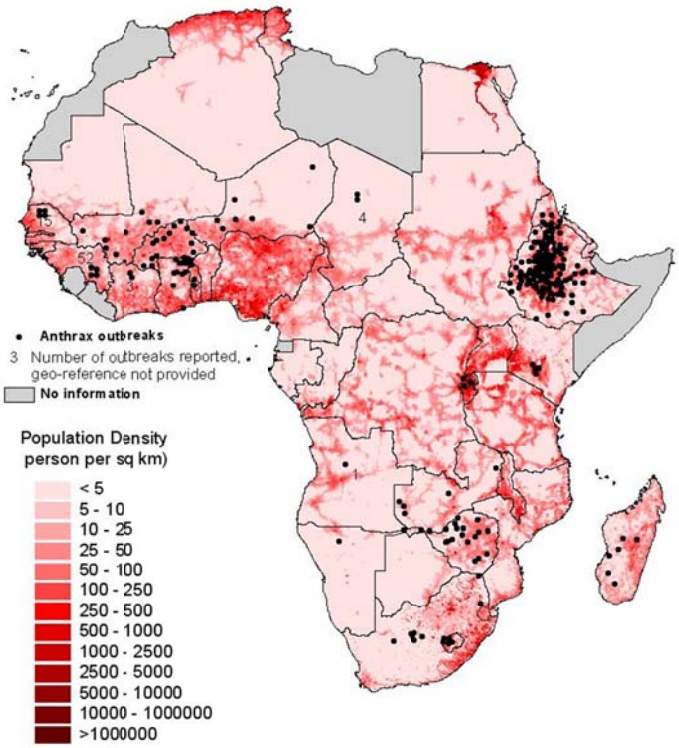


Figure 4.2a Spatial distribution of anthrax outbreaks in relation to human population density, 2009.

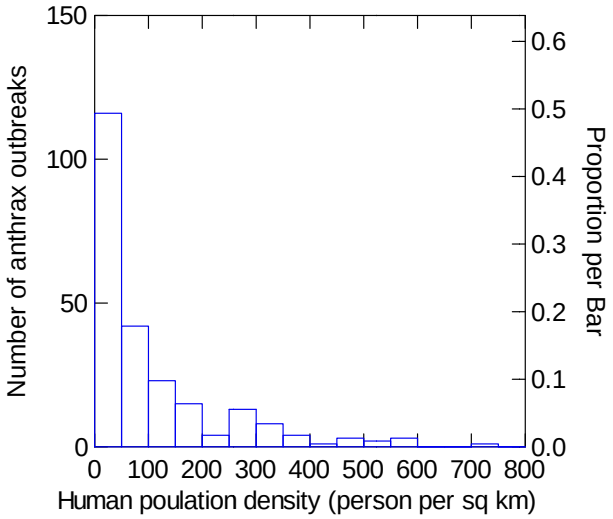


Figure 4.2b Anthrax outbreaks in relation to human population density, 2009.

Studies in Lake Manyara in Tanzania indicate that shrub establishment in the park coincided with anthrax epidemics that drastically reduced the impala population in 1961, 1977 and 1984 (Prins and Vanderjeugd, 1993). A study on a free-ranging population of bison in Canada indicated that more than 50% of morality in bison (*Bos bison athabascae*) occurred in forested or shrub-covered sites (Gates et al., 1995). They used infrared cameras on board helicopters to detect the dead bison. Gates at al., (1995) point out that anthrax bacteria form highly resistant endospores which can, if

conditions are right, maintain anthrax in the environment outside living hosts for decades between epidemics. Dense vegetation can maintain and concentrate these spores for longer times than open areas (Prins and Vanderjeugd, 1993, Gates et al., 1995) before they are trigged by prolonged wet periods followed by dry conditions (Gates et al., 1995).

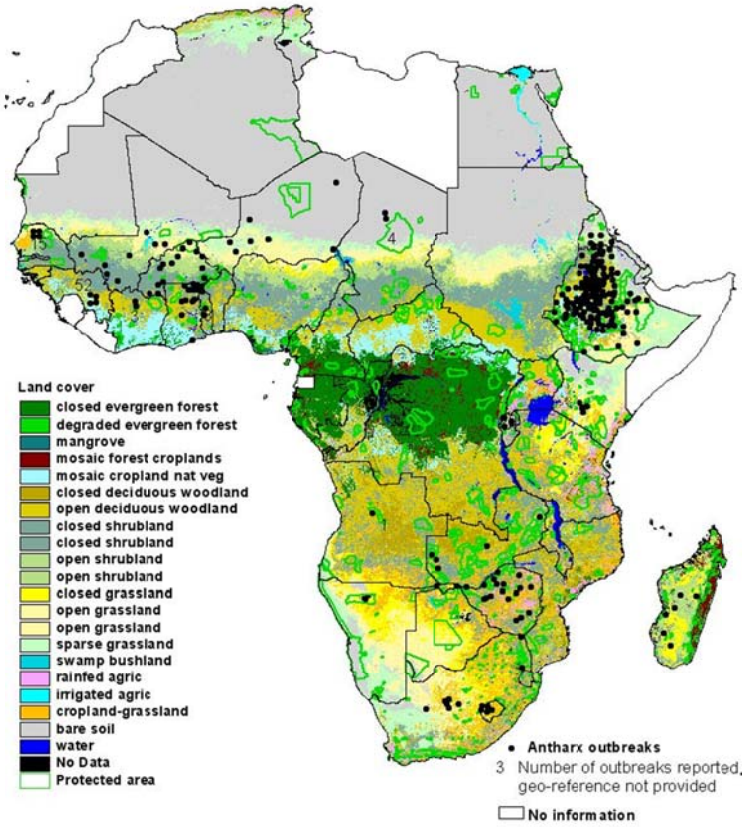


Figure 4.3a Spatial distribution of anthrax outbreaks in 2009 in relation to land cover

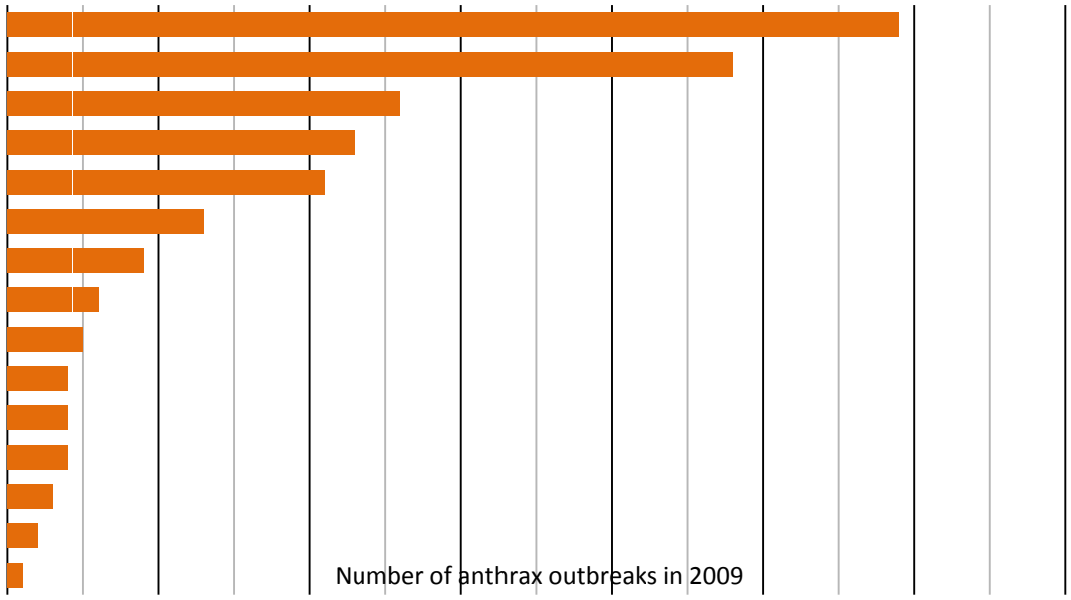


Figure 4.3b Number of outbreaks of anthrax in 2009 relation to land cover

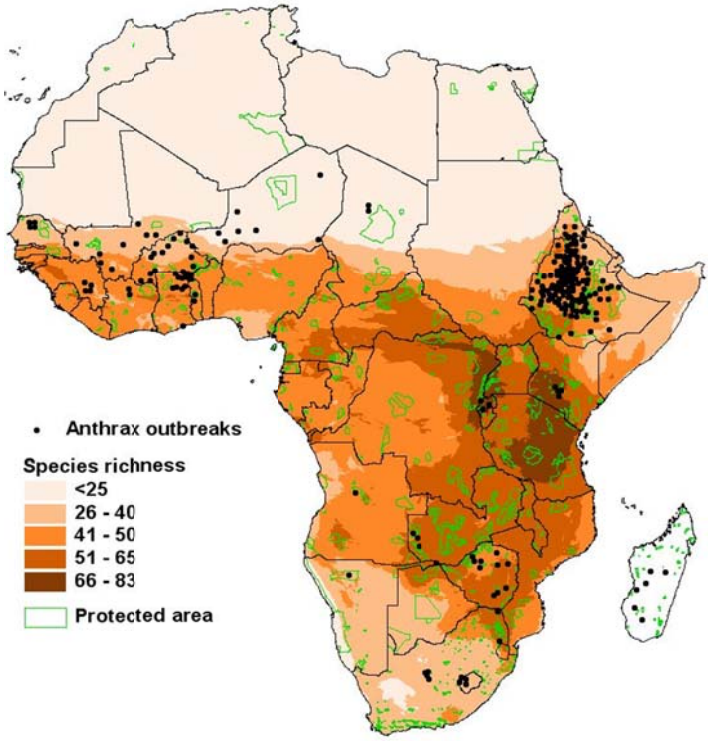


Figure 4.4a Spatial distribution of anthrax in relation to mammal species richness. Species richness was calculated as the number of species in an area.

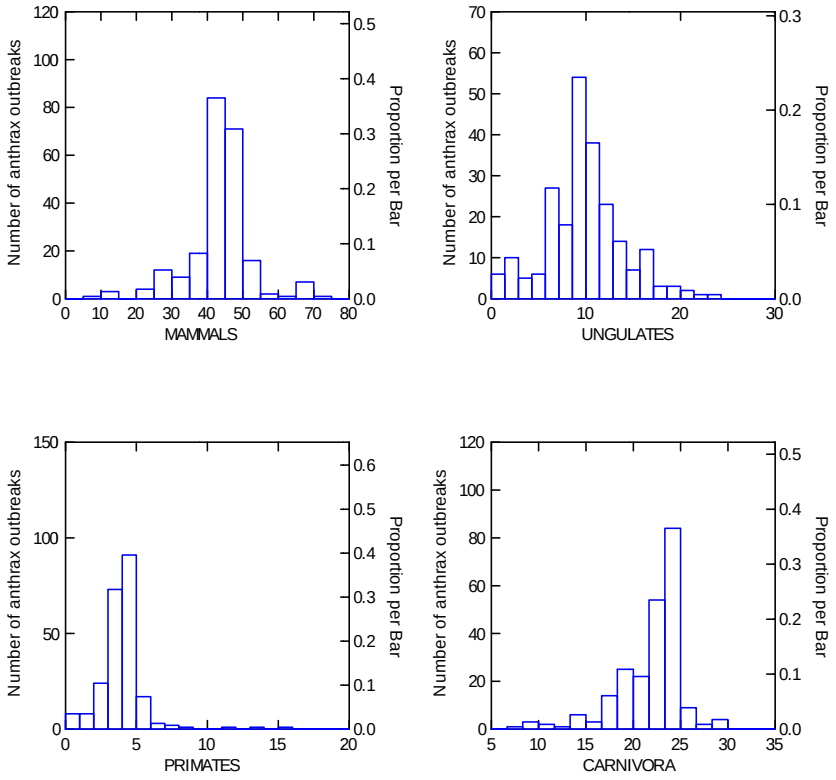


Figure 4.4b Outbreaks of anthrax in relation to species richness of mammals, ungulates, primates and carnivora.

The occurrence of anthrax in relation to mammal species richness shows high occurrence of anthrax in high mammal rich areas (Figure 4.4a). Similar, patterns are exhibited with species richness of ungulates and carnivora (Figure 4.4b). However, the outbreaks of anthrax occurred in areas of low species richness for primates. Many of the primates are found in very dense wooded vegetation where anthrax outbreaks might have been difficult to detect.

Most of the anthrax outbreaks were outside protected areas, but as indicated in the map the species richness of animals goes beyond the park and many of these animals will be in contact with livestock and people. Many of these parks are small in size and in many countries were dry range refuge for livestock. As people and livestock increase, the range for wildlife is becoming smaller and the contact between livestock and wildlife is increasing which will increase transmission of diseases between wildlife and livestock.

Conclusions

Explanatory spatial analysis with the datasets (point data) shows the great potential in characterizing the spatial variation of diseases in relation to a number of environmental (land cover), social (human population) and wildlife (species richness) variables. The potential of spatial temporal analysis has increased due to the resolution of data (geo-referencing using the GPS) in that many diseases are mapped where they did occur.

Tools developed to deal with such data have improved the data integration, correlation analysis, hypothesis setting and also communication of the information to the public. However, as many of the organizations are just starting to develop geo-databases on diseases we still have under-reporting of diseases. Jones et al (2008) suggest that there is a critical need for health monitoring and identification of new, potentially zoonotic pathogens in wildlife populations. They also advocate for re-allocation of resources for smart surveillance of emerging disease hotspots in lower latitudes such as tropical Africa, Latin America and Asia.

The major hurdle in geo-spatial data on zoonotic diseases is data accessibility. Many of these programs are just starting and many institutions find it difficult to share data. It will be helpful for these institutions to develop policy and regulations on data acquisition and data use. Global scale data on environment (land cover and vegetation indices from satellite images), socio-economic and human demography are now widely available compared to 20-30 years ago. Many institutions are making their data available through the internet and also through institutional agreements. Improvement in the modelling of diseases will be possible with accessibility and availability of these data sets.

Lack of reliable geo-referenced data on zoonoses prevalence or even presence hindered mapping; this was partially overcome by collaboration with HealthMap. However, due to limited data it was not possible to carry out detailed investigation of the links between geo-referenced enviro-socio-economic geo-referenced data and diseases, but in the near future this is likely to be possible as these health databases gather and consolidate the information that is scattered in many places and organizations.

5. Disease transmission routes and the relative importance of the wildlife-livestock route

Summary of main messages

- Human habitat expansion, for habitation or agriculture, has contributed to greater contact between humans and wildlife and resulted in the emergence of previously unknown zoonotic diseases from wildlife. Evidence: high.
- Livestock movements (seasonal or all year round) and wet markets provide important mechanisms for zoonotic disease spread. Evidence: high.
- Consumption of bushmeat represents one of the most obvious ways in which humans come into close contact with wildlife and their pathogens. It is an important source of zoonotic disease transmission from wildlife. Evidence: medium.
- Keeping livestock may potentially increase the risk of zoonotic disease transmission from wildlife to humans because livestock may create a new link between wildlife and humans that were otherwise not connected. Evidence: medium.

Introduction

Understanding the diverse transmission routes of infectious diseases from wildlife to humans is a first step in the assessment of any potential risks associated with wildlife. A large number of infectious pathogens are known to be harboured by wild animals, and many have the ability to jump from wildlife to humans and livestock. Many different transmission routes exist for infectious diseases in general, including direct transmission, airborne, vector-borne and indirect transmission via fomites (including food). In the case of zoonoses related to wildlife, there is still no clear understanding of which are the most important transmission mechanisms and whether prioritization is possible as a way to inform allocation of resources. Most zoonotic pathogens found in wildlife are not exclusive to these animals but are also found in domestic animals. The degree of contact between humans and domestic animals is in most cases greater than with wildlife. Nevertheless, there is a potential role for livestock by serving as a link between wildlife and humans hosts that may otherwise not be connected, and facilitating movement of pathogens among those different groups. In some cases domestic animals may act as amplifiers of disease transmission and lead to transmission which would otherwise be impossible. In other cases, the presence of livestock may have a diluting effect if domestic species are not the preferred host for a pathogen. The exact role of livestock and whether livestock keeping in developing countries is a contributor to increased zoonotic disease transmission from wildlife to humans is not clear. This review aims to answer these two essential questions: the transmission routes of zoonoses from wildlife to humans and the relative importance of the wildlife-livestock interface in that transmission.

Methodology

For this theme a total of 98 abstracts were blindly reviewed by two experts. Twenty eight (28) abstracts were selected for full paper review. Of these, 20 were reviews and 8 were original research papers. Full paper review and summary of the main messages was carried out by one expert. Some of the full papers did not provide much information for this review because their focus was not relevant to the questions being asked. Approximately 11 full papers contributed significantly to this review.

Findings

5.1 Transmission routes from wildlife to people

The role of wildlife as reservoirs or amplifiers of transmission of many pathogens to humans is now an unarguable fact. Different wildlife animal species are known to carry a variety of zoonotic pathogens. Wild boars alone, present in many regions around the world, have been found to carry some of the most important zoonotic bacteria including *Mycobacterium bovis*, *Brucella suis*, *B. melitensis* and *B. abortus*, *Coxiella burnetti*, *Yersinia pestis* and *Leptospira* spp., among others (Meng et al., 2009).

But presence of infected wildlife in an area does not necessarily imply risk of zoonotic transmission; various factors influence the likelihood of an infectious disease being transmitted from wildlife to other host population, including humans. In the case of zoonotic transmission, those parameters were summarised by Mathews as: (i) intensity of infection in the wildlife reservoir; (ii) the size and/or density of the wildlife population; (iii) the nature of the contact between wildlife and humans; and (iv) susceptibility of humans to infection (Mathews, 2009).

But many other factors have been found to drive transmission from wildlife to humans and domestic animals. The epidemiology of one specific pathogen will differ in different areas, which may be explained by a different contribution of the various factors driving transmission (Woodford, 2009, Rhyan and Spraker, 2010). For Woodford et al., "there is a clear and solid association between biotic factors (pathogen, host, vector and vegetation) and abiotic factors (geographic landscape, rainfall and soil type) that determines presence and distribution of certain diseases in certain areas" (Woodford, 2009). Ecological factors such as elevation, temperature and rainfall are likely to impact on the distribution of wildlife reservoirs and vectors; air movements are likely to impact on the movement of infectious pathogens and as a result on disease transmission. Soil composition will favour survival of certain agents. The combination of all these factors will therefore determine the distribution of the pathogen, the host and potentially the vector in a specific area, resulting eventually in "the establishment of natural foci of certain infections" (Woodford, 2009).

The role of climatic parameters in disease distribution, especially vector-borne diseases, is also well known. As a result, modification of those abiotic factors will affect zoonoses transmission. Fire that eliminates vegetation has a marked effect on the vulnerability to predation of rodent reservoir hosts. This in turn may facilitate disease transmission between animals, and from these to humans (Woodford, 2009). Similarly, the presence of flooding will modify the landscape and have an effect on disease transmission.

In a review of emergence of diseases from wildlife, Rhyan and Spraker simplify the likelihood of transmission of zoonoses as a function of two main types of factors: (i) human encroachment in wildlife habitat and (ii) increased interest in and popularity of wildlife (Rhyan and Spraker, 2010). While this is a very realistic broad categorization of the factors that may underlie the increasing numbers of outbreaks of zoonotic infections in humans, in this review we have identified a more detailed list of events that have been associated or are believed to contribute to wildlife-human zoonoses transmission. For ease of presentation, we have grouped the transmission routes from

wildlife to humans into three main categories: human encroachment in wildlife habitat, direct contact, and indirect contact with wildlife.

5.1.1 Human encroachment in wildlife habitat

5.1.1.1 Human habitat expansion

Colonization of new areas for human habitation (and/or agriculture) is one of the most prominent examples of humans' incursion into natural foci of certain pathogens. The expansion of the human habitat into forest areas will, with no doubt, lead to greater proximity to wildlife species. This will be translated into a greater potential for zoonotic spillover from wildlife to humans and even the establishment of urban/domestic cycles of otherwise wildlife diseases. This is the case with Chikungunya virus. The virus has an endemic sylvatic cycle in certain areas of the globe where reservoir and competent vectors are present. Human access to those areas will put them in close contact with infected vectors. Infected humans will then carry the pathogens back to their habitation and be responsible for the infection of peri-domestic vectors, resulting in the establishment of a peri-domestic cycle otherwise absent (Gould and Higgs, 2009).

Also deforestation – clearing of forest areas for habitation or agriculture purposes – poses an increased risk of zoonotic infection initially for forest workers, given their closer contact with wildlife reservoirs or vectors of zoonoses, but subsequently for humans inhabiting or making use of deforested areas. The ways in which deforestation leads to increased risk of zoonotic transmission from wildlife are varied. An outbreak of Kyasanur forest disease occurred among forest workers in an area where approx 400 hectares of forest were cleared to set up cashew tree plantations (Chomel et al., 2007). Greater closer contact with wildlife is the event responsible for disease transmission in this example. Also, a study by Goldberg et al. found that people in settlements near a disturbed forest fragment were at increased risk of disease transmission from primates. Investigating transmission of *Escherichia coli* the authors suggest that defragmentation of forest areas may reduce primate biodiversity and alter their demographics and behaviour, with a resulting change in their exposure to pathogens, susceptibility and capacity for disease transmission (Goldberg et al., 2008b). It has also been demonstrated that deforestation alters the patterns of gastrointestinal helminth and protozoal infection of certain primate species. The research by Goldberg et al. found that the degree of anthropogenic disturbance within a fragment affects the rate at which bacteria are transmitted among species, which may be due to increased geographic and ecologic overlap among species.

Nevertheless, it should be emphasized that other human activities apart from deforestation increase the risk of zonootic disease transmission; reforestation of areas suitable for reservoir and other hosts of *Borrelia burgdorferi*, coupled with an increase in human settlements in peri-urban areas, led to increased human incidence of Lyme disease in the US (Chomel et al., 2007).

The degree of zoonotic transmission in areas newly accessed by humans will also be influenced by the abundance of the vector (and often also the density of hosts). Transmission of West Nile Virus between birds and humans has been found to require high mosquito density (Gould and Higgs, 2009). In the same way, the persistence and activity of plague (*Yersinia pestis*) in established foci seems to relate to the abundance of reservoir and vectors. Persistence of plague seems to be determined by the availability of a minimum density of hosts. Increased abundance of vectors in

specific environmental and climatic conditions seemed to be responsible for increases in prevalence of plague in great gerbils (Kausrud et al., 2010).

5.1.1.2 Agriculture

Agriculture expansion in many areas often requires clearing of forest. As explained above, deforestation *per se* leads to closer wildlife-human contact, and the resulting increased risk in the potential for disease transmission. Nevertheless, agriculture has other mechanisms that open new routes for zoonotic transmission from wildlife.

Agricultural activities that result in multi-species land use, or "buffer-zones", where livestock and wildlife make use of the same space will increase contact between these animals and increase transmission. The increased potential for human zoonotic infection derives from livestock filling the gap between wildlife and humans and allowing flow of certain pathogens. A well-known example of this is represented by the outbreak of Nipah virus in Malaysia in 1998-99, as a result of ecological and environmental changes linked to deforestation and the expansion of pig farming, coupled with planting of fruit trees (Chomel et al., 2007).

Another consequence of agricultural expansion is the development of areas that support the presence and expansion of pathogen reservoirs. The emergence of Argentine haemorrhagic fever has been linked to the development of corn plantations that support the main virus reservoir, the corn mouse (Chomel et al., 2007).

And lastly, another well-known aspect contributing to disease transmission is the use of manure as natural fertilizer in agriculture, a common practice in many developing countries – this has the potential to increase transmission of food-borne diseases such as verotoxigenic (VTEC) *E. coli* and *Salmonella* (Newell et al., 2010).

5.1.2 Direct contact

Many human activities have resulted in increased contact between wildlife and humans and an associated increased in the risk of disease transmission. The following is a list of factors that have been found to have increased human contact with wildlife and increased transmission of specific zoonotic diseases:

- Illegal trade of wildlife may result in the spread of exotic pathogens to new areas via infected wildlife. This poses an immediate risk of disease expansion and it is the underlying basis of some of the most well known transboundary diseases. It does not always result in regional or national disease spread, but can represent a risk for people working in close contact with these animals. Customs officers in Belgium developed psittacosis after contact with infected parakeets (Chomel et al., 2007). The outbreak investigation revealed that time of contact with infected animals was a determinant of the risk of infection, with those exposed for more than 2 hours having a risk of contracting infection 3 times higher than those exposed for shorter time (Chomel et al., 2007). Illegal trade of wildlife in some non-industrialized countries is believed to be high and therefore this can present difficulties for control of this transmission route.
- Keeping exotic animals as pets increases the likelihood of humans being exposed to exotic pathogens. The importation of African rodents from Ghana to the US led to an important outbreak of monkeypox in 2003. Prairie dogs housed in contact with the imported reservoir

were infected and subsequent contact with these prairie dogs seemed to be the initial source of infection for affected humans. (Schloegel and Daszak, 2004, Weiss, 2008).

- Other activities that put humans and wildlife into closer contact, such as hunting and butchering, increase the likelihood of zoonosis transmission. Human T-lymphotropic virus types 3 and 4 were found in people exposed to wildlife via these routes in Southern Cameroon (Chomel et al., 2007). In the same way, many cases of *Brucella suis* infection in humans are known to be related to handling of infected wild boars (Meng et al., 2009).
- An emerging leisure attraction, although less so in developing countries, is petting zoos keeping wild animals, often alongside domestic livestock. This represents a risk for its workers and for visitors who are allowed and encouraged to touch the animals. Contact with a contaminated environment can be also an indirect mechanism of transmission of zoonoses. *Escherichia coli* O157 and *Coxiella burnetti* are two classical examples of zoonotic risk in this context (Chomel et al., 2007).
- Another route of entry of zoonotic pathogens is the introduction of new exotic species into a territory. Indirectly, this represents the initial source of pathogens increasing the risk of zoonotic transmission. The introduction of new species of fish to England led to an increased detection of opisthorchid fluke parasite, given that those new species were competent intermediate hosts for the fluke parasite (Fèvre et al., 2006). This aspect is of even greater relevance where exotic animals are introduced into areas already hosting high population densities of either competent hosts of domestic animals or other wild animals. As mentioned before, the importation of African rodents from Ghana led to an outbreak of monkeypox in the US in 2003. Also the release of new raccoon dog species in the ecosystem in Western Russia led to the spread of rabies through north-eastern Europe (Chomel and Sun, 2010).
- Although perhaps with a lower population impact, the use of laboratory animals is another potential source of zoonoses from wildlife to people in contact with these animals. This was the case in 40 cases of meningo-encephalitis (herpes B virus) in people having direct or indirect contact with laboratory macaques (Chomel et al., 2007).

5.1.3 Indirect transmission

The two major mechanisms of indirect transmission of zoonosis from wildlife to humans are represented by water and food.

- Through water: it is well known that using water from the same source as domestic and wild animals results in a greater effective contact among animals/humans and ultimately facilitates disease transmission (Woodford, 2009). A study (Goldberg et al., 2008b) looking into the genetic similarity of *Escherichia coli* strains from primates and humans in Uganda found that using water from an open water source was associated with an increased genetic similarity between strains of primates and humans. Another study (Kankya et al., 2010) found that absence of wild animals from water sources accessed by humans reduced human exposure to mycobacterial infections.
- Food-borne (consumption of bushmeat): food is an important vehicle for many zoonotic pathogens. Consumption of bushmeat represents an ideal mechanism of transmission of zoonotic pathogens. Examples include the simian foamy virus that has been found infecting people who had direct contact with fresh non-human primate meat. Consumption of meat from chimpanzees found dead has been associated with Ebola outbreaks in humans; nevertheless, other investigations indicate that transmission of Ebola may be more likely to be due to handling of dead bodies of infected chimpanzees rather than via ingestion of contaminated meat. 75% of

outbreaks of trichinellosis in Spain were found to be due to consumption of wild boar meat; clear evidence of transmission of hepatitis E virus after consumption of wild boar meat was found in two cases in Japan as well as from the consumption of undercooked pig livers (Meng et al., 2009).

5.2 Relative role of the wildlife-livestock interface in wildlife zoonotic transmission

The second part of the review looked into available evidence on the relative role of the wildlife-livestock interface in zoonotic transmission. Few studies were found to address this key question, and very few studies have directly assessed how much livestock contribute to increased transmission between wildlife and people. It has been already mentioned before that agriculture has proved to be essential in the appearance of certain outbreaks of zoonoses (Nipah virus). The explanation provided above is compatible with livestock (or pets) acting as a link between wildlife and human pathogens that may otherwise not come in contact with each other. So livestock and pets open new transmission routes. Another example also mentioned before is *Brucella suis*; high exposure to this pathogen was found in domestic swine and hunters, suggesting active transmission from wild boar (Meng et al., 2009).

This review found three main mechanisms for amplification of transmission: (i) close contact with livestock, (ii) livestock movements and (iii) livestock markets.

5.2.1 Close contact with livestock

As already mentioned, a study by Goldberg et al. found that tending livestock was associated with an increased genetic similarity among strains of bacteria in humans and non-human primates, demonstrating that livestock could be a factor that facilitates exchange of microorganisms and parasites between primates and humans (Goldberg et al., 2008b). This could be the reason why Kankya et al. found that pastoralists residing in close proximity to cattle or pig night enclosures were at higher risk of acquiring mycobacterial infection, which is compatible with the aerosol transmission of non-tuberculous *Mycobacteria* spp. pathogens and opens the hypothesis of a similar amplifying mechanism for other airborne zoonoses (Kankya et al., 2010). Interestingly, a protective effect of raising livestock was highlighted in the same study, which found that rearing of cattle for more than 5 years seemed to reduce the susceptibility of humans to mycobacterial infections.

It has been also suggested that livestock may naturally minimise their contact (direct and indirect) with other animals, thus reducing risk. Smith et al. explored the wildlife–livestock faecal transmission of pathogens; a selective grazing behaviour of cattle that makes them avoid areas contaminated with faeces from livestock and wildlife is believed to impact on the degree of contact with faeces from certain wildlife species and therefore on the degree of transmission of gastrointestinal parasites and bacteria. Nevertheless, the exact implication of this selective grazing on disease transmission hasn't been investigated (Smith et al., 2009b).

Handling of livestock has also been proven to increase transmission of pathogens. This can be another mechanism of wildlife zoonoses amplification. Pig handlers, including farmers and veterinarians, have been shown to be at increased risk of acquiring infection with hepatitis E virus, probably from wild boars, and possibly amplified through pig farms (Meng et al., 2009).

But it is not only the presence and management of livestock what has the capacity to influence zoonotic transmission. Wildlife management (for example keeping wildlife at increased densities and providing fencing and increased feeding) in deer has been shown to impact on the transmission of disease between livestock and wildlife (Mathews, 2009, Rhyan and Spraker, 2010). Also saiga (*Saiga tatarica*) densities were found to influence the risk of FMD transmission to local livestock, with low densities of this antelope resulting in lower prevalence in livestock in Kazakhstan (Morgan et al., 2006). This shows that land use management and wildlife management could represent important strategies in the management of zoonoses transmission from wildlife. Moreover, stress to wildlife resulting from loss of habitat, higher densities and increased predation leads to changes in behaviour and condition, making them manifest or amplify an otherwise unrecognized infection and perhaps causing spill-back to livestock (Rhyan and Spraker, 2010).

5.2.2 Contact networks / animal movements

Animal movements bring animals from different farms and areas in contact with each other. They represent a very efficient mechanism for dissemination of pathogens in countries or regions. In Africa, where livestock is one of the few tradable commodities, animal movements are of special relevance in terms of disease transmission, for both animal diseases and zoonoses. This is most relevant in the case of nomadic and semi-nomadic pastoralists. A clear example of the impact of animal movements on disease spread is represented by bovine tuberculosis (*Mycobacterium bovis*) and cattle in the UK. *E. multilocularis* was introduced to Northern Japan via movement of infected foxes, with domestic dogs believed to have acted as amplifiers. Also *Trypanosoma brucei rhodesiense* and cattle movements led to a human outbreak of this zoonoses in a new area in Uganda (Fèvre et al., 2006).

The seasonal movement of animals can also influence the epidemiology of certain infectious diseases, including zonooses. Malignant catarrhal fever virus is excreted by wildebeests in the calving season. Brucellosis, excreted in aborted tissues is likely to have a similar seasonal pattern in wildlife reservoirs. In the same way, non-migratory mammals are very important in the aetiology of certain infectious diseases (Woodford, 2009).

5.2.3 Wet markets

Live animal markets are a well-known source of outbreaks. They put different hosts (infected and susceptible amplifying hosts) in contact, facilitating cross-species transmission. This is even further amplified when trade of wildlife occurs in those markets. In China, trade with infected bats and their contact with susceptible amplifying hosts in wet markets may have resulted in the establishment of a market cycle of SARS, which served as the source of infection of people and domestic animals (Fèvre et al., 2006). As with livestock movements, wet markets, where many animals congregate and disperse throughout a region, have a critical role in the dissemination of infectious organisms.

Major gaps and researchable hypotheses

- Food-borne pathogen transmission in developing countries: consumption of bushmeat is probably one of the most important ways of human contact with wildlife. Understanding the risks associated with this type of transmission will improve understanding of food-borne disease transmission and help identify the most important zoonotic diseases transmitted via wildlife handling and consumption.

- Role of livestock markets and the mixing of wildlife/domestic species in amplification of zoonotic transmission from wildlife to humans.
- Wildlife conservation programs, including buffer zones, and their impact on zoonoses transmission.
- Information on zoonoses of wildlife, especially in developing countries, is not only scarce, but likely to be biased due to the nature of surveillance i.e. monitoring that tends to focus on those infections that are associated with more undesired effects in infected humans or those diseases that present with greater mortality in animals. Surveys to identify the most prevalent zoonoses derived from wildlife in various regions will give a better understanding and will also help clarify the hosts involved in the transmission of the most important zoonotic pathogens.

Conclusion

In this review we have highlighted the most important mechanisms for zoonoses transmission derived from wildlife. There is limited original published research looking at transmission mechanisms of zoonoses from wildlife in developing countries. Some lessons can be learned from observations made in industrialized countries, but cultural and geo-ecological factors are likely to have an important role in shaping the exact transmission routes in those countries.

There is even less published information regarding the relative importance of the wildlife-livestock interface in amplification of zoonotic transmission. Certain aspects such as animal movements and wet markets have been suggested to influence zoonoses transmission, but the exact mechanisms are still not well understood.

6. Pathogens of wildlife capable of recombining with analogous organisms in domestic livestock

The review covers those pathogens likely or proven to adapt through genetic recombination or re-assortment to alternative hosts at the wildlife, livestock and human interface and describes the relative risk of such events occurring, suggesting likely drivers of this process. Given the comparatively longer evolutionary times associated with cross-species adaptability in bacteria (apart from the relatively straightforward and unpredictable horizontal transfer of episomal elements) and protozoal pathogens, the review focuses on viruses.

Main messages and strength of evidence

- It is the context in which potential pathogens exist and evolve which matters most to disease emergence and not molecular mechanisms; these have always existed, and are primed to take advantage of opportunities as they are presented. Evidence: strong
- Based on limited evidence, it seems that viruses are more likely to be emerging than other types of pathogen. A wide host range is associated with pathogen emergence. Evidence: medium
- Data on multispecies pathogen transmission and adaptation for viruses is limited to a few families, most of which are RNA viruses, notably; coronaviruses, lentiviruses, flaviviruses, paramyxoviruses and avian influenza viruses. Evidence: strong
- The putative original hosts for these viruses are; bats (3 viruses), primates (2 viruses) and cats, cattle, horses, birds and rabbits (1 virus each); however, there are many other potential candidate pathogens and hosts that have not been properly evaluated. Evidence: medium
- While many organisms have the potential to infect many species, the key to changes in disease transfer is contact rates and host opportunities, often anthropogenically driven. Evidence: medium

Introduction

Jones et al. (2008) concluded that novel diseases are emerging more frequently, with a peak in 1980, and that a high proportion of the emerging zoonotic infections originate in wildlife species (Jones et al., 2008). Woolhouse (2008) commented on both the value and limitations of these frequently cited data (Woolhouse, 2008). The work covers 315 reported emerging infectious disease events through a desk-based review of a single journal's output over 64 years. For 134 of these, wildlife were considered to be the source. This is a relatively crude examination of a complex issue. In truth, available records indicate that quantitative surveillance and reporting of emerging diseases at a global level have been relatively poor. Syndromic (burden of disease) data analysis has been the only practical method for monitoring disease at this scale (Lopez et al., 2006) and even this has considerable constraints (Cooper et al., 1998). Little information is available on the true occurrence of zoonoses, largely because surveillance and reporting systems in veterinary and medical sectors are generally distinct or limited in critical countries. Data on transmission at the human/animal interface generally rely on assumptions (based on molecular epidemiology) and, more often than not, proof of transmission between species is unavailable. In most cases, it is not possible to distinguish between true emergence of diseases and novel detection through improved surveillance and or diagnostic methods.

Based on relatively few data, albeit reported cautiously and with an attempt to correct for reporting bias, this article sparked considerable scientific debate. This highlights the fact that little hard science has been applied to diseases at the animal-human interface. As a result, no conclusive picture is available of the frequency of disease emergence, its geographic patterns, the relative risk of transmission and adaptation (emergence in a host), or the relative importance of different hosts. Nevertheless, available data summarise some of the evidence for pathogen flow between species and emphasise the importance of zoonoses occurring around human concentrations (perhaps not surprisingly) and the increasing susceptibilities of humans as a result of HIV AIDS and other stressors. More importantly, they emphasise the need for greater focus on surveillance and research on diseases at the human-animal interface.

An alternative evidence-based approach to understanding pathogen emergence is to undertake detailed evaluation of published research on selected diseases and, along with expert opinion, extract the key findings. These can then inform extrapolation of likely risks of zoonotic emergence, especially through genetic adaptation at the wildlife-livestock interface, and be used to identify research gaps.

Methodology

As part of a systematic review of zoonoses transmission and livestock-wildlife interactions, available literature was researched and, along with expert opinion, provides the basis for this chapter. A specific methodology for the review of which this chapter is a part, is covered elsewhere in this publication. For this theme 171 papers were selected and relevant abstracts were retrieved, experts agreed on 30 for full paper retrieval from this list and added an additional 36; of these 66, 45 were original research.

Findings

Data on multispecies pathogen transmission and adaptation for viruses are limited to a few families, most of which are RNA viruses. Some of these have received detailed attention in the areas of genomics, mechanisms of transmission and host adaptation, disease ecology and epidemiology, notably: coronaviruses, lentiviruses, flaviviruses, paramyxoviruses and avian influenza viruses. A summary of virus infections for which there is evidence of the pathogen infecting and adapting to alternative hosts is provided in Table 6.1 (Parrish et al., 2008). Cross-species transmission with adaptation to new species is also recognised for a range of other microorganisms, from bacteria to protozoa. However, such evolutionary shifts in host susceptibilities and associated mechanisms are relatively slow when compared to viruses. This is even truer for macroparasites, with frequent host specificity and radiation of ancestral forms occurring over millions of years neatly illustrated with *Digenea* species (Lotfy et al., 2008).

Avian Influenza Viruses (AIV)

There is considerable evidence for recombination and re-assortment in AIV and the associated mechanisms are reasonably well understood (Peiris et al., 2007, Swayne, 2007, Dugan et al., 2008, Hall et al., 2008, Abrahão et al., 2009, Li and Cardona, 2010). Although numerous strains of low pathogenicity circulate in the natural reservoir, wild birds, the key evolutionary step towards virulence was adaptation to domestic ducks, which then through close contact transmit the infection to chickens. Phylogenetic analysis suggests that AIVs circulating in wild birds populations do not

undergo selection to drive emergence of variant strains but exist instead as ephemeral combinations of relatively stable gene segments. Transmission and adaptation to poultry results in emergence of discrete strains, most of which fail to transmit back to wild birds, with H5N1 a notable exception (Dugan et al., 2008). H5N1 diverges from other AIV strains, especially in pathogenesis and its ability to cause disease in a wide host range including epizootic infections in wild birds (Webster et al., 2007, Hu et al., 2011, Li et al., 2011). No reservoir has been found for H5N1 in wild bird populations and it appears that domestic poultry rather than wild birds are the main source of HPAI (and H5N1) for other poultry. The reasons behind this paradoxical behaviour of H5N1 are uncertain but probably relate to selection pressures under particular agro-ecological conditions in China and South East Asia (and, latterly the Nile Valley in Egypt), where the virus evolved and persists.

Chickens are notably susceptible to H5N1 and highly pathogenic strains can devastate poultry flocks. On the other hand, domestic ducks show considerable tolerance and therefore, constitute the main reservoir host (Swayne, 2007, Kim et al., 2009, Li and Cardona, 2010). Other spill-over and dead-end hosts exist for AIV and H5N1 including humans, domestic and wild animals (Hall et al., 2008). Pigs can act as an intermediate or reservoir host of H5N1 and other AIVs and when infected simultaneously with human or swine flu strains can evolve new viruses (Cyranoski, 2005).

The principal contemporary concern regarding AIVs and H5N1 is the potential for evolution of a potential pandemic virus for humans (Peiris et al., 2007). An important focus for research in this regard should be the ecological drivers for emergence of H5N1-like viruses or potential pandemic strains. These are likely to involve particular domestic poultry production systems, around high-density human-poultry landscapes that incorporate domestic ducks. The role of wild birds in this issue remains that of a general reservoir of AIVs that can spill over into more genetically homogeneous poultry populations. Wild birds are therefore an indicator of HPAI H5N1 virus persistence. The role of the wild bird diversity and population dynamics as a buffer or moderator of AIV pathogenicity and the underlying mechanisms of this warrant more study.

Paramyxoviruses

Nipah and Hendra Viruses

Pteropus bats (Fruit) are reservoir hosts for henipaviruses in Australasia and there is evidence that *Eidolon* sp. carry putative henipaviruses in Africa (Lo and Rota, 2008, Drexler et al., 2009). Virus transmission has been confirmed to pigs, horses and humans (directly or indirectly) from these species in Asia. Disease associated with Nipah virus has not been reported in Africa. The amplification of these viruses by pigs, with associated mortality and related human infection led to devastating economic impact and public health concern in Malaysia between September 1998 and April 1999. Outbreaks are generally associated with changing ecology and landscapes, with habitat degradation forcing bats to encroach upon agricultural zones for survival and into contact with humans through contamination of foodstuffs (Breed et al., 2006).

Although Nipah and Hendra disease outbreaks are rare events on a global scale, human Nipah infection is occurring with some regularity in Bangla Desh, where there is advanced ecological change and reliance of fruit bats on mango orchards with high human population densities and poor hygiene practices (Field, 2009).

Table 6.1 Viruses for which there is evidence of pathogen jumping and adaptation to the new host causing disease
Adapted from (Parrish et al., 2008)
* RNA ** DNA viruses

Virus(es)	Original host	New host	Reference	Mechanism and/or time
Measles virus*	Possibly cattle	Humans	(Parrish et al., 2008) Not specified – expert opinion	Host switching and adaptation? Time not known; after the establishment of populations sufficient to allow transmission
Smallpox virus ?Monkey pox virus**	Other primates or camels (?)	Humans	(Parrish et al., 2008) Not specified – expert opinion	Host switching and adaptation? Time 10,000 yr ago?
Influenza A virus*	Water birds	Humans, pigs, horses	(Holmes et al., 2005)	Host switching and adaptation, possible role of intermediate host; many examples. In humans, viruses emerged in the period from 1910–1916 and in 1957 and 1968. Reassortment involved in 1957 and 1968 emergences. Earlier epidemic viruses not characterized. Changes in several genes required for success in new host.
CPV**	Cats or similar carnivores	Dogs	(Hueffer et al., 2003)	Host switching and adaptation; several mutations in the capsid control binding to the canine transferrin receptor. Arose in early 1970s, spread worldwide in 1978.
Lentiviruses: HIV-1&2 STLV foamy viruses*	Old World non-human primates chimpanzees	Humans	(Heeney et al., 2006)	Host switching and adaptation; HIV virus entered human population in approximately 1930s and spread widely in 1970s; multiple introductions likely to give the HIV-1 M, N, and O variants. Broad range of STLV viruses in NHPs with frequent cross-over to human hunters and through handling bushmeat in West Africa. Most lentivirus natural infections apathogenic slow coevolution host specificity rare cross over.

SARS CoV*	Bats Himalayan palm civets or related carnivores – specific source or reservoir species not identified but SARS like bat viruses occur (2011)	Humans	(Zhao, 2007)	Host switching, adaptation; some adaptation for binding to the ACE2 receptor in humans. 2003–2004
Dengue virus*	Old World primates	Humans	(Parrish et al., 2008) Not specified - expert opinion	500 yr before present
Nipah virus*	Fruit bats	Humans (via pigs, or direct bat-to-human contact)	(Wong et al., 2007)	Host switching; adaptation may not be necessary: bat and human isolates identical in some outbreaks
Marburg virus and Ebola viruses*	Reservoir host not proven (bats?)	Chimpanzee, gorilla and humans	(Wolfe et al., 2005)	Host switching; evidence for viral recombination and evolutionary divergence in Africa.
Myxoma virus**	Brush rabbits and Brazilian rabbits	European rabbits	(McFadden, 2005)	spread widely in 1950s by human actions; high virulence, adaptation after host emergence Existing host range, required contact
Hendra virus*	Fruit bats	Horses and humans	(Daszak et al., 2006)	Host switching; adaptation not reported
Canine influenza virus*	Horses	Dogs	(Parrish et al., 2008) Not specified – expert opinion	Host switching; adaptation to dog may be occurring
FMD	Cattle? Buffalo?	Buffalo? Cattle	(Balinda et al., 2010)	Buffalo reservoir of SAT viruses with occasional spillover to cattle but based on evolutionary phylogeny of prevalent virus strains in cattle occurring rarely.
Adenovirus	??	Humans	(Excoffon et al., 2009)	Evidence that adenovirus can be experimentally changed to become more infective through gene manipulation therefore potential for natural selection also to change this attribute

Nipah viruses infect humans readily but the mechanisms whereby the virus adapts and its potential for persistence in human populations is not well understood. Ecological management of the risk is probably the most cost effective option, with a focus on sustaining intact ecosystems and designating agricultural areas well away from bat roosts and their habitat.

Morbilliviruses

There is evidence that molecular adaptations at receptor binding sites are important in determining host cell tropism as a basis for evolution of morbilliviruses. This has been found to be a key mechanism underlying the spread of Canine Distemper Virus (CDV) to other species (McCarthy et al., 2007). CDV has been shown to transmit beyond canidae on a number of occasions, to primates (Yoshikawa et al., 1989), marine mammals (Visser et al., 1993) and felines (Roelke-Parker et al., 1996), causing significant disease and mortality. However, the virus does not appear to have established or persisted in a new form in other species. Changing ecological conditions are likely drivers for these pathogen flows (Munson et al., 2008) and, in the case of felines, the potential for reverse transmission is also possible; there is phylogenetic evidence that CDV originated from this family. The evolution of measles, most probably an adapted strain of rinderpest virus (RPV) of cattle was coincident with the period of domestication of bovidae, when direct contact rates between humans and cattle was increasing. The eradication of rinderpest and coincident rise in the incidence of peste des petits ruminants (PPR) virus across the original range of RPV and its incursion into other species (Khalafalla et al., 2010, Abubakar et al., 2011) is another issue that requires urgent and intensive research. This should focus on the role of molecular adaptation and the ecological niche in evolution of these viruses and their spread to and establishment in new species.

Filoviruses

Ebola viruses

Ebola virus infection of humans and wildlife in Central Africa represents another emerging concern with a bat association, as is the presence of ebolaviruses in other regions of the world. Available evidence is consistent with spill-over of virus from a reservoir forest host into a variety of species including great apes and humans. Consumption of bush meat is considered the most plausible route for transmission of these viruses to human communities. Studies of viruses isolated from gorillas and humans over the last few decades have provided evidence of recombination events that may have facilitated cross-species infection events. More virus lineages are being detected as more samples are examined. The evidence supports a hypothesis of multiple spill-over from an unknown reservoir, although but this is partially confounded by young divergence of lineages (Wittmann et al., 2007). Evidence that the highly pathogenic Zaire strain of Ebola virus (ZEBOV) can infect pigs has raised concerns that this species has the potential to amplify these viruses, as observed with henipaviruses.

Retroviruses

Lentiviruses (HIV, SIV, SFV &, FIV) Deltaretrovirus (STLV)

The adaptation of non-human primate lentiviruses to humans was probably the most significant pathogen species jump in human history. The phylogeny of current circulating Human Immunodeficiency Virus (HIV) strains is consistent with at least two such events (HIV 1 and HIV 2) over

the past century (Gao et al., 1999, Sharp et al., 1999, Korber et al., 2000), from chimpanzee and sooty mangabey. This is believed to have occurred through regular infection of humans with Simian Immunodeficiency Virus (SIV) through consumption of bushmeat and subsequent viral adaptation through mutation or reassortment. SIV transmission between non-human primates (NHP) is also contributing to the evolution of primate lentiviruses. This is also the case for Simian T-lymphotrophic (STLV) and Simian Foamy viruses (SFV) (Liu et al., 2008, Sintasath et al., 2009). The NHP-human jump of SIV and evolution of HIV led to an insidious and pervasive infection dynamic with few signs of host adaptation to the virus but clear evidence for rapid evolution of the virus to changing circumstances. This suggests that evolution in the virus rather than humans will continue to determine progress of the AIDS epidemic in the absence of effective chemotherapy (Levin et al., 2001). Lentivirus infections rarely progress to disease or AIDS-like syndromes in the wild, most probably because incubation periods exceed normal life spans in naturally infected animals. However, recent work amongst Gombe chimpanzee in Tanzania, suggests that SIV may play a more significant role in population health than hitherto believed (Kondgen et al., 2008). Cross-species transmission is a rare event for both primate lentiviruses and Feline Immunodeficiency Virus (FIV), probably as a result of natural barriers - spatial, behavioural and immune-mediated - in free-living populations (Troyer et al., 2008). For example, there is evidence that FIV has jumped species, but co-evolution is largely host specific – recombinations are therefore likely to be ancient events and not common.

It is possible, had humans not chosen to consume primates for food, that HIV would never have evolved from SIV. The serious consequence of a simple life choice of food type highlights the risks inherent in the human-animal interface and the difficulty in predicting such consequences occurring. More research is clearly needed in respect of the drivers for such parameters as pathogen virulence, cross-species transmission and emergence (in humans or livestock) and ecological selection for low pathogenicity viruses in natural populations.

Coronaviruses

Severe Acute Respiratory Syndrome (SARS-CoV)

There is good evidence that interspecies transfer of coronaviruses (CoVs) is facilitated by recombination events. A number of CoVs have been identified in wild birds and bats and most studies in this regard have focussed on the latter. Using genomics and phylogenetic analysis of known strains, virus transmission and adaptation have been demonstrated between bat species and between bats and other mammals e.g. palm civet, domestic animals and humans. In the case of SARS-CoV, this appears to have occurred via an intermediate, perhaps rodent, host. However, the precise evolutionary relationships of these viruses remain largely unknown and cross-taxonomic transfers appear to be relatively rare (Cui et al., 2007, Hon et al., 2008, Ren et al., 2008, Muradrasoli et al., 2010). Although horseshoe bats (*Rhinolophus sp.)* have been shown to harbour SARS-like (SL) CoV, available evidence suggests that they are not the source of the SARS virus. Despite considerable effort, the reservoir host of the SARS CoV therefore remains enigmatic. SL CoVs have also been demonstrated in African bats, although no associated emerging disease event has occurred to date (Quan et al., 2010). This highlights the challenges of predicting and detecting these pathogen jumps in nature. A perhaps surprising implication of the genomic analysis of SARS CoV strains is the apparent rapidity with which these viruses adapted

through other species into humans. This is thought to relate to the opportunities presented by mixing of wild and domestic species in animal markets in China. Like the SIV/HIV jump from chimpanzees to humans, it is likely that humans acquired the virus through consumption of wild species. A considerable amount of work has been carried out on SARS CoV to identify molecular changes that might have underpinned the species jump and these have now been characterised with some precision. However, caution is required in the interpretation of data that are possibly confounded by multiple viruses in individual samples. When subjected to genomic analysis, these can give rise to false impressions of recombination or re-assortment events.

Apthoviruses

Foot and Mouth Disease Virus (FMD)

FMD is a rare zoonosis but has been a disease of major concern globally for decades, largely because of the impacts it has had on regulation of livestock trade. It has also contributed to major landscape changes (with associated ecological consequences) through widespread implementation of fencing to separate wild and domestic species in the belief that cross-species transmission was at the root of frequent epidemics and therefore necessary for control or eradication of the virus (Ferguson and Hanks, 2010). A major constraint to control of FMD is the rapid evolution of new strains of virus through apparent recombination events, making vaccine development and application challenging without extensive biosecurity. Phylogeny of strains circulating in some countries suggests that mixing is local and restricted to a particular host species and region. This suggests that evolution of new strains occurs largely through intra-specific rather than cross-species events. In this regard, two studies in east Africa have provided evidence that cattle and buffalo FMD strains circulate independently (Bronsvoort et al., 2008, Balinda et al., 2010). Transmission and adaptation of the virus between wildlife and livestock species is probably far less frequent than commonly believed (Vosloo and Thomson, 2004).

Orthopoxviruses

Vaccinia Virus

Orthopoxviruses are an important group of which smallpoxvirus is a notorious example. Cessation of the smallpox vaccination campaign gave rise to concerns over the possible transmission of monkeypoxvirus to humans and potential evolution of new smallpox-like strains in the future (Hutin et al., 2001). Ironically, there is good evidence that the vaccine virus, vaccinia, established in wild fauna in Brazil and that cowpoxvirus, which was used early in the vaccination campaign, circulates freely in wild rodents. Studies reporting potential cross-species poxvirus transmission events and therefore the evolutionary potential for adaptation to new hosts through genetic recombination or reassortment are contentious because of the broad host specificity of some poxviruses, notably vaccinia virus. One such transmission link has been demonstrated at an ecological level, using phylogenetic relationships between bovine vaccinia viruses isolated from forest rodents, peri-domestic rodents, cattle and people in one South American study (Abrahão et al., 2009).

Adenoviruses

A variety of adenoviruses circulate in human and animal species but are not known as zoonotic infections. However, a recent cross-over from laboratory monkeys to a human has raised this possibility

(ProMED-mail, 2010). Further evidence of the potential for adaptation of adenoviruses through evolution has emerged from an experimental model of directed evolution. This study demonstrated the feasibility of creating an adenovirus with 100 fold increased infectivity in a human airway model (Excoffon et al., 2009).

Conclusions on general ecology and pathogen evolution

A key message that emerges from this literature study is that co-evolved host-pathogen systems are generally at equilibrium, showing little evidence of disease despite effective pathogen replication. This is exemplified by the endemic stability of influenza A viruses in palearctic wild birds, in which the virus is believed to exist as a constellation of ephemeral variants rather than discrete individual strains (Dugan et al., 2008). This circumstance is made possible by the rich diversity of this wild bird population. Inevitably, some variants within such a virus constellation will be capable of infecting domestic bird populations where appropriate contact events occur. If this model is broadly applicable, the conventional view that emergence of disease results from new pathogen traits acquired through mutation or recombination is over-simplistic. Rather, disease emergence appears to relate to opportunities for contact between domestic animals with relatively low diversity and highly diverse wild animal populations in endemic equilibrium with their pathogens. The population bottle-neck experienced by a virus during such a spill-over results in a discrete strain that, in a suitably permissive new host, can replicate in the absence of resistance mechanisms. Contact opportunity and biodiversity are therefore the key factors that influence emergence of disease. Interestingly, high diversity in the wild host population promotes a broad pool of source pathogens, while low diversity in the domestic animal host promotes expansion of the pathogen after spill-over.

Genomics and molecular adaptation mechanisms, recombination and reassortment are only one aspect of the pathogen transmission story. Novel viruses are tested in nature every day and win or lose. Population heterogeneity is important with respect to mechanisms of virus adaptation and transmission. The levels of population immunity are critical in epidemiology and availability of hosts fundamentally determines transmission potentials. In other words potential pathogens are part of biodiversity but the opportunity for infection and cross-species transmission is dependent on contact rates and immune responses, which might increase or decrease the probabilities for adaptation to a new host. Naturally diverse populations, e.g. avian species, can carry a diverse range of avian influenza viruses with no sign of pathogenicity yet more genetically homogeneous species of domestic poultry determined through artificial breeding are highly susceptible. Disruption of natural ecological processes and homogeneity are therefore key factors in the emergence of new pathogens from wildlife and through domestic animals. This is a complex field of research but it needs to be developed to understand key intervention points for control and prevention of emerging diseases.

Transmission of viral or other genetic material to livestock and people from wildlife sources is often considered to be negative and from this the concept of biosecurity has developed. Although a necessity given the current structure of agricultural systems and breed characteristics this might be too simplistic, short term a view and ultimately detrimental to human health (Dethlefsen et al., 2007). Gene flow from a healthy heterogeneous population to a homogenous one, even in the form of viruses, might transmit

as many positive genetic attributes as negative ones (e.g. in terms of virulence) to the population of viruses circulating.

In this age of so-called disease emergence it must be remembered that increased or decreased intensity of the interface between wildlife, humans and domestic species is not, nor has it ever been static or consistent everywhere. Some countries and even continents have undergone massive landscape and ecological change without total catastrophe, all biological systems are inherently adaptive but it should be understood that considerable resilience has gone from these systems and the emergence of human diseases historically are closely linked to agriculture (Wolfe et al., 2007). To compound this risk, current rates of agricultural encroachment, species movements and biodiversity loss are substantially different due to population growth, anthropogenic impacts, technology, modern travel and transport and it is suggested that increasing rates of novel disease events are likely as a result of this (Keesing et al., 2010).

Major gaps and concrete researchable hypotheses

The most important research gap evident from this review is in qualitative and quantitative epidemiology of a range of pathogens, which have emerged or occur at the interface, to define more specifically the frequency and risks of pathogen flow across species. In the case of many diseases, especially viruses, it is the key ecological changes which need to be more clearly understood which in turn drive pathogen emergence and transmission across species. These changes relate mainly to anthropogenic impacts and in particular agro-ecological change with increasing contact spatially and temporally between a wider range of species and microorganisms with opportunities for amplification and evolution of specific pathogenic strains in increasingly monotypic domestic animal genotypes. The mechanisms of amplification and persistence need to be more specifically researched. On the other side of the coin, research into natural disease and infection processes in bio-diverse animal communities, with respect to microorganisms and their co-evolution, immunity, genetics and population health will provide a guide on key interventions, most probably in domestic animal breeding strategies and husbandry practices that are necessary to encourage more passive co-evolution of microorganisms and reduce pathogen emergence and ensure healthier human and animal populations.

Given that;

- microorganisms have not essentially changed in their character, and,
- that they have the tools for adaptation to new hosts and populations with time and opportunity, most developed and rapidly evolved in viruses,

the key hypothesis to be tested is:

- it is the context in which potential pathogens exist and evolve which matters most to disease emergence and not molecular mechanisms as these have always existed, rather, it is the extraordinary pace of both human and domestic animal population increase and increasing contact rate with biodiversity, which is leading to the emergence of novel diseases across the animal and human domains.

7. Risk factors for disease transmission from wild or domestic animals to people and between wildlife and domestic livestock

Main findings

- There are few studies in the literature on risk factors for transmission from wild or domestic animals to people and between wildlife and domestic livestock. Evidence: strong
- Risk factor studies are rarely used to manage disease. Evidence: strong
- Risk factors are context specific, and the effectiveness of an intervention strategy will vary with context. Interventions based on risk factor assessment are likely to be more effective and efficient than conventional vertical management. Evidence: moderate
- Agro-ecosystem change, especially forest fragmentation, can increase pathogen flows and disease risk. Evidence: moderate
- Agro-ecosystem change can also decrease disease risk, and shift from wildlife to domestic animal hosts can select for decreased pathogenicity. Evidence: moderate
- Socio-economic determinants of health may be more powerful determinants of risk than biological factors. Evidence: moderate.

Introduction

The basis for most epidemiological investigations is the assumption that disease does not occur in a random fashion. Risk factor studies are a central part of analytical epidemiology that attempt to identify the factors associated with increased or decreased likelihood of outcomes such as disease or productivity.

The methodology for risk factor studies is robust and well established. Three main tools are used:

- Cross-sectional studies, the simplest design, are basically surveys. The epidemiologist defines the population to be studied and then collects information on the prevalence of the outcome of interest and potential risk or protective factors. This type of study is very prone to confounding and is the type most abused in the popular press and most misinterpreted by decision makers.
- Cohort studies follow an outcome-free group (often disease) forward in time from the supposed cause (risk factor) to the effect. These longitudinal studies are more expensive and difficult to organize, but make it easier to draw causal inference around potential risk factors.
- Case-control studies are useful for rare outcomes. Subjects with the outcome are identified and their past exposure to suspected aetiological factors is compared with that of controls or referents who do not have the disease. This permits estimation of odds ratios (but not of attributable risks).

Methodology

Literature research resulted in 153 abstracts being sent to the two reviewers. A decision was made that only those which met with the definition of an epidemiological study and that quantified risk would be retrieved (as well as meeting the other criteria of referring to zoonoses, livestock, wildlife and developing countries). On reading the abstracts reviewers agreed on 13 papers to be retrieved. Of these only four referred to quantified risk factors in the abstract; for the others reviewers considered it

possible that the paper might contain risk factor data. Four of the studies were also identified under the theme of risk management. An additional 3 papers were obtained – none of these had quantitative data on risk.

Table 7.1 – Summary of abstracts retrieved by systematic literature search

Bats and emerging zoonoses: henipaviruses and SARS (Field, 2009)	Review
Leptospirosis: risks during recreational activities (Monahan et al., 2009)	Not risk factor. Qualitative discussion of risk
Ecology and epidemiology of tick-borne diseases: which role for the control? (Genchi, 2006)	Not available. Probably not risk factors
Inter- and intra-specific exposure to parasites and pathogens via the faecal-oral route: a consequence of behaviour in a patchy environment (Smith et al., 2009b)	Not a risk factor. Modelling of cattle contact with cattle and wildlife faeces
Ecology and control of ticks as disease vectors in wildlife of the Ngorongoro Crater, Tanzania (Fyumagwa et al., 2007)	No risk factors. Describes how increases ticks associated with increased disease
Forest Fragmentation as Cause of Bacterial Transmission among Nonhuman Primates, Humans, and Livestock, Uganda (Goldberg et al., 2008b)	Risk factors
Factors associated with pastoral community knowledge and occurrence of mycobacterial infections in Human-Animal Interface areas of Nakasongola and Mubende districts, Uganda (Kankya et al., 2010)	Risk factors
Risk factors of bovine tuberculosis in cattle in rural livestock production systems of Ethiopia (Tschopp et al., 2009)	Risk factors
Determining Risk for Severe Leptospirosis by Molecular Analysis of Environmental Surface Waters for Pathogenic Leptospira (Ganoza et al., 2006)	Molecular epidemiology approach to understanding risk
Oral vaccination reduces the incidence of tuberculosis in free-living brushtail possums (Tompkins et al., 2009)	No risk factors given. Also identified under disease control theme
Neglected diseases of neglected populations: Thinking to reshape the determinants of health in Latin America and the Caribbean (Ehrenberg and Ault, 2005)	No risk factors given. Also identified under disease control theme
Canine vaccination - providing broader benefits for disease control (Cleaveland et al., 2006)	No risk factors given. Also identified under disease control theme
Vaccination in conservation medicine. (Plumb et al., 2007)	No risk factors given. Also identified under disease control theme

Results

Only four studies met the criterion that studies should include a quantitative assessment of risk and only three of these were in fact risk factor studies. Of papers that did meet the requirement, three focused on 'charismatic megafauna' that is the larger mammalian wildlife species associated with conservation,

tourism and national parks. The paucity of studies led to our initial conclusion that relatively few risk factor studies are available on zoonoses with a wildlife-livestock interface. An interesting case-study on leishmaniasis from South America suggests that this is a missed opportunity

Risk factors are context specific, and the effectiveness of an intervention strategy will vary with context. Interventions based on risk factor assessment are likely to be more effective and efficient than conventional vertical management. Evidence: moderate

Like many of the zoonoses with a domestic animal-wildlife interface, leishmaniasis has a complex epidemiology and many interventions have been recommended, often as a package (Box 7.1). Delivering these packages is expensive and complicated and has not so far been successful in controlling leishmaniasis in poor communities.

Box 7.1 Recommended interventions for leishmaniasis

Vector control
- ∞ Insecticide spraying
- ∞ Genetic control
- ∞ Biologic control
- ∞ Chemical control

Control of animal reservoirs (domestic and wild)
- ∞ Drugs
- ∞ Vaccine

Personal protection
- ∞ Vaccine
- ∞ Repellents

Early diagnosis and treatment

As for other neglected zoonoses, very little research had been done on risk factors for leishmaniasis and the evidence generated has been little used to plan control. Llanos-Cuentas (2004) argues that the weakness of the strategy is the biomedical mindset (that thinks in terms of cure rather than prevention); the application of interventions through vertical programmes (that follow a formulaic and simplified approach to intervention delivery); and the lack of sustainability in the long term (Llanos-Cuentas, 2004).

He proposes an approach using risk factors as an alternative to this classical approach, reporting a study in West Peru that found a group of risk factors that could be tackled by a single measure (spraying insecticide indoors). The combined population attributable risk for this group was 0.792, which implies that removal of this group of factors with the single measure of spraying would reduce nearly 80% of the human risk. In another area, other risk factors were more important and spraying would reduce only 5.1% of the risk.

For five years, both regions were systematically studied (spraying lambda-cyhalothrin in the home and peri-domestic area every six months for two years, and measuring the incidence rate for an additional three years); reduction in the incidence of leishmaniasis in the first region was 81%, but in the second region was only 4.6%. This is a powerful example of the risk assessment approach: targeting interventions to risk factors in specific contexts can be more successful than conventional recipe-book interventions.

Another example of how epidemiological risk information can inform management is given by Faulde et al. (2008). Leishmaniasis is widespread in Afghanistan but previous reports did not distinguish between anthropotic and zoonotic transmission. Detailed fieldwork revealed sharp differences in epidemiology between anthropotic and zoonotic transmission relevant to the targeting of interventions (bed-nets, spraying and urban rehabilitation for anthroponotic and gerbil control, changed agriculture practice and personal protection for zoonotic leishmaniasis) (Faulde et al., 2008).

While the application of risk-based management to zoonoses at the livestock-wildlife interface appears limited, it has been very successfully applied to food-borne disease and pathogen surveillance, increasing our confidence in recommending it for zoonoses management. Grace et al. summarise how risk assessment can give contra-intuitive findings of great relevance for disease management. For example, personal hygiene was a much less important risk factor than ingredient storage for ensuring the safety of milk sweets in India, and the point of greatest contamination for vended milk was not the farm but the step immediately preceding the consumer (Grace et al., 2010).

Pathogens flow between people, livestock and non-human primates. Evidence: strong

Numerous studies have looked at disease transmission from non-human primates to humans (including the historical emergence of HIV/AIDS and the current alarming increase in monkey pox) and at the transmission of human diseases to non-human primates, including polio, mumps, gastro-intestinal pathogens, human metapneumovirus and human respiratory syncytial virus.

However, much less research has taken place at the interface of livestock with humans and primates, which is the subject of this report. One of several important studies to emerge from a group working in the Bwindi Impenetrable Forest in Uganda establishes clearly the ability for pathogen transmission between humans, non-human primates and livestock. In this study, Goldberg et al. (2008b) report on forest fragmentation as a risk factor for bacterial transmission between primates and humans and their livestock. The especially close genetic relationship between bacteria from humans and bacteria from red-tailed guenons (also paralleled in livestock) probably reflects the propensity of red-tailed guenons to enter human habitats to raid crops (Goldberg et al., 2008b).

Human behaviour could also increase likelihood of transmission: the practice of “maize daubing” has been reported in Kibale (Goldberg et al., 2008a). Farmers mix sand, pepper, and cow dung which they apply on ears of the maize to deter particularly red tailed guenons, a primate species that may be an obligate crop-raider in forest fragments and that has a penchant for maize. This practice will increase contact and transmission opportunities between cattle and guenons.

A study by the same group found humans harboured *Escherichia coli* that were virtually indistinguishable genetically from the *E. coli* of their cattle and goats indicating that the livestock might act as a connection between humans and non-human primates. In another study from the same group, antibiotic resistance was found in the faeces of non-human primates. Although antibiotic resistance does occur in nature this was suggestive of a flow of pathogens from people to non-human primates (Rwego et al., 2008).

Agro-ecosystem change especially forest fragmentation can increase pathogen flows and disease risk. Evidence: moderate

In the study mentioned (Rwego et al., 2008) tending livestock, experiencing gastrointestinal symptoms, and residing near a disturbed forest fragment increased genetic similarity between a participant's bacteria and those of nearby primates. The incursion of farming into natural ecosystems had long been considered a potential risk factor for disease transmission and this paper provides credible evidence that this may indeed be the case. Conceptually, increased "edge effects" would be expected to promote interaction among pathogens, vectors and hosts. This edge effect has been documented for Lyme disease (Glass et al., 1995). Similarly, increased activity in forest habitats (through behaviour or occupation) appears to be a major factor for Leishmaniasis (Weigle et al., 1993).

Agro-ecosystem change can also decrease disease risk and shift from wildlife to domestic animal hosts can select for decreased pathogenicity. Evidence: medium

However, land use changes can also decrease risk disease. It has long been known that agricultural intensification can reduce some diseases. A recent publication summarise studies on the impacts of ecosystem change on tsetse flies, the vectors for human and animal trypanosomosis (no quantitative risk factor data presented) (Bossche et al., 2010). In large parts of tsetse-infested sub-Saharan Africa, the progressive clearing of the natural vegetation for cultivation, the introduction of domestic animals and the almost complete disappearance of large wildlife species have led to near-disappearance of tsetse and the parasites they transmit. It is self-evident that changes resulting in elimination and reduction of wildlife hosts will result in reduced disease risk, providing other hosts are not found.

Interestingly, the same study by Bossche et al. suggests that before tsetse flies have been cleared completely, an intermediate epidemiological process develops in which tsetse flies become highly dependent on livestock for their survival, and the disease reaches a level of endemicity with high morbidity but low mortality. The virulence of a parasite would be expected to decrease when its reservoir changes from a multispecies-tolerant wildlife population to a single-species (or restricted number of species)-susceptible livestock population. This finding was confirmed when the pathogenicity of the trypanosome strains circulating in the cattle population in the endemic area of eastern Zambia was assessed. Almost 80% of the circulating *T. congolense* strains were shown to be of moderate or low virulence, whereas the remaining trypanosome strains (20%) were highly pathogenic.

A molecular epidemiology study by Ganoza et al. (2006) of leptospirosis in Latin America, found that urban leptospirosis was more pathogenic and associated with rodents while rural leptospirosis was less

pathogenic, and associated with livestock and wildlife. This supports other papers in underlining that zoonoses epidemiology and virulence is context specific and dynamic and changes in land use may affect pathogenicity (Ganoza et al., 2006).

The next two risk factor studies focused on pastoralist communities and mycobacterium. Contact with wildlife was only one of several risk factors studies considered.

In pastoralist communities, contact with wildlife is a risk factor for mycobacterial infection; however, socio-economic determinants were more important. Evidence moderate

A study in Uganda investigated factors associated with pastoral community knowledge and occurrence of mycobacterial infections at the human-animal interface in Uganda (Kankya et al., 2010). While contact with wild animals and involvement of cattle-keeping were both risk factors for the occurrence of mycobacteriosis, they accounted for less risk and were less significant than socio-economic factors.

- tribe (pastoralist versus less history of keeping livestock)(OR = 6.4) p=.01
- use of spring vs. stream water for domestic use (OR =4.5) p=.002
- presence of sediments in household water receptacle (OR = 2.32) p=.006
- non separation of water containers for drinking and domestic use (OR = 2.46) p=.004
- sharing of drinking water sources with wild animals (OR = 2.1) p=.024
- duration of involvement of >5 yrs in cattle keeping (OR = 3.7) p=.021
- and distance of household to animal night shelters (>20 meters) (OR = 3.8) p=.029

However, there are some concerns about the methodlogy of this study. These are univariate relations, and it is not clear how many factors were examined raising the possibility that some of these associations are spurious: if you examine 100 risk factors then 20 will be 'significant' at $p<0.05$ by chance alone. Confounding was not sufficiently investigated and some of these factors may be proxies for causal factors not measured.

In a similar study in Ethiopia, risk factors of bovine tuberculosis in cattle in rural livestock production systems were investigated (Tschopp et al., 2009). Encounters between wildlife and cattle were overall rare (observed and reported by 19% of interviewees with the exception of the Bale mountains national park, where 59% of farmers stated that wildlife share common habitat with cattle). Only a few animals per herd were found to have a positive tuberculin reaction, with an overall individual prevalence of 3%. Reported contact between cattle and wildlife was not a significant risk factor for a positive tuberculin reaction in cattle.

Human tuberculosis (confirmed by clinical diagnosis and/or clinical signs of cervical lymphadenitis) was reported in 86 households (19%). At least 20% of the reported cases were extra-pulmonary tuberculosis (cervical lymphadenitis), which is most common in *M. bovis* infection. However, none of the assessed eight variables were statistically significant in the univariable model for having a tuberculosis case in a household (livestock keeping, husbandry practices, livestock product consumption, having a bovine

reactor to tuberculin testing, and altitude). Recorded contact between people and wildlife was not a significant risk factor for a confirmed clinical diagnosis of TB or clinical signs of cervical lymphadenitis.

Conclusion

A thorough investigation of the risk factors, both in terms of practices and actors, is important for risk assessment, management and communication. Context-based risk factor assessment is more complex than standardised approaches to service delivery, and requires capacity-building. There has been little work on risk factors for zoonosis transmission between wildlife and livestock, and the few studies there are give insightful results, which warrant further research

8. Drivers influencing the interaction between wildlife and livestock and the implications for zoonoses transmission

Main messages and strength of evidence

- Growth in human population and consumption is driving widespread environmental change including urbanisation, agricultural spatial expansion and intensification, and wildlife habitat change, which is affecting ecological systems including wildlife-livestock interactions and in some cases has led to zoonotic disease emergence and re-emergence. However, there have been few studies, especially in developing countries, providing evidence for this probable association. Evidence: moderate
- Agricultural spatial expansion disrupts wildlife habitats and brings humans and their livestock into closer proximity to wildlife resulting in changes in host-pathogen dynamics and increased risk of spill-over. Evidence: strong
- Livestock intensification increases the population size and density of livestock and increases the likelihood of livestock becoming an amplifying host, or a source of environmental contamination. Evidence: moderate
- Livestock and wildlife marketing and trade increase the risk of local and international movement of pathogens and spill-over to humans. Evidence: strong
- Wildlife management for conservation or recreational hunting can increase the population size and density of wildlife species resulting in higher disease prevalence in wildlife and increased risk of spill-over to livestock. Evidence: moderate
- Wildlife habitat fragmentation or loss leads to lower biodiversity, which in some ecosystems may result in increased density of particular wildlife species that are reservoir hosts for a particular pathogen or vector and consequentially higher disease prevalence. Evidence: moderate
- Climate change is predicted to affect the geographical distribution and population densities of wildlife species, which will interact with many other factors to have variable effects on disease dynamics. Evidence: weak

Introduction

As much as 73% of emerging human diseases are zoonotic (Woolhouse and Gowtage-Sequeria, 2005) and 26% of human pathogens also infect both domestic animal and wildlife species (Cleaveland et al., 2001). Drivers that influence the interaction between wildlife and livestock will affect host-pathogen dynamics and may influence the emergence of new human diseases or the re-emergence of existing diseases. Increasing human populations and spatial expansion and intensification of agriculture in developing countries is bringing humans and livestock into closer contact with wildlife habitats and, together with urbanisation, have been implicated as the drivers behind some recent emerging disease events. This systematic review aimed to find recent evidence of drivers of livestock-wildlife interactions that have had an effect on the dynamics of zoonotic diseases. Bovine tuberculosis, Nipah virus and Influenza A are discussed as examples of re-emerging and emerging diseases that have been affected by wildlife-livestock interactions.

Methodology

The full methodology is described in Chapter 2. For this subject 124 relevant abstracts were retrieved of which experts agreed on 30 for full paper retrieval and added an additional 13. Out of these, 28 papers were found to be relevant for the subject but only 5 were original studies. An additional 14 papers of original studies were retrieved from the reference lists of the 18 papers.

Findings

Human population growth and consequential increased consumption of food and other commodities are drivers of environmental change such as urbanisation, agricultural spatial expansion and intensification, and habitat alteration. These play an important role in the emergence and re-emergence of infectious diseases by affecting ecological systems at landscape and community levels and host and pathogen population dynamics (Wilcox and Colwell, 2005) (see Figure 9.1). Climate variability interacts with these environmental changes to contribute to disease emergence (Wilcox and Colwell, 2005). Interactions between wildlife and livestock are influenced by several of these environmental changes.

An increasing human population requires increased food production. **Expansion of geographical areas utilised for agriculture, including livestock production**, can bring livestock into closer and more frequent contact with wildlife. The expanded range of Japanese encephalitis virus (JEV) in South East Asia in the last few decades is associated with increasing irrigated rice production and pig farming due to increasing human population (Pfeffer and Dobler, 2010). The primary mosquito vector of JEV, *Culex tritaeniorhynchus,* is associated with irrigated areas and feeds on water birds, especially herons and egrets, and domestic and wild mammals, including pigs, horses and humans. Humans and horses are dead-end hosts but pigs develop a high level viraemia and are amplifying hosts for human infection (Pfeffer and Dobler, 2010). The combination of irrigated fields, which increases the population density of mosquito vectors and water birds, and pig farming, which provides an amplifier host, increases the risk of spill-over into the human population.

Encroachment of livestock production into wildlife habitats increases the risk of spill-over of micro-organisms from wildlife into livestock populations e.g. the emergence of Nipah virus infection of pigs and humans in Malaysia due to the encroachment of large commercial pig farms into forested areas containing fruit bats infected with Nipah virus (Field, 2009) (see below).

Graham et al. (2008) give examples of how **intensive livestock farming** can increase disease transmission from livestock to wild and domestic animals and humans by environmental pathways. Ventilation systems expel material including pathogens such as *Campylobacter* and avian influenza virus into the surrounding environment. Large quantities of animal waste are produced containing a variety of pathogens that can survive for several months if left untreated. Much of the waste is spread on open land where it can come into contact with wild animals and may contaminate surface and ground water, whilst use of animal waste in aquaculture leads to potential contact with wild birds (Graham et al., 2008).

Increased livestock production is associated with **increased marketing of live animals and products** both locally and internationally. In a review of international movement of livestock and wild animals, Fèvre et al. (2006) gave some examples of disease emergence associated with trade. The spread of highly pathogenic avian influenza (HPAI) H5N1 has been associated with live bird markets that provide opportunities for inter-species transmission, whilst legal and illegal international trade in wild birds, some of which have been found to be infected with H5N1, increases the risk of HPAI introduction to disease-free countries. Uncontrolled movement of cattle for trade and grazing or of animal products can spread diseases such as foot-and-mouth disease and Rift Valley fever in Africa and to the Middle East. In Uganda, an outbreak of human trypanosomiasis in an area that had been free of the disease was caused by movement of infected cattle into the area (Fèvre et al., 2006). In some countries there is increasing demand for wild animals and their products for food and medicine: in China an increasing trade in bats through live animal markets may have brought bats infected with precursors of the SARS corona virus into contact with other wild animals, some of which were susceptible to infection and served as amplifying hosts for human infection, such as the masked palm civet (*Pargum larvata*) (Fèvre et al., 2006).

Certain types of **wildlife management** may increase wildlife-livestock interactions and increase the risk of zoonotic disease transmission. Management of wildlife species for recreational hunting or conservation through measures such as fencing, introduction of new animals, supplementary feeding or water provision can increase population density resulting in increased disease transmission and prevalence and increased risk of transmission to livestock and humans e.g. wild boar in southern Spain and white-tailed deer in the United States of America (USA) as sources of bovine tuberculosis for livestock (Mathews, 2009, Meng et al., 2009, Rhyan and Spraker, 2010) (see below), and elk in the greater Yellowstone area, USA, as a source of brucellosis for bison and cattle (Rhyan and Spraker, 2010).

Wildlife habitat change can lead to changes in population structure, migratory patterns, population density, disease susceptibility and contact with livestock and humans, resulting in an increased risk of zoonotic disease transmission (Mathews, 2009). In Brazil, the re-emergence of Chagas disease in humans caused by *Trypanosoma cruzi* has been associated with anthropogenic environmental change leading to low mammal diversity and abundance of the common opossum (*Didelphis aurita*) (Vaz et al., 2007). Comparing continuous forest habitat to fragmented habitat, Vaz et al. (2007) found that *T. cruzi* sero-prevalence in small wild mammals was higher in fragmented habitat due to lower small mammal diversity and increased marsupial abundance. In North America fragmentation of forest habitat has decreased species bio-diversity and increased the population density of white-footed mice (*Peromyscus leucopus*), an efficient host for the causative agent of Lyme disease, *Borrelia burgdorferi*, and its *Ixodes sp.* tick vector, leading to an increased risk of Lyme disease in humans (Mathews, 2009, Pongsiri et al., 2009). The increasing badger population in southwest England may be due to increased availability of improved pasture for cattle grazing which is also good badger habitat (Mathews, 2009). However one study has found that habitat management that is favourable to wildlife is associated with reduced risk of bovine tuberculosis incidence on dairy farms in England (Mathews et al., 2006) (see below).

The recent emergence of several bat-associated viruses in Australia – Hendra virus, Australian bat lyssavirus and Menangle virus – is associated with loss of bat habitat due to deforestation and agricultural expansion leading to changes in the location, size and structure of bat colonies, changes in migration patterns and foraging in suburban and urban fruit trees. This has led to increased contact with livestock and humans with an increased probability of spill-over of pathogens (Daszak et al., 2006, Field, 2009). The establishment of large intensive pig farms together with fruit trees within forest areas populated by fruit bats brought pigs into close contact with Nipah virus infected bats resulting in spill-over of infection (Field, 2009) (see below).

Based on a literature review and extrapolation from observations of short-term climate variation, Mills et al. (2010) identified the potential impact of **climate change** on vector-borne and zoonotic diseases. In relation to wildlife-livestock interactions, climate change may affect the geographic distribution of wildlife species or their population density, both of which could affect contact with other wildlife, livestock, vectors and humans. The interaction of climate change with other factors such as habitat change will have varying effects on pathogen transmission within host and vector populations and to humans so the overall effect is difficult to predict (Mills et al., 2010).

Changes in the geographic distribution of wildlife due to climate change are most likely to be towards higher latitudes and altitudes and there may be either an expansion or contraction of range or no overall change in area occupied. In North America the hispid cotton rat (*Sigmodon hispidus*), a reservoir of hantavirus, has undergone a northward and altitudinal expansion, and the white-footed deer mouse, a reservoir of Lyme disease, human granulocytic anaplasmosis, babesiosis and hantavirus, has extended its range northwards (Mills et al., 2010). It is likely that climate change will change the distribution, composition and migration patterns of wild bird populations that are reservoirs for avian influenza viruses which may affect transmission between wild bird species and between wild birds and domestic poultry (Gilbert et al., 2008).

In the tropics, climate change is likely to cause host and pathogen systems to shift their ranges towards currently sub-tropical and temperate areas, whilst species diversity in lowland tropical areas is likely to decrease with increasing temperatures. Changes in range are likely to occur at different rates for different species leading to changes in species assemblages and new interactions (Mills et al., 2010).

Extreme weather events are expected to increase with climate change and their likely effects can be inferred from phenomena such as the El Nino Southern Oscillation (ENSO). A study in Guadeloupe, French West Indies, compared a series of human patients hospitalised with leptospirosis during a period of high leptospirosis incidence from 2002-2004 and an earlier period 1994-2001 (Storck et al., 2008). Increased rainfall due to two El Nino phenomena during 2002-2004 was associated with increased leptospirosis incidence, and contact with rodents was a risk factor for infection in 2002-2004 but not in the earlier period. The authors concluded that increased rainfall had increased rodent populations and increased the risk of leptospirosis. In south-western USA, the 1997 ENSO event caused higher rainfall and improved vegetation that increased the North American deer mouse (*Peromyscus maniculatus)* population leading to an increase in hantavirus pulmonary syndrome in humans (Mills et al., 2010).

Recent epidemics of Rift Valley fever in east Africa have occurred after heavy rainfall due to ENSO events in 1997 and 2006 (Mills et al., 2010).

Bovine tuberculosis – *Mycobacterium bovis*

Corner (2006) uses the example of bovine tuberculosis to discuss the risk of disease transmission from wild animals to livestock. Transmission depends on the nature of the infection in the wild animal species, the dynamics of the disease in wild animals, their geographic distribution and the type of interaction between the wild animal species and livestock. A wild animal species may be infected with *M. bovis* and excrete the pathogen, and its range may geographically overlap with livestock but if there is no interaction with livestock then transmission is unlikely to occur. Wild animals may be a maintenance host, able to maintain *M. bovis* within the population without the involvement of other species, or a spill-over host i.e. *M. bovis* is introduced to the population from other species but is not maintained (Corner, 2006).

In southern Spain there is an increasing density of wild ungulates, especially wild boar (*Sus scrofa*) and red deer (*Cervus elaphus*), due to intensive management for recreational hunting such as supplementary feeding and watering, fencing and translocation of animals (Naranjo et al., 2008). Most are kept on private estates and share resources with livestock (Parra et al., 2006). Tuberculosis control programmes have reduced the prevalence in cattle but the disease is not yet eradicated. There are areas of higher prevalence in cattle where wild boar and red deer also show high prevalence (Naranjo et al., 2008).

Naranjo et al. (2008) summarize the evidence that European wild boar are a maintenance host for bovine tuberculosis in the Spanish Mediterranean ecosystem; wild boar, domestic and wild animals and humans are infected with the same genotypes of *Mycobacterium tuberculosis* complex (MTBC), there is a high prevalence of tuberculosis in wild boar populations without contact with domestic livestock or other wild ungulates, tuberculosis lesions are commonly found in the thoracic lymph nodes and lungs of infected wild boars leading to respiratory excretion, and extensive tuberculosis lesions are found in more than one part of the body of juvenile wild boar, which is the age group that disperses, leading to geographical spread. The high tuberculosis prevalence is likely to be due to management practices and increasing density of wild boar (Parra et al., 2006, Naranjo et al., 2008).

White-tailed deer in the state of Michigan, USA, were historically considered to be a spill-over host of tuberculosis but changes in their management for recreational hunting during the last century led to the population doubling so they were able to maintain tuberculosis infection. Provision of winter supplementary feeding, hunting restrictions and fencing caused increased population density and a higher prevalence of *M. bovis.* Bovine tuberculosis was eliminated from cattle in Michigan but later re-emerged due to suspected spill-back from white-tailed deer (Corner, 2006, Rhyan and Spraker, 2010).

Importation of European cattle is thought to have introduced bovine tuberculosis to South African wildlife (Michel et al., 2006). Genetic studies in Kruger National Park indicate that there was a point source introduction of *M. bovis* from cattle to African buffalo in 1950-60 with gradual geographic spread and increase in prevalence. African buffalo are now a maintenance host with spill-over to other wild

animal species in the park, and potential for spillback to extensively managed cattle populations neighbouring the park (Michel et al., 2006).

Ward et al. (2006) suggest that the increase in cattle farming and improved grassland in southwest England in the last few decades has contributed to an increase in the European badger (*Meles meles*) population because this is a good foraging habitat for them. Certain farm management practices can decrease the risk of direct or indirect contact between badgers and cattle; strip-grazing rather than set-stocking, lower stocking density, regular removal of badger carcasses, fencing off badger latrines and setts, not providing feed at pasture and only using mains water. Infected badgers forage further away from their setts than healthy badgers and are more likely to enter farm buildings especially during dry spells when earthworms are less available, so badger-proofing feed stores and cattle housing is important (Ward et al., 2006).

Mathews et al. (2006) carried out an unmatched case-control study to identify risk factors for tuberculosis breakdown on dairy farms in England. After controlling for herd size and distance to the nearest infected farm, hedgerow abundance was negatively associated with tuberculosis breakdown: a hedge-poor farm had a 1.6 times greater risk of TB breakdown than a hedge-rich farm (95% confidence interval 1.0-2.4). This effect was thought to be because increased quality and availability of hedgerow habitat provided routes for badger movement and latrines away from cattle pasture thereby reducing direct and indirect cattle-badger contact (Mathews et al., 2006).

Nipah virus

The first known outbreak of Nipah virus infection was in Malaysia during 1998-99. Investigation showed that pig and human cases had occurred in January 1997 on a large intensive pig farm in northern Malaysia (Epstein et al., 2006) where Nipah virus infected fruit bats were attracted to fruit trees planted around the pig farms providing the opportunity for virus spill-over to pigs, which were highly susceptible. At the index farm fruit trees had been planted near to pig sties and these attracted fruit bats. Some branches overhung the pig pens so pigs could eat fruit that was contaminated with bat saliva or urine. The infection spread in pigs by the respiratory route facilitated by high pig and farm density and movement of pigs between farms to the main outbreak area around Nipah (Daszak et al., 2006, Field, 2009). Pigs became an amplifier host for human infection (Field, 2009). Almost all human cases had contact with pigs and there was no evidence of spill-over directly to humans from bats or of human-to-human transmission (Epstein et al., 2006). Live pig exports to Singapore for slaughter resulted in human cases in abattoir workers (Epstein et al., 2006, Field, 2009). The outbreak was controlled through mass culling of pigs and there have been no further outbreaks of Nipah in Malaysia (Epstein et al., 2006).

The causative agent, Nipah virus, was found to be closely related to Hendra virus, for which the reservoir hosts are *Pteropus sp* fruit bats, so Malaysian bats were investigated and high seroprevalence was found in *Pteropus hypomelanus* and *P. vampyrus* throughout Malaysia, and Nipah virus was isolated from a *P. hypomelanus* colony suggesting that these species are reservoirs of Nipah virus and that the virus is endemic (Mohd Yob et al., 2001, Chua et al., 2002, Epstein et al., 2006).

Several possible drivers of Nipah virus emergence in Malaysia have been proposed (Breed et al., 2006, Field, 2009):

- infected flying foxes had migrated from Indonesia to Malaysia due to unfavourable conditions caused by an ENSO-related drought and forest fires in the mid-1990s;
- at the same time legal and illegal hunting of bats had caused abandonment of roosting and feeding sites, created niche vacuums and an influx of neighbouring bat populations to fill those niches;
- deforestation had removed natural bat habitat leading to an increased reliance on crops, bringing bats nearer to humans and livestock;
- an increase in the number, density and distribution of the pig population,
- fruit tree planting near to pig farms that attracted bats.

Daszak et al. (2006) discuss the possibility that Nipah virus was introduced from Indonesia with migrating bats in the mid-1990s and conclude it to be unlikely because the index human and pig cases occurred before the ENSO event, bat migration between Indonesia and Malaysia commonly occurs even in non-ENSO years, and the serological evidence that Nipah virus is endemic in fruit bats throughout Malaysia.

Daszak et al. (2006) examined evidence for deforestation and changes in pig production in Malaysia using Food and Agriculture Organization (FAO) data covering the preceding four decades. They found that there had been a slight increase in pig production, an exponential increase in oil palm production mainly to replace rubber plantations, a decrease in forest cover from 49% in 1979 to 45.3% in 1992, and an increase in agricultural land use from 4.2 hectares in 1961 to 7.9 million hectares in 2001.

Epstein et al. (2006) and Daszak et al. (2006) propose that Malaysian bats have been historically infected with Nipah virus and that there has probably been sporadic undiagnosed bat-to-pig transmission and pig-to-human transmission of Nipah virus. They hypothesise that the initial 1997 outbreak on the index farm caused an epidemic in pigs that burnt out quickly and caused only a few human cases but reintroduction of virus in the following year into a partially immune population resulted in prolonged endemic circulation on the farm that increased the risk of spread to other farms and to humans. When infected pigs were sold from the affected farm to the south, where there was a high density of smaller intensive pig farms and a high human population density, a large outbreak occurred in humans stimulating an investigation and the discovery of Nipah virus as the causative agent (Epstein et al., 2006, Daszak et al., 2006). They conclude that the emergence of Nipah virus was primarily driven by the intensification of the pig industry combined with fruit production in an area populated by Nipah virus infected fruit bats.

Since 2001 Bangladesh and India have experienced seasonal clusters of human Nipah cases with no apparent intermediate host but limited human-to-human transmission (Field, 2009). Serological surveys have found Nipah antibodies in *P. giganteus* fruit bats but no evidence of infection in pigs or other animals (Hsu et al., 2004, Daszak et al., 2006). It appears that in Bangladesh there is transmission from

bats to humans via contaminated date palm sap followed by limited human-to-human transmission, and livestock do not play an important role (Epstein et al., 2006, Daszak et al., 2006).

There is serological evidence that henipaviruses are likely to occur throughout the range of pteropid bats, which stretches from Madagascar to South and South East Asia, Australasia and Pacific Islands (Epstein et al., 2006). Surveys in India, Indonesia, Cambodia, Thailand and Madagascar have found neutralizing antibodies to Nipah virus or Nipah RNA (Epstein et al., 2008, Sendow et al., 2006, Reynes et al., 2005, Wacharapluesadee et al., 2010, Iehlé et al., 2007). Surveys in West Africa have demonstrated that henipaviruses are not restricted to the range of pteropid bats: Nipah and Hendra virus neutralizing antibodies and henipavirus RNA were found in *Eidolon helvum* fruit bats sampled in Ghana (Hayman et al., 2008, Drexler et al., 2009).

Influenza A

Aquatic birds are considered to be the main reservoir hosts of Influenza A viruses (Landolt and Olsen, 2007, Irvine and Brown, 2009). They are segmented RNA viruses that are constantly evolving by re-assortment (antigenic shift) or mutation (antigenic drift) to create new strains of different pathogenicity and host range that may spill over into new host species that have no immunity to the new strain (Landolt and Olsen, 2007, Pekosz and Glass, 2008).

Influenza A viruses have been found in birds, humans, pigs, horses, cats, dogs, seals, whales and other animals (Riedel, 2006, Landolt and Olsen, 2007). Swine influenza caused by several sub-types occurs in pig populations worldwide and infection may be transmitted between pigs, between pigs and birds and between pigs and humans (Landolt and Olsen, 2007, Irvine and Brown, 2009). In wild birds, avian influenza is usually sub-clinical or of low pathogenicity (Artois et al., 2009). Low pathogenic viruses introduced to domestic poultry may mutate to become highly pathogenic avian influenza (HPAI) (Landolt and Olsen, 2007). H5N1 HPAI was probably first introduced to domestic geese in China as a low pathogenic avian influenza (LPAI) virus from wild birds and has since undergone mutation and re-assortment to create multiple HPAI strains that have spread across Asia to the Middle East, Europe and Africa (Sims et al., 2005, Vijaykrishna et al., 2008) by movement of domestic poultry and wild birds, causing localised outbreaks and major epidemics in domestic poultry and sporadic human cases with high case fatality. H5N1 HPAI is now endemic in certain Asian countries and Egypt, where the virus continues to evolve.

In the last century there were three human influenza pandemics; the 1918-1919 Spanish flu H1N1 outbreak, 1957-58 Asian flu H2N2 and 1968-69 Hong Kong flu H3N2 outbreaks (Riedel, 2006). The Spanish flu virus was made up of genes of avian origin, whilst the Asian and Hong Kong flu viruses were a re-assortment of human and avian viruses (Landolt and Olsen, 2007). The 2009 H1N1 human pandemic was caused by a re-assortment of human, avian and swine viruses (Smith et al., 2009a). There have also been sporadic human cases associated with domestic poultry or pig infections (Riedel, 2006, Myers et al., 2007, Smith et al., 2009a).

Certain farming practices increase the risk of spill-over of influenza from wild birds to domestic birds and pigs, followed by amplification in the domestic animals and transmission to humans. Rice farming combined with free grazing duck farming in wetland areas brings wild water birds into close proximity with domestic water birds (Gilbert et al., 2007, Artois et al., 2009), who are not very susceptible to clinical disease but are infectious to other domestic poultry by direct contact or environmental contamination (Sims et al., 2005). Other low bio-security rearing systems such as scavenging poultry, household poultry and small scale commercial poultry allow direct or indirect contact between wild and domestic birds, which may introduce infection, transmit infection between farms, or lead to spill-back into wild birds (Sims et al., 2005, Artois et al., 2009).

The increase in intensive livestock production in the last few decades, particularly for poultry and pigs, creates large high density populations in which there is an increased probability for adaptation of an introduced virus and amplification for transmission between farms, to humans and to wild animals (Kapan et al., 2006, Gilbert et al., 2007, Graham et al., 2008). Increasing poultry production has increased trade in poultry and poultry products, which can rapidly spread infection to new farms, areas or countries whether by small-scale informal trade or large scale commercial trade (Sims et al., 2005, Fèvre et al., 2006). Live bird markets in particular play an important role in disseminating infection and providing opportunities for cross-species transmission between domestic and wild bird species in the market (Sims et al., 2005, Fèvre et al., 2006).

The recent influenza pandemics have not been as serious for human disease as earlier ones because although H5N1 is highly pathogenic for humans so far it has low transmissibility from birds to humans and very limited human-to-human transmission whilst pandemic H1N1 was highly transmissible between humans but of low pathogenicity. The potential continues for the evolution of a variant which is both highly transmissible to humans and of high pathogenicity. This could either be a variant of pandemic H1N1 or H5N1 or a completely new strain (Landolt and Olsen, 2007). Farming systems that allow contact between wild and domestic birds and pigs and have large high density populations that facilitate transmission, adaption and amplification, are increasing the risk that such a pandemic variant will emerge.

Major gaps and concrete researchable hypotheses

There have been few studies of the interactions between livestock and wildlife and its impact on zoonotic disease transmission, especially in developing countries. The few studies that have been carried out are mainly reactive investigations of an emerging disease outbreak and are usually retrospective making causality difficult to establish. Zoonotic diseases involving both wildlife and livestock are complex systems, which are difficult to study and in which changes have unpredictable effects.

It is likely that, for a number of emerging diseases such as Nipah virus, the disease has previously occurred in livestock or humans but the cause was not diagnosed. Only when a larger outbreak occurred with high morbidity or mortality was it recognised as a new disease and fully investigated. Such an outbreak is more likely to happen in higher density livestock or human populations. Trade networks and

live animal markets are very important for pathogen spread. Where wild animals are traded alongside livestock there is the potential for wildlife pathogens to spill over into livestock and be amplified in livestock and human populations.

Some species appear more likely to be reservoirs or vectors of disease pathogens of humans and domestic animals and these should be a focus of research. This should include examination of the factors, genetic or otherwise, that have led to the species acting as a reservoir e.g. buffalo and TB.

Research needs:

- Improve understanding of direct and indirect interaction between relevant wild animal species and domestic animals under differing livestock management conditions.
- Conduct long-term studies of the epidemiology of multi-species infectious diseases to understand incidence, transmission and reservoir species.
- Develop and test risk-based surveillance strategies appropriate to different ecosystems that increase the chances of identifying pathogen amplification scenarios e.g. surveillance of sentinel species.
- Identify sustainable risk management strategies for the wildlife-livestock interface.
- Understand the relationship between wild and domestic animal within-species diversity and pathogen species diversity and pathogen emergence or re-emergence.
- Understand better the association between spatial distribution of disease and demographic, environmental, socio-economic, behavioural and climatic factors.

Conclusion

Certain wildlife species have adapted to and thrived in the ecological landscape created by human settlement and agriculture and become reservoirs for disease in livestock and humans. Anthropogenic changes driven by increasing human population have led to the emergence or re-emergence of some zoonotic diseases involving wildlife and livestock, in particular where intensive livestock production is introduced to wildlife habitats creating the opportunity for pathogen spill-over and amplification. The individual events leading to disease emergence are chance occurrences but a changing ecological situation increases the probability that all the necessary steps occur for pathogen spill-over from wildlife to livestock, amplification in livestock, transmission to humans, and finally human-to-human transmission. In developing countries, increasing human population and agricultural expansion and intensification into high biodiversity wildlife habitats to meet the increased demand for food and animal protein may mean those countries are increasingly likely to experience emerging infectious disease events in the next few decades.

9. Historical changes in transmission, factors which foster novel transmission routes and hosts, and wild animal candidates for future disease transmission

Main messages and strength of evidence

- Historically, changes in prevalent human diseases have been associated with increases in human population, human migration and changing interactions with ecosystems that have led to animal pathogen spill-over and host-switching. Evidence: medium
- Disease emergence is a complex process involving changes in host-pathogen dynamics, ecological dynamics and environmental change. Demographic and social factors are driving regional environmental changes such as urbanisation, agricultural expansion and intensification, and habitat change, which are exacerbated by climate change and deterioration in public health services in lower income countries. Evidence: medium
- Viruses are more likely to be emerging than other types of pathogen. Emergence may occur due to genetic changes that allow the pathogen to adapt to new host species or a new ecological environment. A wide host range is associated with pathogen emergence. Evidence: medium
- Commonly cited factors that influence the emergence or re-emergence of zoonotic diseases:
    - Human demographic and social changes, socio-economic development, deterioration of public health services. Evidence: medium
    - Urbanization associated with biodiversity loss and increase in vector-borne disease. Evidence: strong
    - Urbanization associated with migration of susceptible people or introduction of new pathogens by migrants. Evidence: strong
    - Globalisation of human travel, commercial trade and agriculture, including international trade in livestock, wild animals and their products, can lead to translocation of pathogens, vectors and hosts. Live animal markets provide opportunities for spill-over of pathogens from wild to domestic animals. Evidence: strong
    - Spatial expansion and intensification of agriculture and use of fertilizers. Evidence: medium
    - Water management projects associated with emerging vector-borne diseases. Evidence: strong
    - Intensive livestock production, especially pigs and poultry, provides a large population with limited host genetic diversity that can be a reservoir and amplifier of emerging pathogens, with transmission to humans and animals by occupational and environmental pathways. Evidence: strong
    - Encroachment of people and livestock into wildlife habitats for settlement, agriculture, hunting or tourism, leading to spill-over between wild and domestic animals and humans and adaptation to new hosts. Evidence: strong
    - Deforestation causes biodiversity loss, changes in bird and bat migration patterns, and human exposure to vector-borne diseases and wildlife pathogens. Evidence: medium
    - Loss of biodiversity of vertebrate species causes increases in zoonotic vector-borne diseases due to the loss of the dilution effect provided by high species diversity. Evidence: strong

- Changes in temperature and precipitation due to climate change may affect the distribution of pathogens, the distribution and density of vectors and hosts, and vector competence, but the effects will interact with the other factors listed above leading to unpredictable outcomes. Evidence: medium
- Extreme climatic events can increase the frequency and magnitude of disease outbreaks. Evidence: strong

- Bats have recently been the source of a number of emerging zoonotic diseases, some of which have involved domestic livestock in transmission and amplification. Although the number of emerging diseases from bats is in proportion to the number of bat species, they have been found to be naturally infected with a high number of viruses. Encroachment of humans and livestock into bat habitat and disturbance of bat populations due to hunting and habitat destruction is increasing the likelihood of pathogen spillover and future disease emergence. Evidence: medium

Introduction

Historically there have been huge changes in the burden of human infectious disease, the types of pathogen involved and the geographic distribution of disease, mainly related to human activities. Changes are continuing to occur and a range of factors have been associated with changes in rates of transmission, spatial distribution, routes of transmission and sources of pathogens. Since 73% of emerging human diseases are zoonotic (Woolhouse and Gowtage-Sequeria, 2005) and many recently emerging zoonotic diseases have originated in wildlife in developing countries it is important to have an improved understanding of the drivers and sources of disease emergence. Many authors have reviewed and discussed a range of factors that affect emergence of diseases, including zoonotic diseases. Some focus on particular factors or particular types of disease, whilst others take a more general approach. This systematic review aimed to find recent evidence of factors affecting zoonotic disease transmission and potential wild animal hosts of future emerging diseases.

Methodology

The full methodology is described in Chapter 2. For this subject 182 relevant abstracts were retrieved of which experts agreed on 86 for full paper retrieval (of which 12 could not be obtained) and added an additional 15. Out of these, 58 papers were found to be relevant for the subject but only 16 were original studies. An additional 22 papers were retrieved from the reference lists of the 58 papers of which 12 were original studies.

Findings

9.1 Historical changes in transmission

The epidemiological transition model describes historical changes in human disease patterns (Harper and Armelagos, 2010). The early hunter-gatherer period was characterised by small human populations with low mortality and fertility and a varied diet. The prevalent infectious diseases were those that had co-evolved with humans such as tapeworms, lice and *Staphylococcus*.

The first transition was associated with the change to agriculture about 10,000 years ago, characterised by large human populations with high mortality and fertility and a high crop diet, associated with

nutritional deficiencies. Close association with domesticated livestock resulted in human infection with new pathogens that adapted to human hosts such as smallpox, brucellosis, and measles. Rodents and birds that lived around human settlements were also sources of diseases such as bubonic plague, typhus and salmonella, and the clearance of land for cultivation increased contact with malaria-transmitting mosquitoes. In the last 200 years some countries have gone through a second transition associated with industrialisation and characterised by large human populations with low mortality, high fertility changing to low fertility, increased life expectancy, and a varied diet with over-nutrition. Use of antimicrobials and improved hygiene were associated with a decrease in infectious disease, whilst there was an increase in degenerative diseases, allergies, and sexually-transmitted diseases (STDs).

Harper and Armelagos (2010) propose that a third transition is currently occurring associated with globalisation and characterised by large human populations with decreased life expectancy. Prevalent diseases are the same as for the second transition as well as antimicrobial resistant infections, novel infections and delayed onset of chronic disease. Some low-income countries are experiencing the first, second and third transitions concurrently, with resistant infections, under-nutrition and over-nutrition (Harper and Armelagos, 2010).

Wirth et al. (2008) conclude from molecular studies that the *Mycobacterium tuberculosis* complex (MTBC) emerged from its progenitor approximately 40,000 years ago, when humans migrated out of the horn of Africa. MTBC is composed of two major lineages that arose 20-30,000 years ago, one that spread amongst humans during waves of migration to Asia, Europe and Africa, and one that spread in humans and from humans to animals that is linked to livestock domestication and development of farming societies. During the last 180 years there has been a demographic expansion of all *M. tuberculosis* lineages that coincides with human population increase, western urbanisation and international movements (Wirth et al., 2008).

Translocation of people and animals has historically played an important role in emergence of disease. Population expansion, social and political unrest, natural disasters and wars have resulted in the introduction of exotic pathogens to naive populations (pathogen or biological pollution) e.g. the introduction of smallpox and measles to America from Europe, and the introduction of rinderpest to Africa in the late 1800s (Gummow, 2010). *Echinococcus granulosus* was translocated with domestic animals from the northern to the southern hemisphere during European colonisation (Jenkins et al., 2005). Bovine tuberculosis was imported into South Africa and the Americas with European cattle (Michel et al., 2006, Thoen et al., 2009).

9.2 Factors that foster novel transmission routes and hosts

In their analysis of 1,407 human pathogen species identified by literature review, Woolhouse and Gowtage-Sequeria (2005) found that 13% of species were emerging or re-emerging and 58% of species were zoonotic. Zoonotic pathogens were twice as likely to be emerging or re-emerging as non-zoonotic pathogens (RR 2.0). Viruses were overrepresented in emerging and re-emerging pathogens but there was no difference between virus families in the proportion emerging or between genome type (DNA or RNA), although more RNA viruses had emerged in the last few decades. Emerging and re-emerging

pathogens were not strongly associated with particular types of non-human hosts, but were likely to have a broad host range (Woolhouse and Gowtage-Sequeria, 2005).

Cleaveland et al. (2001) used the same database of human pathogens and a database of 616 livestock and 374 domestic carnivore pathogens to analyse pathogen characteristics, host range and risk factors for disease emergence. 12% of human pathogens, 5% of livestock and 3% of domestic carnivore pathogens were classed as emerging. Viruses, especially RNA viruses, were highly likely to be emerging. An important risk factor for emergence was the ability of the pathogen to infect multiple host species, especially if they were from different taxonomic orders or wildlife species (Cleaveland et al., 2001).

By systematic review of the emerging diseases literature, Woolhouse and Gowtage-Sequeria (2005) identified the main factors that had been associated with (but had not necessarily caused) increased incidence or range of emerging and re-emerging human pathogens and ranked them by the number of pathogens associated with each. The highest ranked factor was change in land use or agriculture practices, followed by changes in human demography and society, poor population health, hospitals and medical procedures, pathogen evolution (drug resistance, increased virulence), contaminated food or water supplies, international travel, failed public health programmes, international trade and, lastly, climate change. For zoonotic pathogens, changing land use and agriculture was more important than for non-zoonoses.

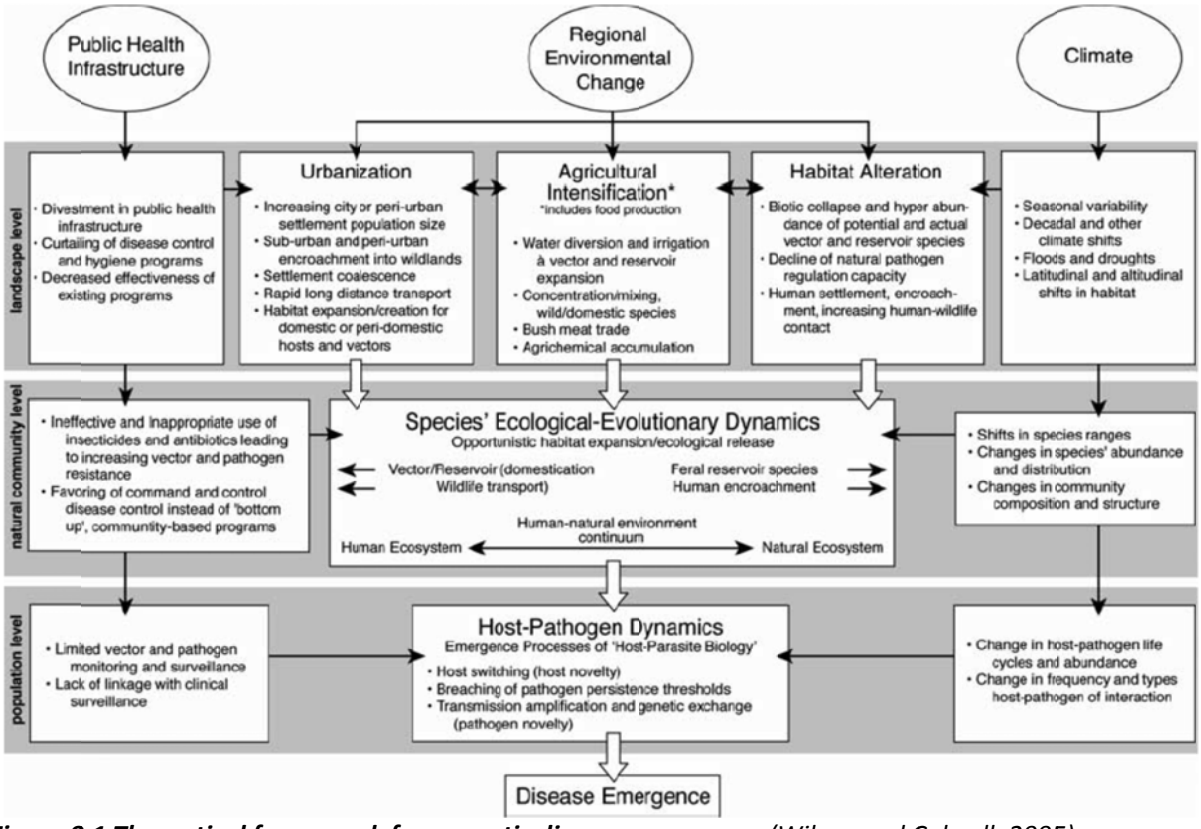


Figure 9.1 Theoretical framework for zoonotic disease emergence *(Wilcox and Colwell, 2005)*

Daszak et al. (2001) state that disease emergence occurs due to changes in the ecology of the host and/or the pathogen resulting from changes in human demography, behaviour or social structure that allows increased transmission between hosts, or increased contact with new host populations or host species. This occurs against a background of pathogen evolution and selection pressure leading to dominance of pathogen strains that are adapted to the new conditions (Daszak et al., 2001).

Wilcox and Colwell (2005) use a social-ecological approach, combining concepts and theory of population, community and systems ecology, to develop a theoretical framework for global zoonotic disease emergence that integrates anthropogenic and biological processes from molecular and cellular level to regional scale. Demographic and social factors (population growth and consumption) are driving regional environmental changes such as urbanisation, agricultural spatial expansion and intensification, and habitat change. These are exacerbated by climate change and deterioration in public health services in lower income countries, causing changes at community level and in host-pathogen dynamics that leads to disease emergence (Figure 9.1).

9.2.1 Human demographic and social changes

Increasing human population size, resulting in increased human population density and distribution, and increased land use for settlement and food production, is an important factor in emergence of diseases (Brown, 2004, Newell et al., 2010, Cutler et al., 2010, Gould and Higgs, 2009, Daszak et al., 2000, Daszak et al., 2001, Vora, 2008).

Level of socio-economic development affects human behaviour, public health infrastructure and medical interventions (Rosenthal, 2009, Gould and Higgs, 2009). Chaves et al. (2008) conducted an ecological study in Costa Rica to explore the association between American cutaneous leishmaniasis (ACL) cases and forest ecosystems. They found that when taking into account social marginality, the effect of living close to a forest on risk of ACL was low and concluded that social factors together with environmental and climatic factors are associated with disease risk (Chaves et al., 2008).

Poor governance in some developing countries coupled with unplanned urbanisation, a deterioration in public health infrastructure, and water and sanitation systems can lead to the re-emergence of disease (Daszak et al., 2000, Daszak et al., 2001, Harrus and Baneth, 2005). In Uganda, Angola, Democratic Republic of Congo and Sudan, there has been a re-emergence of human African trypanosomiasis in the last few decades because health services have been disrupted due to conflict (Polley, 2005, Hotez et al., 2004, Harrus and Baneth, 2005). In Eritrea, Sudan and Ethiopia war and civil unrest has led to a resurgence of leishmaniasis due to displacement of people and disruption of health services (Harrus and Baneth, 2005). After the collapse of the Soviet Union, in the new central Asian states hydatid disease re-emerged due to the deterioration of veterinary and public health services, break up of state farms into small-holdings, cessation of dog treatment, and the closure of abattoirs with safe offal disposal (Jenkins et al., 2005).

Human immunosuppression, caused by infections, medicines, stress or old age can lead to the emergence or re-emergence of disease (Daszak et al., 2001, Newell et al., 2010). HIV infection is

associated with the re-emergence of human tuberculosis (Thoen et al., 2009) and visceral leishmaniasis (Harrus and Baneth, 2005).

9.2.2 Urbanisation

Bradley and Altizer (2007) made a review of studies of the effect of urbanisation on the ecology of wildlife-parasite interactions. Urbanisation is associated with biodiversity loss and an increase in abundance of species that thrive in urban areas. Urban-adapted wildlife may have increased disease prevalence and transmit infection to rarer species in parks or the surrounding rural areas. Vector-borne disease may increase due to lower biodiversity and the predominance of key reservoir hosts, a reverse of the dilution effect. In North America there has been an increased prevalence of Lyme disease in ticks, white-footed mice and humans due to an increased abundance of white-footed mice in peri-urban areas. Similarly in USA there is a higher prevalence of West Nile Virus in low biodiversity areas (see below) (Bradley and Altizer, 2007).

Provision of food for wildlife in the urban environment, whether deliberately or accidentally as waste, results in higher wildlife density, higher contact rates and disease transmission, although foxes that feed on waste food rather than the intermediate hosts of *E. multilocularis* may have a reduced prevalence of this disease, and better nutrition may reduce disease susceptibility in general (Bradley and Altizer, 2007). Conversely Jenkins et al. (2005) and Dorny et al. (2009) describe an increase in *E. multilocularis* parasite density in Europe due to rabies control, increasing urban fox populations and increased fox contact with pets and humans (Jenkins et al., 2005, Dorny et al., 2009).

Urban areas are hubs of transport and trade. If new pathogens are introduced there are many opportunities for cross-species transmission and geographical spread (Bradley and Altizer, 2007). Increasing urbanisation can result in re-emergence of human disease where there are limited health services, water and sanitation (Gummow, 2010, Vora, 2008). Population growth and migration from rural to urban areas can introduce susceptible people to an endemic disease or newcomers may introduce new pathogens and vectors (Harrus and Baneth, 2005). Leishmaniasis in Brazil was formerly a rural disease but increasingly there are outbreaks in cities due to massive population movement into cities (Vora, 2008).

9.2.3 Globalisation, travel and trade

Globalisation of human travel, commercial trade and agriculture, including international trade in live animals and their products**,** provides a means for translocation of pathogens, vectors and hosts (Brown, 2004, Daszak et al., 2000, Daszak et al., 2001, Gummow, 2010, Cutler et al., 2010, Newell et al., 2010, Dorny et al., 2009, Harrus and Baneth, 2005, Gould and Higgs, 2009, Epstein et al., 2006). Trade in animal products is stimulated by changes in eating habits towards a higher protein diet and more exotic foods (Newell et al., 2010, Dorny et al., 2009). The construction of new roads facilitates vector and host movement to new populations (Harrus and Baneth, 2005).

West Nile virus, which originated in central Africa has a mosquito-bird cycle and occurs in Africa, Europe, Asia and Australasia causing a febrile illness in horses and humans as well as infecting rodents and other

small mammals, all of which are dead-end hosts. Epidemics are prevented in temperate areas due to low mosquito populations. In 1999 it was introduced to New York most likely by a transported infected mosquito, bird or human. The availability of the competent vector *Culex pipiens* and a large population of susceptible house sparrows, blue jays and American robins resulted in an epidemic in wild birds and humans, and the disease spread rapidly via infected migratory and resident birds, dispersing mosquitoes, and human-assisted mosquito movements on trains, trucks and airplanes, throughout the USA, and to Canada, Central and South America (Marra et al., 2004, Gould and Higgs, 2009, Daszak et al., 2001, Pfeffer and Dobler, 2010, Schloegel et al., 2005).

The mosquito *Aedes albopictus* has spread during the last two decades from the western Pacific and Southeast Asia to Africa, the Middle East, North and South America and Europe mainly due to the international trade in used tyres in which mosquito eggs have been laid (Vora, 2008, Harrus and Baneth, 2005). Chikungunya virus causes a febrile arthralgia in humans living in or near forested areas in Africa where the *Aedes sp* vector feeds on sub-clinically-infected primates and lays transovarially-infected eggs and human outbreaks occur every few years associated with heavy rainfall. In 2004 – 2006 there were major outbreaks of Chikungunya in the Indian Ocean, India, Malaysia and Sri Lanka. Phylogenetic analysis indicates that the outbreak originated in East Africa and it is suspected that the disease was spread in several waves by infected humans, infected mosquitoes or their eggs carried in car tyres to infect fully susceptible human populations (Gould and Higgs, 2009). It was found that the epidemic virus was a new variant that had adapted to the more widespread vector *Aedes albopticus.* Subsequently in 2007 there was an outbreak of *A. albopictus*-adapted Chikungunya in Italy (Vora, 2008).

Tatem et al. (2006) used air and sea traffic movements and climatic information to map global transport networks in terms of disease vector suitability and found that for ports with a similar climate, the traffic volume on routes to destinations where *Aedes albopictus* had established was twice as high as on those where it had not, but an African mosquito, *Anopheles gambiae,* has rarely spread from Africa probably due to the lower volume of sea traffic and because air traffic from Africa is mainly to areas of unsuitable climate in Europe (Tatem et al., 2006).

Trade in live wild animals for exotic pets or zoos, or for consumption can result in the introduction of new species of host or pathogen that can cause a change in ecological communities and loss of biodiversity (Chomel et al., 2007, Brown, 2004, Polley, 2005, Daszak et al., 2000, Daszak et al., 2001, Bradley and Altizer, 2007, Cutler et al., 2010, Epstein et al., 2006). Fèvre et al. (2006) gave an overview of the international movement of livestock and wild animals and cited some examples of disease emergence linked to animal trade. Increasing trade in bats and bat products for food and medicines may have brought bats infected with the precursor of SARS coronavirus into contact with susceptible amplifying hosts in live animal markets such as the masked palm civet (*Parguma larvata*), which then infected in-contact humans. Live poultry markets are hubs for cross-species transmission of HPAI H5N1. International trade in wild birds has resulted in the importation of H5N1-infected birds; infected hawk eagles were imported illegally from Thailand to Belgium and infected wild birds were imported legally into the UK for the pet market. An outbreak of human African trypanosomiasis in a previously unaffected area of Uganda was caused by movement of infected cattle (Fèvre et al., 2006). Pepin et al.

(2010) suggest that Rift Valley Fever was introduced to Egypt, the Arabian Peninsula and Madagascar by cattle trade from the greater horn region of Africa (Pepin et al., 2010).

Whilst the expansion of the areas affected by bluetongue in southern Europe in the last decade are likely to be due to the effect of climate change on the distribution and competence of *Culicoides sp.* vectors, the sudden appearance in 2006 of an African strain of BTV-8 subtype in northern Europe is likely to be due to transportation of sub-clinically infected ruminants (Gould and Higgs, 2009). The subsequent spread and overwintering of BTV-8 in indigenous European *Culicoides sp.* is an example of how a new pathogen can be introduced and become established in a new ecosystem.

9.2.4 Agricultural expansion and intensification

Modern farming practices and intensified farming systems have been associated with disease emergence and amplification (Daszak et al., 2000, Gummow, 2010, Brown, 2004, Newell et al., 2010, Dorny et al., 2009, Cutler et al., 2010, Gould and Higgs, 2009, Epstein et al., 2006).

Livestock may be reservoir hosts for vector-borne diseases and can act as amplifiers of emerging pathogens. In parts of South East Asia and the western Pacific there has been increased distribution of Japanese encephalitis virus (JEV) spread by wind-blown or transported infected mosquitoes, migratory birds or bats, or infected pigs. Increasing human population with increased irrigated agriculture, especially rice, and pig farming has supported its establishment in new areas (Vora, 2008, Hurk et al., 2009). JEV has a mosquito-water bird cycle (especially ardeid wading birds - egrets and herons). The primary vector, *Culex tritaeniorhynchus*, is associated with rice paddy and irrigated fields, and feeds on domestic and wild animals, including humans and horses, which are dead end hosts. Pigs develop a high viraemia and have a high reproductive rate providing a regular supply of susceptible animals and therefore serve as an amplifier host for human infection (Pfeffer and Dobler, 2010, Hurk et al., 2009). Relocation of pigs away from households has helped to decrease the incidence of human JEV in Japan, Taiwan and Korea (Hurk et al., 2009, Mackenzie et al., 2002).

Graham et al. (2008) reviewed recent changes in food animal production from traditional small-scale to industrial-scale with vertically integrated management and concentrated geographic distribution. Industrial poultry production is widespread in USA and Europe and is expanding rapidly in Asia, Africa, Latin America and the Near East. Intensive swine production is also on the increase. High density poultry and pig production tend to be concentrated in certain geographical areas, often together (Graham et al., 2008, Cutler et al., 2010). From an analysis of Thai 2004 HPAI surveillance data, Graham et al. (2008) found that the odds of HPAI H5N1 outbreaks and infections were higher in large commercial poultry farms than in backyard farms.

Certain disease transmission pathways are intensified by industrial production:

- Occupational pathways; there are a smaller number of workers on intensive farms but they have a greater intensity of exposure. Several cross-sectional studies show evidence of a higher sero-prevalence in farm workers compared to the general community to H1 swine influenza, Hepatitis E and HPAI (H5, H7) (Graham et al., 2008).

- Environmental pathways; pathogens are transmitted to the external environment via ventilation systems, increasing the risk of transmission to wild and domestic animals and humans e.g. *Campylobacter*, H7N1. Animal waste is a source of pathogens that can persist for several months when spread on open land or used in aquaculture, where wild animals or birds may be infected (Graham et al., 2008).

Intensive livestock systems generally use populations that have low genetic diversity. Springbett et al. (2003) used a stochastic model to simulate the effect of genetic diversity in an animal population on infectious disease transmission. They found that whilst genetic diversity did not affect the probability of an epidemic it did affect the severity of an epidemic. Decreasing genetic diversity is associated with an increased probability of a major epidemic or no epidemic whilst a more diverse population has a higher probability of a minor epidemic (Springbett et al., 2003).

Water management projects such as dams and irrigation canals can provide breeding sites for mosquitoes. The emergence of malaria in the Thar Desert in India was associated with the construction of irrigation canals (Vora, 2008) and Rift Valley fever epidemics have occurred after the construction of dams and irrigation canals (Pepin et al., 2010). Schistosomiasis outbreaks have also been associated with dams and irrigation. The Diama dam on the Senegal River reduced water salinity and increased the water pH increasing the population of freshwater snails and introduced *Schistosoma mansoni* to the lower and middle valleys of the Senegal River Basin (Harrus and Baneth, 2005). Irrigation projects in Egypt led to increased schistosomiasis prevalence because irrigation water from the Nile introduced the snail vectors and infected settlers contaminated the water, whilst other settlers had little or no immunity (Vora, 2008).

The effect of fertilizer use (environmental nutrient enrichment - ENE) on disease dynamics varies depending on the pathogen, the host, the ecosystem and the level of ENE (Johnson et al., 2010). It is likely that ENE will increase in the future in tropical and subtropical regions as agricultural development increases and may have an important impact because of the diversity of infectious pathogens in these areas. Many complex life cycle parasites, especially trematodes, increase in abundance under nutrient-rich conditions because the intermediate hosts - snails, worms, crustaceans – have increased population density and an improved ability to survive infection. Johnson et al. (2010) describe several studies on the effects of ENE on vectors:

- In Belize, phosphate-enriched run off and human settlement caused changes in wetland vegetation. Sparse rush vegetation was replaced by tall dense cattail, which is a typical habitat for *A. vestitipennis*, an efficient malaria vector for humans. Spatial data on malaria incidence showed a weak but positive correlation between the distribution of cattail marshes and number of malaria cases in humans.
- Female *C. restuans,* a WNV vector, oviposited more than ten times the number of egg clutches in containers with added nutrients compared to control containers. Larval survival and the mean size of emerging adults were greater in higher nutrient treatments compared with controls.

- In Californian rice fields the application of rice straw led to increased numbers of *C. tarsalis,* a WNV vector.

Martin et al. (2010) reviewed the effect of pollutants on host immune function and infection: whilst pollutants affect immune function through their effect on the physiology or behaviour of the host, or alter disease transmission due to changes in the rate and type of species interaction, their effect on disease emergence, prevalence and distribution is poorly known (Martin et al., 2010). Harrus and Baneth (2005) state that urban and industrial air pollution suppresses precipitation, altering vector habitats and the distribution of pathogens.

9.2.5 Encroachment of people and livestock into wildlife habitats

The encroachment of humans into wildlife habitats for settlement, agriculture, hunting or tourism can introduce new pathogens or hosts or expose people and their livestock to new pathogens or vectors and movement of people and livestock in and out of the encroached area can spread diseases especially along trade routes (Daszak et al., 2000, Daszak et al., 2001, Brown, 2004, Cutler et al., 2010, Polley, 2005, Newell et al., 2010).

Distemper and rabies was introduced into African wild dogs through spill-over from domestic dogs (Daszak et al., 2000, Daszak et al., 2001). Historically, brucellosis spilled over into North American bison from cattle but now that brucellosis has been controlled in cattle, the bison are a source of infection for the cattle (Schloegel et al., 2005). A similar situation has occurred for bovine tuberculosis which historically most likely spread from cattle into wildlife species and some of those species (white-tailed deer in North America, badgers in United Kingdom, brushtailed possum in New Zealand) are now a source of infection for the cattle populations in which the disease has been controlled or eliminated (Thoen et al., 2009). The emergence of HIV in humans is thought to be due to hunting of non-human primates in central African forests, and outbreaks of Ebola are associated with hunting in Gabon and Republic of Congo (Daszak et al., 2000, Gummow, 2010, Leroy et al., 2004). Rabies transmitted by vampire bats to cattle and humans is associated with forest activities in South America (Belotto et al., 2005).

Kyasanur Forest disease is a tick-borne disease affecting monkeys and humans in India that emerged in the 1950s due to encroachment of the rapidly increasing human population into undisturbed forest, clearing forest for agriculture and cattle grazing. The availability of cattle as a host for the tick increased the tick population and caused an epidemic in humans (Varna, 2001, Chomel et al., 2007). Nipah virus emerged in Malaysia due to the encroachment of intensive pig farming into forested areas that were the habitat for fruit bat colonies (Chomel et al., 2007) (see below).

Disruption and encroachment of wildlife habitats causes increased density of wildlife because they are compacted into smaller areas and leads to increased intra and interspecies contact (Brown, 2004). Wildlife may move to a different habitat such as urban areas. The emergence of Hendra, Australian Bat Lyssavirus and Menangle virus are associated with loss of bat habitat due to agriculture and deforestation forcing them to forage in urban trees (Daszak et al., 2000).

Despommier et al. (2006) discuss the role of ecotones (transition zones between two adjacent ecological systems) in disease emergence. Land use change and deforestation increase the area of ecotones as human settlements and agricultural land encroach into natural ecosystems. In ecotones species assemblages from different habitats are mixed, providing opportunities for pathogen spill-over, and genetic diversification and adaptation is intensified. Despommier et al. (2006) reviewed the literature for the 130 zoonotic emerging infectious diseases in the database of Woolhouse and Gowtage-Sequeria (2005) and found associations between emergence and an ecotone for a number of diseases; yellow fever, Lyme disease, Sin Nombre, Nipah, influenza, rabies, cholera, leptospirosis, malaria and sleeping sickness. The endemic cycle for yellow fever is between monkeys and mosquitoes. Yellow fever emerges where human settlement encroaches on forest edges where houses and cropland provide a favourable habitat for the *Aedes sp*. vector leading to increased virus transmission to the increased human host population (Despommier et al., 2006).

9.2.6 Deforestation

Sehgal (2010) reviewed the direct and indirect effects of deforestation on avian infectious diseases. Changes in wild bird habitats may affect flyways and contact between avian populations, which may affect avian influenza transmission. Deforestation causes low biodiversity, which is associated with an increased WNV infection rate in mosquitoes and increased human incidence (see below).

Forest-related human activity has been associated with increased exposure to vectors of yellow fever, Lyme disease, malaria, and cutaneous leishmaniasis (Sehgal, 2010). Savannah blackflies, which are vectors of onchercerciasis, preferentially transmit the more severe form of the disease compared to forest blackflies (Sehgal, 2010, Vora, 2008). In Asia, *Echinococcus multilocularis* is associated with pastoral communities where deforestation creates grassland suitable for the intermediate hosts (Jenkins et al., 2005). Conversely, Ducheyne et al. (2009), in a study of tsetse fly density and level of natural habitat fragmentation in eastern Zambia, found that tsetse fly density was lowest in areas of greatest habitat fragmentation and concluded that where human settlement and habitat clearance for agriculture was heavy the tsetse flies would disappear autonomously (Ducheyne et al., 2009).

In Uganda an increased rate of human gastrointestinal bacteria exchange with non-human primates was found in people and livestock living near forest fragments inhabited by monkeys and the effect was greater with greater disturbance of the forest fragment (Pongsiri et al., 2009).

9.2.7 Loss of biodiversity

Biodiversity loss can occur for a variety of reasons; ozone depletion, pollution, invasive species, global warming and habitat degradation; deforestation, fragmentation or modification (Vora, 2008, Pongsiri et al., 2009). The spread of invasive species and pathogens causes biotic homogenisation (the replacement of local with non-indigenous species) and can cause extinction of local species and loss of diversity at many levels; genetic, microbial, vectors, hosts, community and habitat structure (Pongsiri et al., 2009, Daszak et al., 2000, Martin et al., 2010) .

Biodiversity loss can exacerbate the risk of infectious diseases. The availability of a high diversity of vertebrate hosts for arthropod vectors of zoonotic diseases reduces the risk of human disease because of a dilution effect: the densities of the primary reservoir host and the vector are reduced, which decreases the contact rate between the reservoir host and the vector. In low diversity communities vectors feed more frequently on the primary reservoirs leading to higher pathogen prevalence in vectors (Vora, 2008, Ostfeld, 2009a). In high biodiversity communities, vectors feed on a wider range of hosts, some of which are poor pathogen reservoirs resulting in lower pathogen prevalence in vectors (Ostfeld, 2009a). For example, human WNV incidence in USA is negatively correlated with bird diversity. Ticks occurring in forests with high vertebrate diversity have lower *Borrelia burgdorferi* infection prevalence (the causative agent of Lyme disease) than ticks in low diversity habitats, and there is a greater abundance of ticks in low diversity habitats (Ostfeld, 2009a). An increase in Lyme disease in USA is associated with the abundance of the main reservoir host, the white-footed mouse, in areas of low vertebrate density (Pongsiri et al., 2009). A similar effect has been observed for leishmaniasis, Chagas disease, Rocky mountain spotted fever and schistosomiasis (Vora, 2008).

Where a wildlife species is in small fragmented populations there is likely to be reduced genetic variability within each population which may affect its susceptibility to infectious disease, possibly due to decreased heterogeneity of the major histocompatibility complex and reduced effective immune response (Breed et al., 2009).

9.2.8 Pathogen adaptation and evolution

Pathogen mutation and recombination give rise to new variants with different pathogenic potential; virulence, abundance, adaptation to a different host species or resistance to drugs (Cutler et al., 2010, Polley, 2005, Daszak et al., 2000).

Pekosz and Glass (2008) propose that the most important event in new disease emergence is a genetic change in the pathogen that makes it possible for it to become established in a new host species. They give the following examples of emerging zoonotic viral diseases that have undergone such genetic changes:

- Influenza viruses are RNA viruses with a segmented genome that allows for accumulation of mutations (genetic drift) and re-assortment of segments between virus strains (genetic shift) to give new strains to which hosts have no immunity.
- Comparison of SARS corona virus isolates from animals, from humans early in the epidemic, and from humans later in epidemic indicated that later in the epidemic there was improved binding of virus to human respiratory epithelial cells and more efficient virus replication in the respiratory tract.
- A single genetic change in the Chikungunya virus increased the efficiency of *A. albopictus* mosquito infection and transmission to hosts leading to the 2004-5 epidemic in south and southeast Asia.
- North American strains of West Nile virus have one genetic change that increases the ability of the virus to replicate and cause disease in birds, especially the North American crow (Pekosz and Glass, 2008).

Human-to-human transmissibility is an important characteristic for disease emergence. Most zoonoses are not transmissible between humans or are only minimally transmissible; rabies, RVF, Lyme disease. About 25% of zoonoses are transmissible between humans but do not persist in the population e.g. *E. coli* 0157, *Trypanosoma brucei rhodesiense* and Ebola virus. About 10% of zoonoses have mainly human-to-human transmission e.g. *M. tuberculosis* and measles, or are transmitted mainly from human to human once they have been introduced into the population e.g. influenza A, *Yersinia pestis*, SARS corona virus (Cutler et al., 2010).

Newell et al. (2010) summarized trends in prevalence of infectious agents in the food chain. Food-borne bacterial pathogens are evolving in response to environmental changes and developing new virulence properties or occupying new niches. There was an increase in salmonellosis in the 1980s in developed countries due to *S. enteritidis* phage type 4, which had adapted to colonise the avian reproductive tract and persist in the ovary, oviduct and eggs. Several *Salmonella* species have evolved to attach to and colonise vegetables. Vero cyctotoxin-producing *E. coli* (VTEC) O157 emerged in the last two decades infecting humans from contaminated beef and by environmental transmission. Antimicrobial resistance has developed in species of *Salmonella*, *Campylobacter* and *Staphylococcus* (Newell et al., 2010).

9.2.9 Climate change

Changes in climate will alter the conditions for hosts, vectors and pathogens, which potentially could change the exposure of human and animal populations to infectious diseases. Increases in temperature may cause spatial expansion into higher altitudes and latitudes. Changes in rainfall may increase or decrease habitat suitability for hosts, vectors and pathogens. There may be increased frequency of extreme weather events such as flooding and drought, which may affect the frequency and magnitude of disease outbreaks. Temperate environments are likely to become more suitable for tropical vector-borne diseases (Rocque et al., 2008). Minimum temperatures are increasing more than maximum temperatures so there is likely to be an overall increase in suitable conditions for pathogens and vectors rather than just a shift in distribution (Ostfeld, 2009b).

Rocque et al. (2008) described the likely biological effects of climate change on pathogens and vectors. There will be changes in population dynamics, the development cycle and disease transmission especially for pathogens with a stage in the environment or a vector: an increase in temperature is likely to cause increased disease transmission due to increased vector competence, vector population and disease transmission. Pathogen development within an arthropod vector is affected by the vector's body temperature; there is a temperature threshold below which development will not occur, at lower temperatures the duration of the pathogen development cycle may be longer than the vector's lifespan so transmission will not occur and as temperature increases the pathogen cycle becomes shorter. There will be changes in the distribution and ecological range of both vector and pathogen. The seasonality of life-cycles may be altered. Species with short generation intervals and rapid population growth, such as RNA viruses, will be able to adapt rapidly to a changing ecological situation.

Harrus and Baneth (2005) state that there appears to be an overall expansion in the global distribution of malaria, several vector-borne encephalitis viruses and yellow fever that is at least partially attributable to rising temperatures. Vector-borne diseases such as malaria, dengue, African horse sickness and bluetongue are likely to expand their range as increasing temperatures increase the development rate and winter survival of vectors and pathogens (Daszak et al., 2000, Schloegel et al., 2005, Cutler et al., 2010). Modelling predicts geographical expansion into new areas for diseases such as malaria, nematodes, WNV, Lyme disease, dengue and schistosomiasis (Harrus and Baneth, 2005, Rosenthal, 2009). Tabachnick (2010) has reservations about predicting the effects of climate change because although climate has a direct effect on vectors, pathogens, hosts and their interactions it also affects other factors that affect disease dynamics such as demographics, land use, water management and international trade and travel so the outcome is unpredictable (Tabachnick, 2010).

Outbreaks of Rift Valley fever in East Africa are associated with increased rainfall and flooding due to El Nino Southern Oscillations (ENSO) (Daszak et al., 2000, Daszak et al., 2001, Gummow, 2010, Pfeffer and Dobler, 2010) and the ENSO phenomenon is associated with dengue fever outbreaks in the Asia-Pacific region (Vora, 2008).

Gilbert et al. (2008) discuss the impacts of climate change on the ecology of avian influenza viruses and conclude that it is likely to change the distribution, composition and migration of wild bird populations that harbour the genetic pool of AI viruses but there is little data to link the emergence of H5N1 HPAI to climate change. Northward shifts in distributions have been reported in many bird species, with increased species diversity in northern areas, and reduced long distance migration or earlier migration. These will affect the distribution of AI viruses among different species and flyways. Extreme weather events can cause abnormal population movements: in January 2006 mute swans escaped a cold period in the eastern Caspian Sea basin and spread H5N1 into Western Europe (Gilbert et al., 2008).

Kausrud et al. (2010) used mathematical modelling to explore the relationship between paleoclimatic indices and human plague cases in south east Kazakhstan. Paleoclimatic indices correlated with plague prevalence and population density of the great gerbil (*Rhombomys opimus*) during the 20th century and climate-driven models predicted human plague cases in the early part of the century. They expect that global warming will sustain or increase future plague activity in the region (Kausrud et al., 2010).

9.3 Wild animal candidate species as potential future sources of future pathogens

The probability that a pathogen infects an individual of a new host species increases with the abundance of the reservoir host, the proportion of the reservoir host that is infected, the contact rate between reservoir (or vector) and new host, and the probability of transmission during each contact (Wolfe et al., 2007). The probability of infection decreases with increasing phylogenetic difference between hosts and it also depends on the type of pathogen and whether it has a wide or narrow host range, which is linked to genetic variability and the ability to overcome new host barriers to infection. Chimpanzees have low abundance and low contact rate but a close phylogenetic relationship to humans. Rodents have a distant phylogenetic relationship but have high abundance and frequent contact with humans and are a reservoir for several zoonoses e.g. leptospirosis, plague, typhus. Domestic livestock have high

abundance and close contact with humans and historically have been a source of several human pathogens. Wolfe et al. (2007) state that bats are phylogenetically distant from humans, have low contact and abundance and rarely transmit pathogens to humans but the focus of the literature on wildlife hosts of emerging diseases is predominantly on bats.

There are approximately 925 species of bats (order Chiroptera), comprising about 20% of all mammalian species and widely dispersed throughout all continents except Antarctica, although little is known about many of them (Calisher et al., 2006). Breed et al. (2006) describe some characteristics of bats that make them good candidates as a source of emerging infectious diseases: they are the only mammal that can fly (to forage for food, some species are migratory), which provides an opportunity for transmission within and between species, they have a long life span relative to their size and metabolic rate, many species live in large populations with high population density and colonial roosting behaviour increasing the likelihood of intra and interspecies transmission, and colonies may consist of mixed species. Bats feed by extracting nutrients from the food source and discarding the remains, which may be contaminated and become a source of infection for other species; fruit bats chew fruit to extract sugars and then regurgitate partially digested fruit or drop partly chewed fruit, whilst insectivorous bats discard the heavier parts of the insect (Dobson, 2005).

Calisher et al. (2006) summarised the current knowledge about viruses isolated from naturally infected bats and their role in maintaining and transmitting viruses. Sixty six viruses have been isolated and there are probably more. Most have not been shown to be transmitted to other animals or humans, but transmission has been demonstrated for rabies and other lyssaviruses (Family *Rhabdoviridae*, genus *Lyssavirus*), Nipah and Hendra (Family *Paramyxoviridae*, genus *Henipavirus*), and probably SARS coronavirus-like virus of bats (Family *Coronaviridae*). Arthropod-borne alphaviruses (Chikungunya), flaviviruses (Japanese encephalitis virus) and bunyaviruses (Rift Valley fever) infect bats but it is not known whether they are important reservoir hosts. Influenza A (Family *Orthomyxoviridae*), *Arenaviridae*, *Reoviridae*, *Herpesviridae* (A cytomegalovirus) and *Picornaviridae* have also been isolated as well as other unclassified viruses. There is genetic evidence that henipaviruses and lyssaviruses are of ancient origin, which suggests that they have co-evolved with their bat hosts (Calisher et al., 2006). A wide range of species is susceptible to henipaviruses; as well as pteropid species, natural infection has been found in five terrestrial species in four mammalian orders and experimental infection has been demonstrated in a fifth order, rodentia (Eaton et al., 2006). The cell receptor for both Hendra virus and Nipah virus, ephrin B2, is a surface glycoprotein of ancient origin that has a wide distribution in vertebrates, which explains the wide host range (Eaton et al., 2006).

In spite of the large number of viruses found in bats, the number of emerging diseases associated with bats is in proportion to the number of bat species (Breed et al., 2006). The Hendra and Nipah viruses isolated from humans, livestock and flying foxes are closely related, which indicates that virus emergence is unlikely to be due to a genetic change in the virus but due to a change in transmission (Breed et al., 2006, Calisher et al., 2006). Temporal clustering of the identification of bat-associated viruses in Australia - Hendra, Australian bat lyssavirus and Menangle virus - is consistent with changes in the endemic host population leading to spillover to new susceptible hosts. Bat populations are

decreasing in all continents due to habitat loss and hunting leading to altered foraging and behaviour patterns and closer proximity to humans and livestock. In Australia there has been a redistribution of roosting sites to urban areas (Breed et al., 2006, Calisher et al., 2006, Field, 2009).

Examples of zoonotic diseases involving bats

Hendra virus was first described in 1994 in Australia causing an outbreak of acute respiratory disease and death in horses and in-contact humans and there have been sporadic outbreaks since that time. No evidence was found of a reservoir in terrestrial animals so bats and birds were sampled and Hendra virus was found in all four species of Australian flying foxes (*Pteropus sp*), which were concluded to be the reservoir host (Breed et al., 2006). Genetic analysis has shown that there is a cluster of strains of Hendra virus indicating a series of independent spill-over events (Field, 2009).

The first known outbreak of **Nipah virus** infection was in Malaysia during 1998-99 causing an outbreak of respiratory disease in pigs and high case fatality encephalitis in humans. Nipah virus infected fruit bats were attracted to fruit trees planted around intensive pig farms providing the opportunity for virus spill-over to pigs, which were highly susceptible. The infection spread in pigs by the respiratory route due to high pig density on farms and by movement of pigs between farms; movement of pigs for sale spread infection to farms in the south of Malaysia (Breed et al., 2006, Field, 2009). Pigs became an amplifier host for human infection (Field, 2009). Almost all human cases had contact with pigs and there was no evidence of spill-over directly to humans from bats or of human-to-human transmission (Epstein et al., 2006). Live pig exports to Singapore for slaughter resulted in human cases in abattoir workers (Field, 2009, Epstein et al., 2006).

Investigations indicated that the first known pig and human cases occurred in 1997 on a large intensive pig farm (31,000 pigs) in Ipoh (Epstein et al., 2006) and the disease spread to the main 1998-99 outbreak area around Nipah by the movement of infected pigs (Daszak et al., 2006, Field, 2009). At the index farm fruit trees had been planted near to pig sties and these attracted fruit bats. Some branches overhung the pig pens so pigs could eat fruit that was contaminated with bat saliva or urine. In pigs, the virus caused a severe respiratory and neurological syndrome characterised by coughing. Infected pigs were highly infectious to other pigs and to humans through aerosols and secretions. Sub-clinically infected pigs were also infectious. The outbreak was controlled through mass culling of pigs and there have been no further outbreaks of Nipah in Malaysia (Epstein et al., 2006).

It was found that the causative agent, Nipah virus, was closely related to Hendra virus. The reservoir hosts for Hendra virus were *Pteropus sp* fruit bats, so bats in Malaysia were surveyed for evidence of Nipah virus infection. 324 bats were sampled from 14 species and two species, *P. hypomelanus* and *P. vampyrus,* had a high seroprevalence and they were concluded to be reservoir hosts although no virus was isolated (Mohd Yob et al., 2001, Chua et al., 2002). Subsequently Nipah virus with an almost identical genetic sequence to human isolates was isolated from urine samples and partially eaten fruit collected from below a flying fox colony (*P. hypomelanus*) (Chua et al., 2002). Experimental infection of *P. poliocephalus* caused sub-clinical infection, production of neutralizing antibodies and virus excretion in urine (Middleton et al., 2007). Further surveys have shown that throughout Malaysia there is high

Nipah seroprevalence in colonies of *P. vampyrus* and *P. hypomelanus,* which suggests that these species are reservoirs of Nipah virus and that the virus is endemic (Epstein et al., 2006).

Several reasons for the emergence of Nipah virus in Malaysia have been suggested. Daszak et al. (2006) discuss the possibility that Nipah virus was introduced from Indonesia in the mid-1990s by bats migrating away from unfavourable conditions created by an ENSO-related drought and forest fires. They consider it to be unlikely because the index human and pig cases occurred before the ENSO event, bat migration between Indonesia and Malaysia was later shown to commonly occur even in non-ENSO years, and serological evidence that Nipah virus is endemic in fruit bats throughout Malaysia.

Epstein et al. (2006) and Daszak et al. (2006) propose that Malaysian bats have been historically infected with Nipah virus and that there has been sporadic bat-to-pig transmission and pig-to-human transmission. They conclude that the emergence of Nipah virus was primarily driven by the intensification of the pig industry combined with fruit production in an area populated by Nipah virus infected fruit bats.

Since 2001 Bangladesh and India have experienced seasonal clusters of human Nipah cases with no apparent intermediate host but limited human-to-human transmission (Field, 2009). Hsu et al. (2004) conducted a retrospective outbreak investigation of the 2001 and 2003 outbreaks and found that close contact with human cases was a major risk factor for human infection. A serological survey found no evidence of infection in pigs, dogs, shrews and rodents, whilst 2 out of 25 *P. giganteus* fruit bats were seropositive (Hsu et al., 2004). A survey conducted during the 2004 Bangladesh outbreak found that 15% of 92 *P. giganteus* had Nipah antibodies, but rodents, shrews, other fruit bat species and insectivorous bats were seronegative (Daszak et al., 2006). A case-control study conducted during the 2004 outbreak found a strong association between infection and close contact with cases (Gurley et al., 2007). During the 2005 outbreak there was a strong association between drinking raw data palm sap and Nipah cases: bats have been observed licking sap at the collection sites, contaminating the collected sap with saliva or urine (Luby et al., 2009, Luby et al., 2006).

The outbreaks in Bangladesh have several differences from the Malaysian outbreak. The annual outbreaks are independent spill-over events that occur seasonally between January and May. There is no evidence of a livestock amplifier host (pigs are not very common in Bangladesh) and transmission is apparently from bats to humans via contaminated data palm sap. There is strong evidence of human-to-human transmission; there have been several household clusters with apparent secondary cases, and there were four apparent transmission cycles during the 2004 outbreak (Epstein et al., 2006, Daszak et al., 2006, Gurley et al., 2007). Genetic analysis shows some strain differences between the Malaysian and Bangladesh Nipah viruses (Harcourt et al., 2005, Field, 2009). Greater genetic heterogeneity amongst viruses isolated from the Bangladesh outbreaks compared to the Malaysia outbreak suggests that in Bangladesh there have been multiple introductions to humans from different bat colonies compared to a single introduction to humans from the amplifying host in Malaysia (Harcourt et al., 2005).

Luby et al. (2009) conclude that it is likely that Nipah infection of humans has been occurring before 2001 in the densely populated parts of Bangladesh where date palm sap collection is a traditional activity but it is now being diagnosed because diagnostic tests are available and there is increased surveillance for encephalitis cases (Luby et al., 2009).

There is serological evidence that Henipaviruses are likely to occur throughout the range of pteropid bats, which stretches from Madagascar to South and South East Asia, Australasia and Pacific Islands (Epstein et al., 2006). A survey in northern India found a neutralizing antibody prevalence of 51% in *P giganteus* (Epstein et al., 2008). A serological survey in Sumatra and Java, Indonesia, of *P. vampyrus* found an antibody prevalence of 36% (n=70) (Sendow et al., 2006). Nipah virus antibodies have been found in *P. lylei* in Cambodia and a Nipah virus closely related to the Malaysian strain was isolated (Reynes et al., 2005). Nipah RNA has been found in urine samples from colonies of *P. lylei* in multiple sites across Thailand (Wacharapluesadee et al., 2010). Serological evidence of Hendra, Nipah and Tioman virus infection in three endemic species of fruit bats were found in Madagascar (Iehlé et al., 2007). Surveys in west Africa have demonstrated that henipaviruses are not restricted to the range of pteropid bats: Nipah and Hendra virus neutralizing antibodies were found in *Eidolon helvum* fruit bats sampled from urban and forest sites in Ghana (Hayman et al., 2008) and henipavirus RNA was detected in faeces samples from a colony of *E. helvum* in Kumasi, Ghana (Drexler et al., 2009).

Severe acute respiratory syndrome (SARS) corona virus emerged in China in 2002. The earliest human cases of SARS were associated with wildlife contact and SARS corona virus-like viruses were isolated from wild animals in a live animal market. Several surveys were conducted in domestic animals, poultry and wildlife to identify the natural reservoir of SARS corona virus and two independent groups found SARS corona virus-like virus in several species of insectivorous horseshoe bats (*Rhinolophus sp.*) from different locations in southern China (Lau et al., 2005, Li et al., 2005, Bennett, 2006). Genetic analysis showed that there was greater variation amongst bat viruses than human or civet viruses, and that the human and civet viruses phylogenetically lay within the bat SARS corona virus-like virus cluster and therefore probably originated from bat-associated viruses (Li et al., 2005). It appears that SARS corona virus-like virus of bats was transmitted in the wild or in markets to various species of wild animal such as masked palm civets, racoon dogs and hog badgers, spilled over into humans through contact with these intermediate hosts or their tissues, followed by human-human transmission (Li et al., 2005).

Cui et al. (2007) explored the evolutionary relationships between bat corona viruses and their bat hosts though a phylogenetic study of 67 bat corona virus gene sequences obtained from ten bat species, and bat mitochondrial cytochrome b gene sequences from the ten bat species caught in nine provinces of China. They compared the genetic diversity of corona viruses and the corresponding diversity among bat taxa and concluded that there have been recent host shifts of corona viruses amongst rhinolophid bats, which may have implications for the emergence of SARS and related viruses (Cui et al., 2007).

Lyssaviruses: Badrane and Tordo (2001) conducted a phylogenetic analysis of 55 lyssavirus isolates from 36 carnivores and 17 chiroptera from around the world and found that chiropteran lyssaviruses existed long before carnivoran and that there had been several successful host-switches of rabies virus from

bats to carnivores about 1000 years ago (Badrane and Tordo, 2001). Belotto et al. (2005) analysed data from the PAHO regional information system for epidemiological surveillance of rabies in the Americas for the period 1993 to 2002 and found that 15% of human rabies cases are infected by haematophagus and non-haematophagus bats. *Desmodus rotundus*, a haematophagus bat that feeds on mammalian blood, is the species of greatest epidemiological importance. The frequency of vampire bat attacks on humans is associated with environmental activities such as livestock grazing, deforestation and mining and transmission of rabies to cattle is a major constraint to livestock production (Belotto et al., 2005).

Ebola: Amongst the Filoviridae there are four types of Ebola virus (Sudan, Zaire, Ivory Coast, Reston) and Marburg virus. The natural reservoir of Ebola is not yet known although Ebola virus RNA has been detected in animals in Central African Republic and experimental infection and virus replication has been demonstrated in several bat species (Calisher et al., 2006). Leroy et al. (2005) tested small vertebrates trapped near to infected gorilla and chimpanzee carcasses during Ebola outbreaks from 2001 to 2003 in humans and great apes in Gabon and the Republic of Congo and found Ebola virus IgG in 3 species of fruit bat (16 bats out of 192) and Ebola virus RNA in 13 of 279 fruit bats. They concluded that fruit bats may be a reservoir and that the increase in great ape Ebola mortality during the dry season may be due to increased contact between animals as they compete for scarce food resources (Leroy et al., 2005).

Major gaps and researchable hypotheses

This systematic review found many papers that discussed the likely factors leading to the emergence or re-emergence of zoonotic diseases but there were few published studies that provided evidence for the role played by the different factors, especially in relation to zoonotic diseases involving wildlife and livestock developing countries.

Research needs:

- Improve understanding of the co-evolution of hosts and pathogens.
- Understand within-host interaction between pathogens e.g. immune-compromising infections.
- Assess effect of reduced diversity of pathogens through increased hygiene on disease susceptibility.
- Screening of bat populations for pathogens.
- Develop targeted surveillance methods for early detection of emerging pathogens.
- Understand key pathways of disease spread subsequent to exposure.
- Model within complex system interactions.
- Understand the effect of genetically homogenous livestock populations on infectious disease emergence.
- Increase understanding of human behavioural aspects of wild animal interaction and exposure through for example hunting, harvesting, consumption and recreation.

Conclusion

Historically, changes in prevalent human diseases have been associated with increases in human population, human migration and changing interactions with ecosystems that have led to animal

pathogen spill-over and host-switching. Disease emergence is a complex process involving changes in host-pathogen dynamics, ecological dynamics and environmental change. Commonly cited factors that influence the emergence or re-emergence of zoonotic diseases are human demographic and social changes, urbanization, globalisation of human travel and commercial trade, spatial expansion and intensification of agriculture, intensive livestock production, encroachment of people and livestock into wildlife habitats, deforestation and loss of biodiversity, but there is limited evidence for each factor.

Bats have recently been the source of a number of emerging zoonotic diseases, some of which have involved domestic livestock in transmission and amplification. Although the number of emerging diseases from bats is in proportion to the number of bat species, they have been found to be naturally infected with a high number of viruses. Encroachment of humans and livestock into bat habitat and disturbance of bat populations due to hunting and habitat destruction is increasing the likelihood of pathogen spillover and future disease emergence.

10. Key factors influencing the risk of the transfer of infections between livestock and wildlife in developing countries – production and socio-economic factors

Main messages

In covering the area of socio-economics and production there are a number of unwritten yet commonly accepted issues around disease emergence. These are listed as:

- Human behaviour is a critical component in:
    - the modification of the environments in which the host and pathogen circulate be they production systems or urbanisation;
    - the type and frequency of contacts at which a host and a pathogen are brought together.
- Human behaviour underlies:
    - the emergence of a disease;
    - the likelihood that a disease it will become established in the human population;
    - the impact of the disease, as many of the costs are related to response.
- Human behaviour is influenced by cultural norms, legislation, private standards – broadly known as the institutional environment – as well as by economic incentives.
- The institutional environment can be both negatively and positively affected by public services and law structures and hence impact on the likelihood of disease emergence and establishment.
- There are difficulties in studying the relationship between disease emergence and human behaviour in that:
    - running controlled trials would be ethically and morally challenging;
    - quantification of human behavioural influences is methodologically challenging and therefore rarely attempted;
    - analysis that leads to documenting and in some cases quantification of the importance of human behaviour requires interdisciplinary teams with individuals who are experts in their own field yet sufficiently humble to accept the opinions and ideas of others;
    - in general, research into linkages between behaviour and disease emergence requires systems research, not reductionist thinking.

The latter point often means that funding to look carefully at socio-economics and production is difficult to obtain and studies tend to be limited to partial overviews of the more complex nature of looking at disease emergence through a human behavior lens. The published evidence base is therefore weak, meaning that the evidence to support the above conclusions can be stated to be weak. This does not mean that these issues are unimportant, they remain largely untested hypotheses that require further fieldwork studies that ideally become integral components of risk analyses and epidemiological studies. The gap in this area actually calls into question the sort of questions being used to research disease emergence, maintenance and spread and the need for work that gets to a more fundamental basis of risk factors. The brief review of material supports this view.

Introduction

The objective of the paper is to synthesise and analyse existing evidence on the factors relating to production system and socio-economic characteristics that influence or could influence (positively or negatively), the risk of the transfer of infections between livestock and wildlife in developing countries. As stated by Cutler et al. (2010) a majority (>70%) of the pathogens of concern come from wildlife (Cutler et al., 2010). According to Chomel et al. (2007) the leading causes of disease emergence are human behaviour and modifications to natural habitats, changes in agricultural practices, and globalization of trade (Chomel et al., 2007). Weiss (2008) has a similar list and adds more emphasis on the use of bushmeat in the exposure of pathogens (Weiss, 2008).

For the synthesis the following categories of socio-economic and production characteristics have been identified:

a. Increasing human population
b. Use of greater levels of intensification
c. Changes in land use
d. Changes in livestock value chains

Further explanation and details of the characteristics are described in the following sections.

10.1 Increasing human population

The increases in human population over the last two hundred years have led to:

- higher levels of urbanisation,
- greater concentrations of humans,
- more frequent travel and interactions over long distances;
    - rapid spread of SARS and H1N1,
    - jumps in the distribution of diseases such as bluetongue and West Nile virus.

These increases in population and a number of associated impacts have not generally been accompanied with government responses and institutional change, leading to issues that are problematic for disease control such as the rule of law, the existence and performance of local implementing structures, and political sustainability at national and global levels (Mills et al., 2008). Impoinvil et al. (2007) also report a lack of sustainable funding as a common problem in disease management with particular reference to malaria (Impoinvil et al., 2007).

The problems of keeping pace with demographic change are also seen at local levels with Dongus et al. (2007) reporting that in Dar es Salaam the registering of housing and new settlements was not keeping pace with the expansion of the city creating problems with targeting resources for malaria control (Dongus et al., 2007). Similarly David et al. (2007) describe the difficulties of informal settlers not being captured in health statistics and not being given access to proven interventions. They go on to state that the underlying causes of inequity result in poorer health and worse health outcomes for the urban poor (David et al., 2007).

Accepting that population increases will continue in some regions of the world and these lead to greater issues associated with urbanisation, there needs to be policies that strengthen public services in terms of monitoring change, disease outcomes that these changes stimulate, and response mechanisms that can adequately manage and control disease.

10.2 Intensification of production

On the supply side livestock production has seen a rapid increase both in terms of the size of populations and the output per animal. This has been achieved through:

- Changes in how we manage the genetics of the food animal species, with perhaps the most dramatic changes being in the poultry sector, and significant changes in the pig and cattle sectors.
- Changes in the feeding of livestock with the globalisation of sourcing of feed inputs such as maize and oilseed meals, plus a variety of minor products.
- An increase in the density in which we keep animals either through housing or fencing systems.
- Changes in movement patterns of livestock through advances in technologies of transport. a Again the extremes are in the poultry sector with the ability to move day-old chicks or ducks thousands of miles by plane. The importance of livestock movements and disease spread and control are well covered in the literature (Fèvre et al., 2006, Prasad and Minakshi, 2006, Rushton, 2006, Rushton, 2008).

There are implications to these changes stimulated by the socio-economics of the societies we live in. For example, researchers have shown that there are risks with production units due to the constant movement on and off farms to deliver feed or to remove products for sale and that these are issues that need to be including in models and disease control programmes (Leibler et al., 2010). In intensified systems, anti-microbials are used in large amounts for growth promotion or to control the diseases associated with high population densities. Many researchers raise concerns around the use of anti-microbials in the production of feed for pigs and poultry with regards to the emergence of anti-microbial resistance (Gilchrist et al., 2007). Likewise, intensive producers are likely to use vaccines and while this can help manage disease, inadequate development, monitoring and use of vaccine for disease agents – H5N1 (Indonesia and probably China) being the classic case – can paradoxically lead to disease persistence by reducing the susceptibility of hosts and hence the likelihood of disease 'burn-out'. Recent analysis suggests that the risks of disease such as avian influenza are greater in the more intensive units that the extensive scavenge-based systems (Graham et al., 2008).

10.3 Changes in patterns of land use

Changes in land use has been divided into different areas, the urban and peri-urban, and the use of agricultural or rural areas and the ocean.

10.3.1 Urban and peri-urban areas for livestock production units

The greater density of urban areas and the human activities associated with these changes lead to greater contact with rodent populations and also an increased tendency to have companion animals in closer contact. Much attention is given to the problems of rabies and its control (Cleaveland et al.,

2006). Another important factor for companion animals but with relevance to any livestock or wildlife sharing the environment is the feeding of raw meat to dogs leading to increased prevalence of pathogens such as *Campylobacter jejeuni* or *Salmonella enterica* in the faeces (Lenz et al., 2009). This was associated with a lack of acceptance of the dog owners to recognise this risk.

Spread of dog and cat populations and their contact with wild populations fosters endemic rabies in both populations. Though essentially a manageable problem, rabies is considered to persist in poor countries because:

- low priority is given for disease control as a result of lack of awareness of the rabies burden;
- epidemiological constraints exist such as uncertainties about the required levels of vaccination coverage and the possibility of sustained cycles of infection in wildlife;
- operational constraints exist including accessibility of dogs for vaccination and insufficient knowledge of dog population sizes for planning of vaccination campaigns;
- limited resources for implementation of rabies surveillance and control are available.

Water source changes and watershed management are associated with changes in prevalence of many zoonoses including cryptosporidia (Weiss, 2008).

10.3.2 Rural Areas

In the already settled areas of agricultural production the sheer intensity of land use can create disease burdens. For example Nguyen Thi Lan et al. (2009) indicate the problems of intensification of aquaculture in areas with large numbers of humans and domesticated animal species with the consequence of the circulation of fish-borne zoonotic trematodes (Nguyen Thi Lan et al., 2009). In other areas the interface between agriculture and wild populations are important with the following examples:

- Meng et al. (2009) describe the problems of increasing contact with wild boars that is associated with a number of infectious diseases in domestic animals, such as classical swine fever, brucellosis and trichinellosis, and in humans, diseases such as hepatitis E, tuberculosis, leptospirosis and trichinellosis (Meng et al., 2009).
- Goldberg et al. (2008b) indicate that the population of gastrointestinal bacterial in humans that have settled in forest fringes of Uganda resemble those of the primates around them, and that the association increased with greater disturbance of the forest (Goldberg et al., 2008b).
- Judge et al. (2007) describe the interface between cattle and rabbit populations leading to potential problems in the maintenance of paratuberculosis (*Mycobacterium avium* subspecies paratuberculosis; *Map*) (Judge et al., 2007).
- Similarly a well reported issue is the interfaces between bat populations and the transmission of henipaviruses viruses with the best case being Nipah virus from fruit bats due to the close proximity of pig populations (Breed et al., 2006).

Social and political change can also create challenges that lead to problems of disease control. Joyner et al. (2010) describe the problems with anthrax in Kazakhstan where carcass disposal is poorly supervised

and there is inadequate access to vaccines. This was related to periods of instability and a lack of facilities (Joyner et al., 2010).

10.3.3 Oceans

Kite-Powell et al. (2008) state that risks on acute health caused by toxins associated with shellfish poisoning and red tide are relatively well understood (Kite-Powell et al., 2008). However, risks posed by chronic exposure to many anthropogenic chemicals, pathogens, and naturally occurring toxins in coastal waters, are less well quantified. There is also a lack of data on economic and social consequences of ocean health related problems. Watterson et al. (2008) add that there is little work on occupational health issues despite the fishing industry employing many millions of people (Watterson et al., 2008).

10.4 Changes in value chains

The livestock supply chains have experienced increasing volumes of animals and products. This has included bushmeat species and the trade in wild animal species (Pavlin et al., 2009). There is significant mixing and crossover of species in live animal markets and, in general, little or no regulation or infrastructure investments.

- The use of bushmeat as a food source has been linked to the emergence of several zoonotic diseases such as SARS and HIV (Weiss, 2008).
- Pavlin et al. (2009) assessed the potential of the 246,772 mammals from 190 genera (68 families) that were imported to the USA between 2000-2005 to host 27 selected zoonoses. The zoonotic agent that was capable of infecting the greatest number of genera was rabies virus (78 genera of mammals), followed by *Bacillus anthracis* (57), *Mycobacterium tuberculosis* complex (48), *Echinococcus* spp. (41), and *Leptospira* spp. (35). Mammalian genera that were capable of harboring the greatest number of the selected zoonoses were *Canis* and *Felis* (14 each), *Rattus* (13), *Equus* (11), and *Macaca* and *Lepus* (10 each).
- Inadequate public resources, capacity and regulation to manage zoonotic diseases within more complex and longer chains (Zinsstag et al., 2007, Lembo et al., 2010).
- Spread and maintenance of H5N1 virus in SE Asia.

Gender issues

Men and women have different exposure to risk depending on their roles and responsibilities. Socio-economic factors such as increasing proximity between humans and livestock accentuate these risks. LaBeaud et al. (2008), in a study on Rift Valley fever (RVF), highlight the large variability in exposure and RVFV seropositivity among Kenyan villages and emphasize the effect of age, gender, location, and animal husbandry in RVF transmission. Bivariate statistical analyses showed that RVF seropositivity varied significantly according to age and gender (male participants were more at risk, $p = 0.011$). Multivariable logistic regression models used to predict adjusted odds of RVFV seropositivity showed that location was significant when age and gender were controlled for. Seropositivity also varied by gender when age and location were controlled for; male participants had >3 times the risk of women participants (20% vs. 9%; adjusted OR 2.78, 95% CI 1.18– 6.58 for male participants vs. female participants). The increased seropositivity among male participants may have a biological basis, given

that outcome of infection and resultant immune response to other viruses has been linked to gender differences (LaBeaud et al., 2008).

A gendered assessment of avian influenza (AI) in Egypt (Lambert and Radwan, 2010) found relations also are important in understanding the pattern of human infection and mortality from AI in Egypt. Women in Egypt are more exposed to AI than men. Since AI's emergence in Egypt, 104 people have been infected and 30 have died. 60% of the victims have been female, whilst the majority of the victims have been children aged 15 or less. Women are more likely to succumb to the effects of AI than men: most of the fatalities have been adults, and in particular adult women who accounted for 73% of all deaths. There is no evidence that the greater vulnerability of adult women is due to biological factors or to differences in care. Rather, it is attributed to factors linked to gender roles including greater contact with live birds and delay in seeking care. Statistics showed a clear correlation between recovery and the amount of time that passes between the onset of symptoms and the beginning of treatment. Women's delay in seeking medical assistance may be tied to denial of symptoms because of household and childcare responsibilities; the inconvenience of travelling to a medical centre because of the need for male accompaniment; and the fear of losing the poultry flock to culling if an AI infection is confirmed. By contrast, both parents are likely to respond quickly to any influenza symptoms in their children.

In Vietnam and Thailand, Velasco et al. (2008) found that women faced particular problems and risks because of their direct contact with backyard poultry, a significant form of poultry production. The risk factor is potentiated by women's lower level of education compared to men. The widespread acknowledgment of women's key roles in backyard poultry production and marketing had not successfully informed the targeting of women as both communicators and as beneficiaries of AI campaigns and training. Women poultry keepers rarely received adequate support and services or resources and training. Neglect of this important production group exacerbated the effects of socio-economic shocks resulting from AI outbreaks (Velasco et al., 2008).

Key Issues

Endemic zoonoses are found throughout the developing world, wherever people live in close proximity to their animals, affecting not only the health of poor people but often also their livelihoods through the health of their livestock (Maudlin et al., 2009). The contact with animals is a consequence of socio-economic change and urbanisation leading to increasing density of human populations that both create larger rodent populations and increase the populations of domesticated populations that either act as liaison hosts or actual sources of infection to humans. The diseases that are emerging and re-emerging in this situation are not just zoonoses; they are also food-borne pathogens due to increases in the use of intensive, poorly managed livestock production systems and relatively poorly managing processing and marketing systems.

Chomel et al. (2007) and Lembo et al. (2010) talk of ignorance of the human population and the need for greater education on the risks associated with disease emergence. They discuss aspects of human behaviour, some of which are due to ignorance and others that relate to people breaking rules.

Pekosz and Glass (2008) describe that human activities play a role in the changing levels of disease emergence risk, and that a relative lack of severe clinical disease and non-specific presentations can contribute to making impacts difficult to assess. However, they also argue that genetic changes in pathogens are key to making the transmission to humans easier or pathology more significant. With their evidence they believe that our ability to specifically predict or to prevent the occurrence of an emerging pathogen is difficult if not impossible. Their suggestion is therefore to have careful monitoring of human populations in order to recognise unusual disease patterns. With regards to basic science they state that more research is required on what leads to an increase in virus transmission between species and better viral replication in a new species (Pekosz and Glass, 2008).

Mazet et al. (2009) argue for a focus on gender differentiated roles that may define risk exposure. Men's contact with sick animals and women's contact with animals, particularly poultry and lactating cows and goats increase the likelihood of contracting diseases. Further studies are however required to examine the epidemiologic, biological, and genetic basis for gender variations in risk and to quantify the potential public health impact of these risks (Mazet et al., 2009). Velasco et al. (2008) recommend the use of gender analysis to conduct country-level assessments of gender differentials of socioeconomic and livelihood impact of the AI crisis among different types of poultry production and marketing systems in South Asia with a particular focus on changes in gender patterns among ethnic minorities, and in areas of persistent food insecurity. Identification of gendered AI vulnerabilities and potential roles and contributions in AI control and responses as well as analysis of the gender differentials in knowledge, attitudes and behaviour as a result of AI communication campaigns is essential. Also required is analysis of gender impacts of national policies on bio-security controls on poultry production and livelihoods.

Researchable points

There is a need for further research in the following areas;

- How to assess the "health" of institutional environments in terms of their roles in encouraging risk taking and rule breaking.
- Application of the health of institutional environments to the food systems and chains that are believed to have the greatest biological risks.
- Development of political science methods to turn conclusions from these areas of research into achievable and implementable actions.

These research items need to be systems centric, not disease centric, and need to be strongly focussed on the understanding of human behaviour with the triangle of disease emergence.

11. Management of zoonoses at the livestock-wildlife interface

This chapter covers possible interventions that could limit the interaction of the key wildlife species with domestic livestock and their potential economic and social impacts and governance issues associated with zoonosis control. Few of the papers reviewed dealt with detailed efficacy and impact assessments of interventions to limit contact between livestock and wildlife. Although not fully germane to the issue we also capture some of the broader lessons around managing zoonoses with a livestock and wildlife interface as these condition the environment in which more specific interventions take place.

Main messages and strength of evidence

Justification for control of zoonoses with a livestock-wildlife interface:

- Zoonoses impose a high burden on human health, are under-diagnosed and under-reported. Evidence: strong
- Zoonoses have multiple burdens and control has multiple benefits. Evidence: medium
- High burden of diseases does not necessarily imply high prioritisation for control. Evidence: strong
- The likelihood of successful disease control and the importance of zoonotic transmission are inversely correlated. Evidence: medium

Evidence on intervention methods that limit interaction of livestock with wildlife:

- Elimination of wildlife populations as a means to disease control is probably not feasible. Evidence: medium
- Reducing wildlife population can reduce risk to livestock, but partial measures can make things worse. Evidence: strong
- Becoming wealthy is one of the most effective ways of reducing zoonoses. Evidence: strong
- Innovations may radically improve control even in poor countries. Evidence: weak

Current approaches to control:

- Ability to measure disease burden has led to new emphasis on tackling the biggest problems first. Evidence: strong
- Both top down and community-based programs have had little success in tackling epidemiologically complex disease at the human-livestock-wildlife interface. Evidence: medium
- Focus on high-burden but intractable disease is a missed opportunity for controlling lower-burden but more tractable diseases (the low-hanging fruit). Evidence: weak/medium
- Integrated and One Health approaches lead to better control. Evidence: weak

Introduction

Depending on how they are defined, zoonoses with a livestock-wildlife interface include some of the most significant diseases in developing countries as well as serious threats to global health security. The examples of brucellosis, tuberculosis, avian influenza, SARS, human African trypanosomosis, rabies and anthrax give an idea of the depth and breadth of impacts, from massive human sickness and mortality, to huge economic loss, to disruption of global trade and tourism, to potential for bio-terrorism. Diseases with a human-livestock-wildlife interface are also of concern because of the risk they pose to

endangered wildlife; transmission of disease from domestic animals to wild carnivores, and between livestock, humans and non-human primates are well-described in recent literature.

Methodology

The team of experts formulated questions relevant to the area of management of zoonoses through interventions that could limit the interaction of the key wildlife species with domestic livestock and the potential economic and social impacts (at both state and household level) of those interventions. These questions were developed into search terms and algorithms; using these in the PubMED and CABDirect databases resulted in 2,259 abstracts. These were screened for relevance and 74 were sent to experts. An additional 20 were sent which had been identified in searches around other themes but were considered relevant to the theme on management. Of these 94, both reviewers agreed that 24 should be retrieved. The full paper was obtained for 22 of these plus another 7 papers identified in the reference list of the 22 papers obtained or because the reviewer considered they were relevant to the topic (even though not identified in the search).

Findings

11.1 Benefits and challenges of control of zoonoses with a livestock-wildlife interface

Zoonoses impose a high burden on human health, and are under-diagnosed and under-reported. Evidence: high

Several papers considered the burden of disease and benefits of control. The literature agrees that the burden of zoonoses in general is both high and underestimated; several of the zoonoses referred to are at the wildlife-livestock interface (human African trypanosomiasis, brucellosis, rabies, Chagas disease and anthrax). Zinsstag et al. (2007) cites evidence that the combined effects of human disease caused by zoonoses, as part of the neglected infectious diseases, are in the same range as the classical diseases of poverty such as HIV/AIDS, tuberculosis, and malaria (Zinsstag et al., 2007). Maudlin et al. (2009) argue that zoonoses are under-diagnosed because they are confused with other diseases (brucellosis with malaria) and under-reported (citing 92% of the deaths from sleeping sickness in Uganda are not reported) (Maudlin et al., 2009). Budke et al. (2009) consider cystic echinococcosis to be a neglected zoonosis. Its burden is probably similar to zoonoses featured in Global Burden of Disease, and its neglect is partly due to difficulties in diagnosis, the chronic nature of the disease and expense of treatment (Budke et al., 2009).

An example of under-reporting is given by Lembo et al. (2010) citing evidence from modelling approaches and, using the incidence of dog-bite injuries and availability of rabies post-exposure prophylaxis, suggest that incidence in Africa is about 100 times higher than officially reported, with 24,000 deaths in Africa each year (Lembo et al., 2010).

Summarising many authors, Utzinger and de Savigny (2006) attribute this neglect of tropical diseases (many of which are zoonoses with a livestock-wildlife interface) to the diseases' primary impact on the poorest of the poor in rural and deprived urban settings, the underestimation of their public health and

economic significance, and the lack of coordinated research and control efforts (Utzinger and de Savigny, 2006).

Zoonoses have multiple burdens and control has multiple benefits. Evidence: high

An important literature is emerging around the multiple burdens of zoonoses, their distribution and assessment. The two diseases best evaluated from the perspective of multiple burdens are both at the livestock-wildlife interface (brucellosis and rabies). The Swiss Tropical Public Health Institute has been a leader in this research and some results are summarized in Zinsstag et al. (2007). In Mongolia, an economic analysis of brucellosis included both medical and veterinary costs and benefits. This found that the public health sector reaps only 11 per cent of the benefits, and, regarded solely from a cost per DALY-averted perspective, brucellosis control was less attractive than other disease control expenditure options. But when the benefits for the livestock sector were added and the costs of the intervention are shared between the public health and the agricultural sector in proportion to their benefits, the control of brucellosis actually had a net gain for both sectors and the adjusted cost per DALY averted was reduced to $19.1 per DALY averted. As a rule of thumb, interventions that cost less than US $150 per DALY averted are 'attractive' from a public health perspective, while those that cost US $25 per DALY averted are 'highly attractive'.

Integrated economic assessments have also been made for rabies with very different results. Most costs are associated with post-exposure treatment (83%) of which 60% are losses borne by the patient associated with seeking treatment; 15% of costs are associated with dog vaccination or population control and only 2% with livestock loss (Knobel et al., 2005).

Cleveland et al. (2006) draw attention to psycho-social burdens of rabies: studies in Tanzania found that people are more concerned about the potential threat from rabies than from malaria, despite the higher prevalence of the latter. When human cases do occur, the distressing clinical signs and invariably fatal outcome result in considerable psychological trauma for families, communities and health-care professionals involved with the victim (Cleaveland et al., 2006).

Of obvious and increasing relevance to zoonoses at the livestock-wildlife interface is the impact associated with spill-over of disease to endangered or otherwise valued wildlife. The same paper summarises the threats to wild carnivores (including lions, wild-dogs, Ethiopian wolves and seals) posed by rabies and canine distemper virus.

High burden of diseases does not necessarily imply high prioritisation for control. Evidence: high

Of course, disease burden is only one consideration in deciding the feasibility of control. FAO/WHO/OIE (2003) point out that as well as the disease being of importance, there must also be effective methods for stopping or reducing agent transmission; epidemiological features that allow good case detection; and good surveillance for measuring progress and providing information (FAO/WHO/OIE, 2003). An important feature that is propitious for eradication, as opposed to long-term management and control, is when there are no animal or environmental reservoirs for the disease; by definition zoonoses at the wildlife-livestock interface do not meet this criterion.

Several detailed frameworks have been developed to systematically assess the controllability or eradicability of diseases. These have not been applied to zoonoses at the livestock-wildlife interface but as a group, some individual diseases have been assessed. The International Task Force for Disease Eradication used specific criteria for assessing eradicability to consider 94 diseases, and reviewed 35 of them in depth. None of the zoonoses with a substantial livestock-wildlife interface are considered eradicable (Table 11.1)

Table 11.1: Eradicability of a disease in relation to transmission

	Eradicable	Some aspects eradicable	Not now eradicable	Not eradicable
All diseases	7	9	12	7
Zoonoses	2	3	5	2
Zoonoses with wildlife-livestock interface	0	3	3	1

The likelihood of successful disease control and the importance of zoonotic transmission are inversely correlated. Evidence: moderate

The papers reviewed covered several success stories in the control of diseases in developing countries. It is notable that most of these diseases did not involve multiple hosts and were amenable to relatively simple interventions. Smallpox and rinderpest, the only two diseases eradicated from the planet have limited host ranges (capable of maintaining the disease) as do measles and polio, which are other human diseases considered eradicable.

Among other infectious diseases of poverty for which control has been attempted, polio, lymphatic filariasis, trachoma and onchocerciasis, and guinea worm are considered successes (Solomon et al., 2009). These diseases have in common a limited host range and are either not vector-borne or have vectors with limited ranges susceptible to insecticides. Using a similar argument, Maudlin et al. (2009) suggest that the success of the 'Southern Cone' initiative to eliminate Chagas disease can be attributed to the fact that the only vector, *Triatoma infestans*, is an obligate human feeder and is restricted to human habitations. They believe that successful control may prove difficult to replicate elsewhere in Latin America where there are many different vector species, each with distinct feeding, infestation behaviour patterns and wild reservoirs.

11.2 Methods of limiting contact between livestock and wildlife

Limiting contact between livestock and wildlife is one of many control strategies

Zinsstag et al. (2007) point out that when zoonoses are maintained in animal reservoirs, with humans as incidental hosts, then control will usually require intervention at the animal level (Zinsstag et al., 2007). The same logic applies to wildlife zoonoses that also affect livestock.

The literature reflected different objectives: protection of livestock populations from zoonotic pathogens (e.g. cattle from tuberculosis in badgers); protection of people from zoonoses with reservoirs in livestock or wildlife (e.g. Chagas disease); protection of wildlife from domestic animal pathogens (e.g. wild carnivores from domestic dogs with rabies).

There are many different perspectives for viewing disease control; but none of the papers reviewed focused on limiting contact between livestock and wildlife. Veterinary services often consider four functions: preparedness, prevention, surveillance and response, and improving surveillance is currently a major focus of international effort. One systematic review looked at surveillance systems. A minority of the papers reviewed focused on outbreak response, but little attention was given to inter-species contacts.

We organize control around the environment, the hosts (wildlife and livestock), and the points of contact between them while recognizing that control programs can target several hosts. Given that the TOR of this review were to identify possible interventions (and outline associated governance structures) that could limit the interaction of the key wildlife species with domestic livestock and the potential economic and social impacts (at both state and household level) of those interventions, we focus on interventions aimed at limiting contact between wildlife and domestic systems. The next section will consider governance structures, and this section looks at specific interventions and evidence for their impacts.

Box 11.1: Synthesis of different interventions to manage zoonoses by reducing contact between livestock, wildlife and human hosts

Managing ecosystems and environment to promote health in wildlife
- a. Reducing opportunities for transmission around water and other resources
- b. Burning pasture to decrease tick populations
- c. Stocking densities and landscapes that allow livestock to avoid wildlife

Wildlife-focused programs
- a. Population control of wildlife
  - i. Elimination of populations
  - ii. Reduction of populations (culling; birth control)
  - iii. Replacement of populations by disease-free animals
- b. Managing disease in wildlife
  - i. Increasing host resistance (vaccinations, general health)
  - ii. Treating disease in wildlife
- c. Removing incentives for killing/trading wildlife
  - i. Protected areas, anti-poaching laws
  - ii. Regulation/prohibition of trade in wildlife
  - iii. Education and sensitisation
  - iv. Linking benefits to conserving wildlife (schools, natural resource use)

Reducing contact between livestock and wildlife
- a. Confining wildlife to conservation areas
- b. Improving biosecurity on farms and along the value chain, including wet markets

c. Controlling trade in wildlife

Livestock focused programs

a. Eliminating diseased individuals or populations
b. Husbandry practices to manage disease (all-in, all-out; Swiss depopulation; virus exposure)
c. Increasing host resistance (vaccines, general health, manipulation gut microbes)
d. Treatment

Human focused programs

a. Decreasing contact with infection sources
b. Meat inspection and hygienic slaughter
c. Increasing resistance of people (general health; vaccines; HIV treatment)
d. Treatment of people

Of the papers reviewed, few compared multiple control measures in a systematic way. Only a minority of the papers were original studies and most of these were from one context only. This makes it difficult to draw firm conclusions. Some general findings were:

- A lack of evidence on efficacy; generally better evidence in human focused programs than livestock focused programs than wildlife focused
- But even less evidence on economics, acceptability and sustainability.

Specific findings include the following:

Elimination of wildlife populations is probably not feasible. Evidence - Moderate

This has been the traditional strategy based on the concept that wildlife are a reservoir of disease. Over historical time scales, many species of animals have been eradicated from countries or regions (e.g. large carnivores from Europe) and a thought experiment suggests that if any of these had been reservoirs for disease, then eliminating the reservoirs would have also eliminated the disease. However, Wobeser (2002) in a detailed review of limited evidence concludes that total eradication of a wild population is probably impossible in the short term. A fundamental problem is that as population is reduced the effort required for further extirpation increases markedly (Wobeser, 2002).

Other studies suggest that a more nuanced concept of zoonoses dynamics is needed than the traditional 'hydraulic model', where wildlife act as a reservoir from which Infection ''spills over'' into livestock, with a more dynamic picture including substantial transmission both within and between alternative host species. Woodruffe et al. (2006) cite the case of suspension of cattle TB controls during a FMD outbreak in the UK which substantially delayed removal of TB-affected cattle, and was associated with a widespread increase in the prevalence of *M. bovis* infection in badgers, underlining the importance of two-way transmission (Woodroffe et al., 2006).

Reducing wildlife populations can reduce risk to livestock. Evidence strong

Reducing wildlife populations will theoretically reduce contact rates, possibly under a threshold necessary to sustain disease in the wildlife population. The concept of 'crowd diseases' requiring high populations and crowded conditions for persistence is well established in human medicine; for example,

in populations of less than 500,000 or so measles cannot establish. However, there is little empirical evidence for persistence thresholds in wildlife populations (Lloyd-Smith et al., 2005), and the relationship between transmission rates and host abundance may be nonlinear (Barlow, 1996, Smith, 2001).

Nonetheless, there is clear empirical evidence that wildlife population control can limit contacts and reduce disease risk. Wobeser (2002) summarises the longest running program of wildlife culling: poison baiting of bushtailed possums in New Zealand over the last half century in order to reduce transfer of tuberculosis to cattle. While short-term population reduction was not effective, sustained reduction of populations to around 22% of their starting level led to marked reduction of tuberculosis in possums and cattle (although not eradication).

Population reduction has been more effective in preventing disease entering an area than in eliminating it when established. For example, intensive wild carnivore reduction in advance of spreading rabies appears to have protected domestic animals in Argentina, Switzerland and Denmark (Wobeser, 2002).

However, short-term and un-sustained attempts to reduce population are often ineffective and can make things worse. Evidence: strong

Several papers from the well-studied research area of tuberculosis in cattle and badgers draw attention to the possible paradoxical effect of culling wildlife (Woodroffe et al., 2006, Carter et al., 2007).

- Repeated badger culling in the same area is associated with increasing prevalence of *M. bovis* infection in badgers, especially where landscape features allow badgers from neighbouring land to re-colonize culled areas
- The Randomised Badger Culling Trial showed that although culling badgers reduced cattle TB incidence where widespread (100 km^2) culling occurred, incidence was increased on neighbouring un-culled lands and in areas where culling was restricted to small patches of land (average, 5.3 km^2).

Improving biosecurity in wet markets and informal value chains is very difficult: Evidence: strong

The avian influenza pandemic has drawn attention to the difficulty of changing the informal value chains and wet-markets that predominate in developing countries in order to reduce contact between wildlife and livestock. Disease control in developed countries often relies on the ability to impose compliance on farmers. In developing countries this is very difficult as witnessed by a case study from Vietnam. A new law was introduced in 2005 prohibiting the movement and sale of wild and ornamental birds in cities, and this was followed by a significant decline in the scale of the wild bird trade in Hanoi. In 2007, 2 years after the law saw a 39.7% decline from 2000 and 74.1% decline from 2003. Nevertheless, 91.3% (21/23) of bird vendors perceived no risk of H5N1 infection from their birds, and the trade continues, albeit at reduced levels, in open market shops (Brooks-Moizer et al., 2009).

Fencing interventions are reasonably successful but expensive to maintain

Fencing is a logical measure to prevent contact between farmed and wild animals, and has been extensively used to protect standing crops from wildlife damage, domestic animals from predation,

livestock from disease, and wildlife from poaching and incursion. A recent review edited by Ferguson and Hanks (2010), brings together extensive research on the environmental, social and economic impacts of game and veterinary fencing in Africa and elsewhere. Their major findings include:

- Fencing is a major driver of habitat fragmentation, and it is this disruption caused by fencing and other forms of habitat fragmentation that constitutes the greatest threat to semi-arid savannas.
- Some species (such as blue wildebeest) and ecosystems (particularly arid and semi-arid) are highly susceptible to the disruption induced by fencing.
- Impacts of fencing on landscape epidemiology need to be re-visited. As well as preventing disease transmission, wildlife corridors designed to connect protected areas can serve as biological bridges for vectors and the pathogens they carry.
- Disease-free fenced areas are not essential to the production of safe livestock products; but current rules governing international trade mean they are often required.
- Sedentarization of pastoralists, with subdivision of land being enforced by fencing, leads to sharp declines of wildlife populations. This is likely to lead to reduced livestock-wildlife contact.
- Fences have denied some communities access to natural resources, marginalising natural resource-based livelihoods and escalating resource conflicts; at the same time, fencing has decreased stock-thefts and pressure on labour.
- There is no generic set of impacts for all types of fencing, as this will vary with the types of fencing, extent, aims and purposes of the fencing and the species, ecosystems and diseased management regimes involved.

Innovations may radically improve our ability to control disease even in poor countries. Evidence: weak

Although only indirectly relevant to the topic of interventions that could limit livestock-wildlife interaction, several papers (Matthews et al., 2006, Zhao, 2007, Paton et al., 2009) summarise promising technological innovations that may improve the ability to manage zoonoses at the livestock-wildlife interface in developing countries.

- Real-time RT–PCR for diseases such as FMD,
- Digital cameras and cellular phones make it possible to get distant advice on the interpretation of clinical signs and lesions,
- Infrared cameras can help screen stock for those with fevers or inflamed feet, possibly even from the air (Bashiruddin et al., 2006, Dunbar, 2008),
- Disposable chromatographic strip tests perform with similar accuracy to antigen detection ELISAs used in laboratories and are able to confirm the presence of antigens in serum or tissue within 20 minutes of sample collection, at the animal's side,
- Even more sensitive portable nucleic acid-based equipment,
- Air sampling devices in strategic positions to detect airborne virus emissions remotely,
- Better understanding of epidemiology (e.g. phenomenon of super-shedders) allowing better targeting of innovations.

Following the TOR, this chapter focuses on interventions to limit livestock-wildlife interactions. However, systems-based, integrated approaches to control are more likely to be useful than interventions aimed only at limiting livestock-wildlife interactions. Box 11.2 contrasts the actual situation with a scenario.

Box 11.2 An ideal integrated approach to managing a zoonosis with a livestock-wildlife interface compared with the actual situation

What if? scenario

- A handheld device can rapidly test for tuberculosis and distinguish between anthroponotic and zoonotic.
- Finding a zoonotic case triggers a response by the veterinary services, who then visit the household farm or trace back from milk vendor to farm of origin.
- Accurate animal tests allow cases to be confirmed in the herd and neighbours and at risk animals identified.
- An accelerated slaughter scheme is in place for in-contact cattle to reduce the cost of culling, compensation and destruction. Women are compensated for milk loss and men for animal loss.
- Once slaughtered, meat is tested or specially treated to ensure it is safe for consumption.
- Repeated infections in cattle trigger investigation of tuberculosis in wildlife.
- These lead to ecosystem-based approaches to limit contact between livestock and wildlife.
- Data from human and veterinary health services go to a central location and are regularly reviewed to adjust funding of zoonotic versus anthroponotic tuberculosis interventions.

Actual situation

- Tuberculosis cases are not routinely tested for zoonotic strains
- Human health and veterinary services are largely de-coupled
- Poor incentives for farmer compliance with disease control
- Little information on the role of wildlife in maintaining zoonoses
- No accurate information on the relative burden of zoonotic tuberculosis or appropriate control

11.3 Approaches to control and governance structures

Molyneux et al. (2005) provide a useful summary of changes in the global health environment over the last few decades (Molyneux et al., 2005). We expand this with other concepts from current literature and assess the implications for zoonoses with a livestock-wildlife interface in Table 11.2. Some of these issues are reviewed in more depth later in this chapter.

Table 11.2. Changes in the global health environment over the last decades

	Overall effects health sector	Zoonoses at livestock-wildlife interface
Economic development	South America and Asia continue to improve economic and human development indicators - less progress or stagnation in sub-Saharan Africa. Recent global economic shocks chill donor investments in health for	One of the most effective ways to control zoonoses at livestock interface. Conflict in some sub-Saharan African countries, Afghanistan (and more lately, North Africa and

	development.	the Middle East) are major challenge to the control of zoonoses.
Innovation and technology	Technological innovation around diagnostics, vaccines, therapy and surveillance	Technology an opportunity but little impact on the ground yet
Health security	Emergence of SARS and avian influenza and fears of terrorism	Brings attention to zoonoses which present a risk to rich countries and fosters One Health approaches
Decentralisation of health systems	Impact on health provision unclear: should make health more responsive to local needs but problems of co-ordination, governance and capacity have emerged.	Zoonoses are especially challenged as often multi-sectoral approaches are needed for effective control
Financing initiatives	Insurance, user fees, debt relief, World Bank loans, and debt relief and poverty reduction strategies	Should increase resource flows – impact on zoonoses unclear
Health related public-private partnerships	Bring substantial new finance and some demonstrate significant progress; leadership remains western.	Address specific issues and zoonoses have not been well represented to date.
Global burden of disease studies	Assessment of the global health burden leads to focus on high burden disease and reduction DALYs	Diverts attention and resources from neglected zoonoses
Philanthropists	Increasing involvement of large philanthropic foundations in health and development	Often focus on numbers and targets which tends to divert attention from zoonoses
Expansion in drug donation programmes		Only a few address zoonoses

Adapted from (Molyneux et al., 2005)

Top-down control campaigns have success (at least short-term) in the case of widespread and epidemiologically complex diseases in poor countries. Evidence: medium

Two major approaches to control are salient in the literature. Well-organized, centralized, vertical campaigns with highly motivated professional and massive funding were applied to diseases of high importance from the middle of the last century on. Military-style control typifies the traditional vector control programs used to control zoonoses such as Chagas and human African trypanosomosis as well as non-zoonotic diseases such as smallpox and onchocerciasis and the animal disease rinderpest. According to Gurtler et al. (2007) these were characterized by a centralized vertical structure with highly motivated professional spray workers and technicians, frequently with the time-limited goal of vector elimination, and massive funding (Gürtler et al., 2007). These approaches had successes, but in the case of vector-borne diseases with multiple hosts (HAT, malaria, Chagas in parts of South America) success has been more limited. The Onchocerciasis Control Programme in West Africa (1974 - 2002) was not only one of the most successful large scale operations ever carried out in the field of vector transmitted diseases it also demonstrated that a programme without any medical intervention could eradicate a disease, on a

scale of several countries over several decades. However, after roughly 30 years, there remains a doubt concerning the sustainability of these impressive results as all around the controlled area, blackflies are present and since stopping the spraying of insecticides, not only flies are coming back to reinvade the areas of population settlement but resistance has been detected to the drugs used to treat river-blindness in people (Rougemont, 2007, Osei-Atweneboana et al., 2007). The failure to eliminate the disease from defined regions led to more emphasis on control (suppression) and long-term sustainability through community-based broad social participation.

But community-based approaches also have poor success in controlling complex diseases. Evidence: moderate

Other papers report on the challenges in sustaining community-based control without external support. Pilger et al. (2008) reported on an intervention package to tackle sand-flies in a fishing community in Brazil. Humans and reservoir animals were treated, and premises sprayed with insecticide. At baseline, prevalence of tungiasis was 43% and 37% in control and intervention villages, respectively. During the 12-month study, prevalence of tungiasis dropped to 10% in the intervention village, while remaining at a high level in the control village. However, after one year, at the end of the study, in both communities the prevalence of the infestation had reached pre-intervention levels. They conclude that a long-lasting reduction of disease occurrence can only be achieved by the regular treatment of infested humans and the elimination of animal reservoirs. They speculate that while poverty remains, so will the disease and that substantial changes that only development is likely to bring (paved streets, cement floors, changes in the way people interact with environment and animals) are needed to reduce disease (Pilger et al., 2008).

Gurtler et al. (2007) use the example of Chagas control in northern Argentina since the 1980s. Control campaigns led to an immediate drop in disease, but in the absence of follow-up and the persistence of poverty, diseases came back in 2-3 years. Sustained, supervised, community-based vector control was an order of magnitude better in controlling disease than intermittent, minimally supervised community-based control. However, it did not eliminate disease (Gürtler et al., 2007).

A comprehensive study on rabies control in Chad showed that effective rabies control by vaccination could not be achieved by private funding only (Dürr et al., 2007). Researchers organized two pilot mass vaccination campaigns for dogs against rabies under equal conditions in N'Djaména, Chad. The first one was free of charge for the dog owners and succeeded in vaccinating 3000 dogs in five days, enough to break transmission of the disease. In the second campaign four years later, owners had to pay 3 Euros (enough to cover the costs of the campaign), and only 393 dogs were vaccinated which was not enough to break transmission. Lembo et al. summarises data from 14 mass vaccination studies in Africa which show coverage is typically very low and does not reach the 60% required to break transmission (Lembo et al., 2010).

Although most of the papers contrast community-based with centralized approaches, Holveck et al. (2007) point out that these are not mutually exclusive. The virtual elimination of river blindness, or onchocerciasis, from west Africa focused on an appropriate division of labour between central

governments and local communities. In this instance, large-scale vector control activities were carried out by the government while local communities managed the distribution of the anti-helminthic drug ivermectin to fight the disease. Ivermectin was made available through public-private partnerships and drug donations (Holveck et al., 2007).

Ability to measure disease burden has led to new emphasis on tackling the biggest problems first. Evidence: strong

Maudlin et al. (2009) describes how the 'Big Three' diseases of HIV, tuberculosis and malaria came to dominate the global health agenda. He attributes this to the landmark Global Burden of Disease study carried out by WHO/World Bank in 1995 and repeated in 2004, which for the first time estimated the burden of sickness, disability and death due to a range of important diseases. Together, AIDS, tuberculosis (TB) and malaria, are estimated to kill over six million people each year and make up 23.5% of the disease burden in Africa. With the Millennium Development Goals providing strong pressure to attain visible success, it seemed to made sense to tackle the biggest causes first. The Global Fund was created to finance the fight and to date has spent 21.7 billion USD in 150 countries to support large-scale prevention, treatment and care programs against the three diseases (www.theglobalfund.org). However, Molyneaux et al. (2005) argue that despite being undeniably big, HIV, TB and malaria, are unusually intractable for biological and epidemiological reasons and that "We are ignoring the low hanging fruit". They contrast successes in controlling chronic biologically stable infections with the difficulty of controlling malaria, TB and HIV/AIDS.

Several papers call for linking an integrated neglected disease strategy with the newly emerging global partnerships addressing HIV/AIDS, tuberculosis and malaria, in order to take advantage of the economies of scale that occur during the scaling up process of these global initiatives (Holveck et al., 2007).

Becoming wealthy is a successful method of controlling zoonoses and remaining poor is a major challenge to control. Evidence: strong

Whether comparing the same country over time, different countries, or different populations within a country, there is a clear and well-established positive correlation between wealth and health, and as the world has grown richer over the last decades and centuries the risk of infectious disease has declined by orders of magnitude (Levy et al., 2005). A telling case study from South Korea reviews the burden of zoonotic parasites (many with a wildlife interface) over the last century (Youn, 2009). Four trends emerge, which are likely to be applicable elsewhere:

1. Cyclo-zoonotic parasites (which require a human host) and sapro-zoonotics (common infections) have been declining in Korea over the last decades and centuries as humans seek and obtain better treatment and human health improves.
2. Parasites persist in vulnerable populations; parasites were at higher levels among the mentally ill.
3. In the general population, infection is increasingly localised into sub-groups with special risk factors (those who consume raw meat/fish and wildlife in the studies summarised).
4. While widespread parasitism is decreasing with economic development, new diseases emerge. These are mainly directly transmitted parasites such as *Cryptosporidium parvum.*

Integrated approaches improve management of zoonoses. Evidence: moderate

Integration is recommended at different levels. The simplest is linking inter-sectoral interventions. Several authors point out that programmes with similar delivery strategies and interventions - such as those for onchocerciasis, lymphatic filariasis, and soil-transmitted helminthiasis - could be managed on the same platform. Utzinger and de Savigny (2006) cite Hotez and colleagues who suggest that large-scale deployment of just four safe, efficacious, and orally administered drugs, i.e., albendazole, azithromycin, ivermectin, and praziquantel, to target over 90% of the neglected disease burden will result in additional health benefits. This is now being increasingly adopted by the large disease control campaigns. Of course any mass medication programme carries a risk of fostering resistance – this was not discussed in the literature and is an area where veterinary health may bring insights to human health.

At the same time Utzinger and de Savigny (2006) raise the concern that the nearly unique focus on large-scale drug administration reflects the lack of concern within the global health community for prevention strategies such as emphasising access to clean water, improved sanitation and hygiene activities that could serve as the backbone of multi-component integrated and sustainable disease control programmes.

One health approaches lead to better management. Evidence: weak/moderate

In fact, several of the papers reviewed call for more systems-based, holistic, multi-disease-based, integrated, inter-programmatic, and/or inter-sectoral approaches to disease control than the current medical model. However, this was mainly based on *a priori* logic rather than impact evaluations. Ehrenberg and Ault (2005) argue that many of the determinants of disease lie outside the purview of the health sector. These determinants include poor living conditions such as unsafe drinking water, inadequate sanitation and excreta disposal, poor drainage, inadequate solid waste removal, poor housing, and indoor air pollution (Ehrenberg and Ault, 2005). The fact that determinants lie outside the health sector is an argument for integrated approaches. Holveck et al. (2007) argue that integrated, multi-sectoral approaches can add value a) by decreasing costs through shared delivery and b) through contributing to non-health goals such as economic development, education, and environmental protection. They cite several examples from South America of multi-sectoral initiatives which were successful. Although conceptually attractive, the impacts are anecdotal and no comparison of costs and benefits with other delivery models is provided.

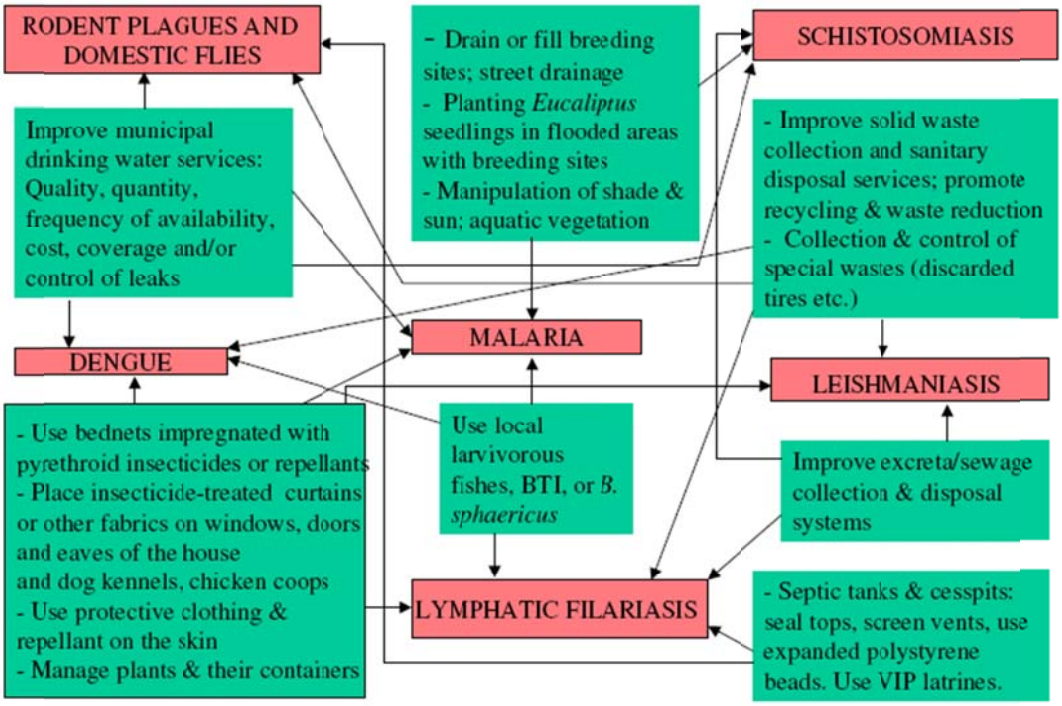
Ehrenberg and Ault (2005) propose a typology of nine different types of multi-sectoral interventions for neglected diseases.

1. Linking within the health sector – integrated chemotherapy
2. Environment and sanitation
3. Education and school health
4. Nutrition and food security
5. Economic development
6. Urban improvement

7. Agriculture (including forestry and animal husbandry
8. Primary and environmental care
9. Promotion of tourism

Figure 11.1 shows how combinations of health and non-health interventions can target multiple neglected zoonoses. Interestingly while four of these health problems are zoonoses, none of the suggested interventions are directed at domestic animal or wildlife reservoirs.

Figure 11.1. Multi-disease interventions for the prevention and control of vectors in urban areas – conceptual model.



(From Ehrenberg & Ault, 2005)

One Health has emerged in the last ten years, with SARS and avian influenza epidemics being major drivers. Interestingly, there is little reference to this approach in reviews and papers from the medical discipline.

Public health problems have biological, epidemiological, social, economic, political and environmental dimensions. This does not mean that they are impossibly complex. Sometimes an effective solution will be conceptually very simple, vaccination being an example or routine boiling of milk. However, consideration should be given to all aspects before opting for a solution or package of solutions and attention should be paid to trade-offs, paradoxical effects and externalities.

Programmes are in advance of evidence. Evidence moderate

The last decade has seen major initiatives around health (avian influenza control; global fund for health; public private partnerships around diagnostics, vaccines and delivery; Roll back malaria, Stop TB, Presidents fund for HIV; the USAID Predict/Prevent/Respond) but little research has emerged from these. At the end of the last century the Global Forum for Health Research coined the phrase 10/90 gap to capture the discrepancy between health research spending and disease burden (a small amount of the world's resources for health research applied to the health problems of low- and middle-income countries, where most of the world's preventable deaths occurred). Molyneaux et al. (2005) states that the real proportion of funding for targeted research that will directly affect the outcomes to achieve the MDGs by 2015 is probably 1/99. This reflects the time to 2015 on the one hand and the bias towards high-end research with the unlikelihood that science can deliver any products by 2015 which can affordably address the needs of the majority of the poor.

The disconnect between research and delivery is a possible cause of the neglect of tropical zoonoses and the failure of medical programmes to fully and sustainably reach their objectives.

Conclusion

Of the papers reviewed, none focused specifically on zoonoses with a livestock-wildlife interface as a category of disease; around half covered management of zoonoses or neglected diseases, while the remainder dealt with specific diseases or interventions. Most of the papers reviewed deal with the management of zoonoses by interventions targeted to or including livestock and wildlife populations, but passing mention was made of the role of livestock and wildlife as sentinels for human disease. Apart from one very rich (but non peer-reviewed) collection of papers there was little detail on interventions to reduce contact between livestock and wildlife and impact assessments were too sketchy to allow any coherent synthesis of social and economic impacts or governance aspects.

This gap was partly filled by providing more details on broader aspects of control of zoonoses involving livestock and wildlife. Historically there has been an evolution from laissez faire, to suppression of wildlife (nineteenth and early twentieth century), to well organised campaigns for specific diseases (mid-twentieth century), to greater involvement of communities (late-twentieth century), to understanding of disease burden and focus on high burden disease (early twenty-first century), and in parallel, to renewed interest in integrated and multi-sectoral approaches.

A broad conclusion is that, management of zoonoses with a livestock-wildlife interface is more challenging than management of other zoonoses or non-zoonotic diseases. Where wildlife and animals have an important role in disease maintenance then control usually requires or benefits from interventions directed at the animal host. The relative involvement of humans, livestock and wildlife in disease transmission is variable, dynamic and often unknown. As a consequence, control often fails because of lack of understanding of the importance of both livestock and wildlife in maintenance of disease.

Key research gaps

- Risk-based management: management strategies based on an epidemiological and objective understanding of risk and targeted to the actors and actions that are key to risk management.
- Impact assessment of current strategies to generate high quality evidence on firstly the technical effectiveness of management strategies, and secondly, the economic, social, environmental and political impacts and sustainability.
- Adapting innovations: action research to adapt technological, organisational and social innovations for better managing disease to developing country contexts.

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Annex 1. Assumptions around DALY calculations

In order to estimate the importance of zoonoses in contributing to the Global Burden of Disease we had to make some assumptions about the proportions of different diseases that are zoonotic. In many cases, information was lacking and we took 'best estimates' from the literature and our opinion. Given good evidence of widespread under-reporting of zoonoses and the absence of important zoonoses from the Global Burden of Disease (rabies, cystic echinococcosis, cysticercosis) we preferred to be liberal in our estimates.

Diarrhoea: There is much uncertainty over the proportion of the burden of diarrhoea that is zoonotic. Zoonoses are common causes of diarrhoea and food-borne illness and a significant proportion of these illnesses are caused by food-borne transmission of the pathogens (40-90+% (Cressey and Lake, 2005); direct contact, and consumption of water or fresh produce contaminated by animal faeces are other important routes. Worldwide, bacterial zoonotic infections are the most common cause of reported food-borne cases of human diarrhoea (Bloomfield et al., 2009). The importance of food in the aetiology of diarrhoea is not known but various estimates range from 30% to 70% (Schlundt et al., 2004). We assumed that 50% of the diarrhoeal burden is zoonotic. As the non-diarrhoea burden of food-borne disease is estimated as equivalent to the diarrhoeal burden, this is likely to be an under-estimate for total burden.

Tuberculosis. There is little detailed information on zoonotic tuberculosis but prevalence varies from 0-25% (Cataldi and Romano, 2007). Given that the disease is believed to be greatly under-estimated and was historically an important cause of human tuberculosis we estimate 10% of tuberculosis in developing countries to be zoonotic.

Tetanus is a zoonosis that is directly transmissible between animals and humans by bite injuries, a disease common to animals and humans (contamination of wounds or perinatal tetanus), and a disease where animals contaminate the environment by shedding spores in their faeces. Although much of the human burden from tetanus is from contaminated environment, we consider tetanus to be a zoonosis.

HIV arose from several crossover events involving sooty mangabeys and chimpanzees, probably in the 1930s in west central Africa (Wolfe et al., 2005). We classify it as a disease recently emerged from animals and not as a zoonosis, as now the disease is maintained through human-to-human transmission.

Bancroftian filiariasis, present in Africa, Asia and South America has no animal reservoir. Brugian filiariasis present in South East Asia and South India has an animal reservoir and is estimated to account for 10% of the total burden (King and Freedman, 2000).

Dengue we consider a zoonosis as the sylvatic (monkey) cycle is well documented. Currently most disease is transmitted between humans and insect vectors, but the presence of a sylvatic cycle has implications for control.

Japanese encephalitis is a mosquito–borne viral infection of horses, pigs, and humans. It is found throughout the temperate and tropical regions of Asia. Humans and horses appear to be dead–end hosts. Cattle are often infected in endemic regions, but do not become ill or develop viremia. Swine develop clinical signs and also amplify the virus. We consider Japanese encephalitis to be a zoonosis.

Amongst 15 well-recognised *Leishmania* species known to infect humans, 13 have zoonotic nature, which include agents of visceral, cutaneous and mucocutaneous forms of the disease in both the Old and New Worlds. Furthermore, for the two species considered as having an exclusive or predominant anthroponotic transmission pattern, i.e. *L. donovani* and *L. tropica*, the presence of animal reservoir hosts has been indicated in several endemic settings. Hence we consider all leishmaniasis as zoonotic (Gramiccia and Gradoni, 2005).

Chagas disease is a zoonosis (or an anthropozoonosis) caused by the flagellated protozoan parasite *Trypanosoma cruzi.*

Schistosomiasis: the species responsible for most human infections are *Schistosoma mansoni,* which is endemic throughout Africa and South America, *Schistosoma haematobium,* which also occurs in Africa and the Middle East, and *Schistosoma japonicum,* which causes schistosomiasis in China, the Philippines and Indonesia. Humans are the reservoir hosts for *S. mansoni* and *S. haematobium* but primates are also susceptible and may have a role in epidemiology. A range of animals including sheep, cattle and horses act as natural definitive hosts for *S. japonicum* and hence this parasite can be considered truly zoonotic. We consider 10% of the burden of schistosomiasis to be zoonotic, a conservative estimate given the lack of information.

Table A1 Estimates of zoonotic component of diseases appearing in the Global Burden of Disease

Zoonotic diseases and diseases recently emerged from animals	
Diarrhoea	50% zoonotic
Tuberculosis	10% zoonotic in poor countries
Tetanus	All zoonotic
HIV	Emerging
Trypanosomiasis (African)	All zoonotic
Chagas disease	All zoonotic
Schistosomiasis	10% zoonotic
Leishmaniasis	All zoonotic
Lymphatic filariasis	10% zoonotic

Dengue	All zoonotic
Japanese encephalitis	All zoonotic