Rev. sci. tech. Off. int. Epiz., 2004, **23** (2), 497-511

The role of wildlife in emerging and re-emerging zoonoses

R.G. Bengis [1], F.A. Leighton [2], J.R. Fischer [3], M. Artois [4], T. Mörner [5] & C.M. Tate [3]

(1) Veterinary Investigation Centre, P.O. Box 12, Skukuza, Kruger National Park, 1350, South Africa
(2) Canadian Cooperative Wildlife Health Centre, Department of Veterinary Pathology, University of Saskatchewan, Saskatoon, Saskatchewan S7N 5B4, Canada
(3) Southeastern Cooperative Wildlife Disease Study, College of Veterinary Medicine, University of Georgia, Athens, GA 30602, United States of America
(4) Ecole Nationale Vétérinaire de Lyon, Département de santé publique vétérinaire, Unité de pathologie infectieuse et épidémiologie, 1, avenue Bourgelat, 69280 Marcy l'Etoile, Lyons, France
(5) Department of Wildlife, National Veterinary Institute, 751 89, Uppsala, Sweden

Summary

There are huge numbers of wild animals distributed throughout the world and the diversity of wildlife species is immense. Each landscape and habitat has a kaleidoscope of niches supporting an enormous variety of vertebrate and invertebrate species, and each species or taxon supports an even more impressive array of macro- and micro-parasites. Infectious pathogens that originate in wild animals have become increasingly important throughout the world in recent decades, as they have had substantial impacts on human health, agricultural production, wildlife-based economies and wildlife conservation.

The emergence of these pathogens as significant health issues is associated with a range of causal factors, most of them linked to the sharp and exponential rise of global human activity. Among these causal factors are the burgeoning human population, the increased frequency and speed of local and international travel, the increase in human-assisted movement of animals and animal products, changing agricultural practices that favour the transfer of pathogens between wild and domestic animals, and a range of environmental changes that alter the distribution of wild hosts and vectors and thus facilitate the transmission of infectious agents.

Two different patterns of transmission of pathogens from wild animals to humans are evident among these emerging zoonotic diseases. In one pattern, actual transmission of the pathogen to humans is a rare event but, once it has occurred, human-to-human transmission maintains the infection for some period of time or permanently. Some examples of pathogens with this pattern of transmission are human immunodeficiency virus/acquired immune deficiency syndrome, influenza A, Ebola virus and severe acute respiratory syndrome.

In the second pattern, direct or vector-mediated animal-to-human transmission is the usual source of human infection. Wild animal populations are the principal reservoirs of the pathogen and human-to-human disease transmission is rare. Examples of pathogens with this pattern of transmission include rabies and other lyssaviruses, Nipah virus, West Nile virus, Hantavirus, and the agents of Lyme borreliosis, plague, tularemia, leptospirosis and ehrlichiosis. These zoonotic diseases from wild animal sources all have trends that are rising sharply upwards.

In this paper, the authors discuss the causal factors associated with the emergence or re-emergence of these zoonoses, and highlight a selection to provide a composite view of their range, variety and origins. However, most of these diseases are covered in more detail in dedicated papers elsewhere in this *Review*.

Keywords

Emerging disease – Re-emerging disease – Species barrier – Wildlife – Zoonosis.

Introduction

Zoonoses are infectious diseases that have been transmitted from animals to humans. Emerging and re-emerging zoonoses are infectious diseases that:

– are newly recognised

– are newly evolved

– have occurred previously but have more recently shown an increase in incidence or expansion into a new geographic, host or vector range.

The concept of 'emerging diseases' developed as health scientists documented and tried to explain the apparent abrupt rise in the number of new and important infectious diseases over the past two decades. The processes and factors that may have given rise to emerging or re-emerging infectious and zoonotic diseases which originated in wildlife (55) include the following:

– expanding human populations and increased contact with wild animals or their products

– ecosystem changes of natural or anthropogenic origin, with climatic and geographic influences on pathogens and vectors

– increased human-assisted movement of animals and animal products

– wildlife-associated microbes entering intensive livestock-based agricultural systems

– intensive farming of formerly wild species

– increased frequency and speed of local and international travel

– changes in the microbes themselves, or their host spectrum (crossing the species barrier)

– improved technical diagnostic and epidemiological techniques, which have resulted in the recent detection of an existing or novel disease agent.

It may be useful to consider that zoonoses generally fall into one of the two following categories:

a) diseases of animal origin in which the actual transmission to humans is a rare event but, once it has occurred, human-to-human transmission maintains the infection cycle for some period of time. Some examples include human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), certain influenza A strains, Ebola virus and severe acute respiratory syndrome (SARS)

b) diseases of animal origin in which direct or vector-mediated animal-to-human transmission is the usual source of human infection. Animal populations are the principal reservoir of the pathogen and horizontal infection in humans is rare. A few examples in this category include lyssavirus infections, Lyme borreliosis, plague, tularemia, leptospirosis, ehrlichiosis, Nipah virus, West Nile virus (WNV) and hantavirus infections.

Over all, approximately 60% of recognised human pathogens are zoonotic, so it is not surprising that many of these relatively recent emerging infections can also be traced back to animals. Approximately 75% of the diseases that have emerged over the past two decades have a wildlife source (56).

Recent emerging zoonoses

Viral zoonoses

Simian immunodeficiency viruses and human immunodeficiency virus/acquired immune deficiency syndrome

Human immunodeficiency virus/AIDS is caused by two of the 26 simian immunodeficiency virus (SIV) strains known to occur in African primates. The HIV-1 and HIV-2 viruses have evolved from a chimpanzee (*Pan troglodytes*) strain and a Sooty mangabey (*Cercocebus torquatus*) strain, respectively (24, 34). The available evidence and genetic analysis suggest that transmission of these SIV strains to humans was a rare event, but one that has occurred on at least seven separate occasions over the past century. These initial transmissions in equatorial Africa appear to be linked to hunting apes and using them for food. From these transmission events, virus strains which were both highly adapted to humans and contagious among humans evolved as HIV-1 and HIV-2, and these are now maintained and spread in human populations, independent of their simian origin.

The emergence of HIV-AIDS in the twentieth century appears to be the result of a complex set of largely ecological and sociological changes in Africa, including the following:

– expanding human populations

– deforestation

– rural displacement (people moving from rural areas to urban areas to seek employment, education or new social relationships)

– urbanisation and its attendant poverty

– sexual behaviour

– parenteral drug use

– increased local and international travel (4, 23).

The HIV infection is probably becoming one of the biggest zoonotic pandemics in recent human history. At the end of 2003, the United Nations (UN) estimated that 40 million people were infected worldwide, with more than three million HIV-associated deaths during that year (53).

Sub-saharan Africa was the region most severely affected. International public health initiatives have not yet been successful in reducing the impact of this zoonosis; its prevalence and geographic distribution around the world are rising and its full impact on human well-being, economies and security has yet to be experienced.

Ebola virus

Ebola virus infection of humans was first described in Central Africa in 1976, in the southwestern Sudan and the northern region of the Democratic Republic of the Congo with high mortality (28). From 1992 to 1999, further lethal outbreaks were recorded in Gabon, the Republic of the Congo and the Democratic Republic of the Congo. Also in 1994, human cases were linked to high mortality in chimpanzee colonies in Côte d'Ivoire, and the virus was isolated from a chimpanzee (62). Several human and animal Ebola outbreaks have occurred over the past four years in Gabon and the Republic of the Congo. The human outbreaks consisted of multiple simultaneous epidemics caused by different sub-types of the virus (31). Each human epidemic has been linked to the handling of a distinct gorilla (*Gorilla sp.*), chimpanzee or duiker (*Sylvicapra grimmia*) carcass, themselves incidental victims of infection. It is important to note that populations of these animals declined markedly during the period of human Ebola outbreaks, apparently also as a result of Ebola infection. Recovered carcasses were infected by a variety of Ebola strains, suggesting that Ebola outbreaks in great apes result from multiple virus introductions from a yet undetermined wildlife maintenance host of these viruses. The possible involvement of arthropod vectors during primary infection has not been ruled out. Thereafter, apparent horizontal transmission from ape to ape has resulted in the disappearance of several known and well-studied gorilla and chimpanzee groups.

Most human Ebola outbreaks in Gabon and the Republic of the Congo were directly linked to the handling of dead animals by villagers or hunters, followed by horizontal human-to-human spread. Surveillance of animal mortality may help to predict high-risk periods for Ebola outbreaks.

Hantavirus

In Europe and Asia, hantaviruses are the causative agents of haemorrhagic fever with renal syndrome (HFRS), and in the Americas they cause hantavirus pulmonary syndrome (HPS). The pathogens responsible for HFRS include Hantaan, Seoul, Dobrava and Puumala hantaviruses, whereas HPS is caused by the Sin Nombre group of hantaviruses. All these viruses are maintained in wild rodent reservoirs, and human infections occur through the respiratory route as a result of aerosolisation of rodent excreta. The infection is chronic and apparently asymptomatic in these natural maintenance hosts (18).

Peaks in the incidence of HPS in the United States of America (USA) have coincided with climatic events driven by the *El Niño* Southern Oscillation (ENSO). (The ENSO generally has opposing effects in the northern and southern hemispheres: when the northern hemisphere experiences increased precipitation the southern hemisphere experiences droughts, and vice versa.) The documented increase in rain in the USA frequently resulted in environmental conditions that supported denser rodent populations. Human activities such as rodent trapping, farming, cleaning rodent-infested premises, camping and hunting have also been identified as risk factors in the occurrence of hantavirus disease. The mortality rate for HFRS varies from 0.1% to 10%, whereas for HPS the rate averages 45% (60). Human-to-human transmission has not been recorded.

Hendra virus

In 1994, two outbreaks of a novel, often fatal, viral disease affecting horses and humans occurred in Queensland, Australia. The outbreaks were caused by a previously unknown paramyxovirus, which was named Hendra virus (39). Experimental infection of horses could be achieved by the parenteral as well as the oro-nasal route, and cats and guinea pigs were also experimentally infected (54). The virus does not appear to be directly contagious among people or horses, and human cases were linked to very close exposure, including an equine necropsy. Virological and serological testing suggests that bats of the Megachiroptera family (*Pteropus* spp.) are the natural reservoirs of the virus (61). The method of transmission from bats to horses is unknown, but the presence of significant amounts of virus in the urine of bats may point to urinary contamination of feed or water.

Nipah virus

From 1998 to 1999, a new highly contagious respiratory and neurological disease of pigs was reported on the Malaysian peninsula. There was a simultaneous epidemic of viral encephalitis among employees on affected pig farms and abattoirs. A novel paramyxovirus, distinct from Hendra virus, was isolated from both porcine and human victims, and named Nipah virus (36). Dogs and cats were also found to be susceptible. Evidence from virological and serological techniques implicated fruit bats of the genus *Pteropus* as the natural host and reservoir for this virus.

A mortality rate of up to 40% was seen in suckling piglets. In humans, 265 cases of viral encephalitis were recorded, with 38% mortality (14, 36). The Nipah virus epidemic was controlled using an initial 'stamping out' policy in outbreak areas, followed by a peninsula-wide farm/herd testing and slaughter programme. The cost to the national pig herd was enormous, with almost 45% of the existing pig population destroyed.

Nipah virus emerged as a new human pathogen under changing ecological conditions that point to a complex interplay of human activities as the ultimate cause of this disease emergence (14). The key determinants appear to have been the accelerated rates and scales of deforestation in Southeast Asia, severe drought associated with the ENSO of 1997 to 1998, and the recent expansion of pig farming in Malaysia. The resulting depletion of resources displaced fruit bats from their natural forest habitat, and they moved into agricultural areas that had productive fruit orchards. These agricultural areas also had large numbers of pigs, thus increasing the probability of transmitting the virus from bats to pigs, and thence to people.

Human infection with Nipah virus was also confirmed in Bangladesh in 2001, 2003 and 2004, with high fatality rates. Highly mobile fruit bats with large home ranges were again implicated as the source of infection, which may have occurred directly through human consumption of contaminated fruit (57).

Menangle virus infection

Another recently identified paramyxovirus, designated Menangle virus, has been linked to illness in pigs and humans in Australia. Four species of fruit bats (genus *Pteropus*) have been serologically implicated as reservoirs of infection (44).

West Nile virus infection

Since 1999, WNV has emerged in North America, presenting a threat to human and equine health, and the health of certain wild bird populations. West Nile virus, a flavivirus of the Japanese encephalitis complex, is a well-known virus of Europe, western Asia and Africa (47), which is maintained in a wide species range of wild birds and bird-feeding mosquitoes. This virus can cause febrile disease and encephalitis in a number of mammal species, including humans (49), although these are 'dead-end' hosts that play no role in the maintenance of the virus. Current international interest in WNV has been sparked by its unexpected arrival in North America in 1999 and its unprecedented and well-documented spread across the continent in only a few years. The public health costs of WNV in North America have been significant. The 2002 and 2003 WNV epidemics will be recorded as the largest recognised arbovirus meningo-encephalitis epidemics in the western hemisphere, with more than 500 deaths. During these two years, a total of 13,278 human cases of WNV infection were reported in the USA, with a mortality rate of between 2% and 7%. Infection was also detected in more than 4,000 horses, of which some 20% developed neurological disease (10). Clinical disease and death have been documented in 155 resident avian species in North America, with morbidity and mortality most frequently observed among Corvids, which are now used as a surveillance sentinel species. West Nile virus infection was confirmed in more than 11,000 dead birds in 2003 (41). The ecological effects on wild bird populations have yet to be evaluated.

West Nile virus serves as an important case study of the capacity for introduced alien pathogens to spread widely through the biota of an entire continent, establishing firm 'footholds' or bases, imposing new long-term costs and strains on public health systems, and potentially altering ecological relationships, as well as menacing rare species.

Moreover, now that WNV has become firmly established in North America, it has the potential to move southwards in migratory birds and establish itself in the Caribbean, and in Central and South America.

Severe acute respiratory syndrome

During 2002 and 2003, a novel viral respiratory disease emerged in humans in Southeast Asia. The disease presented as a severe, acute, sometimes life-threatening respiratory syndrome, which gave rise to its name: severe acute respiratory syndrome or SARS. This disease was found to be caused by a novel coronavirus, unrelated to coronaviruses that were commonly associated with human infections, or known to infect livestock. The disease was directly contagious between people, especially from so-called 'superspreaders', and became rapidly disseminated by international travel. Infections of humans appear to have occurred first in the southern region of the People's Republic of China (58), and a virus that may have been the initial source virus was subsequently isolated in masked palm civets (*Paguma larvata*) in that area. This small carnivore has recently become highly commercialised and is intensively farmed for health food and other products in that region, which may have increased opportunities for close contact with humans. It is not yet known whether these civets or other 'wet market' animals (similar coronaviruses have also been isolated from foxes and domestic cats in the southern People's Republic of China) are the reservoir for this virus, or are just transient permissive hosts. Nonetheless, most evidence points to an epidemiological linkage between the emergence of SARS and the expanding commercial trade in live wild or pseudo-domesticated animals in southern Asia. These wild animal or 'wet' markets of Southeast Asia, where humans, livestock and wild animals are gathered together in an intensive milieu, may offer an ideal setting for pathogens to cross over between species.

Avian influenza (Influenza A)

Influenza A viruses are responsible for highly contagious acute illness in humans, pigs, horses, marine mammals and birds, occasionally resulting in devastating epidemics and pandemics. Phylogenetic studies suggest that aquatic birds

could be the original source of the genetic material of all influenza A viruses in other species (25). The influenza A virus strains isolated from wild birds have generally been weak pathogens that cause little or no disease in the natural host or in a range of other species that have been experimentally infected. However, through genetic mutation or recombination, these strains may become both pathogenic and well adapted to host species such as poultry, pigs and humans (8). There is evidence that both pigs and poultry may act as 'mixing vessels' for different influenza A strains, facilitating genetic re-assortment, and serving as sources for newly evolved virus strains, which have resulted in pandemics of severe disease in people. The most serious of these pandemics occurred in 1918, during which an estimated 20 to 50 million people died. This has been followed by some lesser but significant pandemics in 1957, 1968 and 1977 (1).

Other influenza A strains have caused severe mortality in poultry. Outbreaks of influenza A that are highly pathogenic to poultry generally lead to international trade embargoes on poultry and poultry products, until such time as the virus is eradicated (40).

Until recently, there had been no evidence that influenza A viruses causing severe disease in people had ever been acquired directly from poultry. However, in 1997, an H5N1 virus sub-type, causing high mortality in poultry on farms and in markets in Hong Kong, also caused eighteen human cases of disease with a mortality rate of 33%. There was no evidence of human-to-human transmission, and each case was assumed to represent a direct transmission from infected poultry. This poultry outbreak was eventually controlled by the slaughter of over 1.5 million chickens (1).

In March 1999, seven cases of avian influenza infection in humans, involving an H9N2 sub-type, were reported from Hong Kong and the mainland of the People's Republic of China.

In 2003 and 2004, outbreaks of an H5N1 virus sub-type occurred in intensive poultry farms over large areas of Southeast Asia (19). Spillover infections into humans were reported in Vietnam and Thailand, with some mortalities.

Thus far, the human infections reported in all the outbreaks of severe influenza A in poultry occurred in people who were closely associated with poultry. No human-to-human transmission appears to have occurred. These infections probably represent the direct transfer of the poultry virus to humans. However, the development of such poultry viruses into new virus sub-types, which may become well adapted to humans and highly contagious among them, raises the fear of a new pandemic, and is of major concern to people and public health services around the world.

Monkeypoxvirus infection

Historically, monkeypoxvirus infection of humans occurred as isolated or, at the most, focal clusters of cases in West and Central Africa. The virus reservoir is among tree squirrels and other rodents in these African tropical rain forests, and humans became infected by hunting and handling these animals. Horizontal human transmission has been documented, but appears inefficient, and transmission chains beyond secondary are rare (27). In addition, smallpox vaccination (vaccinia) imparts cross-immunity to monkeypox. The main interest in monkeypox was related to the global discontinuation of smallpox vaccination in the 1980s, and concern whether this would create an immunological void which may be exploited by other related pox viruses (43). The endemic monkeypox situation in Africa in the 1980s and 1990s increased slightly (26) as a result of many years of war, when people relied heavily on subsistence hunting, and also as a result of increased susceptibility after vaccinia vaccination had been discontinued. During outbreaks in the Democratic Republic of Congo after 1983, a monkeypox-related case fatality rate of up to 9.8% was recorded in people who had not been vaccinated against smallpox. With subsequent changes in lifestyle, due to increasing urbanisation and intensified agriculture over recent years, the reported incidence of monkeypox in Africa has decreased.

During June and July 2003, 71 suspected cases of monkeypox were reported in the states of Illinois, Indiana, Kansas, Missouri, Ohio and Wisconsin in the USA. A total of 35 cases were confirmed by laboratory tests (11). Most of these people became infected by contact with pet prairie dogs (rodents of the genus *Cynomys*), sourced from a commercial pet trade distributor. The prairie dogs at this facility were probably caught in the wild, and apparently became infected through contact with Gambian giant rats (*Cricetomys* spp.) and dormice (*Graphiurus* spp.) that had been shipped in from Ghana. This highly publicised disease outbreak in humans and pet prairie dogs occurred because of the international trade and transport of non-domesticated animals, and the growing trend of private exotic animal and captive wildlife ownership in the USA (42).

Bacterial/rickettsial zoonoses

Lyme borreliosis

Lyme borreliosis has become the most common vector-borne infection in the northern hemisphere. This disease is caused by spirochaetes belonging to the *Borrelia burgdorferi* complex, and is a good example of a recently discovered infection that has probably been present at a low incidence for many years. The sylvatic maintenance hosts and reservoirs are a range of small and medium-sized mammals and ground-feeding birds in the endemic areas. In Europe,

the vector of infection is the tick, *Ixodes ricinus*, whereas, in North America, two primary tick vectors exist, namely *I. scapularis* and *I. pacificus*.

The spirochaetes cause a multi-systemic disease, affecting the skin, nervous system, heart and joints. Treatment of human cases in the early stages of the disease is usually uncomplicated, involving a slightly prolonged course of appropriate antibiotics. In cases which are not detected and treated early, multi-systemic pathology may occur, and the disease appears to become more resistant to treatment (22).

The emergence of Lyme borreliosis in North America in the 1970s is a further example of new patterns of disease occurring as emergent properties of complex ecological changes.

In this instance, changes in land-use practices, such as the abandonment of less productive farmlands, deforestation (2) and a massive expansion of suburban human settlement resulted in dense populations of white-tailed deer (*Odocoileus virginianus*), and an increase in wild rodent reservoirs (*Peromyscus* spp. and *Tamias* spp.) of the bacterium. The increased number of preferred hosts supported high tick-vector populations in close proximity to outdoor environments which were near to suburban areas and heavily used by people (6).

Ehrlichiosis

Ehrlichia and *Anaplasma* spp. are obligate intracellular tick-transmitted bacteria in the order Rickettsiales. Each organism exhibits tropism for a specific host blood cell in which it forms characteristic clusters known as morulae. Three of these rickettsial agents, *E. chaffeensis*, *E. ewingii* and *A. phagocytophilum*, cause human disease in the USA. Human infection with these bacteria commonly presents as a flu-like illness, but may be asymptomatic. Rarely, it may even cause fatal disease. Laboratory findings include leukopenia, thrombocytopenia and elevation of liver enzymes.

Ehrlichia chaffeensis, recognised as the causative agent of human monocytic ehrlichiosis in 1987 (3), is primarily maintained in nature by white-tailed deer (*O. virginianus*) and the lone-star tick (*Amblyomma americanum*) as host and vector, respectively (16).

Ehrlichia ewingii is the causative agent of both canine and human granulocytic ehrlichiosis. Recognised very recently as a human pathogen (7), *E. ewingii* appears to be vectored by *A. americanum*, but other tick species may play a role. Molecular evidence of the bacteria has been demonstrated in wild white-tailed deer (59).

Anaplasma (Ehrlichia) phagocytophilum, the causative agent of human granulocytic anaplasmosis, was first detected as a human pathogen in 1994 (13). In North America, the white-footed mouse (*Peromyscus leucopus*) is a competent mammalian host, while the ticks *I. scapularis* and *I. pacificus* are the primary vectors. Molecular evidence of infection has been demonstrated in a variety of wild rodents, as well as in medium-sized and large mammals, such as white-tailed deer (16). This is the same ecological complex that maintains Lyme borreliosis, and the emergence of *A. phagocytophilum* as a human pathogen may relate to the same complex of ecological factors.

Re-emerging zoonoses

The re-emergence of well-documented zoonotic diseases appears to be driven by climatic, habitat and population-density factors that affect hosts, pathogens or vectors – frequently causing natural increases and decreases in disease activity in different geographical areas and over various periods of time.

Viral infections

Rabies and related Lyssavirus infections

Rabies is an ancient disease that can affect most mammals and is endemic in many parts of the world, with sporadic epidemics. There are a large number of different host-adapted strains of the rabies virus and these are maintained in nature, exclusively within specific host species. Occasionally spillover occurs into other sympatric species (species occurring in the same or overlapping geographical areas), especially during epidemics in the host species, but perpetuation through time occurs only within the specific host species. Epidemics are usually associated with climatic or environmental events which increase numbers and densities of regional wildlife hosts or domestic dogs, and are frequently described as so-called 're-emergences'. There is great regional variation as to which strains of the rabies virus predominate in which animal host, as well as which strains pose significant risks to human health (45). Most human exposures are linked to domestic and feral dogs. Rabies reportedly kills between 50,000 and 100,000 humans annually, the vast majority in developing countries. In the developed countries of the northern hemisphere, rabies control has been effective, through the regular vaccination of domestic pets and oral bait vaccination of important regional sylvatic hosts.

The lyssaviruses include classical rabies and other rabies-related viruses, of which there are seven genotypes and many different strains within some of the genotype categories. The construction of phylogenetic trees indicates that, in general, lyssavirus isolates cluster into distinct

lineages, according to geographical origin and maintenance host species (51).

Lyssavirus genotype 1 is the classical multi-species rabies virus with a worldwide distribution. There are multiple, highly species-adapted strains of this genotype, maintained almost exclusively in one host species in different regions of the globe. In this regard, rabies has adapted to the following:

– jackals (*Canis mesomelas, Canis aureus* and *Canis adustus*), bat-eared foxes (*Otocyon megalotis*) and various mongoose species in Africa (48)

– various foxes, raccoon dogs (*Nyctereutes procyonoides*) and bats in Europe and Asia

– vampire bats in South America

– raccoons (*Procyon lotor*), skunks (*Mephitis mephitis*), coyotes (*Canis latrans*) and bats in North America.

It is important to note that, in the Americas, only lyssaviruses that belong to genotype 1 have been isolated from bats. Dogs, however, remain the major maintenance host and source of human infection in the developing world.

Bats, which represent approximately 24% of all known mammalian species, are frequently the maintenance hosts for many strains of rabies viruses. They are, however, the exclusive maintenance hosts for five of the lyssavirus genotypes. These genotypes cause low mortality in bats and sero-conversion occurs in many of the bats that survive (33).

Genotype 2 (Lagos bat virus) preferentially circulates in fruit bats (*Macrochiroptera*) in Africa.

Genotype 3 (Makola virus) appears to have multiple small African mammal hosts, including shrews and cats, while genotype 4 (Duvenage virus) circulates in African insectivorous bats (29).

Genotypes 5 and 6 (European bat lyssaviruses 1 and 2) circulate in insectivorous bats (*Microchiroptera*) in Europe.

Genotype 7 (Australian bat lyssavirus) circulates in fructivorous and insectivorous bats in Australia. Australia has always been considered free of classical rabies, and the discovery of this virus in *Pteropus* bats in 1996 sparked intensive research. It was found to be clearly a lyssavirus, but genetically distinct from genotype 1.

This suggests a rather precise adaptation of these genotypes to bats, and a long-term co-evolution. Thus, it is questionable whether bat lyssavirus infections are a true emerging disease. It may be that these lyssaviruses have only recently been detected, due to better surveillance and laboratory tools, not that there has been any recent increase in incidence.

Standard laboratory techniques used to diagnose rabies in terrestrial mammals may also be used to confirm *Lyssavirus* infection in bats (35). These routine laboratory techniques, however, do not identify the genotype involved.

It is important to note that, as of June 2004, commercial rabies vaccines developed for classical genotype 1 rabies provide little if any protection against genotypes 2 (Lagos) and 3 (Makola), and the immune response conferred by these vaccines against genotype 5 (EBL 1) is weak. This need is currently being addressed.

Rift Valley fever

Rift Valley fever (RVF) is a peracute or acute mosquito-borne viral disease of domestic and some wild ruminants in Africa. The disease is characterised by abortions, necrotic hepatitis and a haemorrhagic state, although many infections are inapparent or mild. Humans become infected by contact with infected tissue or by mosquito bites. Infection in humans is usually associated with influenza-like symptoms, but severe complications, including ocular sequelae, encephalitis and haemorrhagic disease, occur in a small proportion of patients.

Rift Valley fever activity is related to climatic conditions that favour the mosquito vectors. Documented epidemics of RVF occurred in southern and eastern Africa in the 1950s and 1970s (wet cycles), during which thousands of abortions and deaths were reported in livestock. Thereafter, with the exception of a large outbreak in West Africa between 1987 and 1988, a period of relatively reduced disease activity was noted in the 1980s and early 1990s. More recently, following some of the heaviest (ENSO-associated) rainfalls ever recorded in East Africa, an exceptionally severe outbreak of RVF in both domestic livestock and humans commenced in Kenya in 1997, and spread rapidly into Somalia and Tanzania. The number of human cases was estimated to be 89,000, which suggests that this may be one of the largest outbreaks of RVF on record (46).

The current theory as to survival or 'over-wintering' of the RVF virus during the period between epidemics is that the virus is maintained principally through transovarial transmission and the hatching latency of the eggs of floodwater-dependent mosquitoes of the genus *Aedes* (32).

However, the role of potential wild vertebrate maintenance hosts needs further investigation because RVF disease has been documented in buffalo (*Syncerus* spp.), antelope (*Tragelaphus* spp.) and camels (*Camelus* spp.), and wildlife sero-surveys frequently test positive for the presence of antibodies, even though such results are unrelated geographically or temporally to livestock outbreaks.

Marburg virus

In 1967, the first human cases of Marburg virus infection were detected in laboratory workers in Marburg (Germany) and Belgrade (Yugoslavia), who had been exposed to African green monkeys (*Cercopithecus aethiops*) or handled monkey primary cell culture suspensions. Later, sporadic cases were reported from Zimbabwe in 1975 and Kenya in 1980 and 1987 (37). More recently (1999), a major focus of Marburg disease was confirmed in the north-eastern province of the Democratic Republic of the Congo, with tens of deaths in the Durba area.

Bacterial infections

Bovine tuberculosis

Mycobacterium bovis is a bacterium, which causes chronic debilitating disease in cattle, many wild animal species and humans. It is a bacterium of ancient lineage with a separate evolutionary trajectory from that of human-maintained *M. tuberculosis* (15).

In Africa, *M. bovis* has become established in certain populations of the following species:

– buffalo (*Syncerus caffer*)
– lechwe (*Kobus leche*)
– warthog (*Phacochoerus africanus*)
– kudu (*Tragelaphus strepsiceros*).

In North America, this disease is known to occur in one population of bison (*Bison bison*) and certain populations of wapiti (*Cervus elaphus*) and white-tailed deer. In Europe, bovine tuberculosis (TB) is found in wild boar (*Sus scrofa*), and certain cervid populations. In the United Kingdom and Ireland, infection is maintained in the European badger (*Meles meles*). In New Zealand, *M. bovis* infection is maintained in brush-tailed opossums (*Trichosurus vulpecula*) and ferrets (*Mustela furo*). In Australia, the disease was previously present and maintained in feral water buffalo (*Bubalus bubalis*), but has subsequently been controlled by a major depopulation exercise (5). Most of these infections originally crossed into wildlife from infected cattle in areas where the two populations came into contact with each other, and have now become established and maintained in certain free-ranging wild populations.

Bovine TB in wild animals is most often considered a disease issue because of its zoonotic potential and, indeed, wild animals can and do serve as reservoirs of infection and may pose a direct health risk to consumers of infected wildlife products. However, it is the indirect risk path, whereby wildlife reservoirs may infect livestock, that is the greatest cause for concern, because it is the bovine link which poses the greatest risk for human infection. This is especially relevant in developing countries with high human HIV prevalence, particularly in communities where human consumption of raw (unpasteurised) milk is normal practice, and meat inspection is, at most, rudimentary. For this reason, many countries have bovine TB eradication policies in place, which have been implemented and executed at great cost over a number of years. This has resulted in the eradication of the disease in some countries, or has brought the prevalence rate down to fractional levels, where eradication appears attainable in the near future. The current concern is that the presence of infection in certain wild maintenance hosts may impede the control of the disease in sympatric livestock.

Over the past two decades, *M. bovis* infection has achieved new prominence, as populations of free-range and farmed wild ungulates, formerly believed to be free of the disease, have been discovered with high prevalences of infection, particularly in North America, Europe and parts of Africa. At least some of these new occurrences in the northern hemisphere appear linked to ecological changes and changes in land-use practices, resulting in high population densities of susceptible wild species.

Control efforts in wildlife are very difficult, and are further hampered by the lack of effective ante-mortem diagnostic tests. The effect of bovine TB on infected wild animal populations is generally not known. However, at least in Africa, there are early indications that a sustained high prevalence of infection may have an impact on the population growth and structure of buffalo herds and on the social organisation and stability of lion prides, with reduced reproductive success and recruitment (20).

Brucella species in wild animals

Several species of *Brucella* infect wild animals. Infection of livestock by any of these species, whether or not the infection results in disease, may cause the animals to test 'positive' in standard screening tests used to identify and eliminate infected domestic animals or herds. *Brucella abortus* and *B. melitensis* are the species most regularly transmitted between wild and domestic ungulates, and are most frequently associated with the conflicting needs of wildlife and agriculture, and the risk of human disease. Each species can cause significant disease in livestock (*B. abortus* in cattle and *B. melitensis* in sheep and goats), and both can cause serious disease in humans. Human health risks are generally associated with the handling or consumption of infected animals or products.

Other *Brucella* species found in wild animals include *B. suis*, which occurs widely in wild and feral animals. Biotype 4 occurs in caribou and reindeer (*Rangifer tarandus*) over their entire range, biotype 2 is found in the European brown hare

(*Lepus capensis* Linnaeus) and biotype 1 in feral swine. These *Brucella* species also pose potential health risks to people who handle or consume infected animal products. Indeed, at least 91 species of wild mammals, from nine different orders, demonstrate some evidence of infection with one or more species of *Brucella* (50). Recently, a number of incompletely characterised species of *Brucella* have been isolated from whales and seals of various species, and also from rare human infections. These are currently collectively referred to as marine *Brucella*, pending more complete characterisation. The effects of *Brucella* infections on wildlife at the population level are generally not known. Infections can result in abortion, lameness and sterility on the individual level, but many infections appear to be sub-clinical.

Tularemia

Tularemia is a bacterial disease caused by strains of the bacterium *Francisella tularensis*. This bacterium appears to have co-evolved with lagomorphs and rodents in the northern hemisphere, where it occurs on most continents. More specifically, both a type-A strain and a type-B strain have been identified and are associated with different epidemiological patterns. These organisms have an extremely broad host range, having been reported in 190 species of mammals, 23 species of birds and three species of amphibians. Tularemia is also an important zoonosis. Despite the broad host range, it primarily causes clinical disease in lagomorphs and rodents. Carnivores generally have lower susceptibility.

Transmission of tularemia may occur through the following:

– the bites of haematophagous insects and ticks

– direct contact with infected exudates and tissues

– mucous membrane contamination

– inhalation

– ingestion.

Tularemia may also be water-borne.

Epidemiologically, two main cycles have been identified. The type-A cycle is associated with lagomorphs, ticks and biting flies (38), and this form of the disease may serve as a regulatory mechanism in rabbit populations in North America. This cycle appears to be responsible for 70% of human cases of tularemia in the USA. Cases that occur during the summer months are usually associated with tick bites, whereas cases occurring in the fall are frequently associated with the hunting and handling of rabbits. The type-B cycle in North America and some parts of Russia causes clinical disease in muskrats (*Ondatra* spp.) and beavers (*Castor* spp.). The actual reservoir species are probably less susceptible rodents, such as voles, and transmission is usually water-borne. The type-B cycle also occurs in Europe as a vector-borne cycle, as does transmission from infected lagomorphs to humans. Tularemia may be seen either as a localised focal outbreak or a widespread epidemic. Human cases usually occur during the summer, during the winter hunting season, or in association with handling carcasses.

In recent years, an increasing number of human and animal cases of tularemia have been observed in Sweden, and the disease is now occurring in areas where it has not been seen before (41). More than 500 human cases were recorded in Sweden in 2003, and epidemic outbreaks appear to be on the increase in other areas of Europe. The reason for this expansion has yet to be determined.

Plague

Plague, caused by *Yersinia pestis*, was a disease of great historical impact on human populations, and continues to re-emerge as a zoonotic disease on a reduced scale. When plague is endemic in wild animal populations, the bacterium is usually maintained in rodent reservoir species and transmitted by fleas. This bacterium was spread around the world from its central Asian site of origin by people and the rodents that accompanied human movements. Global distribution of the plague occurred only at the end of the nineteenth century, when the last pandemic coincided with the development of rapid transportation by steamship. Plague can persist for some time in urban environments as a disease of rats and their fleas. The bacterium can produce serious, usually fatal, disease in rats and fleas, and infected rats and rat fleas are important sources of infection for humans in urban settings, as was the case in historical descriptions of classical plague. A recent urban outbreak has also been described in Madagascar (12).

The establishment of endemic foci of plague in many parts of the world during the twentieth century has made *Y. pestis* a much more widespread and available zoonotic threat than in the past (21). Close association with reservoir rodent populations is the primary risk factor for human plague which originates from wild animal sources. The extension of suburbs into plague-endemic areas and outdoor recreation in plague-endemic habitats are common mechanisms of human exposure. Flea bite is thought to be the most common route of human infection in these settings, but companion animals, such as domestic cats, can also serve as bridges for human infection. Infected cats frequently develop buboes and draining sinuses in the cervical region, and some 10% of infected cats develop the pneumonic form of the disease (17). Both forms are then highly infectious for their owners.

Leptospirosis

Leptospirosis is the disease caused by clinical infection with any one of the many serovars of the bacterium *Leptospira interrogans*. Each serovar of the bacterium is maintained in nature by non-clinical persistent infection of one or more wild or domestic mammals. These mammals are the maintenance hosts.

Leptospirosis as a clinical disease occurs when mammals of other susceptible species, such as humans, become infected. The disease is associated with septicaemia, haemolytic anaemia, hepatitis, nephritis, jaundice, abortion and still births. The bacteria persist in the kidneys of the maintenance hosts, are shed (excreted) in the urine, and can survive for some time in aquatic and moist environments. Infection can occur through the following ways:

– ingestion of contaminated water
– handling or ingesting infected milk or tissues
– transplacental invasion
– sexual contact
– social grooming.

In humans, farm and abattoir workers, hunters and trappers, wildlife handlers and zoo-keepers have traditionally been the high-risk groups (30). Epidemic outbreaks may be associated with periods of high rainfall, particularly in habitats with poor drainage and a high density of carrier animals. A recent significant outbreak of human leptospirosis in Nicaragua was associated with regional flooding. Contamination of ground water by infected domestic dogs appears to have been the source of infection (52).

Another major outbreak of leptospirosis occurred in 1998, involving ninety athletes participating in a triathlon in the upper Midwest of the USA. This outbreak was associated with swimming in a contaminated lake, bordered by both livestock-producing areas and wildlife refuges (9). However, the actual animal source of infection was never determined.

There have also been increasing reports of leptospirosis diagnosed in emergency rooms in urban settings, with the source of infection thought to be rodents.

Thus, while leptospirosis has been an acknowledged zoonosis for many years, recently it appears to be gaining new importance as a public health threat.

Conclusion

Emerging zoonoses are assuming a new importance, probably as a result of the following elements:

– the globalisation of trade
– expanding human populations
– intensification of wildlife farming
– microbes associated with wildlife entering intensive livestock production enterprises.

Some pathogens and/or their vectors appear to have expanded their geographic or host range as a result of global warming and other associated climatic changes. Other contributing factors may include habitat changes caused by humans and resource depletion, causing the displacement of traditional wild hosts.

The veritable collision between humans and wildlife, as human populations advance into new habitats and ecosystems, will continue to unmask cycling native pathogens, which can cross-infect humans and their livestock. Future occurrences of newly emerging diseases are most likely to erupt at these intensifying interfaces. In less developed countries, the communities most likely to be affected by such outbreaks are those that are poor or in less accessible areas. Such communities frequently rely on inadequate methods of medical surveillance and diagnostics, as well as traditional treatment methods. As a result, it is unfortunately quite likely that an emerging disease with high epidemic potential may only be detected after it has become established in humans or their livestock, and has already spread significantly. The logical pre-emptive counter to this scenario would be to increase disease surveillance and monitoring activities, and create a rapid response capability to investigate any unusual disease event in humans or animals around the globe.

These new animal and human health challenges will require innovative measures to improve vigilance. International hazard identification, risk communication and risk management strategies will become increasingly important as new diseases emerge in the future. Organisations such as the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the UN and the World Health Organization will have a decisive role to play in the detection and management of emerging diseases.

■

Le rôle de la faune sauvage dans les zoonoses émergentes ou réémergentes

R.G. Bengis, F.A. Leighton, J.R. Fischer, M. Artois, T. Mörner & C.M. Tate

Résumé

La taille des populations mondiales et la diversité de la faune sauvage sont immenses. Chaque paysage et chaque habitat présentent un kaléidoscope de niches qui font vivre une innombrable variété d'espèces vertébrées et invertébrées, et chaque espèce ou taxon entretient une diversité encore plus impressionnante de macro-et micro-parasites. Les agents pathogènes infectieux qui proviennent d'animaux sauvages ont pris ces dernières décennies une importance croissante dans le monde entier, à cause de leurs effets notables sur la santé humaine, la production agricole, les économies fondées sur la faune sauvage et la conservation des espèces sauvages.

L'émergence de ces agents pathogènes en tant que problèmes importants de santé est due à une série de facteurs, dont la plupart sont liés à l'augmentation brusque et exponentielle de l'activité humaine dans le monde. Au nombre de ces facteurs figurent l'explosion de la population humaine, la fréquence et la vitesse accrues des voyages locaux et internationaux, l'augmentation des mouvements d'animaux et de produits d'origine animale provoqués par l'homme, le changement des pratiques agricoles qui facilite le transfert d'agents pathogènes entre animaux sauvages et domestiques, enfin une série de modifications de l'environnement qui transforment la répartition des hôtes et vecteurs sauvages, facilitant ainsi la transmission des agents infectieux.

On constate dans ces maladies zoonotiques émergentes deux modes différents de transmission des agents pathogènes entre les animaux et les humains. Selon le premier, la transmission effective de l'agent pathogène aux humains est rare, mais quand elle se produit, la transmission interhumaine entretient l'infection pendant une certaine période ou de façon permanente. On peut donner comme exemples d'agents pathogènes fonctionnant selon ce mode de transmission le virus responsable du syndrome d'immunodéficience acquise, celui de l'influenza A, le virus Ebola et celui du syndrome respiratoire aigu sévère.

Dans le second mode, la transmission animal-homme directe ou par l'intermédiaire d'un vecteur constitue la source habituelle des infections humaines. Les populations d'animaux sauvages sont les principaux réservoirs de l'agent pathogène et la transmission interhumaine de la maladie est rare. On peut donner comme exemples d'agents pathogènes fonctionnant selon ce second mode de transmission le virus de la rage et les autres lyssavirus, le virus Nipah, le virus West Nile, l'hantavirus et les agents de la maladie de Lyme, ceux de la peste, de la tularémie, de la leptospirose et de l'ehrlichiose. Ces maladies zoonotiques dues à des sources animales sauvages ont toutes tendance à augmenter rapidement.

Dans cet article, les auteurs examinent les facteurs qui provoquent l'émergence ou la ré-émergence de ces zoonoses et mettent l'accent sur certaines d'entre elles pour offrir un point de vue synthétique sur leur portée, leur variété et leurs origines. La plupart de ces maladies sont traitées de façon plus détaillée dans les articles qui leur sont consacrés dans ce même numéro de la *Revue*.

Mots-clés

Maladie émergente – Maladie réémergente – Barrière des espèces – Faune sauvage – Zoonose.

El papel de la fauna salvaje en relación con las zoonosis emergentes y reemergentes

R.G. Bengis, F.A. Leighton, J.R. Fischer, M. Artois, T. Mörner & C.M. Tate

Resumen

Las poblaciones de animales salvajes que habitan el planeta son extraordinariamente numerosas y diversas. Cada paisaje y hábitat contiene un caleidoscopio de nichos que albergan una miríada de especies de vertebrados e invertebrados, y cada especie o taxón da cobijo a un conjunto aún más impresionante de macro y microparásitos. De unos decenios a esta parte, los patógenos animales procedentes de la fauna salvaje han cobrado una importancia creciente en todo el mundo por los notorios efectos que tienen sobre la salud humana, la producción agrícola, las economías dependientes de la fauna salvaje y la protección de ésta.

La aparición de esos patógenos como problema importante de salud pública guarda relación con una serie de factores causales, ligados en su mayoría al aumento súbito y exponencial de la actividad humana. Entre dichos factores se encuentran el pujante crecimiento demográfico, la mayor frecuencia y rapidez de los viajes locales e internacionales, la intensificación del movimiento de animales y productos de origen animal por obra del hombre, la evolución de las prácticas agrícolas hacia sistemas que favorecen la transferencia de patógenos entre animales domésticos y salvajes y una serie de cambios ambientales que alteran la distribución de huéspedes y vectores salvajes y facilitan así la transmisión de los agentes infecciosos.

Se distinguen con claridad dos modelos según los cuales los agentes patógenos de esas enfermedades zoonóticas emergentes pueden transmitirse de la fauna salvaje al hombre. En uno de ellos, el salto del patógeno al ser humano es en realidad muy poco frecuente, pero a partir del momento en que se produce el contagio entre seres humanos perpetúa la infección, ya sea durante un tiempo o de manera permanente. Como ejemplos de patógenos que siguen este modelo de transmisión cabe citar el virus del síndrome de inmunodeficiencia adquirida humana, el de la influenza A, el Ebola o el agente del síndrome respiratorio agudo severo.

En el segundo modelo, la vía habitual de contagio humano es la transmisión del animal al hombre, ya sea directa o mediada por un vector. Las poblaciones de animales salvajes constituyen el principal reservorio del patógeno, y rara vez se da la transmisión entre personas. Entre los ejemplos de patógenos que actúan de este modo figuran el de la rabia y otros lyssavirus, el virus Nipah, el virus West Nile, el hantavirus o los agentes de la enfermedad de Lyme, la peste, la tularemia, la leptospirosis y la erliquiosis. Todas estas enfermedades zoonóticas que provienen de la fauna salvaje muestran una acusada tendencia a aumentar. Los autores examinan los factores causales asociados a la aparición o reaparición de estas zoonosis, y describen algunas de ellas para ofrecer una visión de conjunto de su alcance, variedad y orígenes. En otros artículos de este número de la *Revista*, sin embargo, se examinan con más detenimiento la mayoría de esas enfermedades.

Palabras clave

Barrera interespecífica – Enfermedad emergente – Enfermedad reemergente – Fauna salvaje – Zoonosis.

References

1. Alexander D.J. & Brown I.H. (2000). – Recent zoonoses caused by influenza A viruses. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 197-225.

2. Allan B.F., Keesing F. & Ostfeld R.S. (2003). – Effect of forest fragmentation on Lyme disease risk. *Conserv. Biol.,* **17** (1), 267-272.

3. Anderson B.E., Dawson J.E., Jones D.C. & Wilson K.H. (1991). – *Ehrlichia chaffeensis*, a new species associated with human ehrlichiosis. *J. clin. Microbiol.*, **29** (12), 2838-2842.

4. Barnett T. & Whiteside A. (2002). – AIDS in the twenty-first century: disease and globalization. Palgrave MacMillan, New York, 432 pp.

5. Bengis R.G. (1999). – Tuberculosis in free-ranging mammals. *In* Zoo and wild animal medicine: current therapy, Vol. 4, Chap. 16 (M.E. Fowler & R.E. Miller, eds). W.B. Saunders and Company, Philadelphia, 101-114.

6. Brown R.N. & Burgess E.C. (2001). – Lyme borreliosis. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 435-454.

7. Buller R.S., Arens M., Hmiel S.P., Paddock C.D., Sumner J.W., Rikhisa Y., Unver A., Gaudreault-Keener M., Manian F.A., Liddell A.M., Schmulewitz N. & Storch G.A. (1999). – *Ehrlichia ewingii*, a newly recognized agent of human ehrlichiosis. *N. Engl. J. Med.*, **341** (3), 148-155.

8. Castrucci M.R., Donatelli I., Sidoli L., Barigazzi G., Kawaoka Y. & Webster R.G. (1993). – Genetic reassortment between avian and human influenza A viruses in Italian pigs. *Virology*, **193**, 503-506.

9. Centers for Disease Control and Prevention (1998). – Update: leptospirosis and unexplained acute febrile illness among athletes participating in triathlons – Illinois and Wisconsin, 1998. *JAMA*, **280** (17), 1474-1475.

10. Centers for Disease Control and Prevention (1999). – Update: West Nile virus encephalitis – New York, 1999. *MMWR*, **48** (41), 944-955.

11. Centers for Disease Control and Prevention (2003). – Update: Monkeypox – 2003. *MMWR*, **52** (27), 642-646.

12. Chanteau S., Ratsifasoamanana L., Rasoamanana B., Rahalison L., Randriambelosoa J., Roux J. & Rabeson D. (1998). – Plague, a reemerging disease in Madagascar. *Emerg. infect. Dis.*, **4** (1), 101-104.

13. Chen S.M., Dumler J.S., Bakken J.S. & Walker D.H. (1994). – Identification of a granulocytotropic *Ehrlichia* species as the etiologic agent of human disease. *J. clin. Microbiol.*, **32** (3), 589-595.

14. Chua K.B. (2003). – Nipah virus outbreak in Malaysia. *J. clin. Virol.*, **26** (3), 265-275.

15. Clifton-Hadley R.S., Sauter-Louis C.M., Lugton I.W., Jackson R., Durr P.A. & Wilesmith J.W. (2001). – Mycobacterial diseases: *Mycobacterium bovis* infections. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 340-371.

16. Davidson W.R. & Goff W.L. (2001). – Order rickettsiales. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 455-470.

17. Eidson M., Thilsted J.P. & Rollag O.J. (1991). – Clinical, clinicopathologic, and pathologic features of plague in cats: 119 cases (1977-1988). *JAVMA*, **199** (9), 1191-1197.

18. Escutenaire S. & Pastoret P.-P. (2000). – Hantavirus infections. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 64-78.

19. Food and Agriculture Organization (FAO) (2004). – Report of the avian influenza technical task force. FAO, Rome, Bangkok, 9 pp.

20. Gallagher J., Macadam I., Sayer J. & van Lavieren L.P. (1972). – Pulmonary tuberculosis in free-living lechwe antelope in Zambia. *Trop. anim. Hlth Prod.*, **4** (4), 204-213.

21. Gasper P.W. & Watson R.P. (2001). – Plague and yersiniosis. *In* Infectious diseases of wild mammals (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 313-329.

22. Gern L. & Falco R.C. (2000). – Lyme disease. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 121-135.

23. Grmek M.D. (1993). – History of AIDS: emergence and origin of a modern pandemic. Princeton University Press, Princeton, New Jersey, 290 pp.

24. Hahn B.H., Shaw G.M., De Cock K.M. & Sharp P.M. (2000). – AIDS as a zoonosis: scientific and public health implications. *Science*, **287** (5453), 607-614.

25. Horimoto T. & Kawaoka Y. (2001). – Pandemic threat posed by avian influenza A viruses. *Clin. Microbiol. Rev.*, **14** (1), 129-149.

26. Hutin Y.J., Williams R.J., Malfait P., Peabody R., Loparev V.N., Ropp S.L., Rodriguez M., Knight J.C., Tshioko F.K., Kahn A.S., Szczeniowski M.V. & Esposito J.J. (2001). – Outbreak of human monkeypox, Democratic Republic of Congo, 1996-1997. *Emerg. infect. Dis.*, **7** (3), 434-438.

27. Jezek Z., Grab B., Szczeniowski M.V., Paluku K.M. & Mutombo M. (1988). – Human monkeypox: secondary attack rates. *Bull. WHO*, **66** (4), 465-470.

28. Khan A.S., Sanchez A. & Pflieger A.K. (1998). – Filoviral haemorrhagic fevers. *Br. med. Bull.*, **54** (3), 675-692.

29. King A.A., Meredith C.D. & Thomson G.R. (1994). – The biology of southern African lyssavirus variants. *In* Lyssaviruses (C.E. Rupprecht, B. Dietzschold & H. Koprowski, eds). Springer-Verlag, Berlin, 267-295.

30. Leighton F.A. & Kuiken T. (2001). – Leptospirosis. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 498-502.

31. Leroy E.M., Rouquet P.K., Formenty P., Souquiere S., Kilbourne A., Froment J.-M., Bermejo M., Smit S., Karesh W., Swanepoel R., Zaki S.R. & Rollin P.E. (2004). – Multiple Ebola virus transmission events and rapid decline of central African wildlife. *Science*, **303** (5658), 387-390.

32. Linthicum K.J., Davies F.G., Kairo A. & Baily C.L. (1985). – Rift Valley fever virus (family *Bunyaviridae*, genus *Phlebovirus*). Isolations from Diptera collected during an inter-epizootic period in Kenya. *J. Hyg. (Camb.)*, **95** (1), 197-209.

33. McColl K.A., Tordo N. & Setién A.A. (2000). – Bat lyssavirus infections. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 177-196.

34. Mahy B.W.J. & Murphy F.A. (1998). – Emergence and re-emergence of viral infections. *In* Topley and Wilson's microbiology and microbial infections, Vol. 1, 9th Ed. (B.W.J. Mahy & L. Collier, eds). Edward Arnold, London, 1011-1025.

35. Meslin F.-X., Kaplan M.M. & Koprowski H. (1996). – Laboratory techniques in rabies, 4th Ed. World Health Organization, Geneva, 476 pp.

36. Mohd Nor M.N., Gan C.H. & Ong B.L. (2000). – Nipah virus infection of pigs in peninsular Malaysia. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 160-165.

37. Monath T.P. (1999). – Ecology of Marburg and Ebola viruses: speculations and directions for future research. *J. infect. Dis.*, **179** (Suppl. 1), S127-138.

38. Mörner T. & Addison E. (2001). – Tularemia. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 303-312.

39. Murray K., Selleck P., Hooper P., Hyatt A., Gould A., Gleeson L., Westbury H., Hiley L., Selvey L., Rodwell B. & Ketterer P.J. (1995). – A morbillivirus that caused fatal disease in horses and humans. *Science*, **268** (5207), 94-97.

40. OIE (World Organisation for Animal Health) (2002). – Highly pathogenic avian influenza. Chap. 2.1.14. *In* International Animal Health Code: mammals, birds and bees, 11th Ed. OIE, Paris, 158.

41. OIE (World Organisation for Animal Health) (2004). – Report of the meeting of the OIE Working Group on wildlife diseases, 9-11 February, Paris. OIE, Paris, 5.

42. OIE (World Organisation for Animal Health) (2004). – Report of the meeting of the OIE Working Group on wildlife diseases, 9-11 February, Paris. OIE, Paris, 8.

43. Pattyn S.R. (2000). – Monkeypoxvirus infections. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 92-97.

44. Philbey A.W., Kirkland P.D., Ross A.D., Davis R.J., Gleeson A.B., Love R.J., Daniels P.W., Gould A.R. & Hyatt A.D. (1998). – An apparently new virus (family *Paramyxoviridae*) infectious for pigs, humans, and fruit bats. *Emerg. infect. Dis.*, **4** (2), 269-271.

45. Rupprecht C.E., Stöhr K. & Meredith C. (2001). – Rabies. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 1-36.

46. Sall A.A., Zanotto P.M., Vialat P., Sene O.K. & Bouloy M. (1998). – Origin of 1997-1998 Rift Valley fever outbreak in East Africa. *Lancet*, **352** (9140), 1596-1597.

47. Smithburn K.C., Hughes T.P., Burke A.W. & Paul J.H. (1940). – A neurotropic virus isolated from the blood of a native of Uganda. *Am. J. trop. Med. Hyg.*, **20** (4), 471-492.

48. Swanepoel R. (1994). – Rabies. *In* Infectious diseases of livestock, with special reference to Southern Africa (J.A.W. Coetzer, G.R. Thomson & R.C. Tustin, eds). Oxford University Press, Cape Town, Oxford and New York, 493-552.

49. Taylor R.M., Work T.H., Hurlbut H.S. & Rizk F. (1956). – A study of the ecology of West Nile virus in Egypt. *Am. J. trop. Med. Hyg.*, **5** (4), 579-620.

50. Thorne E.T. (2001). – Brucellosis. *In* Infectious diseases of wild mammals, 3rd Ed. (E.S. Williams & I.K. Barker, eds). Iowa State University Press, Ames, Iowa, 372-395.

51. Tordo N., Badrane H., Bourhy H. & Sacramento D. (1993). – Molecular epidemiology of Lyssaviruses: focus on the glycoprotein and pseudogenes. *Onderstepoort J. vet. Res.*, **60** (4), 315-323.

52. Trevejo R.T., Rigau-Perez J.G., Ashford D.A., McClure E.M., Jarquin-Gonzalez C., Amador J.J., de los Reyes J.O., Gonzalez A., Zaki S.R., Shieh W.-J., McLean R.G., Nasci R.S., Weyant R.S., Bolin C.A., Bragg S.L., Perkins B.A. & Spiegel R.A. (1998). – Epidemic leptospirosis associated with pulmonary hemorrhage – Nicaragua, 1995. *J. infect. Dis.*, **178** (5), 1457-1463.

53. United Nations & World Health Organization (2004). – AIDS epidemic update 2003. Joint United Nations Program on HIV-AIDS (UNAIDS), Geneva, 48 pp. Website: http://www.unaid.org (accessed on 12 March 2004).

54. Westbury H.A. (2000). – Hendra virus disease in horses. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 151-159.

55. Williams E.S., Yuill T., Artois M., Fischer J. & Haigh S.A. (2002). – Emerging infectious diseases in wildlife. *In* Infectious diseases of wildlife: detection, diagnosis and management (R.G. Bengis, ed.). *Rev. sci. tech. Off. int. Epiz.*, **21** (1), 139-157.

56. Woolhouse M.E. (2002). – Population biology of emerging and re-emerging pathogens. *Trends Microbiol.*, **10** (10 Suppl.), S3-7.

57. World Health Organization (WHO) (2004). – Nipah virus outbreak(s) in Bangladesh, January-April 2004. *Weekly epidemiol. Rec.*, **79** (17), 168-171.

58. Xu R.-H., He J.-F., Evans M.R., Peng G.-W., Field H.E., Yu D.W., Lee C.K., Luo H.M., Lin W.S., Lin P., Li L.H., Liang W.J., Lin J.H. & Schnur A. (2004). – Epidemiologic clues to SARS origin in China. *Emerg. infect. Dis.*, **10** (6), 1030-1037.

59. Yabsley M.J., Varela A.S., Tate C.M., Dugan V.G., Stallknecht D.E., Little S.E. & Davidson W.R. (2002). – *Ehrlichia ewingii* infection in white-tailed deer *(Odocoileus virginianus)*. *Emerg. infect. Dis.*, **8** (7), 668-671.

60. Young J.C., Mills J.N., Enria D.A., Dolan N.E., Khan A.S. & Ksiazek T.G. (1998). – New World hantaviruses. *Br. med. Bull.*, **54** (3), 659-673.

61. Young P., Halpin K., Field H. & MacKenzie J. (1997). – Finding the wildlife reservoir of equine morbillivirus. *In* Recent advances in microbiology, Vol. 5 (V. Asche, ed.). Australian Society for Microbiology, Melbourne, 1-12.

62. Zeller H. & Bouloy M. (2000.) – Infections by viruses of the families *Bunyaviridae* and *Filoviridae*. *In* An update on zoonoses (P.-P. Pastoret, ed.). *Rev. sci. tech. Off. int. Epiz.*, **19** (1), 79-91.