Rev. sci. tech. Off. int. Epiz., 2004, **23** (2), 467-484

Ecological sources of zoonotic diseases

J. Slingenbergh [(1)], M. Gilbert [(2)], K. de Balogh [(1)] & W. Wint [(3)]

(1) Animal Production and Health Division, Food and Agriculture Organization of the United Nations, Viale delle Terme di Caracalla, 00100 Rome, Italy
(2) Biological Control and Spatial Ecology, Free University of Brussels, avenue F.D. Roosevelt 50, 1050 Brussels, Belgium
(3) Environmental Research Group Oxford, P.O. Box 346, Oxford OX1 3QE, United Kingdom

Summary

Although of zoonotic origin, pathogens or infections posing a global threat to human health such as human immunodeficiency virus, severe acute respiratory syndrome or emerging influenza type A viruses may actually have little in common with known, established zoonotic agents, as these new agents merely underwent a transient zoonotic stage before adapting to humans. Evolution towards person-to-person transmission depends on the biological features of the pathogen, but may well be triggered or facilitated by external factors such as changes in human exposure. Disease emergence may thus be depicted as an evolutionary response to changes in the environment, including anthropogenic factors such as new agricultural practices, urbanisation, or globalisation, as well as climate change. Here the authors argue that in the case of zoonotic diseases emerging in livestock, change in agricultural practices has become the dominant factor determining the conditions in which zoonotic pathogens evolve, spread, and eventually enter the human population. Livestock pathogens are subjected to pressures resulting from the production, processing and retail environment which together alter host contact rate, population size and/or microbial traffic flows in the food chain. This process is illustrated by two study cases:

a) livestock development in the 'Eurasian ruminant street' (the area extending from central Asia to the eastern Mediterranean basin) and the adjacent Arabian peninsula

b) poultry production in Southeast Asia.

In both scenarios, environmental factors relating to demography, land pressure and imbalances in production intensification have led to an unstable epidemiological situation, as evidenced by the highly pathogenic avian influenza upsurge early in 2004, when the main outbreaks were located in areas which had both large scale, peri-urban commercial holdings and a high density of smallholder poultry units.

Keywords

Agricultural intensification – Animal production – Disease ecology – Ecological change – Emerging zoonosis – Epidemiology – Population increase – Urbanisation.

Introduction

Disease emergence and zoonotic disease agents

Zoonoses are defined as infectious diseases that can be transmitted naturally between humans and wild or domestic animals. These diseases are particularly important in the context of emerging infectious diseases of humans as the majority of these are of zoonotic origin: a comprehensive review by Cleaveland *et al.* (6) identified 1,415 species of infectious organisms known to be pathogenic to humans, including 217 viruses and prions, 538 bacteria and rickettsia, 307 fungi, 66 protozoa and 287 helminths. Out of these, 868 (61%) were classified as zoonotic and 175 pathogenic species were considered to be associated with emerging diseases. Of this group of 175 emerging pathogens, 132 (75%) were zoonotic.

The definition of zoonoses actually fits a wide array of epidemiological situations. Some pathogens are largely confined to animal reservoirs – human cases are infrequent or represent dead-end infections (e.g. anthrax, rabies, West Nile and Nipah/Hendra viruses), whereas others are well-established in both animals and humans (e.g. bovine tuberculosis, salmonellosis). Others present an intermediate situation with animals as the main hosts, but with occasional outbreaks occurring in humans, but with a transmission chain leading to eventual extinction (e.g. monkeypox, Hanta, Lassa and Ebola viruses). There are also some zoonotic agents that gradually adapted to human-to-human transmission and are now readily transmissible between humans (human tuberculosis). Finally, there are pathogens of animal origin that suddenly appear in human populations (human immunodeficiency virus [HIV], influenza type A and, probably, severe acute respiratory syndrome [SARS]).

The more classical zoonotic diseases may still be classified as emerging diseases, but only if an emerging zoonosis is defined as 'a zoonosis that is newly recognised or newly evolved, or has occurred previously, but shows increases in incidence or expansion in a geographic, host or vector range. Some of these diseases may further evolve and become effectively and essentially transmissible from human to human' (9, 45). An emerging zoonosis may thus be an existing infection or disease which appears again or invades new territories. Many diseases, zoonotic or otherwise, which had once been controlled in many parts of the world, have started to re-emerge: cholera, tuberculosis, dengue fever, yellow fever and malaria. In the United States of America (USA) the infectious disease mortality rate increased at an annual rate of 4.8% between 1981 and 1995. This compares to a decrease of 8.2% between 1938 and 1952, the period when antibiotics and immunisation became commonplace (7).

Zoonotic diseases have relatively little impact on human health when compared to major diseases such as influenza (flu), measles, smallpox, diphtheria, or HIV/acquired immune deficiency syndrome (AIDS). It is, however, increasingly clear that most of these diseases started out as zoonotic (12), and the aetiology of the pandemics that have occurred during the 20th Century tend to support the notion that emerging diseases in humans originated directly from animal reservoirs rather than gradually evolving from known and existing zoonotic agents. What the major influenza type A epidemics of 1918, 1957 and 1968 all had in common was that a novel pathogen was suddenly seen to circulate in the human population. Indeed, the level of susceptibility of humans to these new strains may have dictated the size of the human influenza epidemic (44). The human immunodeficiency viruses (HIV type 1 and 2) have long since abandoned their zoonotic status and despite the fact that HIV viruses may have been present for many years before assuming pandemic proportions, there was no sign of development towards an equilibrium stage. Instead, there may have been a somewhat delayed visible emergence because of the specific structure of the host contact network (scattered rural villages) in the early stages of HIV evolution (31).

It appears, therefore, that particular attention should be paid to those pathogens which may undergo a transient, perhaps hardly discernable zoonotic stage, characterised by haphazard outbreaks that may go largely unnoticed by local health authorities, and then adapt and shift to humans as their main hosts. In the latter stages of this process, environmental change may increase the basic reproductive number (R_0) leading to longer transmission chains, which provide an opportunity for the pathogen to adapt to human hosts, and thus for the disease to emerge (3). Whilst the pace of evolution towards full human-to-human transmission is strongly influenced by the biological features of a pathogen relating to genetic shift, drift or quasi-species behaviour, external factors may be equally important (38).

Factors affecting the emergence of zoonotic diseases

Rather than concentrating solely on zoonotic disease agents, the conditions affecting disease emergence in general will be considered first, followed by an examination of factors which may explain why and how pathogens found in animal reservoirs become progressively introduced into human populations and evolve exclusively into either a human or a zoonotic pathogen.

Factors associated with the emergence of pathogens in human, wildlife and domestic animals have been explored by Morse (32), Schrag and Wiener (38) and more recently by Daszak *et al*. (10), Dobson and Foufopoulos (13) and Cleaveland *et al*. (6).

Schrag and Wiener (38) argued that changes in pathogen and/or host ecology are primarily responsible for the majority of emerging diseases and that those resulting from evolutionary changes alone are comparatively rare. 'Ecological changes' embrace a number of very different processes under the same umbrella: changes in agricultural practices, urbanisation, globalisation or climate change. The latter is a factor of growing concern as it may affect the areas where primary agricultural production takes place, alter vector distribution and abundance, change the migration patterns of birds and other wildlife, and affect the survival time of pathogens outside the host (32, 38). A common feature of all these processes is that they are largely a consequence of human activity. The title of Schrag and Wiener's paper 'Emerging infectious disease: what are

the relative roles of ecology and evolution?' could actually be substituted by 'Emerging infectious disease: what are the relative roles of human activities and evolution?' In recent years, it seems that humans have probably been responsible for many emerging diseases through creating and maintaining the conditions for existing pathogens to enter, persist and develop in new host populations (13).

The reason that most emerging diseases are reported to be related to ecological changes rather than evolution may also be a matter of time-scale: environmental change may have been the main factor influencing disease emergence over the last few decades because such changes have been fast, whilst evolution has played a major role in the emergence of diseases over the longer term (12). This does not, however, prevent evolution from playing a role in the short-term adaptations of pathogens to human hosts (14, 23), and assessing the respective roles of environment and evolution separately is therefore unwarranted, as they are closely intertwined. One can simply view emerging diseases as an evolutionary response to (anthropogenic) environmental change.

From another perspective, disease emergence is the result of two sequential processes:

a) the adaptation of a pathogen to a new host: as elegantly demonstrated by Antia *et al*. (3), pathogen strains entering a new host population may initially have an overall reproductive number of less than one ($R_0 < 1$) that leads to the extinction of the pathogens, but prior to extinction, some may evolve and increase their virulence to give $R_0 > 1$, allowing them to persist and spread into a new host population

b) the spread of the pathogen into the new population.

Different questions relate to each of these processes. How did a pathogen enter a human population? What are the characteristics of potentially invasive pathogens? These questions relate to the adaptation of a pathogen to a new host, and can be addressed by comparisons between emerging diseases and invasive plant and animal species. Invasive alien species are defined as species introduced outside their natural, past or present, distribution (42). Generally introduced by human activities, these species have adverse effects on indigenous fauna and are now considered to be the second most important cause of the global biodiversity crisis (43). They are also recognised as a clear threat to ecosystems, habitats or species, with severe economic and environmental consequences (42).

Questions concerning emerging diseases and invasive species essentially address how an organism adapts to a new environment and then spreads (31, 37). In biological invasion ecology, it has long been recognised that successful invaders are generally those species able to maximise fitness in changing environments, i.e. r-strategists (organisms can be classified according to their strategies to maximise their fitness: in a predictable environment, it pays to invest resources in long-term development and long life [K-selection] whereas in a risky environment, it is better to produce as many offspring as quickly as possible [r-selection]). Such organisms are generally characterised by a short generation time and high numbers of offspring and usually have efficient ways of dispersing to new habitats (26), e.g. weeds (as opposed to trees), or generalist herbivores (as opposed to specific herbivores). Although not expressed in such terms, emerging disease pathogens are acknowledged to follow approximately the same pattern (6), i.e. most successful emerging pathogens are ribonucleic acid (RNA) viruses (r-strategists, that are small, with a short generation time, and for which minor changes in the genome may change host-specificity), whereas helminths are considered to be unlikely candidates to jump host-species barriers (K-strategists, with longer generation times, and higher host-specificity). Likewise, endemic diseases are generally linked to a static environment whilst epidemic agents are more usually associated with changing ones.

Following introduction and initial 'colonisation', the spread of disease within the new host population will determine the success of an emerging pathogen in the newly invaded host. Factors facilitating the spread into new populations are not specific to emerging diseases and apply equally to any epidemic disease. As developed by May *et al*. (31), the spread mainly depends on the overall reproductive number being higher than one, which is subject to change as a consequence of both a better adaptation to the host and changes in the spatial structure of the host population (e.g. changes in the geography of human population may have contributed to drive the R_0 above one in the emergence of HIV/AIDS in Africa) (28, 31).

Standard epidemiological models predict that the size of an epidemic relates to the size of the susceptible population. If one thinks of the susceptible population as a network of susceptible hosts, then this general statement can be refined by taking into account the spatial structure of social groups (28). For diseases which trigger lifelong immunity, local extinctions are observed, and if one considers a network where each node is a group of hosts, i.e. a village or city, the analogy with metapopulation can be used to explore the spatial dynamics of diseases (25). If the size of the epidemic is closely related to the number of the susceptible hosts, then using the metapopulation analogy, it is also related to the size of the host metapopulation (in the rest of this text, we will use the term metapopulation to mean a set of host-subpopulations connected by possible microbial traffic). Therefore, in a given landscape for a given disease affecting a given host species, the risk that a disease will assume epidemic proportions can be assessed on the basis of the size and structure of the host

metapopulation, and the level of isolation of each sub-population. Naturally, this also applies to the spread of emerging diseases. For example, the current global network of human populations meets all the basic requirements for a novel disease agent to turn into a pandemic.

The factors cited in the literature as contributing to the emergence of livestock diseases and associated zoonotic infections may be assigned to four main epidemiological risk categories (Table I):

– production intensification (which determines production structure and the local biosecurity level)

– the host metapopulation, i.e. the 'static' environment in which disease spread is taking place

– the transmission pathways other than those within the animal host populations, comprising the entire food chain (from feed, to live animals, processing, marketing/distribution, food preparation and consumption)

Table I
Factors influencing the spread of livestock (including zoonotic) diseases, categorised according to four main epidemiological domains

Factors	Husbandry [a]	Host metapopulation [b]	Transmission pathways [c]	Pathogen characteristics [d]
Human demography	x	x	x	
Technological progress	x	x	x	
Economic development	x	x	x	
Land pressure	x	x	x	
Animal movement and trade	x	x	x	
Urbanisation	x	x	x	
'Peri-urbanisation' of livestock	x	x	x	
Veterinary services/campaigns	x	x	x	
Wildlife contacts (including birds and rodents)	x		x	x
Farming systems/intensification	x	x	x	
Agro-ecological zones		x		x
Dietary habits/demand elasticity			x	
Waste management	x		x	
Hobby/cultural animals		x		
Infrastructure	x		x	
Seasonality in livestock management	x	x	x	
Population structure (age, sex, etc.)	x	x	x	
Phylogeography/gene flows:				
Pathogens				x
Animals				x
Globalisation:				
Mobility of people			x	
Trade and traffic		x	x	
Climate change:				
Primary production location	x	x	x	x
Vector distribution/abundance		x		x
Migration pattern wildlife/stock		x	x	
Pathogen survival outside host			x	x
Distribution of rural population	x	x	x	

a) Animal husbandry factors pertaining to feeding, breeding, housing/animal movement management, and health protection practices are together responsible for the production structure
b) Metapopulation, the 'static' animal host environment in which the disease spread is taking place, made up of the number and size of holdings, the spatial structure (clumping) of production units; the metapopulation fixes the possible microbial traffic within the host population
c) Pathways external to the host population are also important and include the flow of pathogens originating from live hosts passing into the food production-processing-distribution chain, germs in animal waste products contaminating open land and water resources, and the spread of pathogens through giving feed of animal origin to live animals. Pathogens are also dispersed through food preparation and consumption and can also spread to water bodies via the sewage system
d) Factors relating to the innate biology of the pathogen: reproductive (r/K) strategy, host range, mode of transmission, virulence and infective period

– the innate ecological characteristics of the pathogen (virulence, host-range, infective period, vector distribution, reproductive strategy).

Zoonotic infections originating from wild animal reservoirs are generally associated with anthropogenic forces involving high contact rates with the wild animal host (e.g. rodents can be host to several zoonotic diseases) or biological invasions by vectors (e.g. West Nile virus, Lyme disease) or by the pathogen itself (e.g. anthrax spores).

Many zoonotic diseases and human pathogens result from our intimate contacts with domesticated animals, a process that has continued since the early days of domestication. The capture and controlled breeding of the major animal domesticates was part of a suite of transformations in human society known as the Neolithic transition. This is best described in the archaeological record of the Near East, particularly the Fertile Crescent, which witnessed the development of the first agricultural economy in the world, starting more than 10,000 years ago. The biological products of this remarkably innovative region are now widespread and include plants such as barley, the wheats, lentils, and four of the major domestic livestock species (in temporal order: goats, sheep, pigs and cattle) (Fig. 1). It is likely that 'crowd diseases' such as smallpox, measles, rubella and pertussis emerged following the advent of agriculture and associated settlements. The domestication of farm animals enabled surplus food production, and this paved the way for human population clusters, and the first urban centres, which were large enough for these infections to be maintained (1, 12).

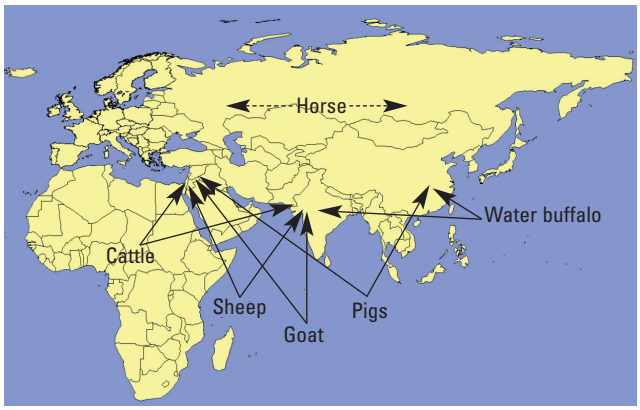

Fig. 1
Approximate locations of suggested domestication centres for sheep, goat, cattle, pig and water buffalo from 10,000 BP onwards
Horse domestication probably occurred in more diffuse locations over a longer period of time (20)

Identifying the processes underlying the transformation of livestock production and its intensification are thus central to an understanding of the forces affecting disease emergence and spread. For example, in large areas of the developing world, the majority of livestock production still takes place in extensive systems, varying from pastoral livestock kept in drylands and other harsh environments, to free ranging, scavenging smallstock in backyards of village dwellings characteristic of the humid, perennial cropping areas. In most areas where there is sufficient rainfall, but where technology levels are low, inputs are scarce and markets are poorly developed, the integrated crop/livestock system remains the most efficient and sustainable means of increasing off take from a fixed land base (30).

However, this resource driven pattern has been supplanted in some of the densely populated patches of the moister agro-ecological zones where population pressure has triggered a progressive intensification of agriculture (4, 35), most notably during the 20th Century. This is best illustrated by the Green Revolution that took place in Asia during the sixties and seventies and which led to a successful and rapid technology driven increase in crop productivity, made possible by improved seeds, fertilisers, pesticides, irrigation and other inputs.

Similarly, it can be argued that the current 'livestock revolution' is a response to an increased demand for the production of animal protein, e.g. eggs, milk and meat (8, 11). However, whilst crop production levels are constrained by the physical limits of the available land resource, no such limit applies to modern livestock industries that can be detached from the land where feed crops are grown. Unlike the Green Revolution, therefore, an important feature of the intensification of the livestock sector is the severance of the traditional links between the amount of available local land and feed resources. The location of livestock production and the associated processing industries has shifted to be close to markets that supply, and are usually close to, urban centres.

As a consequence, major geographical imbalances – in terms of concentration of production – can develop. This is best demonstrated by the recent history of the poultry sector. Most of the demand for poultry protein stems from the emergence of a global middle income class living in the megacities of transition economies and developing countries. This has triggered the establishment of large scale peri-urban poultry industries that supply meat and eggs to the urban centres of Latin America, the Near East, North Africa, East Asia and, also, South Asia (29). Only in sub-Saharan Africa has this development yet to become firmly established.

Extrapolating from the spatial patterns of the livestock systems discussed above, and guided by events in the world poultry sector, four distinct, sequential, albeit overlapping, stages in the intensification of livestock production may be distinguished.

a) Low input, low output production systems typical of pastoral communities and remote villages beyond the reach of the urban markets and in which animal production is characterised by a rich diversity of livestock well adapted to environmental stress. The subsistence farmers keep ruminants, pigs, backyard poultry or other small stock and today they can be found in large areas of the developing world where population pressures are low.

b) Specialised, commercial production units that are more developed than integrated crop/livestock farms and that generate a surplus for the market. This involves the creation of production environments free of OIE (World Organisation for Animal Health) List A diseases (34), genetic selection of animals for higher yields and more efficient feed conversion, provision of balanced nutrition, and health care. Large numbers of animals are housed in confined feeding operations, mostly located in a rural setting, though processing and marketing operations tend to be moved nearer to the urban centres.

c) Producers find themselves in areas of high land pressure, feed is brought in from outside and both animal production and processing become integrated in a vertical chain. Industrial scale production, 'harvesting', processing and marketing thus form one continuum. The process is driven by automation and standardisation, with bulk production of protein commodities to supply the regional market, or to export to other countries.

d) Animal productivity plateaus and feed conversion rates reach their limits in all modern production units, irrespective of the geographical setting. Production and processing are driven by multinational enterprise and tend to shift to areas and countries where grain is relatively cheap – often where agricultural land is plentiful, such as in southern Brazil, the USA Corn Belt or the Ukraine – or to coastal port areas which can sustain high levels of imports by ship (Southeast Asia).

Thus, with the advent of modern livestock production, (particularly of poultry, but also of swine), the local enterprises with expertise in the exploitation of economies of scale have little problem meeting upsurges in protein demand from the growing number of megacities in the world. A consequence of this rapid intensification is, however, that the traditional smallholder producers have less of a role to play. This chain of events also explains why animal populations keep expanding in the most populous places on earth while most of the income generated from livestock remains concentrated in rich countries and a few transition economies (Fig. 2).

The intensification process can be illustrated by pig production dynamics in the People's Republic of China. According to the size of the pig holding, farmers may be grouped as follows:
– backyard production (one to five pigs)
– specialised (5-1,000)
– industrial (> 1,000).

For the country as a whole, most production remains in backyard units, but intensification matches the exponential increase in demand for pig meat (Fig. 3). The change is most prominent near urban centres.

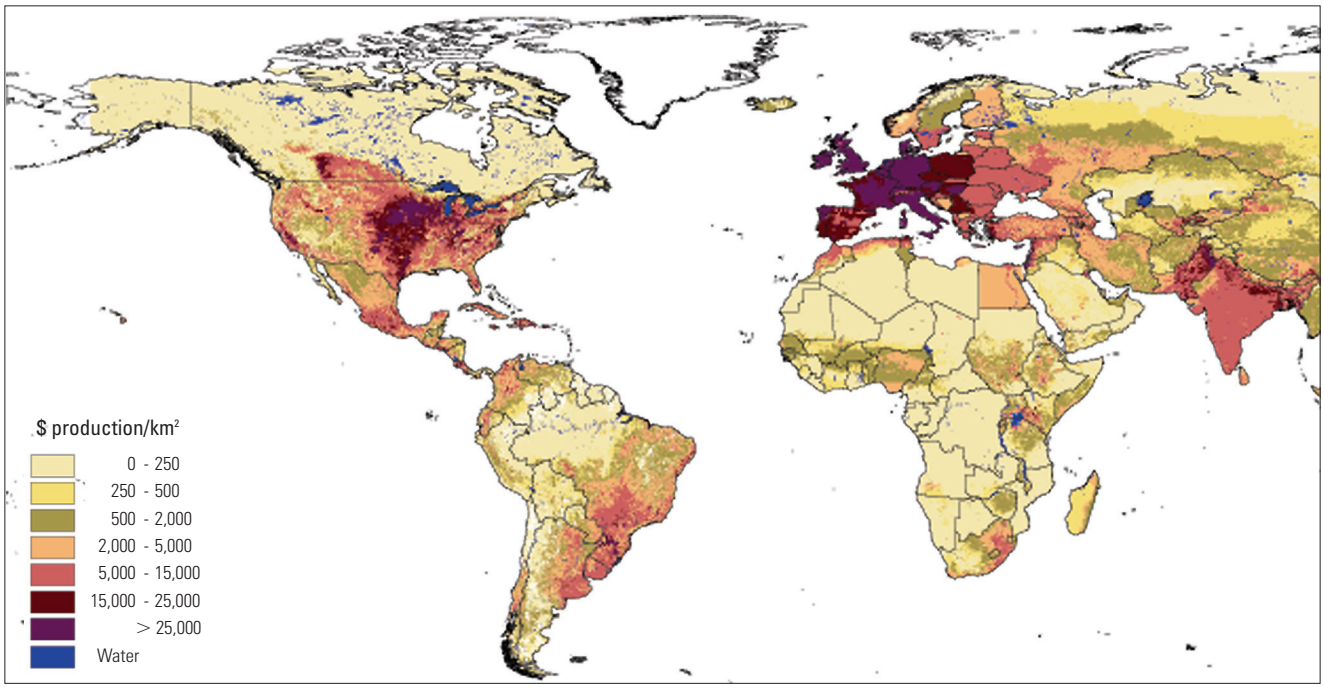

Fig. 2
World livestock farm income generation for 2002 (all continents except Oceania) (16)

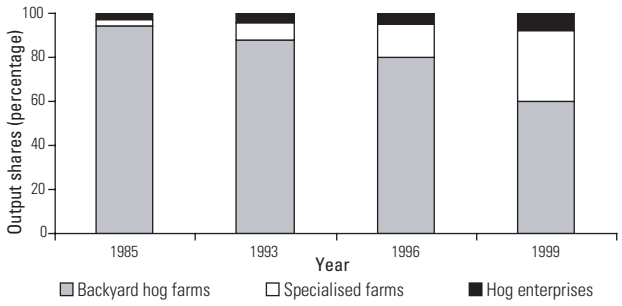

Fig. 3
The evolution of the pig production structure in the People's Republic of China from 1985 to 1999 (40)

The 'livestock revolution', supported by advances in biotechnology and life sciences (aggregation of production, biosecurity, vaccination, multiple stage production systems), coupled with 'global change' events and associated risk factors, has thus profoundly altered the conditions in which livestock diseases may emerge, evolve, spread, and eventually enter the human population. If we consider that many important human diseases may have emerged as a consequence of changes that took place during the Neolithic era, we have to also accept the reality that new diseases may emerge in response to the profound changes taking place today (39).

Hence, the remainder of this review considers how ecological changes may affect patterns of disease in two contrasting production environments and geographical areas:

a) the 'Eurasian ruminant street' and the Arabian Peninsula, with extensive ruminant livestock and localised, modern poultry and dairy plants

b) the monogastric livestock sector in East Asia, mainly with peri-urban, industrial poultry and pig production which may be pushing the very high number of smallholders out of the market.

Disease ecology and emergence: the Eurasian ruminant street and the Arabian Peninsula

The area extending from central Asia to the eastern Mediterranean basin, and including the Arabian Peninsula, forms an area of particular interest as it presents an environment where disease spread frequently goes unchecked. A number of zoonotic and other diseases are believed to be on the increase in the area, particularly in sheep, e.g. peste des petits ruminants (PPR), sheep pox, bluetongue (BT), Rift Valley fever (RVF), old world screwworm (OWS) as well as other forms of myiases and foot and mouth disease (FMD). The 'Eurasian ruminant street' is formed by a high ruminant livestock density area stretching from southern Asia to the Mediterranean basin, creating a narrow east-west connection just south of the Caspian Sea in Iran (Fig. 4), and acting as a corridor for the spread of pathogens (e.g. FMD) (17). In the harsh and often dry environments of Central Asia, livestock husbandry forms a pivotal role in the economy. Iran has over eighty million small ruminants and is believed to play an active role in the international livestock trade, with animals imported from Turkmenistan, Afghanistan and Pakistan and exported to countries to its west. The local animal movement is considerable, with seasonal contraction and expansion as transhumance patterns respond to grazing availability (Fig. 5).

Livestock production in the Arabian Peninsula has been extensively reviewed in a recent report from the Food and Agriculture Organization (FAO) (19). Pastoral livestock production mainly involves sheep and, to a lesser extent, goats and cattle. Sheep production in the rangelands has intensified through the use of crop residues from expanding cultivation and increasing use of supplementary feeds. The main market for live animals in the region is the Gulf States, especially Saudi Arabia and Kuwait, where the principal demand is for sheep to use in religious festivals. Over the past half century, completely new methods of production have been introduced, though to relatively small areas, and traditional forms of livestock production have been adapted to changing circumstances. Feedlot ruminant production has, however, been expanding in the region for decades; there has been increasing use of imported animal feed concentrates (33), and widespread subsidies for these grain imports (animal feeds) have encouraged the processes of intensification and modernisation.

Historically, traditional livestock movements in the Arabian Peninsula were related to one of three primary activities: trade and the passage of caravans between markets; stock for sale or slaughter at markets near permanent settlements; and seasonal transhumance/nomadism in response to rainfall and fodder availability. There is much evidence to suggest that seasonal and tribal movement patterns of traditional nomadism and transhumance have been transformed by oil wealth and the various changes in livestock production. Vehicles are widely used to move animals and transport feed and water supplies. Modern telecommunications provide access to information on rainfall, rangeland condition, pasture availability and market prices. Pastoral livestock production is therefore no longer as dependent on rainfall and range condition as it used to be. Traditional seasonal patterns of movement to and from specific areas are no longer followed, and have been replaced by more erratic

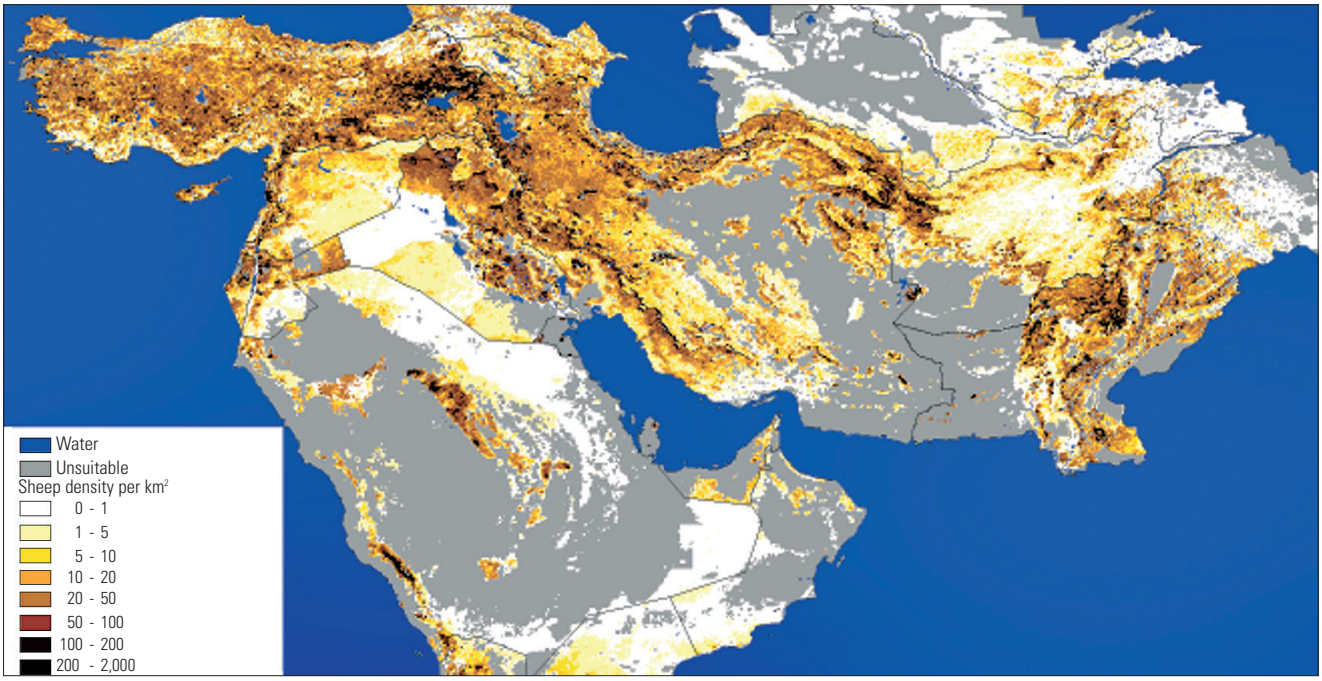

Fig. 4
Sheep density in the Middle East (17, 21)

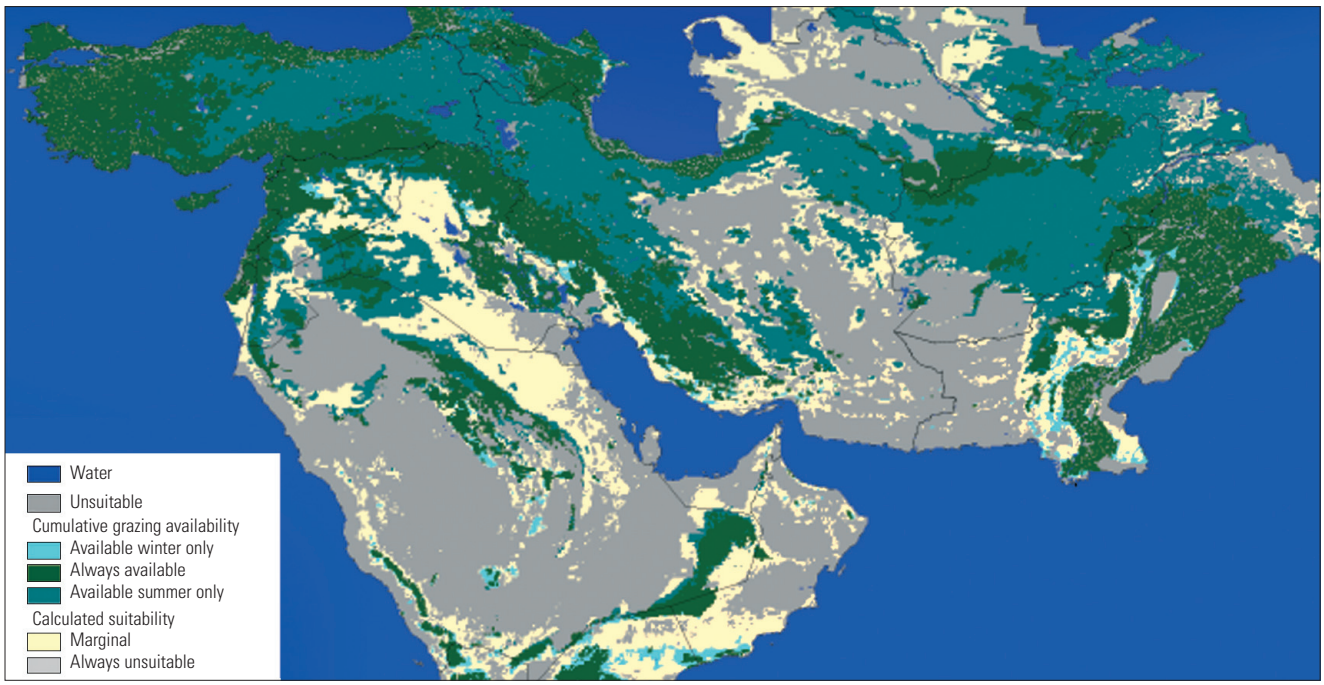

Fig. 5
Cumulative presence of grazing during different seasons along the Eurasian ruminant street (17, 21)

and opportunistic transport to areas with pasture and/or areas where water and supplementary feed can be supplied.

As the human population becomes more urbanised, towns and cities generate the principal demand for animal protein, which traders and producers supply from local production and/or by importation from further afield (Fig. 6). Accordingly, a dichotomy in livestock production has emerged, with 'high-tech' capital-intensive poultry and dairy units at one extreme, and transitional, relatively small-scale, 'low-tech' dairy and sheep producers at the other. Levels of capital investment in the two systems are obviously very different, as are abilities to afford and implement disease control measures.

In this scenario, the urban demand cannot usually be met by local producers and a substantial transport of live animals is required. This raises the probability of long-distance disease dispersal, as has been shown for FMD type O incidence in Turkey (Fig. 7). The disease persists in provinces such as Ankara, which has a deficit of small ruminant meat, and Ezurum, which has a surplus. It would seem, therefore, that meat production-demand discrepancies, both for cattle and small ruminant meat, may be an indicator of the disease risk that can arise from domestic trade in live animals, given that provinces with the highest difference between demand and supply have more movement of live animals and thus a higher disease transmission risk (publication in preparation by M. Gilbert *et al.*).

International and national level trade and traffic also have an effect on local patterns of disease behaviour, other influencing factors being the structure of the animal population, the diversity of husbandry practices and the considerable temporal and spatial heterogeneity of livestock production systems. However, a fuller understanding of sub-national level disease patterns requires more information than is currently available, particularly where this concerns data on local gene flows as revealed by molecular fingerprints of disease agents, vectors and host associations (27). In the example of FMD spread in Turkey, genetic analysis of FMD types O and A, spanning over four decades, showed evolutionary rates (1% nucleotide substitution per year in type A and 0.6% per year in type O) far below those implied by the nucleotide differences between the (sub-)lineages encountered (e.g. type A: 18% nucleotide difference between the isolates taken in 1995 and those taken in 1997) (18). The fact that these isolates were found to match isolates from the Middle-East, indicates that most, if

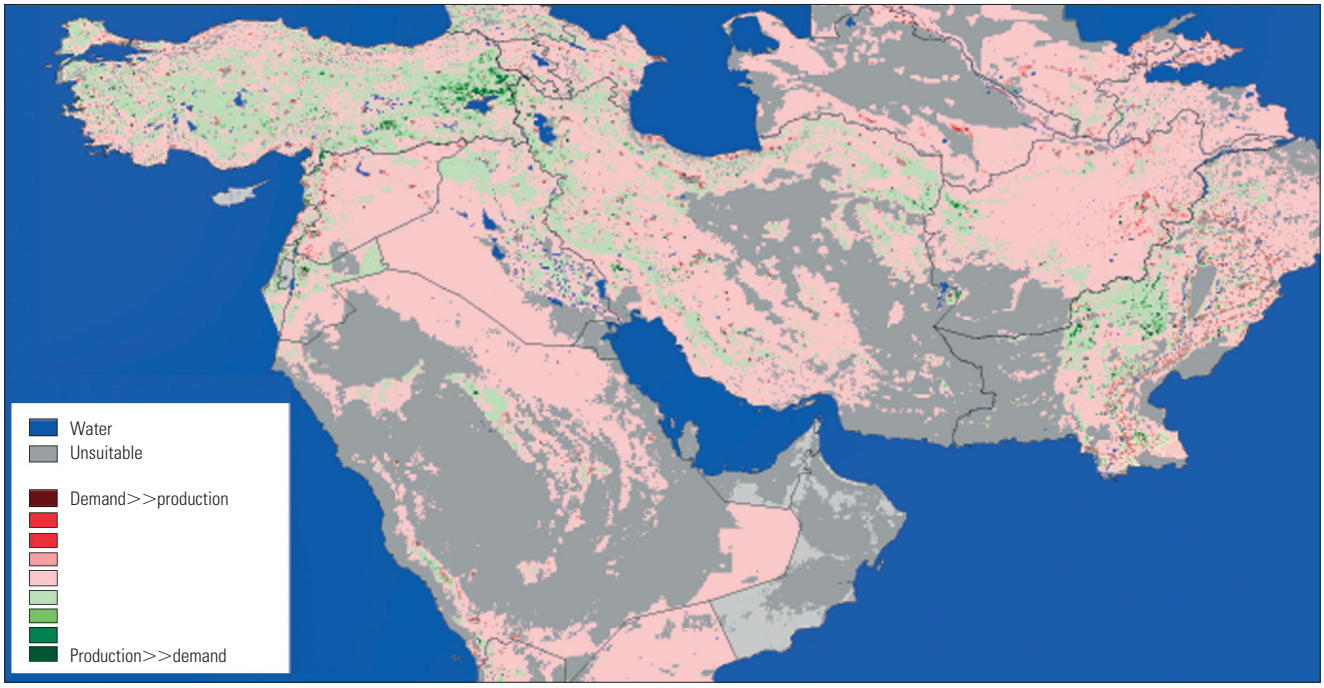

Fig. 6
Animal protein production-demand discrepancies in the Middle East, 2000 (22)

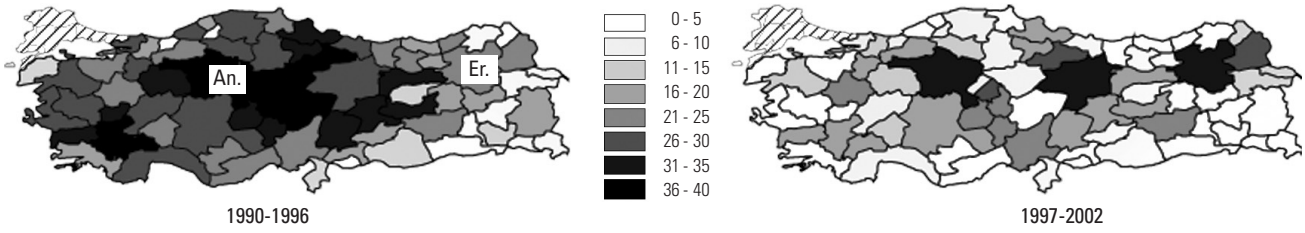

Fig. 7
The number of new outbreaks in Turkey, by province, of foot and mouth disease (FMD) type O in 1990-1996 (left), when FMD type O declined, and in 1997-2002 (right), during which period type O stabilised and was concentrated in 3 major hotspots, including the provinces of Ankara (An.) and Erzurum (Er.)

not all FMD virus strains entering and spreading into Turkey arrive from the east (18). This corroborates with the fact that live animals enter Turkey at the eastern border and are then trucked towards the western half of the country where most consumption centres are located. Again, the demand-supply discrepancy triggers the movement of live animals and presents a risk of disease introduction, both at sub-national and international level.

Not only do environmental changes favour disease spread across a wider geographical area, but indications are that FMD type O may also be broadening its host range and developing a greater affinity for sheep (17). Furthermore, the increasingly closer links, in terms of trade and traffic, between the Eurasian ruminant street, the Middle East, the Horn of Africa and the Sudano-Sahelian ruminant populations also encourage ruminant disease agents to become more aggressive and may lead to increased exposure of humans. Trade of live animals is also reported to contribute to the spread of Crimean-Congo haemorrhagic fever (CCHF) (36), an important zoonotic disease affecting cattle, sheep and goats throughout Central Asia, the Balkans, the Middle East and North Africa. Unofficial records available to the FAO suggest a rising incidence in most of these areas of RVF, FMD, PPR, sheep pox, OWS, BT, CCHF and tick-borne encephalitis; this increase is unlikely to be due to improvements in disease reporting alone.

Structural changes in the East Asian livestock sector and the risk of disease emergence

The FAO has a statistical database (FAOSTAT) that provides general statistics on trends in world food and agriculture, including livestock and animal protein commodities. The projections presented in a recent study on the future of world agriculture (5) suggest that the current world population of 6.2 billion will reach 7.2 and 8.3 billion in the years 2015 and 2030 respectively. Over half of the population of the world will be concentrated in East and South Asia (15). With a projected per capita gross domestic product growth of 5.3% and 3.9% for East and South Asia respectively, running to the year 2015, meat and milk consumption in East Asia will rise to 50 kg and 14 kg/capita/year, while the figure for South Asia will show the opposite proportions, with 88 kg of fresh milk equivalents and only 7.6 kg of meat per capita per year.

The related FAO cereal balance sheets suggest that by 2015 East and South Asia jointly will require 42% of the total world demand of 2,379 million tonnes of grain. It is estimated that the feed required in East Asia by 2015 will be 218 million tonnes, or 24% of total world feed demand. With this amount of feed, it is speculated that by 2015 East Asia may produce 35% of the global meat production of 300 million tonnes.

Animal disease risk following rapid shifts in production systems are poorly documented because in most countries where monogastric production systems are now industrial, intensification has been a gradual process, lasting several decades and involving the entire production sector (e.g. Belgium, the Netherlands, Denmark). In East and South Asia the rapid establishment of specialised farms and industrial production units mostly takes place in areas with high densities of small production units, with relatively low biosecurity, and thus comparatively high prevalence and persistence of disease pathogens. Intensification implies the creation of relatively disease-free production environments and this condition becomes hard to sustain when surrounded by abundant smallholder units.

Hence, one possible way to characterise the likelihood or risk of disease spread or emergence is to consider this to be a function of:

a) the productivity level or degree of production intensification (i.e. open, extensive systems in which pathogens freely circulate and animals become carriers or suffer chronic infections, or large scale, confined production units in which all animals are susceptible and in which major clinical disease problems arise if disease is introduced)

b) the spatial structure of production units, taken as the set of sub-populations of hosts between which microbial traffic occurs.

For example, a high density of smallholders surrounding intensive or industrial production units would create a particularly risky situation. These two critical variables, productivity level and production structure, can be derived from surrogate variables of which statistics are available at the country level: the productivity level can be estimated from the output/input ratio (kg meat/animal/year), whereas the density of the agricultural population (AgPop) forms a surrogate estimate of the density of smallholders. Thus we may plot, for individual animal production subsectors, and for any given country or region, the data pairs, for each year, for smallholder density (x-axis) and productivity (y-axis). The pattern formed by the sequence of years forms a trajectory of agricultural intensification for the period under consideration. The FAO country statistics are available from 1961 onwards whilst future trends in agricultural development, including the productivity levels and labour force dynamics, have been projected for the years 2015 and 2030 (5). The thus observed trajectories of agricultural intensification may now be used to explore the patterns of disease risk.

Figure 8 illustrates the agricultural intensification trajectories of countries grouped by continent (adapted

from Bruinsma [5] – publication in preparation by M. Gilbert *et al.*). The first and most obvious observation is the marked difference between the continents. Very little change in the size of the AgPop is observed in industrial countries and a sharp rise in chicken meat productivity is seen over the last forty years. For the same period, developing countries show very little increase in productivity, and a very significant increase in the AgPop density, mostly as a consequence of generally rising population levels. North America and Australia had a low and stable AgPop density at the start of the period, and have steadily increased their productivity since then; Europe and South America have reduced their AgPop and progressively enhanced the levels of intensification; and in Asia and Africa there has been a very significant increase in AgPop density with relatively little productivity increase (although the increase in productivity in Asia is higher than in Africa and projections are that in Asia, unlike Africa, the density of smallholders will start to decline in the decades ahead).

These trajectories support three main observations. Firstly, countries in Asia, and East and Southeast Asia in particular, are distinct from other regions in the world, and are characterised by relatively minor overall increases in productivity alongside a very significant rise in the AgPop density. The implication is that this area should not be compared to other regions in the world in relation to epidemic risk estimations. Secondly, the fact that intensification is not accompanied by a reduction of AgPop density suggests that any decline in the number of producers due to production intensification is outweighed by the increase in farmer numbers resulting from rising overall populations. Thirdly, epidemic risk may be higher where production is in the process of transformation. Certainly, this applies to Asian countries where gradual intensification proceeds in the face of persisting high density smallholder producers.

In some countries, intensification creates a dichotomy in production structure, with a very high number of smallholders and a restricted number of large scale, intensive production units concentrated around consumption areas, which are responsible for the gradual overall productivity increase at national level. The mismatch between increases in productivity and demographic growth can be examined further by modelling the intensification trajectory of a hypothetical country in Southeast Asia (Fig. 9). The model shows that with a logistic population growth (Fig. 9a) the proportion of farmers decreases inversely as a function of gains in productivity (Fig. 9b). This implies that the number of farmers reaches a peak (Fig. 9c) and a bump is observed in the plot of changes in productivity as a function of the

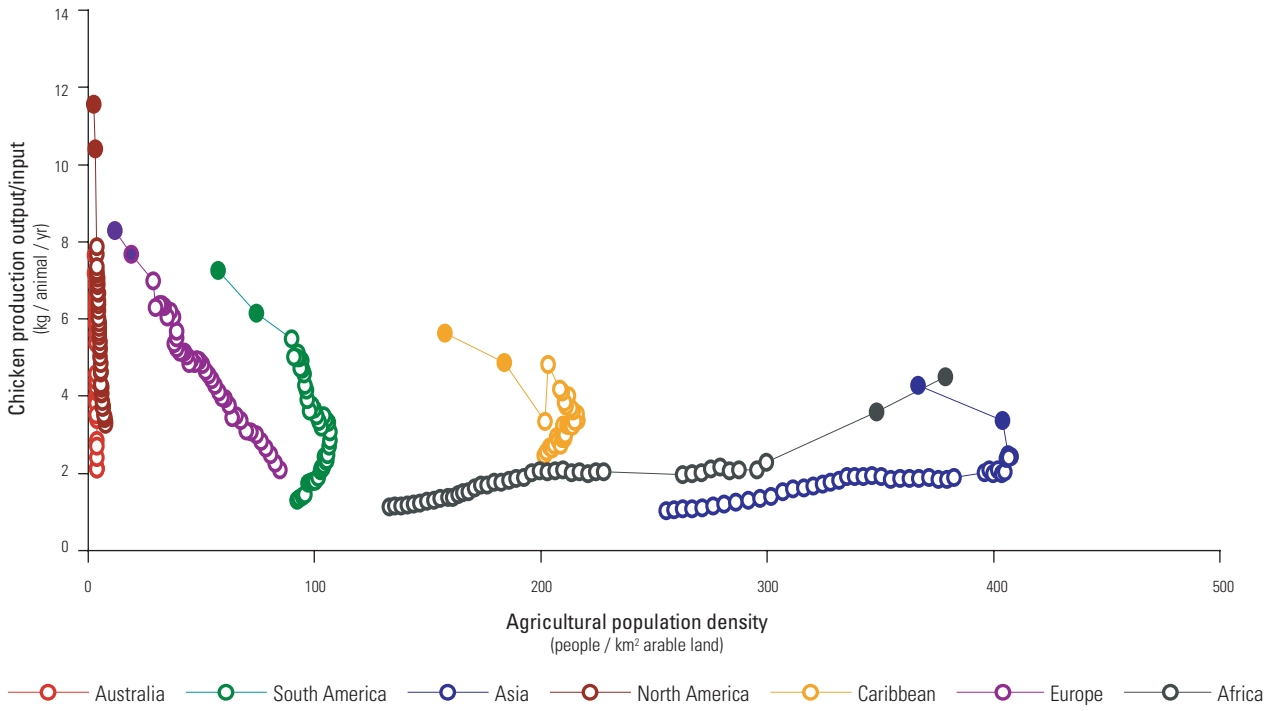

Fig. 8
Change in chicken meat output/input and agricultural population density grouped by continent between 1961 and 2001 (empty circles) and predictions for 2015 to 2030 (full circles)
(adapted from Bruinsma [5] – publication in preparation by M. Gilbert *et al.*)

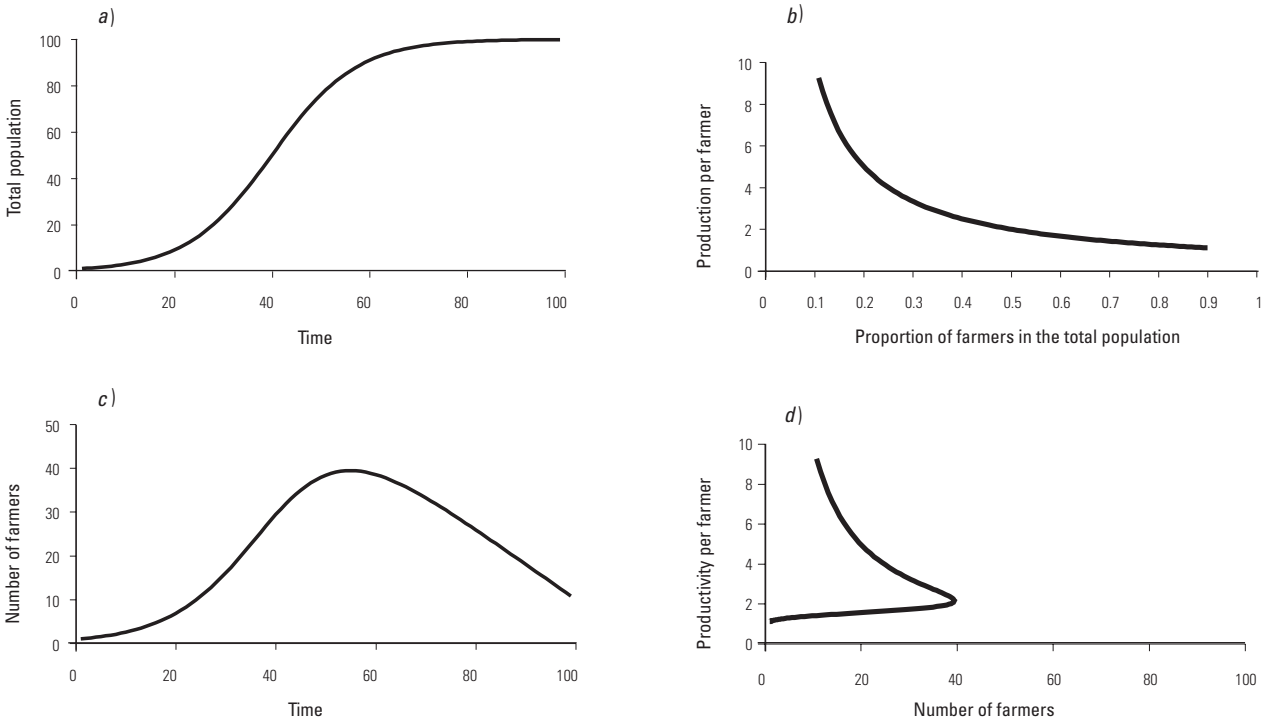

Fig. 9
A model of the intensification trajectory of a hypothetical country in Southeast Asia
If the total population increases with a logistic growth (*a*), the proportion of farmers decreases inversely as a function of gains in productivity (*b*), then the number of farmers shows a maximum (*c*), and a bump is observed in the plot of changes in productivity as a function of the number of farmers (*d*) **(26)**

number of farmers (Fig. 9d). The slope of the latter trajectory in the productivity versus AgPop plot is determined by the pace at which the density of smallholders increases in response to general increases in human population compared to the pace of the reduction in the number of smallholders as a result of production intensification. These results suggest that, irrespective of the pace of intensification, high densities of smallholder producers will remain a reality for a considerable period and that this trend is an inherent characteristic of the intensification process in countries with ever increasing human populations.

In Southeast Asia the transformation of animal production is largely a response to, and is driven by, the growing demand in major urban centres. It follows that the location of poultry and pig production and feed crops is a function of the geographical distance to the nearest megacity (24) (Figs 10 and 11). In fact, land utilisation pattern and livestock density may be the outcome of two main, underlying forces working in opposite directions. Firstly, as animal protein products are highly perishable and require swift processing, distribution and retail, production must be in the vicinity of urban centres, particularly where there is no adequate infrastructure. Following the upsurge in urban

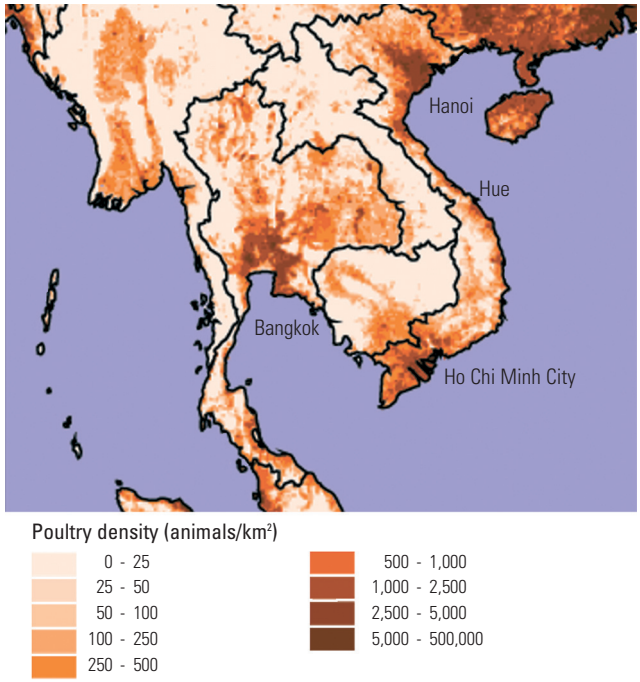

Fig. 10
Estimated poultry density in Thailand, Laos and Vietnam (animals per km²) (24)

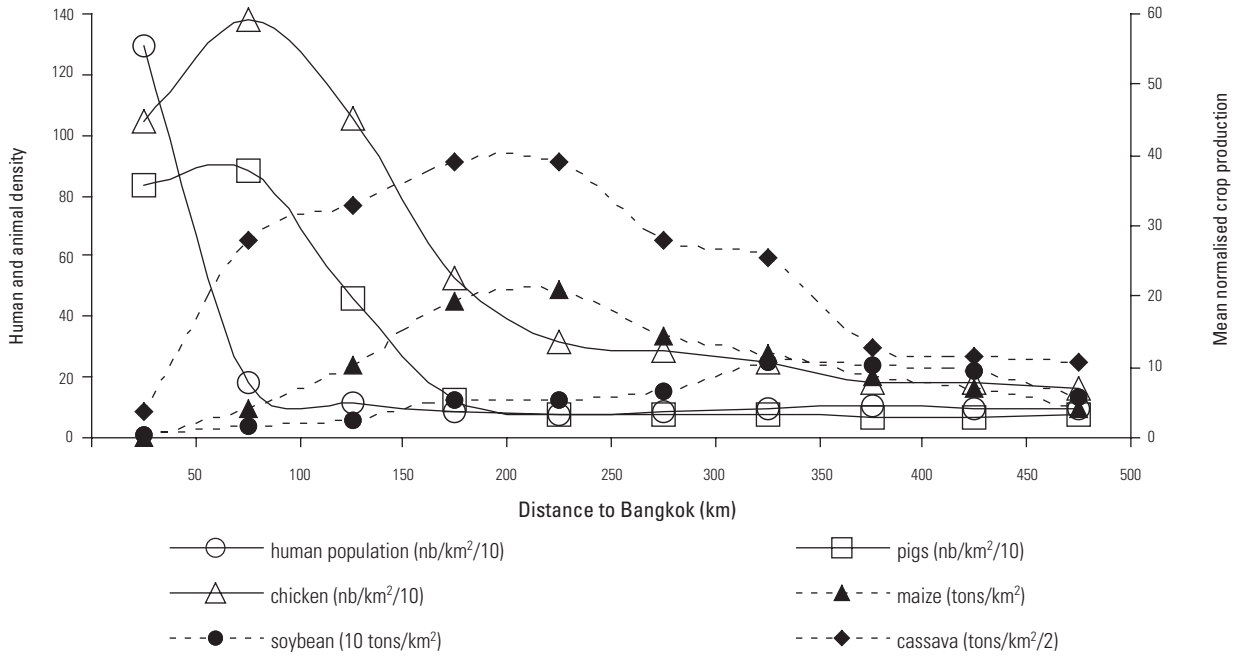

Fig. 11
Spatial distribution of humans, livestock and feed-crops around Bangkok, 2001 (24)

demand, there is a progressive concentration and contraction of animals into peri-urban environments. Secondly, there is an opposite, centrifugal force, acting at the same time, resulting from the progressive increase in population and land pressure around expanding cities, which is forcing rural people to disperse into the more remote land areas hitherto considered less attractive. This creates a decline in the level of agricultural productivity along an urban to rural transect, with high input/high output systems more prominent in the peri-urban settings whilst extensive low input systems are typical of the more remote environments.

This productivity gradient becomes particularly pronounced in situations where agricultural technologies take full advantage of the economies of scale. For example, modern poultry production units mostly count many thousands of birds and produce low-cost animal protein of standard quality. These poultry units may be located wherever it is considered convenient.

The heterogeneity in the production structure of poultry holdings is also reflected in the differential animal health protection strategies. Commercial production enterprises will invest more to protect their birds because of the economic gains acquired when keeping more healthy and productive livestock. The return from animal health investment rapidly decays in remote areas. Also, the cost of health protection is proportional to the size of the area protected, irrespective of the number of animals kept. It follows that biosecurity measures progressively improve near a city.

This geographic stratification in disease protection and risk may be considered in relation to the epidemiology of the highly pathogenic avian influenza (HPAI) H5N1 epidemic in Asia in 2003/2004. Virus introduction from wild waterfowl is most likely to occur in extensive smallholder production units, and therefore, areas with a higher density of poultry smallholders are more prone to the initial spread of infection. For a subsequent spread of the disease some of the more sizeable holdings must be infected, whereupon the considerable movement of people, live animals, and feed between small commercial-scale holdings promotes secondary spread of infection. In this way, the commercial broiler chains may well have played a major role in the 'seeding' of HPAI H5N1. The highest outbreak risk is thus likely to be where smallholders and commercial units coexist. This is confirmed by exploratory quantitative analyses of the recent HPAI distribution which show the distribution of avian flu outbreaks to be concentrated at the interface of extensive and commercial poultry production (publication in preparation by M. Gilbert *et al.*). Similarly, as was observed during the HPAI outbreaks in 2003 in the Netherlands, poultry kept by smallholders or hobby farmers for recreational purposes in the vicinity of large-scale commercial units appear to have been an important risk factor and may have fuelled the epidemic.

In addition to the unstable avian influenza situation in East and Southeast Asia, there is evidence that changes in food demand and agricultural practices play a role in a number of other zoonotic infections. Apart from SARS, of which the animal origin remains uncertain, there is evidence that Nipah/Hendra-like viruses are now found to occur in a number of countries where intensification is widespread, including Australia, Malaysia, Singapore, Cambodia and Bangladesh (2). Similarly, Japanese encephalitis appears to be increasing its range in South Asia (41).

The potential future role of disease ecology

The study of the ecology of invasive diseases may arguably assist in identifying the links between environmental change, new forms of disease and microbial adaptation, though the approach is still in its infancy. Lessons learned from epidemics of existing pathogens have highlighted some of the factors associated with the spread of a disease within a population, and methodological tools are available to explore these patterns (1). In parallel, some of the processes of environmental change (e.g. demographic pressures, critical contacts with wildlife animals, the rate at which climate change or deforestation may occur, etc.) have also been quantified. The missing link is how pathogens currently restricted to wildlife or domestic animals will evolve toward humans in response to abrupt environmental changes. In this context, it may be helpful to consider the full spectrum of pathogens that affect animals and/or humans:

a) true animal pathogens

b) pathogens confined to an animal reservoir but sometimes producing limited human infection

c) well established multiple host and zoonotic pathogens

d) pathogens increasingly affecting human populations but moving towards extinction

e) transient agents which evolve into human pathogens

f) full blown human pathogens.

It is likely that new pandemics will occur in the future, that RNA viruses in animal reservoirs will be implicated and that food and agricultural practices will play an important role in the emergence of disease in human populations as well as in veterinary health and food safety hazards. Agricultural intensification will be fraught with structural problems such as unchecked land pressures and imbalances in socio-economic development. For all these reasons, it would perhaps be advisable to pay fuller attention to the inherent epidemiological instability that is caused by innate characteristics of livestock development and food chains in some parts of the world. Of particular concern is the progressive 'urbanisation' of animal production and processing. Not only does the enhanced contact of people with live animals, perishable meat and dairy commodities and waste products increase the number of occupational hazards, also the general public is at risk through the microbial contamination of water sources, food poisoning and of course flare-ups of zoonotic infections.

Disease ecology shows us that disease spread and the emergence of zoonotics and other veterinary public health concerns are largely the product of human activity. Hence, the solution to these problems is also a matter of human choice.

Acknowledgements

The authors wish to thank David Bourn, Pierre Gerber, Jim Hancock, Maarten Hoek, Raffaele Mattioli, Peter Roeder, Awatif Siddig, Maria-Grazia Solari and Sarah Wint for their most helpful support and comments.

L'origine écologique des zoonoses

J. Slingenbergh, M. Gilbert, K. de Balogh & W. Wint

Résumé

Bien que d'origine zoonotique, les agents pathogènes ou infectieux qui menacent la santé publique mondiale (le virus de l'immunodéficience humaine, le syndrome respiratoire aigu sévère ou les virus émergents de type A de la grippe, par exemple) ont vraisemblablement peu de choses en commun avec les agents zoonotiques connus et déjà bien établis, dans la mesure où ces nouveaux agents ont simplement traversé une phase zoonotique passagère avant de s'adapter à l'homme. Bien que l'évolution vers la transmission de personne à personne soit tributaire des caractéristiques biologiques de l'agent pathogène, elle pourrait néanmoins être déclenchée ou favorisée par des facteurs exogènes tels que des changements dans l'exposition humaine. Par conséquent, l'émergence des pathologies pourrait être décrite comme une réaction évolutive aux modifications de l'environnement (y compris aux facteurs anthropogènes comme les pratiques agricoles, l'urbanisation ou la mondialisation) et du climat. S'agissant de l'émergence de zoonoses dans le bétail, les auteurs estiment que le bouleversement des pratiques agricoles joue désormais un rôle prépondérant et détermine les conditions qui régissent l'évolution et la propagation des agents pathogènes zoonotiques, voire leur irruption au sein de la population humaine. Les agents pathogènes du bétail subissent des pressions liées à la dynamique de la production, à la transformation des protéines et au commerce de détail, qui, en combinant leurs effets, modifient le taux de contact de l'hôte, la taille des populations et/ou les flux microbiens dans la chaîne alimentaire. Ce processus trouve son illustration dans deux situations :

a) le développement de l'élevage dans la « ceinture eurasienne des ruminants » (une zone qui s'étend de l'Asie centrale à l'est du bassin méditerranéen) et dans la péninsule arabique limitrophe ;

b) la dynamique de la production avicole en Asie du Sud-Est.

Dans ces deux cas, les facteurs environnementaux associés à la démographie, à la surexploitation des terres et aux déséquilibres causés par la production intensive ont créé une situation épidémiologique instable, comme en attestent la forte hausse de l'influenza aviaire hautement pathogène en 2004 et la présence des principaux foyers dans une zone où l'on trouve à la fois une forte densité de petits élevages avicoles et de grands élevages périurbains à vocation commerciale.

Mots-clés

Accroissement démographique – Changement écologique – Écologie de la maladie – Épidémiologie – Intensification de l'agriculture – Production animale – Urbanisation – Zoonose émergente.

Génesis ecológica de las enfermedades zoonóticas

J. Slingenbergh, M. Gilbert, K. de Balogh & W. Wint

Resumen

Es muy posible que ciertos patógenos o infecciones que amenazan la salud del hombre a escala mundial (virus de la inmunodeficiencia humana, síndrome respiratorio agudo severo o virus emergentes de la influenza de tipo A, por ejemplo), a pesar de su origen zoonótico, tengan poco en común con otros agentes ya conocidos y descritos, puesto que esos nuevos agentes simplemente han pasado por una fase zoonótica transitoria antes de adaptarse al ser humano. Aunque la adquisición evolutiva de la capacidad de transmisión de persona a persona depende de las características biológicas del microorganismo, factores externos como un cambio en los niveles de exposición con el hombre podrían muy bien desencadenar o favorecer esa adaptación. En este sentido, cabe describir la aparición de nuevas enfermedades como una respuesta evolutiva a los cambios del medio, entre otros los de origen antrópico como los nuevos procedimientos agrícolas, la urbanización, la globalización o el cambio climático. En lo que concierne a las nuevas enfermedades zoonóticas del ganado, los autores postulan que la modificación de las prácticas agrícolas se ha convertido en el principal factor determinante de las condiciones en que un agente zoonótico evoluciona, se propaga y acaba afectando a poblaciones humanas. Los patógenos del ganado están sometidos a presiones resultantes del dinamismo de las actividades de producción, tratamiento de las proteínas y venta al por menor, presiones que en conjunto modifican parámetros tales como la tasa de contacto con los animales hospedadores, el tamaño de la población y/o los movimientos del microbio en la cadena alimentaria. Dos estudios de casos ilustran este proceso:

a) desarrollo ganadero en el 'corredor euroasiático de rumiantes' (que se extiende desde el Asia Central hasta la cuenca mediterránea oriental) y la vecina Península Arábica;

b) dinámica de la producción avícola en Asia Sudoriental.

En ambos casos, una serie de factores ambientales relacionados con la demografía, la demanda de tierras y los desequilibrios ligados a la intensificación productiva han desembocado en una situación epidemiológica inestable, de la que da muestra el rebrote de influenza aviar altamente patógena acaecido en 2004, cuyos principales focos se localizaban en áreas donde coexisten zonas con gran densidad de minifundios avícolas y grandes explotaciones periurbanas de carácter industrial.

Palabras clave

Cambio ecológico – Crecimiento demográfico – Ecología de las enfermedades – Epidemiología – Intensificación agrícola – Producción animal – Urbanización – Zoonosis emergente.

References

1. Anderson R.M. & May R.M. (1991). – Infectious diseases of humans: dynamics and control. Oxford University Press, Oxford, 766 pp.

2. Anon. (2003). – Outbreaks of encephalitis due to Nipah/Hendra-like viruses, Western Bangladesh. Reported by the Division of Viral and Reckettsial Disease, National Centre for Infectious Diseases, Centres for Disease Control and Prevention, United States of America and the Health Systems and Infectious Diseases Division and Clinical Sciences Division of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B). *Hlth Sci. Bull.* **1** (5), 1-6. Website: www.icddrb.org/pub/publication.jsp (accessed on 29 July 2004).

3. Antia R., Regoes R.R., Koella J.C. & Bergstrom C.T. (2003). – The role of evolution in the emergence of infectious diseases. *Nature*, **426** (6967), 658-661.

4. Boserup E. (1981). – Population and technological change: a study in long term trends. The University of Chicago Press, Chicago, 255 pp.

5. Bruinsma J. (ed.) (2003). – World agriculture towards 2015/2030: an FAO perspective. Earthscan, London and FAO, Rome, 432 pp.

6. Cleaveland S., Laurenson M.K. & Taylor L.H. (2001). – Diseases of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergency. *Philos. Trans. roy. Soc. Lond., B, biol. Sci.*, **356** (1411), 991-999.

7. Cohen M.L. (2000). – Changing patterns of infectious disease. *Nature*, **406** (6797), 762-767.

8. Cunningham E.P. (1988). – Global patterns of supply and demand for livestock products. Economic Development Institute, World Bank, Washington, DC, 111 pp.

9. Daszak P., Cunningham A.A. & Hyatt A.D. (2000). – Emerging infectious diseases of wildlife: threats to biodiversity and human health. *Science*, **287** (5452), 443-449.

10. Daszak P., Cunningham A.A. & Hyatt A.D. (2001). – Anthropogenic environmental change and the emergence of infectious disease in wildlife. *Acta trop.*, **78** (2), 103-116.

11. Delgado C., Rosengrant M., Steinfeld H., Ehui S. & Courbois C. (1999). – Livestock to 2020: the next food revolution. Food, Agriculture and the Environment Discussion Paper 28. International Food Policy Research Institute, Washington, 72 pp.

12. Diamond J. (2002). – Evolution, consequences and future of plant and animal domestication. *Nature*, **418** (6898), 700-707.

13. Dobson A. & Foufopoulos J. (2001). – Emerging infectious pathogens of wildlife. *Philos. Trans. roy. Soc. Lond., B, biol. Sci.*, **356** (1411), 1001-1012.

14. Earn D.J.D., Dushoff J. & Levin S.A. (2002). – Ecology and evolution of the flu. *Trends Ecol. Evol.*, **17** (7), 334-340.

15. Food and Agriculture Organization (FAO) (1999). – Agro-ecological zones, farming systems and land pressure in Africa and Asia. Consultant report (W. Wint, J. Slingenbergh & D. Rogers, eds). Environmental Research Group Oxford, FAO and TALA (Trypanosomaiasis And Land-use in Africa) Research Group. FAO, Rome, 42 pp. Website: http://ergodd.zoo.ox.ac.uk/download/index.htm (accessed on 29 July 2004).

16. Food and Agriculture Organization (FAO) (2001). – CD-ROM livestock geography: new perspectives on global resources. Animal Production and Health Division of the FAO, Rome. Last update December 2002. Website: http://ergodd.zoo.ox.ac.uk/livatl2/.

17. Food and Agriculture Organization (FAO) (2003). – CD-ROM animal disease dynamics on the Eurasian ruminant street. Animal Production and Health Division of the FAO, Rome.

18. Food and Agriculture Organization (FAO) (2003). – Genetics of foot and mouth disease in Turkey. Consultant report (S. Aktas, ed.). FAO, Rome, 48 pp.

19. Food and Agriculture Organization (FAO) (2003). – Livestock dynamics in the Arabian Peninsula: a regional review of national livestock resources and international livestock trade. Consultant report (D. Bourn, ed.). Environmental Research Group, Oxford and FAO, Rome, 78 pp. Website: http: //ergodd.zoo.ox.ac.uk/download/ (accessed on 29 July 2004).

20. Food and Agriculture Organization (FAO) (2003). – Livestock phylogenetics and geography: the clarification of disease spread from South Asia to the Mediterranean basin, including the Arabian Peninsula. Consultant report (D. Bradley & A. Freeman, eds). Trinity College, Dublin. FAO, Rome, 98 pp.

21. Food and Agriculture Organization (FAO) (2003). – Ruminants, seasons and grazing in the Middle East. Consultant report (W. Wint, ed.). Environmental Research Group, Oxford and FAO, Rome, 27 pp.

22. Food and Agriculture Organization (FAO) (2004). – Global trends in livestock production and epidemiological instability. Consultant report (W. Wint & J. Slingenbergh, eds). Environmental Research Group, Oxford and FAO, Rome, 86 pp.

23. Galvani A.P. (2003). – Epidemiology meets evolutionary ecology. *Trends Ecol. Evol.*, **18** (3), 132-139.

24. Gerber P., Wassenaar T., Chilonda P., Menzi H. & Steinfeld H. (2004). – Geographical shifts of the livestock production: land use and environmental impact implications. *In* Proc. 'Structural change in the livestock sector – social and environmental implications for policy making': a conference organised by the Food and Agriculture Organization of the United Nations (FAO) Livestock Environment and Development Initiative (LEAD), 27-29 January, Bangkok. FAO, Rome, 16 pp. (in press).

25. Grenfell B. & Harwood J. (1997). – (Meta)population dynamics of infectious diseases. *Trends Ecol. Evol.*, **12** (10), 395-399.

26. Heylighen F. (2000). – r-K selection: the development-reproduction trade-off. Principia Cybernetica Web. Website: http://pespmc1.vub.ac.be/RKSELECT.html (accessed on 29 July 2004).

27. Holmes E.C. (2004). – The phylogeography of human viruses. *Molec. Ecol.*, **13** (4), 745-756.

28. Keeling M.J. (1999). – The effects of local spatial structure on epidemiological invasions. *Proc. roy. Soc. Lond., B, biol. Sci.*, **266** (1421), 859-867.

29. Lotterman E. (1998). – Broilers of the world, unite! Fed gazette. Federal Reserve Bank of Minneapolis, April. Website: http://www.minneapolisfed.org/pubs/fedgaz/98-04/broilers.cfm (accessed on 29 July 2004).

30. McIntire J., Bourzat D. & Pingali P. (1992). – Crop-livestock interaction in sub-Saharan Africa. World Bank Regional and Sectoral Studies. World Bank, Washington, DC, 264 pp.

31. May R.M., Gupta S. & McLean A.R. (2001). – Infectious disease dynamics: what characterizes a successful invader? *Philos. Trans. roy. Soc. Lond., B, biol. Sci.*, **356** (1410), 901-910.

32. Morse S.S. (1995). – Factors in the emergence of infectious diseases. *Emerg. infect. Dis.*, **1** (1), 7-15.

33. Nordblom T.L. & Shomo F. (1993). – Livestock and feed trends in West Asia and North Africa: past, present and future. *Cah. Options méditerr.*, **1** (5), 15-30.

34. OIE (World Organisation for Animal Health) (2004). – Terrestrial Animal Health Code 2003, 12th Ed. OIE, Paris, 515 pp.

35. Pingali P., Bigot Y. & Binswanger H.P. (1987). – Agricultural mechanization and the evolution of farming systems in sub-Saharan Africa. Published for the World Bank by Johns Hopkins University Press, Baltimore, 128 pp.

36. Rodriguez L.L., Maupin G.O., Ksiazek T.G., Rollin P.E., Khan A.S., Schwarz T.F., Lofts R.S., Smith J.F., Noor A.M., Peters C.J. & Nichol S.T. (1997). – Molecular investigation of a multisource outbreak of Crimean-Congo hemorrhagic fever in the United Arab Emirates. *Am. J. trop. Med. Hyg.*, **57** (5), 512-518.

37. Sakai A.K., Allendorf F.W., Holt J.S., Lodge D.M., Molofsky J., With K.A., Baughman S., Cabin R.J., Cohen J.E., Ellstrand N.C., McCauley D.E., O'Neil P., Parker I.M., Thompson J.N. & Weller S.G. (2001). – The population biology of invasive species. *Annu. Rev. Ecol. Syst.*, **32**, 305-32.

38. Schrag S.J. & Wiener P. (1995). – Emerging infectious disease: what are the relative roles of ecology and evolution? *Trends Ecol. Evol.*, **10** (8), 319-324.

39. Slingenbergh J., Hendrickx G. & Wint W. (2002). – Will the livestock revolution succeed? *AgriWorld Vision*, **2** (4), 31-33.

40. Somwaru A.S., Xiaohui Z. & Tuan F. (2003). – China's hog production structure and efficiency. A paper presented at the Annual Meeting of the American Agricultural Economics Association, 27-30 July, Montreal, 29 pp.

41. Tsai T.R., Chang G.W. & Yu Y.X. (1999). – Japanese encephalitis vaccines. *In* Vaccines, 3rd Ed. (S.A. Plotkin & W.A. Orensetin, eds). WB Saunders Inc., Philadelphia, 672-710.

42. United Nations Convention on Biological Diversity, (CBD) (2003). – Pilot Assessments: the ecological and socio-economic impact of invasive alien species on island ecosystems. CBD, Montreal, 38 pp. Website: http://www.biodiv.org/doc/ref/alien/ias-inland-en.pdf (accessed on 15 October 2004).

43. Vitousek P.M., Mooney H.A., Lubchenco J. & Melillo J.M. (1997). – Human domination of the earth's ecosystem. *Science*, **277**, 494-499.

44. Webster R.G. (1998). – Influenza: an emerging disease. *Emerg. infect. Dis.*, **4** (3), 436-441.

45. World Health Organization (WHO) (2004). – Report of the WHO/FAO/OIE joint consultation on emerging zoonotic diseases, 3-5 May, Geneva. WHO, Geneva.