ENVIRONMENTAL JUSTICE FOUNDATION

Protecting People and Planet

Viral diseases from wildlife in China

Could SARS happen again?

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Protecting People and Planet

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Wet market - Wuhan, China. © Animal Equality

PREFACE

It is important to note that this report was written 17 years ago in 2003. We are publishing it here as it was then. There are, of course, sections that could be updated; for example, we could add information on 'swine' flu H1N1 in 2009, MERS in 2012, the 2014-2016 Ebola epidemic, and plenty of research which points to bats as the original source of coronaviruses.

However, we publish it here exactly as it was in 2003 to show how much we did know at the time. Looking back from 2020, the six case studies in chapter 2 make sobering reading, especially those on Ebola and SARS. Consider the table in Appendix II (pages 34-39), listing 76 viruses known then to be transmissible directly from animals, of which 52 were classed as public health problems and 49 were new or increasing. The six recommendations to reduce the risk of another previously unknown viral disease emerging in China (page 31) could be repeated without much alteration.

We had all the knowledge we needed to curb dangerous practices and lower the risks of tragic pandemics such as the one we are living through in 2020. Now we are scrambling to sequence the new coronavirus that causes COVID-19, develop tests, drugs and conduct trials within a few weeks. It is amazing what science can achieve. However, translation of knowledge into policies is seriously lacking. We are not even prepared when it comes to the very basics of protective equipment for frontline medical staff. Nor did we heed the lessons of SARS in 2003. Instead "business as usual" continued, including commerce and practices known to be risky. In 2003, we had a chance to shut the stable door before the horse bolted. This time, we are not so lucky. It is imperative that we use the pandemic to learn our lesson.

Steve Trent (EJF), Wolfgang Preiser (University of Stellenbosch) and Lynn Dicks (University of Cambridge), April 2020.

EXECUTIVE SUMMARY

As demonstrated by the recent outbreak of Severe Acute Respiratory Syndrome (SARS), viruses can emerge suddenly in the human population and spread rapidly, with devastating effect. This report reviews knowledge of viruses that transmit directly from animals to humans and asks whether anything can be done to reduce the risk of further virus outbreaks from animals in China.

The report begins with an outline of virus biology and important concepts such as zoonosis (transfer of pathogens between humans and animals). Six detailed case studies of emerging viral zoonoses are presented: influenza A; Ebola; HIV; hantavirus pulmonary syndrome; hendra viruses and SARS. These illustrate the range of factors associated with transfers of disease from animals to humans.

A detailed review of documented viral zoonoses not carried by arthropod vectors is given. 76 viruses are found to fit this description. The review compiles scientific knowledge about the animal origins, severity and distribution of these diseases and the factors responsible for the transfer to humans. 49 are new or increasing in the human population; 52 cause fatality or widespread infection; 36 are found in Asia. The majority come from primates, even-toed ungulates and rodents. Factors associated with viral disease transfer from wildlife are reviewed from the literature. The most important are ecological change, including climate change and changing agricultural practises; and increasing human populations, both of which can entail increased contact with wildlife. RNA viruses, transmitted by arthropods, with a broad host range are the most likely pathogens to emerge as new diseases from wildlife.

The SARS virus is assessed in the context of this review. It fits some of the categories of a virus likely to emerge, but it could not have been predicted, because it comes from a group of viruses that do not have a broad host range, and apparently from a group of animals with little history of zoonosis.

Three main factors are outlined that make China a likely place for further emergence of directly acquired zoonotic viruses. The first is widespread consumption of wildlife species in China. The risk of zoonosis is during contact with live animals, their blood and raw meat, or in eating poorly cooked meat. In a review of studies of species consumed in China, 226 species were documented. 77% were birds, reptiles and amphibians; 23% were mammals. Since mammals form the vast majority of sources of previous direct zoonoses, these are considered in more detail. Most are primates and carnivores, with a significant proportion of rodents and ungulates. Of these groups, primates, ungulates and to a lesser extent rodents have the greatest history of viral disease transfers. Primates, especially monkeys, are of particular concern because they represent three of the seven most popularly eaten mammal species. This group are the source of around a fifth of documented viral zoonoses, and Asian macaques are known to carry viruses with zoonotic potential such as a strain of Ebola virus.

Secondly, China is found to be experiencing significant ecological changes that have been linked directly to increased risk of zoonosis – specifically deforestation, climate change and increasing rodent populations. Finally, the high and increasing number of Chinese carrying HIV (1.5 million) makes the population vulnerable to new viruses establishing themselves.

Overall, the risk of further viral zoonoses emerging in China can be considered substantial. Six recommendations are suggested to reduce the risk, including reducing the number and quantity of wild species eaten, particularly primates, wild pigs and rodents; warning hunters, traders and consumers of the risk of viral zoonosis; encouraging well-inspected farming rather than hunting of wildlife and further research to anticipate zoonoses.

INTRODUCTION

"If there is any conceivable way a germ can travel from one species to another, some microbe will find it"

(McNeill, 1976).

Viruses are probably the largest threat to the continued prosperity of mankind. Despite nominal success in combating the smallpox virus (*Variola*), most viruses evade eradication, by continually changing or switching between hosts. The majority of human viruses originated in animals. Some scientists claim there has been a dramatic increase in the occurrence of new pathogenic viruses in the human population over the last 25 years (Crawford, 2000), and there has been an increase in global mortality from infectious disease (Ludwig, Kraus *et al*., 2003). These increases can be expected to continue as a result of increasing ecological change and environmental degradation, and increasingly mobile human populations (Morse, 1995; Stöhr and Meslin, 1997; Osterhaus, 2001). As demonstrated by the recent outbreak of Severe Acute Respiratory Syndrome (SARS), viruses can emerge suddenly in the human population and spread rapidly, with devastating effect.

This report reviews our knowledge of viruses that can transmit directly from animals to humans and asks whether anything can be done to reduce the risk of further virus outbreaks from animals. It does not include other human parasites, such as bacteria, which also pose a threat of infection from animals and include well-known zoonoses such as the plague bacteria *Yersinia pestis*, Weil's disease from rats and *Salmonella* food poisoning. The report is divided into four chapters. Chapter one outlines virus biology, describes some important principles and concepts in virology and introduces the concept of zoonoses. Chapter two is a series of six case studies of emerging viral zoonoses. Chapter three is a detailed review of documented viral disease transfers, their animal origins and the factors responsible for the transfer to humans. Chapter four considers the current situation in China, and how it relates to risk factors identified in chapter three. The report ends with a set of recommendations on how to reduce the likelihood of future viral zoonotic diseases emerging in China.

CHAPTER 1 – BASIC VIRUS BIOLOGY

Structure and Replication

Viruses are distinct from other living organisms, because they do not carry the cellular machinery to metabolise. They consist simply of genetic material and a protein coat, and rely on the cells of living organisms to reproduce. When an infectious virus particle, known as a virion, infects an organism, it attaches onto its cells and hijacks the cellular machinery by injecting virus genes into the nucleus. The cell then produces new virus particles, which in some cases rupture the cell as they emerge.

Most viruses are specific to certain types of cell within their host. Hepatitis viruses recognize liver cells, for example, while respiratory viruses infect epithelial cells in the respiratory tract and lungs. Viruses recognise specific receptor molecules on the surfaces of cells. A wide variety of different receptor molecules have been identified for different viruses, including proteins, carbohydrates or lipids involved in a variety of functions from cellular signaling to adhesion. Closely related viruses do not necessarily use the same type of receptor, and some viruses such as hepatitis C use more than one (Baranowski, Ruiz-Jarabo *et al.*, 2001).

Proteins that stick out from the outer coat of the virus bind to these receptors and initiate infection. These 'spike' proteins are often called glycoproteins, because they have a sugar molecule attached. They may be a target of the host's immune response, which learns to recognize the virus by particular sequences in these surface proteins. In the case of influenza, a change in a single amino acid can change the cell surface receptor that is used (Baranowski, Ruiz-Jarabo *et al.*, 2001). This is why the same person can repeatedly suffer the disease, because the target for the immune system changes.

Types of Virus

According to the universal system of virus taxonomy, devised by the International Committee on Taxonomy of Viruses (ICTV), there are currently 71 families of viruses. 24 of these contain viruses that infect humans and animals (listed in Appendix I). The universal system classifies viruses according to their biochemical structure and method of replication. Specifically, they are divided according to what type of nucleic acid they have (DNA or RNA, single or double stranded); whether their genome is a single piece of nucleic acid, or segmented into separate sections, a bit like our chromosomes; which way the genome is read (positive or negative) and whether the virus particle is surrounded by a membranous envelope or not. Most human pathogenic viruses use RNA although there are notable exceptions, such as pox- and herpes viruses.

To some extent, this method of classification is reflected in the epidemiology of the viruses, in that viruses in the same taxonomic group often have similar methods of transmission, clinical signs and affect similar types of organism. For example, viruses in the family *Orthomyxoviridae*, the influenza type viruses, are respiratory infections, acquired by inhalation or direct contact with mucous membranes. The family Flaviviridae contains viruses causing fever and encephalitis, and transmitted by arthropod vector, such as yellow fever, dengue fever and rocio. Viruses in the family Arenaviridae usually cause haemorrhagic fever in humans. All but one are carried by rodents mostly from the Muridae (mice and rats) and the Cricetidae (voles, lemmings and gerbils) families. The exception, Tacaribe virus from Trinidad, is carried by the fruit bat *Artibeus* sp (Howard, 1998). This pattern is not without exceptions. Almost all the viruses in the family Bunyaviridae, for example, are arthropod-borne except for those in the genus Hantavirus, which are transmitted by murid rodents (Clement, McKenna *et al.*, 1998).

Viruses can also be classified according to their mode of transmission. **Enteric** viruses are intestinal and acquired by ingestion. **Respiratory** viruses are acquired by inhalation of 'fomites' – small droplets transmitted between hands, nose, mouth and eyes. **Arboviruses** enter directly into the bloodstream via the bites of arthropod vectors, such as ticks or mosquitoes. Many other viruses are acquired by close contact, such as sexual contact, involving host body fluids. Most virus families contain examples of several of these categories.

Within a virus family, viruses are classified into genus, then species. Proper names for viral species are decided by the ICTV and listed on Index Virum (ICTV, 2003). Identifying and separating different species is difficult, especially because viruses cannot be cultured outside host cells and do not survive long alone. A variety of methods are used, falling into three categories: serological methods, structural characterisation and genetic methods.

Serological techniques involve using antibodies created by the host immune system to identify and distinguish different viruses. Antibodies are virus-specific molecules produced by an infested organism, which bind to virus particles and are instrumental in disabling them. In most cases, they appear in large quantities in host serum, during primary infection with a virus. Some serological techniques, such as **neutralization**, directly measure the capacity of the antibody to block a specific viral function. Others focus on the chemical reaction between the antibody and virus. Serological techniques are particularly useful in circumstances where isolation of the virus itself is difficult, or in demonstrating previous infection rates of non-persistent viruses (see Epidemiology section below). Certain viruses show **cross-reactivity** with antibodies created against other virus species. For example, cowpox antibodies provide protection against smallpox, which is why dairy workers largely escaped the latter disease. In other cases, such as influenza, different strains of a single virus species produce different antibodies – the strains are called different **serotypes**.

Virus groups have different shapes and can be viewed under an electron microscope. Coronaviruses, for example, are round particles covered in surface projections, or spikes. Filoviruses such as Ebola are long filaments.

Genetic characterization of viruses plays an increasingly important part in diagnostics and taxonomy. Genome sequences specific to many viruses are now available and small quantities of virus can be detected in clinical samples either by hybridization with a nucleic acid probe, or by amplifying the viral genome using the polymerase chain reaction (PCR). Since virus genomes can mutate and change rapidly, there is currently considerable effort to identify sequences that remain stable within virus groups (e.g. Rota, Oberste *et al.*, 2003).

A Word on Epidemiology

Epidemiology is the study of the dynamics of infectious diseases: how they survive and change as populations, and interact with their host populations. An important dichotomy in epidemiology is between pathogens that are short-lived in their host, usually leaving them immune but virus-free, and those that persist, creating a population of more or less healthy hosts that carry the virus.

Short-lived pathogens need to infect at least one other host after each infection for the population to persist (Anderson and May, 1992). Since they leave the host either dead or immune, they need a host population large enough for there always to be naïve host individuals available. The number of new individuals infected after each case can be used to predict whether novel viruses, such as the SARS coronavirus, are likely to create an epidemic in a new host population (Bull and Dykhuizen, 2003). It is believed that in low density populations, with small social groups isolated from one another, as in pre-agricultural humans and many wildlife species, microbes tend to co-evolve with their hosts, establishing the latter type - persistent infections that are not highly pathogenic (Weiss, 2001). Examples in humans are the herpes viruses and the chickenpox virus. Similarly, many viruses carried by wild animals do not make them sick.

When humans developed agriculture, our population densities became high enough to support non-persistent, pathogenic parasites of the former type (Anderson and May, 1992).

Virus Transfers Between Humans and Animal Species (Zoonoses)

Viruses that naturally transfer between humans and animal species are known as **zoonotic** viruses, or **zoonoses** (Palmer, Soulsby *et al.*, 1998). Most human infections originally came from an animal source (Weiss, 2001). 61% of all human pathogens and 76% of all human viruses are zoonotic (Taylor, Latham *et al.*, 2001). Some, such as the 'flu virus, are well known and have been present in human populations for a very long time. Others are brand new arrivals. The dynamics of such diseases are complex. Often there is a 'reservoir' population of one or more species, which holds the disease permanently in a stable equilibrium (Haydon, Cleaveland *et al.*, 2002). From the reservoir, the disease can occasionally transmit to a different host and establish itself in the new population. In other zoonoses, like rabies, each new case represents a new infection from an animal.

Many of our most deadly zoonotic pathogens are arboviruses, carried by insects. They frequently change hosts and their dynamics can be affected by changes in patterns of settlement, agriculture or irrigation that affect populations of the vectors, and their contact with humans. A list of known arboviruses is included in this report (Appendix IV), but the diseases are not dealt with in detail. Prevention and control of arbovirus infections is built almost exclusively on diagnosis and treatment in humans, and control of invertebrate hosts (Stöhr and Meslin, 1997), indicating that direct transmission from animals is not an important route.

Viruses transmitted directly[1] between vertebrate animals and humans are of interest because the likelihood of this kind of transfer is closely related to the degree of contact between humans and animals. A detailed review of these viruses is given in chapter three.

Changes in virulence when a virus switches host, are frequent, and difficult to predict (Frank and Jeffrey, 2001). Many zoonotic viruses, such as the arenaviruses, hendraviruses and hantaviruses, produce a tolerated persistent infection in the reservoir host, with no ill-effects and no detectable immune response (Clement, McKenna *et al.*, 1998; Howard, 1998). On transfer to humans, they are deadly killers. The opposite can also happen. The arbovirus Sindbis, for example, causes disease in birds, but is only dangerous to humans that are immunosupressed (Weiss, 2001). Herpes B virus (Cercopithecine herpes virus type 1) is highly prevalent in wild Asian macaques, in 80-100% of which it causes small skin lesions of low severity (Meurens, Gallego *et al.*, 2002). In a human bitten by an infected monkey, the virus often leads to fatal encephalitis. The disease has killed 24 humans since its discovery in 1932 out of around 40 reported cases (Meurens, Gallego *et al.*, 2002). Considering the widespread use of macaques in biomedical science, this low rate of transmission between human and animal host has led one author to suggest there may be an unknown immunological mechanism preventing cross species transfer of this type of virus (Skinner, Ahmad *et al.*, 2001).

Many authors writing on the subject of zoonotic viruses include a stark warning about the likelihood of future incidences producing highly transmissible or pathogenic epidemics (Morse, 1993; Weiss, 2001; Ludwig, Kraus *et al.*, 2003). Close surveillance and careful preparation of medical and public health institutions is consistently suggested, rather than any attempt to reduce the risk of new zoonoses occurring.

[1] 'Direct' in this context, and later 'direct zoonoses', refers to the lack of intermediate arthropod vector, and should not be understood to exclude viruses transmitted between humans and animals via body fluids or environmental reservoirs.

There are virus types common in animals that have not transferred to humans but may have the potential to. Canine Distemper virus (Paramyxoviridae), for example, seems to have expanded its host range this century, infecting many species of carnivore, including marine mammals (Baumgartner, Alldinger *et al.*, 2003). There has long been concern about the zoonotic potential of the cancer causing retroviruses which occur in cows, birds and cats, because of our close contact with these animals, and the existence of a similar virus (HTLV-1) already infecting humans (Platt, 1994). The latter has since been suggested to be a primate zoonosis (Voevodin, Johnson *et al.*, 1997). Mice have been experimentally infected with cow retrovirus via their milk. Analysis of genetic sequences shows that these retroviruses have switched species several times over the last 70 million years (Platt, 1994).

How are zoonoses detected?

Identifying a zoonosis event is not easy. Five lines of evidence are available: prevalence in the natural host; geographic coincidence; plausible routes of transmission; similarities in viral genome organization and phylogenetic relatedness to viruses in animals.

In some cases, the coincidence of events alone provides very strong evidence. For example, a recent outbreak of monkeypox in the mid-West United States was traced to African rats imported as pets (Lutz, 2003). Similarly, Ebola virus has been transferred in shipments of monkeys for biomedical research on a number of occasions, although primates are probably not the main reservoir. In others cases, this sort of evidence is weak, such as the unproven link between bats and Ebola (see case study two).

Molecular genetic ways of identifying the source of a virus can be applied retrospectively. A virus that has co-evolved with the human species, rather than being a zoonotic infection, will have a relationship with similar viruses in other animals that reflects our own evolutionary relationship with them. Our herpes viruses, for example, are more similar to chimpanzee herpes than to a rabbit version (Weiss, 2001). But if a virus appears in humans that is very similar, or indistinguishable from one present in an animal species not particularly closely related to ours, this is strong evidence of a zoonotic transfer, especially if the virus is associated with an illness not previously observed. A zoonotic origin for measles is postulated on the basis of the genetic structure of the virus, although it is an event that probably happened 7000 to 8000 years ago, when humans first domesticated ruminants (Diamond, 1997).

For some viruses, scientists are unsure. There is uncertainty, for example over the origin of the hepatitis B virus (Bollyky, Rambaut *et al.*, 1997; MacDonald, Holmes *et al.*, 2000; Odemuyiwa, Mulders *et al.*, 2001; Simmonds, 2001). In 1997, Bollyky et al postulated it was a zoonosis from new world monkeys in the last 500 years. More recently, the same group has shown that the related viruses are dispersed throughout the Old World Apes, suggesting we carried the virus before we were humans (Macdonald 2000). But one group of human hepatitis B viruses in West Africa is very similar to a local chimpanzee form (Odemuyiwa, Mulders *et al.*, 2001).

To avoid catching zoonoses, the best strategy is to identify the natural host reservoir, and sever links with it (Haydon, Cleaveland *et al.*, 2002). Those links could be direct or via an intermediate host such as a domestic animal. As we shall see, this is not always possible.

CHAPTER 2 – CASE STUDIES OF EMERGING VIRAL ZOONOSES

An **emerging virus** is one that has appeared in a new host population, or whose incidence is increasing (Woolhouse, 2002). Six case studies of well-known emerging viral zoonoses are presented below. These have been chosen to illustrate the range of factors that can influence the transfer of disease from wildlife to humans.

CASE STUDY ONE: INFLUENZA A

Influenza is a highly contagious acute respiratory illness. It is not usually fatal, although a flu epidemic often causes death in the old and weak. Three types of the virus are known to infect humans: influenza A, B, C. They have very high epidemic potential. Up to 25% of the world's population could become ill during a single epidemic, and the virus has the potential to kill 30% of its victims (Enserink, 2003). There are 50,000 influenza deaths per year in the United States (Murphy, 1994).

Until recently, influenza A was the only one known to move between species under natural conditions. It is commonly found in humans, horses, pigs, chickens, aquatic birds, and more rarely occurs in seals, whales, mink and cattle. Current understanding is that wild ducks and shorebirds are the primary and most stable reservoir of the disease, but versions of it frequently transfer to other animals. Influenza A is known as a re-emergent virus, because of this dynamic. The best evidence for transfer of influenza A between species is the sporadic transmission of swine influenza to humans (Slemons and Brugh, 1994). Normally, such infections occur in people in direct contact with pigs. They are no more serious than ordinary human 'flu and transmission to other humans is limited. There is also direct evidence of transfers of influenza A between humans and chickens and humans and seals. In the latter case, the seal flu virus infected the eyes of men investigating the outbreak, causing conjunctivitis (Webster, Geraci *et al.*, 1981). In both instances, the infection died out of its own accord.

The danger of a **pandemic**, or worldwide epidemic, is when a new and highly virulent strain arises. The labels given to different strains of influenza A refer to the type of two surface glycoproteins on the outer envelope – hemagglutinin (HA) and neuraminidase (NA). Currently there are 15 HA and 9 NA subtypes identified (Horimoto and Kawaoka, 2001). Human and swine influenzas are limited to a few of these varieties, but birds can be infected by every combination, forming a vast global reservoir of the virus.

New strains usually occur when two different versions of the virus meet in a single host and the genome segments are re-sorted in a process called **antigenic shift**. For example, if a human already carrying the flu virus becomes infected with an avian variant, a new combination of envelope glycoproteins can arise. Sometimes the new strain is particularly virulent, as in the catastrophic 'Spanish influenza' epidemic in 1918. This was the most devastating viral disease of the twentieth century, and killed more than 20 million people worldwide (Granoff and Webster, 1999).

Since the first human influenza virus was isolated in 1933, three more major pandemic strains have been described: 'Asian flu (1957) H2N2, Hong Kong flu (1968) H3N2 and Russian flu (1977). These strains caused global outbreaks and high death tolls. The first two strains arose in China, when a human flu acquired new genes from the wild duck flu. The same process brought us the Spanish flu. Russian flu was an identical strain to the 1968 Hong Kong flu and may have been stored in a freezer in the intervening years. The low death rate in this pandemic could be explained by immunity of people over 20 years old acquired during the Hong Kong pandemic (Horimoto and Kawaoka, 2001).

It has been suggested that the emergence of new flu strains often occurs in China because of the practice of combined pig and duck agriculture there (Brown and Alexander, 1998). In this context, natural hosts of influenza A are in direct and continuous contact, increasing the chances of a new strain arising by antigenic shift.

Avian influenza is enteric and can be spread in water contaminated with faeces. It is less host-specific than versions of the virus in mammals and is found in a very wide variety of birds, including poultry, game and wild birds. The current strategy for controlling flu involves watching for new strains in pigs or chickens, particularly in China. The regularity of pandemics suggests that the likelihood of another increases over time. Although significant measures are taken to control avian, swine and equine influenza, there is no feasible method for control of influenza in wild free-flying birds.

Zoonosis of influenza A has generally been considered a rare event. A review of the literature reveals only 18 cases of pure swine fever directly crossing into people (Wuethrich, 2003). But this is probably a serious underestimate of the actual incidence of such a transfer. Usually, only molecular biology can distinguish between the different strains of flu, and in the absence of mortality or unusual infection pattern, most cases are assumed to be ordinary human flu. A study last summer found that 23% of pig farm workers and their families carried antibodies to swine flu strains, compared with less than 1% of urban dwellers (Olsen, Brammer *et al.*, 2002).

In the last seven years, outbreaks of two new strains of avian-derived influenza have been reported in humans, in 1997 (H5N1) (Osterhaus, 2001), 1999 (H9N2) (Lin, Shaw *et al.*, 2000) and 2003 (H5N1) (WHO, 2003a). Fortunately none of these developed into a pandemic, partly because human-human transmission was inefficient and partly due to the widespread slaughter of poultry in the affected areas (Shortridge 2001). In each case, the flu was passed directly from birds to humans, without any involvement of pigs as a 'mixing vessel'. It is normally in pigs that the switch happens from the enteric avian form to the respiratory mammalian form. In each case, the transfer occurred in Hong Kong. In the case of H5N1 in 1997, the event was traced to the Hong Kong waterfowl markets, where the virus had transferred from wild birds to chickens. Eighteen people caught the disease, six of them died. There is increasing concern among scientists that a new pandemic strain of influenza could arise at any time (Horimoto and Kawaoka, 2001; Li, Xu *et al.*, 2003; Webster and Walker, 2003).

This year an old strain (H7N7) has reappeared in poultry farms in the Netherlands with apparently new potential for human infection. This virus has caused conjuncitivitis in at least 83 people and killed one person. Although human-human transmission seems weak, it is possible. Flu specialists are worried, because of the potential for an avian flu to recombine with genes from a human strain of flu inside a person. In addition, antibodies to the H7N7 strain have already been found in Dutch pigs (Enserink, 2003).

CASE STUDY TWO: EBOLA

Ebola virus and its cousin Marburg virus are killers. Their source and natural ecology have vexed the scientific community for 35 years and remain a mystery. Both cause haemorrhagic fever, with massive internal bleeding often resulting in death. Marburg virus first appeared in 1967. 31 laboratory workers in Germany and Yugoslavia were infected. They had been exposed to tissues from African green monkeys (*Cercopithecus aethiops*) imported from Uganda. Seven of them died. When the virus was identified, it was placed in a new viral family, the Filoviridae. There have been three subsequent outbreaks of Marburg in South Africa (1975), Kenya (1980 and 1987) and in the Democratic Republic of Congo and Zaire in the 1990s.

In 1976 and 1979 there were several outbreaks of another Filovirus causing lethal hameorrhagic fever in Zaire and Sudan. It was named Ebola virus. It was mostly confined to hospitals, and transmission between people appeared to be by direct contact with infected tissue, or close personal contact. Mortality rates in the initial outbreak were 88% in Zaire and 53% in Sudan. There have been seven subsequent outbreaks of the disease in Africa, with mortality rates ranging from 50-81%. All have been confined to relatively small areas. Currently an epidemic is occurring in Gabon and the Republic of Congo, which so far has affected 143 people, and killed 128 (90%) (WHO, 2003a). In 1994, a scientist became infected with a different strain of Ebola, the Ivory Coast strain, after performing an autopsy on a wild chimpanzee.

Scientists suspect the disease is initially caught in each outbreak from an infected animal, perhaps a primate hunted for 'bushmeat' (CDC, 2003). But monkeys and chimpanzees are unlikely to be the natural reservoir of Filoviruses, because they become ill and die when they are infected (Ludwig, Kraus *et al.*, 2003). Extensive surveys of wildlife, including mammals, birds and insects in the outbreak areas have identified no natural host. In 1987, a boy was infected with Marburg virus after spending considerable time in a cave on Mount Elgon filled with bats. Bats were also present in large numbers in a cotton factory where there were outbreaks of Ebola in 1976 and 1979. They are a strong candidate for the reservoir, because they can be artificially infected without becoming ill (Ludwig, Kraus *et al.*, 2003). But no one has managed to isolate the virus from wild bats. Scientists remain convinced that the disease is zoonotic, and that outbreaks are triggered by initial infection from wildlife (CDC, 2003). Temporal patterns of the outbreaks suggest that the natural host has contact with monkeys and or humans for only a short period of the year. Most outbreaks begin in November or December (Guenno, 1997). The lack of a natural host is mystifying, leading some scientists to speculate that the disease may even be an arthropod or plant virus (Monath, 1999).

In 1989 a new Ebola-type virus appeared in America, in a shipment of macaques (*Macaca fascicularis*) from the Phillipines. No African connection could be found for these monkeys, but they themselves were dying. To the horror of scientists, antibodies to the virus were also found in some of the human laboratory workers, but they showed no disease symptoms. Rapid euthanasia of monkeys and disease control tactics prevented the spread of the outbreak. The disease, named the Reston strain of Ebola, after the quarantine site in America, was subsequently found to be present in captive macaques in the Philippines. During a further outbreak of the same virus in 1990, also at Reston, the disease was noted to have respiratory involvement. There was high concentration of viral antigens in pulmonary secretions and post mortem showed the virus to be reproducing in the lung tissue. 80% of infected monkeys died and several workers at the laboratory were infected without having had direct contact with the monkeys (Peters, Johnson *et al.*, 1993). The same virus was isolated from monkeys from the Philippines in Italy in 1999 and again in the US in 1996 (Rollin, Williams *et al.*, 1999) but no humans were infected, due to employment of careful screening and barrier precautions. Again, captive macaques and primate facilities in the Philippines were investigated, and the virus was concluded to be rare (Miranda, Ksiazek *et al.*, 1999). There have been no surveys for this virus in other Asian wildlife species.

This case demonstrates the epidemic potential of the Filoviruses. It happens that the Reston strain does not cause human disease. But in the words of Peters, Johnson *et al* (1993), "the seriousness of the efficient (airborne) spread of a filovirus cannot be overestimated." There seems to have been little further investigation into the natural ecology of this strain of Ebola, perhaps due to the lack of immediate public health implications. Ebola research is concentrated in Africa.

It is not clear whether there are increasing numbers of Ebola virus outbreaks in central Africa or whether more are recorded due to better surveillance from the international health community. If outbreaks are increasing in frequency, this has been linked to ecological perturbations caused by deforestation (Guenno, 1997).

CASE STUDY THREE: HIV

HIV-1 is currently responsible for an extremely serious global pandemic, particularly affecting the poor and undeveloped nations of the world, with no end in sight (Weiss and Weiss, 2001). 42 million people are infected and the numbers are still increasing. In some African countries more than 30% of the adult population have the virus (Ludwig, Kraus *et al.*, 2003).

The disease caused by HIV, Acquired Immune Deficiency Syndrome, AIDS, is invariably fatal. It was first recognized in the USA in 1981 (Gottlieb, Schroff *et al.*, 1981), and a few years later, scientists realized the disease was already widespread in Africa (Bayley, Cheingsongpopov *et al.*, 1985; Serwadda, Sewankambo *et al.*, 1985). It is a particularly formidable pandemic, because it presents opportunities for other infections, and possible zoonoses, to establish themselves in populations with severely weakened immunity. The virus is transmitted by direct contact of body fluids and evolves extremely rapidly, both within an individual host and around the world (Piot, Bartos *et al.*, 2001).

It is well established that HIV-1 came to humans from the simian immunodeficiency virus, chimpanzee SIV (Gao, Bailes *et al.*, 1999). Analysis of the genetic sequences of the different strains of HIV indicates there have been seven separate zoonotic incidents, in the last 100 years. All happened in Africa, where there is the greatest variation. HIV-1 appears to have crossed the species barrier 3 times, resulting in the M, N and O groups. These groups are as distinct from one another as they are from the chimpanzee SIV (Gao, Bailes *et al.*, 1999). It is the group M that has spread around the world and caused the pandemic. Another form of HIV, HIV-2, which is less transmissible but causes local epidemics, also appears to be of primate origin. It arrived from the sootey mangabey, *Cercocebus atys*, and can be subdivided into six or more groups that appear to represent separate zoonoses (Gao, Yue *et al.*, 1992). HIV-2 is endemic in West Africa, but has spread to Europe (Portugal) and India (Weiss, 2001).

The exact route of HIV zoonosis has been a matter of heated debate amongst scientists. In the case of HIV-2, the contact between humans and host is through mangabeys hunted for food and orphans kept as pets (Hahn, Shaw *et al.*, 2000). Hunting and field-preparation of chimpanzees, a common practice in West Africa, is also blamed for the transfer of HIV-1. However, some scientists argue that the 'cut-hunter' theory, as it is known, has not been carefully studied. It is assumed to be possible, but not proven (Martin, 2001; Weiss and Weiss, 2001). Another theory suggests that HIV originally infected humans through the preparation of live polio vaccines using chimpanzee kidneys (Hahn, Shaw *et al.*, 2000; Hooper, 2000; Martin, 2001; Weiss and Weiss, 2001). The polio vaccine theory has been intensely scrutinized and now looks unlikely. Comparison

between human and primate HIV/SIV viruses suggest that HIV-1 was present in the human population 10-50 years before the polio vaccines trials began. It is not clear why HIV remained geographically isolated in the intervening years, before suddenly enlisting a pandemic in the 1970s.

The natural primate hosts of HIV/SIV harbour similar levels of the virus to infected humans, but they do not become ill or die of AIDS-like illnesses. Twenty-four other species of African primate harbour types of SIV, but there is no evidence that any of these have infected humans (Hahn, Shaw *et al.*, 2000). Asian macaques do not have SIVs (Granoff and Webster, 1999).

CASE STUDY FOUR: HANTAVIRUS PULMONARY SYNDROME

Until 1993, Hantaviruses were recognized zoonoses, mostly carried by Murine rodents (Old World rats and mice) and causing haemorrhagic fever with renal syndrome, HFRS – that is acute renal failure in the context of a flu-like febrile illness. Epidemics of this disease have been documented as far back as the American Civil War, but the virus was first described in the 1950s, during the Korean War (Earle, 1954). A number of outbreaks have since been documented in Asia, Europe and America, largely caused by three strains of hantavirus named Hantaan virus, Seoul and Puumala virus (Chu, Rossi *et al.*, 1994). There are tens of thousands of cases of Hantaan virus annually in China. But the disease was not particularly feared. Rather, it was considered a "somewhat arcane zoonosis, of interest to kidney and rodent specialists" (Jacobson, 2003).

Then, in the early 1990s, a group of new forms of the virus exploded on the scene in Europe and North America, prompting global concern. These viruses attacked not the kidneys, but the lungs. The viruses were classified in the same genus, *Hantavirus*, and a new syndrome was named, hantavirus pulmonary syndrome (HPS), characterized by acute respiratory distress in adults, and often fatal pulmonary or cardiac failure (Clement, McKenna *et al.*, 1998) (Täger, Vial *et al.*, 2003). From 1993 until now, new HPS viruses have been recognised almost every year and there are approximately 200 HPS cases annually throughout the Americas (Khan and Khan, 2003).

The outbreaks of HPS were not caused by new viruses, but by viral agents having long existed in their Sigmodontine (New World) rodent hosts (Nerurkar, Song *et al.*, 1994). Hantaviruses are single-stranded RNA viruses, with a genome segmented into three. Studies have shown that the newly emerged hantaviruses are not a re-assortment of segments from other viruses. Each of the three segments are quite independent of previously known viruses (Spiropoulou, Morzunov *et al.*, 1994). The diversity and evolutionary relationships of the viruses reflect the evolutionary relationships of the rodent species, indicating a close and ancient relationship between rodents and viruses (Clement, McKenna *et al.*, 1998; Monroe, Morzunov *et al.*, 1999).

However, this also seemed to be true for HIV/SIV viruses, but a recent paper has suggested that frequent transmissions between closely related species of host could produce the same pattern (Charleston and Robertson, 2002). Overlapping distributions between different rodent species in South America provide opportunities for host-switching events (Plyusnin and Morzunov, 2001) and there is increasing recognition that host switching may have a role in generating hantavirus diversity (Bohlman, Morzunov *et al.*, 2002). Some authors suspect other types of hantavirus may occur in human populations, but are not noted because they do not cause severe disease (Täger, Vial *et al.*, 2003).

Hantaviruses are all transmitted from infected rodents to man via excretions in urine, faeces or aerosolized

respiratory droplets (Clement, McKenna *et al.*, 1998). Most sufferers of the disease report sightings of rodents, but almost never mention a physical contact. The rodent carriers appear healthy. Person to person transmission of hantaviruses has rarely been reported, despite extensive epidemiological studies. As a result, the diseases remain localized. However, it seems to be possible in the case of Andes virus. During an outbreak in Argentina in 1996 two people were infected who had been in contact with infected people but neither visited the locality of the outbreak nor had high exposure to rodents (Wells, Estani *et al.*, 1997). This also happened in Chile the following year (Toro, Vega *et al.*, 1998) and research is underway to establish the mechanism of transmission (Khan and Young, 2001).

The New World hantaviruses are causing serious public health problems in South America in the early 21st Century, having been first discovered in North America. Two main factors are thought responsible for the repeated outbreaks. One is changing weather conditions. The original outbreak of Sin Nombre virus in 1993 was clearly related to unusual weather conditions. Heavy rains and snow in the previous spring, after a long drought, led to an abundance of rodent food, such as piñon nuts and grasshoppers. The numbers of deer mouse (*Peromyscus maniculatus*), the Sin Nombre virus host, were up tenfold on normal levels during that year (Stone, 1993). During the nineties, several years of high precipitation caused by El–Niño events increased rodent populations generally in the Americas and may have been associated with other outbreaks of hantavirus disease (Childs, Ksiazek *et al.*, 1994; Hjelle, Jenison *et al.*, 1994; Spiropoulou, Morzunov *et al.*, 1994; Hjelle, Jenison *et al.*, 1995; Engelthaler, Mosley *et al.*, 1999; Hjelle and Glass, 2000; Täger, Vial *et al.*, 2003)

The second factor is changes in land use, which have increased people's contact with rodents. A recent study (Täger, Vial *et al.*, 2003) found infection with the Andes strain of Hantavirus to be correlated with those working in the forestry industry. The natural host of this strain is the long-tailed pygmy rice rat (*Olgoryzomys longicauatus*), a species that occurs primarily in temperate forest and is associated with the abundant bamboo-like forest understorey plant *Chusquea quila*. The increasing development of the forestry industry has caused humans to interact more closely with this rice rat species, and acquire its virus.

Hantaviruses are prevalent in wild rodent populations all around the world. In China for example, Old World hantavirus isolates or antigen were found in 55 species of vertebrate, including 37 rodent species (Chen and Qui, 1993). The field mouse (*Apodemus agrarius*) and the brown rat (*Rattus norvegicus*) were the most important vectors with 5.3% and 4.9% testing positive, respectively. A more recent study have found Hantaan-like viruses in 9.9% of wild rodents in Ningxia province, China (Kariwa, Zhong *et al.*, 2001). Hantaan virus causes an estimated 50-100,000 infections a year in China (Khan and Khan, 2003). Rates of 2.1% have been found in rodents in Thailand (Nitatpattana, Henrich *et al.*, 2002). In Uruguay, hantavirus Central Plata strain is carried in 2.6% of its host, the yellow pygmy rice rat *Oligoryomys flavescens* (Delfraro, Clara *et al.*, 2003). Seoul virus persists at even higher levels, having been found at frequencies of 33.9% in *Rattus norvegicus* in Taiwan (Chin, Chiueh *et al.*, 2000) and up to 56% in Brazil (Leduc, Smith *et al.*, 1985).

Although rodents are considered the primary reservoir, the viruses have been detected in other mammals, and birds – a total of 164 different species from eight different orders, including bats and cats (Clement, McKenna *et al.*, 1998). Cat ownership has been described as a risk factor for hantavirus disease in China (Xu, Tang *et al.*, 1987). Although a recent study in the Netherlands searched for Puumala virus in over 2000 domestic animals, including dogs and cats, and found none (Groen, Gerding *et al.*, 1995).

No-one understands why the old and new world strains of Hantavirus cause different diseases. But the virus genetics and host range suggest they have evolved independently for a very long time and make it relatively unlikely that an HPS-type virus will naturally emerge in the Old World.

CASE STUDY FIVE: HENDRA VIRUSES

In the 1990s, a group of three previously unknown viruses suddenly appeared in the human population in Australasia, causing highly pathogenic encephalitis in one case. These viruses – Hendra (1994), Menangle (1997) and Nipah (1998) virus – belong to the family Paramoxyviridae, and are unusual for that family in being able to switch between hosts from different vertebrates classes. Nipah virus was the most serious public health incident, killing 105 people, with separate outbreaks in Malaysia and Singapore (Chua, Bellini *et al.*, 2000; Field, Young *et al.*, 2001). Menangle virus causes embryonic mortalities, stillbirths, mummified foetuses and congenital malformation in pigs (Love, Philbey *et al.*, 2001). Similar symptoms have not been recorded in humans, but all the people found carrying antibodies to this virus were men, not women (Chant, Chan *et al.*, 1998).

The natural host reservoir for all three turned out to be flying foxes, or fruit bats (Pteropid bats). They had transferred to humans via an intermediate. In the case of Nipah and Menangle viruses, outbreaks were traced to pig farms and abbatoirs (Bowden, Westenberg *et al.*, 2001; Chua, 2003). Hendra virus came from horses (Barclay and Paton, 2000). Why did these viruses all suddenly emerge, within a few years of one another? Molecular genetic studies of Hendra and Nipah viruses indicate they are not new or newly recombinant viruses. Rather they are 'old' and have persisted unknown and non-pathogenic in their hosts, for perhaps millennia. Field *et al* (Field, Young *et al.*, 2001) argue that ecological change is the most plausible explanation for their sudden emergence as people killers. Fruit bats are in decline in Australia and southeast Asia, due to habitat loss, particularly deforestation, and hunting. They are struggling to find food, and increasingly living in closer proximity to man. Nipah virus jumped the species barrier into pigs when pig farms were established in the hosts' natural range in the mid 1990s. It is a classic case of a zoonotic virus emerging in a newly encountered host species and may be a direct result of the clearance of rainforest, the bats' natural habitat (Weiss, 2001). The virus then spread rapidly within and between farms due to the intensity of the husbandry and frequent transfer of animals. Extensive sampling of wildlife has shown that these viruses reside in no other peridomestic species, except for dogs (Field, Young *et al.*, 2001).

Although the viruses themselves have only so far been isolated from species of *Pteropus* (flying fox), antibodies to Nipah virus were found in five species of bat: four species of fruit bat, two of which were not flying foxes and one insectivorous bat (Field, Young *et al.*, 2001).

Scientists warn that this could happen again. The stresses on fruit bat populations have not gone away. During the investigations on bats, two further new viruses were found. One, Tioman virus (Chua, Wang *et al.*, 2001) comes from the same virus family, but has not been recorded in other species. The other, Australian bat lyssavirus, is in the Rhabdoviridae and closely related to the rabies virus. Either of these has the potential also to emerge as a serious disease in humans.

CASE STUDY SIX: SARS

Severe acute respiratory syndrome (SARS) appeared in the Chinese province of Guangdong in late 2002, and was first reported by the World Health Organisation in February 2003. It is a respiratory disease akin to pneumonia, easily transmitted between people and with an apparent fatality rate of nearly 10% (WHO, 2003e). A previously unknown coronavirus was isolated from SARS patients in March 2003, and is now identified as the principle cause of the disease (Kuiken, Fouchier *et al.*, 2003; Drosten, Günther *et* al, 2003; Ksiazek, Erdman *et* al., 2003; Peiris, Lai *et al.*, 2003).

Where did the SARS virus come from? Although there is no direct evidence that SARS infected humans via wildlife, most experts, including Zhong Nanshan (China's leading respiratory disease expert), are convinced there is a link (Anon, 2003a) and evidence of SARS as an emerging zoonosis is amassing.

The genome of the SARS coronavirus, which has been fully sequenced (Marra, Jones *et al.*, 2003), shows that it belongs to a completely new group (group 4) of coronaviruses. Analysis of the sequence suggests it is an animal virus for which the natural reservoir host is still unknown and that has recently developed the ability to infect humans (Tobler, Ackermann *et al.*, 2003). It is not a mutant of a known coronavirus or a recombinant between known viruses. However, a genetic mutation or recombination of an unknown animal virus may have happened in a new animal host, as commonly happens with flu (Harnden and Mayon-White, 2003; Shaila, 2003). The genome has been stable as the virus passed between humans, suggesting it is well adapted to its new host (Kamps and Hoffman, 2003).

Research shows that SARS coronavirus isolated from humans can easily infect both ferrets (*Mustela furo*) and domestic cats (*Felis domesticus*), two distantly related carnivores, and transmit from these animals to uninfected co-habiting animals (Martine, Haagmans *et al*, 2003). The ferrets become ill, but the cats do not. This research suggests the virus can pass easily between humans and animals and the reservoir may involve a range of animal species.

In May 2003, Chinese researchers isolated viruses genetically very similar to the SARS coronavirus from masked palm civets (*Paguma larvata*) and racoon dogs (*Nyctereutes procyonoides*) collected at Dongmen wildlife market in Guangdong (WHO, 2003d; Guan, Zheng *et al.*, 2003). The virus isolated from masked palm civets reacts serologically with the human SARS virus and its genome is virtually identical, with the exception of a small additional sequence of 29 nucleotides. Four of the six civets included in the study harboured the virus. The team also found antibodies reactive against human SARS coronavirus in one Chinese ferret badger (*Melogale moschata*. The researchers carried out the survey following reports that a disproportionate number of the first SARS patients were working in southern China's food industry, often as chefs (Normile and Enserink, 2003).

This evidence does not mean the civet, or other animals harbouring the virus are the reservoir of the SARS coronavirus, nor that it arrived in the human population from this source. The survey was limited, involving only 25 animals, in eight species, from one market. A subsequent survey by a team from the China Agriculture University in Beijing apparently found no trace of SARS in civets or sixty-four other domestic and wild species (Enserink, 2003; Normile and Enserink, 2003), despite testing 732 animals. But the specificity and reliability of these tests have been questioned (Enserink and Normile, 2003). The WHO want to send four teams of international animal-virus hunters into China to work with local researchers and test hundreds of species in many markets, but the progress of negotiations is slow according to one report (Enserink and Normile, 2003). So far 100 species have been tested and 'some' are positive (Ansfield, 2003). In June 2003, Yi Guan, a virologist from the University of Hong Kong, said related viruses had been found in about 6 species, apparently

including pigs, snakes, monkeys and bats (News24, 2003). In October, PCR evidence of SARS coronavirus in fruit bats (*Cynopteryx sphinx*), Rhesus macaques (*Macaca mulatta*), Chinese water snakes (*Enhydris plumbea*) and Chinese pangolins (*Manis pentadactyla*) collected at markets in Guangdong, was presented to the WHO SARS Scientific Advisory Committee (SARS Animal Reservoir Studies Working Group, 2003). This research is not yet published with peer review (Cyranoski, 2003). Evidence of infection with the SARS virus has been found in a pet dog and domestic cats in Hong Kong (Martina and Haagmans, 2003; Ng, 2003).

Masked palm civets are generally captured from the wild and raised in farms. They could have caught the virus from another wild animal, as pigs catch avian flu viruses. But the predominance of the virus in civets suggests that this species was its 'springboard' from wildlife to humans (Enserink, 2003). It is possible that the loss of 29 nucleotide sequence made the virus able to prey on humans. Two isolates of the human SARS virus, early cases from Guangdong, still contain these additional nucleotides (Enserink, 2003). More research is required to establish the true dynamics and zoonotic nature of the SARS coronavirus (WHO, 2003e). If a natural reservoir host is found, steps can be taken to minimize contact with that host, either direct or indirect, as they have with the flying foxes that carry hendra viruses.

Like other coronaviruses, SARS is transmitted between people via respiratory droplets. It is also stable for up to four days in faeces and urine from infected people at room temperature, and for one to two days on dry surfaces, suggesting there may be a chance of catching the disease indirectly from environmental sources (Kamps and Hoffman, 2003; WHO, 2003c). A large outbreak in a private housing estate, Amoy Gardens, in Hong Kong in March was traced to an overnight visit by a single patient, leading scientists to suggest the disease may have been carried in the ventilation system, and thus is airborne. WHO officials have since announced this was unlikely (Anon., 2003b). Instead, Stephen Ng from the Mailman School of Public Health, USA, has argued the disease was spread by rats (Ng, 2003). The involvement of black rats, *Rattus rattus*, explains several unusual features of this outbreak, including the distribution of sufferers in floors above the apartment visited by the infected man. However, there is no direct evidence – the rats of the apartment block were exterminated when the people were evacuated. Rats caught subsequently showed no sign of the disease and scientists have been unable to infect other rats with SARS. Ng believes the local Hong Kong rats may have been susceptible, or carried a viral cofactor that made them susceptible to the disease. He has strong support amongst his colleagues for this hypothesis (pers. comm. Ng, August 2003).

A combination of global panic and well-coordinated scientific and public-health effort seems to have succeeded in containing SARS. The last reportable case was detected in Taiwan on June 15th (WHO, 2003f). The disease infected 8437 people and killed 813 in over 30 countries (WHO, 2003b). Re-emergence cannot be ruled out, either as part of a seasonal pattern (Normile and Enserink, 2003), or via re-infection from an animal reservoir, and some scientists think it likely because there has been no reduction in contact between people and potential reservoirs in southern China (Enserink and Normile, 2003; pers. comm. Ng 2003; MacKenzie, 2003). Continued surveillance is intense.

The SARS outbreak cost China an estimated $2.2 billion dollars, and the entire far-east economic region $10.6 - $15 billion dollars (WHO, 2003e).

CHAPTER 3 – REVIEW OF DIRECT VIRAL ZOONOSES

"SARS reminded us just how little we know about virus transmission and zoonoses."

Simon Wain-Hobson, Pasteur Institute, Paris. Editor, Journal of General Virology.

A list of viral diseases known or suspected to be transmitted naturally between animals and humans, without involvement of an arthropod vector, is presented in Appendix III. This list includes viruses such as AIDS that were transmitted in the past and have subsequently evolved in the human population. Measles is not included, although generally agreed to be an historic zoonosis, because the transfer occurred thousands of years ago and the evidence is theoretical (Anderson and May, 1992). The list includes the prion agent (not strictly a virus) responsible for Creutzfeldt-Jakob Disease.

The following sources were used: BIOMEDLINE, PUBMED, ISI Web of Science, world wide web search, Centers for Disease Control and Surveillance (CDC, 2003) and World Health Organisation disease reports (WHO, 2003a). References are given in Appendix III. Appendix IV provides a list of 98 known arboviruses.

- **76** zoonotic viruses were found that transmit or have transmitted from animals to humans or vice versa without an arthropod vector.
- **49** are newly discovered or increasing in the human population in the last 20 years, and classed as 'emerging'.
- **52** have caused fatality or widespread infection, and therefore represent serious public health concerns.
- **36** are found in Asia.

In 67 of these zoonoses, scientists agree the disease naturally transmits between human and animals. In nine cases – borna virus, hepatitis B, hepatitis E, HIV-1, human parainfluenza virus 2, influenza B and C, respiratory synctial virus and SARS there is still uncertainty in the literature.

The majority of direct zoonoses (55 viruses, or 72%) are transmitted by relatively close proximity to a living animal, or its excretions. Many do not need actual contact, because the virus travels in aerosol, or urine. A smaller proportion (13 viruses, 17%) require body fluid contact for example with a wound or freshly butchered meat.

What Types of Animal do they Come From?

Of the 76 viruses, almost all are transmitted from mammals. Only two are transmitted to humans from birds. One is influenza A, for which the natural host reservoir comprises many species of waterfowl around the world. This potentially very serious disease is also transmitted from an intermediate host, pigs. The other is Newcastle Disease, not a particularly serious pathogen to humans. It is usually caught from poultry but the natural reservoir comprises many species of waterfowl and tropical birds (Khan, 1994).

No viruses are transmitted from the other main vertebrate groups, reptiles, amphibians or fish (with the possible exception of the SARS coronavirus, which may be carried by reptiles, although evidence is sparse at this stage - see case study six).

Figure 1a shows the proportion of virus species originating from different mammal taxa. Viruses were assigned to the taxon of their natural reservoir host, where this was known or suspected. If not, they were assigned according to species that harbour the virus. In cases where no natural host is known but there is a strong suggestion of a group of animals in the literature, based on closely related viruses (some hantaviruses, for example), the virus is assigned to that group.

The largest proportion of species carrying disease are rodents, followed by primates, and even-toed ungulates. In the latter group, it is mostly from pigs and cows that diseases jump to humans. Pigs are often an intermediate host between the natural reservoir and humans, as in influenza and Nipah viruses.

It is arguable that this analysis is skewed by the large number of different hantavirus and bunyavirus species, which are similar and have rodent hosts. To avoid this problem, figure 1b shows the proportion of virus genera originating from different host taxa[2]. In this analysis, rodents are far less important. More than a quarter of the zoonoses came from primates and nearly a fifth from even-toed ungulates.

Figure 1a. Zoonotic virus species by mammal taxa

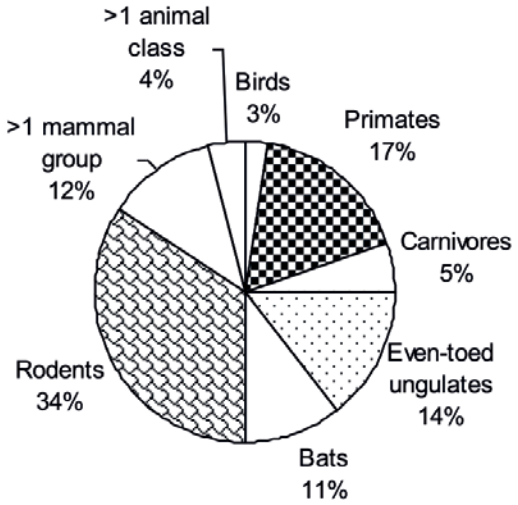
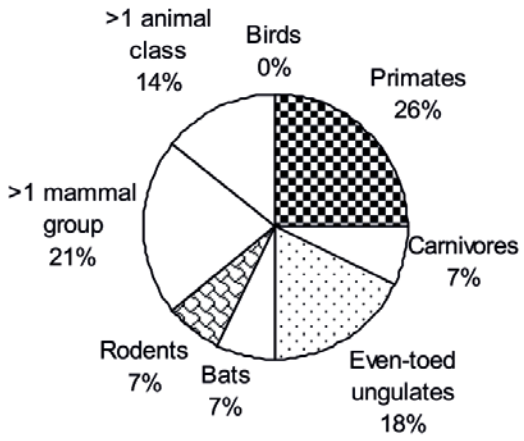


Figure 1b. Zoonotic virus genera by mammal taxa



What Factors Promote the Emergence of New Viruses?

There are two main routes by which new viruses emerge. One is the evolution of brand new strains. The other is the movement of viruses into new species or populations. Despite some notable examples, such as influenza A, the appearance of brand new strains of virus is not a major cause of the emergence of new viruses (Morse, 1993).

Specific factors precipitating disease emergence can be identified in virtually all cases of emerging disease (Morse, 1995). They include ecological, environmental and demographic factors that place people in increased contact with a previously unfamiliar microbe. According to Ludwig (Ludwig, Kraus *et al.*, 2003), the complexity of interactions between all these factors render it difficult to predict future viral zoonosis emergences.

Below is a summary of factors associated with disease emergence in the literature, and prominent examples of zoonotic viruses associated with each.

[2] Virus genera not given in Appendix III. Refer to (ICTV, 2003).

Factors associated with disease emergence (not mutually exclusive):

- Ecological disturbance – includes climate change, agricultural change e.g. Hantaviruses
- Increasing human populations/habitat encroachment leading to increased contact with wildlife e.g. Nipah virus, possibly Ebola and AIDS
- Movement of people/animals transferring virus to naïve population e.g. West Nile virus, monkeypox
- Change in animal husbandry e.g. Nipah virus; vCJD
- Immunosuppression – no examples yet (Weiss, 2003)

According to Morse (1995), agricultural change is one of the primary causes of new human disease. The emergence of the South American haemorrhagic fever diseases known as Junin and Machupo, for example, is attributed to changed conditions in maize agriculture favoring the rodent host *Calomys musculinus*. Increasing human populations have also been blamed for increased contact with wildlife, through invasion of natural habitat, particularly deforestation (Stöhr and Meslin, 1997; Ludwig, Kraus *et al.*, 2003). Globalisation, the widespread and rapid movement of people, livestock and other animals has hugely increased the potential for spread and emergence of new and devastating pathogens.

A number of authors have recently expressed concern that the large proportion of immunosuppressed people in some countries due to high levels of infection with AIDS could allow an easy route for zoonotic diseases to establish in humans (Weiss, 2001; Ludwig, Kraus *et al.*, 2003). The use of animal tissues in medicine, particularly xenotransplantation, also poses a substantial risk of virus transfer, particularly from endogenous retroviruses that are held in a passive state in an animal's genome. Again, immunosuppression of recipients is an important factor (Weiss, 2001; Ludwig, Kraus *et al.*, 2003; Weiss, 2003). So far, there are no specific reports of diseases emerging in the human population by this route.

The number of potentially pathogenic viruses present in wild animals is impossible to know. At least 520 different viruses have been identified from arthropods, and most are of unknown disease potential (Karabostas, 1985). 100 of them cause human disease, and another 25 are pathogenic to domestic animals that are known to share human diseases (Monath, 1993).

It seems that certain types of virus are more likely to emerge than others, as a result of their structure and biology.

Recent studies have looked for patterns in the type of pathogen likely to emerge as a human disease (WHO, 2000; Cleaveland, Laurenson *et al.*, 2001; Taylor, Latham *et al.*, 2001; Woolhouse, 2002). Certain taxonomic groups of pathogen are more likely to emerge than others. Viruses, particularly RNA viruses, are the most likely to emerge (Cleaveland, Laurenson *et al.*, 2001). RNA viruses are also much more likely to be zoonotic than DNA viruses (Wain-Hobson and Meyerhans, 1999). RNA viruses have high mutation rates, resulting from a high error rate during replication and a lack of proof-reading or correction mechanisms (Ludwig, Kraus *et al.*, 2003). They can change and evolve rapidly to suit a new environment, such as a new host.

In Taylor's review of all human pathogens (Taylor, Latham *et al.*, 2001), zoonotic viruses were the category with the largest proportion of emerging diseases. Viruses transmitted by direct or by indirect contact (via food or an environmental reservoir) have a much higher proportion of emerging diseases than arboviruses (Taylor, Latham *et al.*, 2001), but arboviruses are more likely to emerge because there are more of them.

Infectious agents with a broad host range are much more likely to emerge. Zoonotic pathogens are almost twice as likely as non-zoonotic pathogens to emerge (Taylor, Latham *et al.*, 2001). And zoonotic pathogens that can infect both wildlife and domestic animals are really the ones to watch (Cleaveland, Laurenson *et al.*, 2001). Woolhouse (Woolhouse, 2002) attempts to prioritise the features of pathogens that make them likely to emerge into the human population. Amongst viruses, host range is the most important factor.

What type of virus has a broad host range? Hantaviruses have been shown to infect birds and mammals across eight different orders (Clement, McKenna *et al.*, 1998). There is some evidence that the type of cell receptors used by a virus alters its ability to switch between hosts. Viruses with a host range crossing several taxonomic orders are more likely to use 'conserved' receptors – that is receptor molecules that are similar in many different species, from human to mouse. Examples are the rabies virus and the foot-and-mouth disease virus (Woolhouse, 2002).

According to Cleaveland, Laurenson *et al.* (2001), most zoonotic *pathogens* (including bacterial, Chlamydial, Rickettsial and parasitic zoonoses, and arboviruses) are associated with ungulate, carnivore or rodent reservoirs, and a substantial minority reside in primates, bats, marine mammals and birds.

The success of a virus that has newly appeared in the human population depends on its ability to transmit from human to human. Efficient inter-human transmission is required for a virus to pose a pandemic threat. However, there are several high profile cases of deadly zoonotic viruses that did not transmit easily between humans – in which every case was a new infection from an animal. For example, the majority of hantavirus infections are primary infections from rodents. The same is true for fatal cases of the Hong Kong H5N1 influenza A virus in 1997 (Wain-Hobson and Meyerhans, 1999). It is feasible that such viruses could alter and become transmissible, as for example in the Ebola Reston virus, or the Andes hantavirus.

Profile of an emerging pathogen (Woolhouse, 2002)

- An RNA virus
- Zoonotic, with a reservoir host range that is both taxonomically and ecologically broad
- Transmitted by vectors, especially by biting flies that are generalist feeders
- Able to use a cell receptor that is conserved across host species
- Potentially transmissible between humans but currently rare
- Found in areas that are experiencing ecological, demographic or social change

In those cases where a genetically new strain of virus emerges, viruses with large or segmented genomes are most likely to produce new strains. Antigenic shift – or re-shuffling of genetic segments, rather than change by mutation, can result in far more severe diseases (Wain-Hobson and Meyerhans, 1999).

Another factor that may contribute to the risk of zoonosis becoming a public health issue is the increasing sanitisation of society, and the reduction in number of individuals employed in agriculture, or in direct contact with animals. This is seldom mentioned in the literature, because it goes against the public health grain. Wain-Hobson argues that zoonosis is probably far more frequent than we think, because it often does not result in disease. And because infection can prime the immune system to resist other, related viruses, exposure to a wide variety of animal viruses can be protective. Dairy workers did not suffer from smallpox, perhaps because many of them had unknowingly been infected with cowpox and become immune (Wain-Hobson and Meyerhans, 1999). Similarly, there is slight cross-reactivity in immunity between some strains of hantavirus (Sin Nombre and Black Creek Canal) (Hjelle, Chavezgiles *et al.*, 1994; Chu, Jennings *et al.*, 1995) However, in other cases, prior exposure to similar viruses can fool the immune cells into encouraging viral replication, as happens in dengue virus, where a second infection by a different strain can be even more severe (Ananthaswamy, 2003).

Where Does SARS Fit?

If SARS is shown to be a zoonosis, which looks increasingly likely (see case study six), it will be the first time a coronavirus has been shown to naturally move across a species barrier from an animal into humans. No members of this family are mentioned in (Palmer, Soulsby *et al.*, 1998) or (Beran, 1994). However, antibodies to one other human coronavirus have been found in pigs (Hirano, Suzuki *et al.*, 1999), implying that the viruses naturally move the other way, from people to pigs.

Coronaviruses (CoV) are responsible for around 30% of common colds in humans (Rota, Oberste *et al.*, 2003). They spread easily through the respiratory droplets or the faecal-oral route. Coronaviruses are widespread in animals, causing hepatitis in mice, gastroenteritis in pigs and bronchiolitis in birds. They are classified into three groups, on the basis of serological cross-reactivity and genome sequence. Groups 1 and 2 contain viruses that infect a variety of mammals. Group 3 contains bird coronaviruses. Coronaviruses tend to be very species-specific, and most are restricted to a single species (Granoff and Webster, 1999). The two known previously human coronaviruses (HCoV-229E and HCoV-OC43) are in groups 1 and 2 respectively, and are associated with mild disease, although occasionally causing serious infections of the lower respiratory tract in children, and dangerous gut disease in newborns. SARS may be the first coronavirus to regularly cause severe disease in humans (Kamps and Hoffman, 2003).

Does SARS CoV fit the criteria outlined by Woolhouse for a typical emerging pathogen? It is an RNA virus, and it appears to be zoonotic. It is almost certainly not transmitted by arthropod vectors.

Does it have a broad host range? SARS CoV seems to have a much broader host range than other known coronaviruses, having been found in at least eight different species, from widely different taxa, including reptiles and humans (see case study six). It is not clear what makes SARS CoV different from the other coronaviruses in this respect. Other coronaviruses use very species-specific cell receptors, such as the feline aminopeptidase A identified as the receptor for feline infectious peritonitis virus (Granoff and Webster, 1999), but the cell receptor used by the SARS CoV is not yet known. Because the SARS virus is as different from any of the three known coronavirus groups as they are from each other, reading its genome sequence does not provide any further clues to the nature of its animal origins.

SARS does transmit easily between humans and it did emerge in an area subject to considerable ecological disturbance and degradation (see chapter four).

If SARS was transmitted to humans from the masked palm civet, as is currently suspected (Normile and Enserink, 2003), then it is unusual amongst direct viral zoonoses for emerging from a terrestrial carnivore. Only three other viruses came from carnivores, and all are mild diseases, contracted from sealions or seals (see Appendix III). However, it remains possible that SARS CoV originally came from rodents, a group with a long history of zoonoses.

Finally, does SARS have a large segmented genome? The coranoviruses have the largest genome of any of the RNA viruses (Rota, Oberste *et al.*, 2003), and although it is not segmented, they have a high mutation rate during replication (Granoff and Webster, 1999). Their tendency to re-shuffle genes was demonstrated by Haijema et al (Haijema, Volders *et al.*, 2003), when feline coronavirus was induced to take up coat protein genes from a mouse virus, creating a new strain that could also infect mice. This implies that genome shuffling can happen if two different strains of coronavirus co-occur in a single host.

In the context of other direct viral zoonoses, SARS could not have easily have been predicted. While it shares some of the characteristics of viruses likely to emerge, it is not a prime candidate. It is from a group of viruses previously believed to have narrow host ranges. It seems to have come from an animal group with little history of zoonoses, and belongs to a virus group with only one previously known zoonosis. Its emergence should be taken as a sincere warning about the risk of direct contact with a large number of wild animal species.

CHAPTER 4 – IS CHINA A LIKELY AREA FOR FURTHER ZOONOTIC VIRUSES TO EMERGE?

"Why does this region (China and Hong Kong) keep throwing up viruses that have the potential to threaten the lives of people around the world?"

David Cyranoski, Asian-Pacific correspondent for Nature.

Disease emergence in China has been the focus of international attention, as a result of influenza A and SARS. The continuing re-emergence of flu strains in the region has been blamed on the close proximity of people, pigs and ducks in rural areas (see case study). Three more general factors make China a likely area for further zoonotic viruses to emerge: widespread hunting and consumption of wildlife; ecological change; and high levels of immunosuppression due to AIDS. Finally, there is some evidence that a nutritional selenium deficiency in parts of China renders the population more susceptible to the emergence of new viral strains.

1 - Widespread Consumption of Wildlife

Wildlife species are widely sold in markets and eaten in restaurants in China, particularly in the southern provinces such as Guangdong and Guangxi. Many species are also caught and traded for use in traditional medicines. Both practices are ancient and well-established traditions in China, and the trade in wildlife is economically important (Li and Li, 1998). However, demand for wildlife has increased with rapid economic development over the last two decades, as more people can afford to enjoy wildlife goods (Li and Li, 1998) (ACAP, 2003). Such consumption is already recognized as a public health risk (Anon., 2003a), because the contact between people and large numbers of animal species creates ample opportunity for disease transfer.

The risk of contracting a new virus from eating cooked meat is low. Only in one case has cooked meat been the cause of a zoonosis, and that is the case of Creutzfeldt-Jakob disease (CJD), a poorly understood infectious agent contracted by eating infected nervous tissue. Incidences of cannibalism, either in farmed cattle, in the UK in the 1980s, or in people as in Papua New Guinea in the 1950s (Gajdusek 1977) led to outbreaks of the disease. Although a similar disease in sheep, scrapie, is naturally transmissible without cannibalism, this type of infectious agent does not appear to cross the species barrier readily (Weiss, 2001).

However, the risk of contracting zoonoses when handling livestock or animal products is substantial (Jemmi, Danuser *et al.*, 2000). At a conference in Munich in 1997, entitled 'Viral zoonoses and food of animal origin: a re-evaluation of possible hazards for human health', the opening speaker considered the consumption of raw meat products, a custom in some European countries, to pose the greatest risk of disease transfer (Böhm, 1997; Büttner, Oehmig *et al.*, 1997).

Eating poorly cooked shellfish can result in the transmission of virus infections, because these animals can harbour live viruses through bioaccumulation if they have been harvested from sewage-contaminated water (Hetrick, 1994). Large outbreaks of viral gastroenteritis have been traced to shellfish in Australia in the 1970s and in North America. The biggest ever outbreak of disease from shellfish was a huge epidemic of Hepatitis A in Shanghai in 1988 that hospitalised 310,000 people and killed 31 (SINA, 2003). It was traced to consumption of contaminated ark shells. Caliciviruses such as Norwalk virus have caused the highest number of shellfish related outbreaks worldwide (Potasman, Paz *et al.*, 2002). Because the viruses have not actually infected the shellfish, these incidents are not classed as zoonotic disease transfer.

As a source of food contamination, zoonotic viruses are a greater (although less frequent) threat than external contamination with human pathogens, because they are distributed throughout the tissues, and cannot be removed by washing or other decontamination treatments (Büttner, Oehmig *et al.*, 1997).

Arboviruses, normally transmitted by arthropod vectors, have also been contracted from eating poorly cooked meat products. This route was implicated in an outbreak of Rift Valley Fever, caused by Phlebovirus, in Egypt in 1977 (Morse and Schluderberg, 1990). The virus was caught from sheep/ goat meat and unpasteurised milk during an intense epidemic of the disease amongst domestic animals.

Hunting wild animals, and the subsequent butchering and preparation of the meat poses a serious risk of exposure to unencountered and unknown viruses. Inspectors from the US Fish and Wildlife Service consider bushmeat imports to be a dangerous biohazard (Lutz, 2003). Three diseases (six virus species) – AIDS, Ebola/Marburg haemorrhagic fever and monkeypox - have been linked to acquisition of zoonotic viruses through hunting bushmeat, and four from contact with wild primates used for medical science. However, hunting wildlife is unlikely to have previously occurred on the scale of the current practice in China. Many restaurants in southern China keep live animals on the premises and slaughter them as needed, a custom that could expose restaurant workers to virus-laden blood and excrement (Enserink, 2003). The conditions in the wildlife markets of southern China, where animals of many species are held together in close quarters, are ideal for cross-species transmissions promoting the emergence of new zoonotic viruses (Normile and Enserink, 2003).

Böhm (Böhm, 1997) stressed that scientists could not expect people to give up culinary customs as a result of newly understood risks. Similarly, AIDS expert Simon Wain-Hobson, of the Pasteur Institute in Paris, considers it unreasonable to expect poor people in developing countries to stop hunting and consuming 'bushmeat' when their livelihoods depend on it (pers.comm. Wain-Hobson, 2003). Rather, scientists must find other ways of minimising the risks, such as stringent veterinary controls during the production process. This is far more feasible when meat is farmed, less so when meat is transferred directly from the wild to the market (Stöhr and Meslin, 1997).

Types of wildlife eaten

A list of 226 species sold in wildlife markets or consumed in restaurants in China is presented in Appendix III. This list is compiled from four systematic surveys of the wildlife trade, carried out by Chinese scientists in the last ten years (Li, Fuller *et al.*, 1996; Zhijun, Huojie *et al.*, 1996; Li and Li, 1998; Anon., 2000). It is almost certainly not exhaustive, and because some animals listed were not identified to species, the number of species given should correctly be prefixed by 'at least'. However, this list gives a good idea of the range of different species that are eaten.

Figure 2. Wild species consumed or sold for food in southern China, by Class

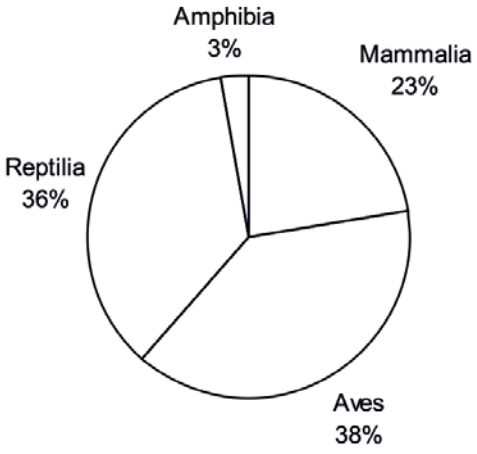


Figure 3. Types of mammal eaten, or sold to be eaten in China

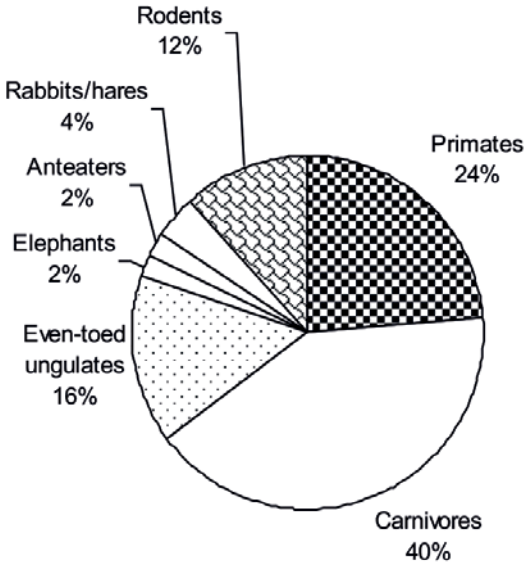


Figure 4a. Mammals observed frequently in at least one study

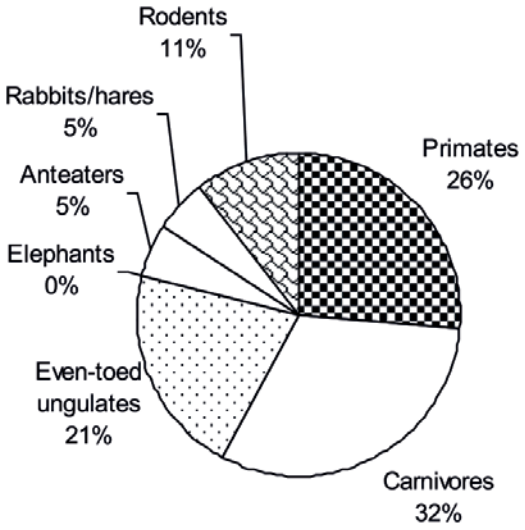
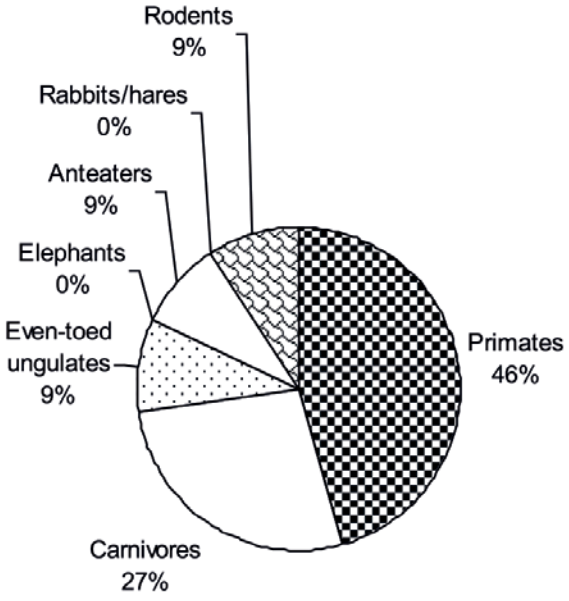


Figure 4b. Mammal species observed in three or more studies



The proportion of species in different classes is presented in figure 2. It is clear that birds and reptiles are the most popular fare for consumption in China. In the case of birds, the largest risk of contracting zoonoses seems to be associated with waterfowl. We have seen from chapter three that the greatest risk of non-arthropod-borne viral zoonoses come from mammals. A significant number of wild mammal species are eaten, and the remainder of this section focuses on mammals.

The proportion of mammals in each of seven different taxonomic orders is shown in figure 3. To give an idea of which mammals are most popular, figure 4a shows mammals that were observed frequently in at least one study. These are animals that were recorded at five or six different ports in study 1, in large quantities in study 2, at more than 10% of restaurants in study 3, or included in the list of most common species from study 4. Figure 4b shows mammal species that were recorded in 3 or more of the 4 studies.

A relatively small number of mammal species fall into both 'popularity' measures, being observed frequently *and* observed in three or more studies. They are the rhesus macaque (*Macaca mulatta*), the pigtail macaque (*Macaca nemestrina*), the slow loris (*Nycticebus coucang*), the masked palm civet (*Paguma larvata*), the large Indian civet (*Viverra zibetha*), the pangolin (*Manis* sp.) and the Chinese bamboo rat (*Rhizomys sinenssis*) These seven are China's favourite wild mammals to eat, or perhaps easiest to catch. Wain-Hobson and Meyerhans (1999) and Jemmi, Danuser *et al.* (2000) recommend screening animals for unknown viruses on a global scale, to pre-empt future emerging zoonoses. These seven species would be good starting points in China. Macaques are of particular concern, because these monkeys are known to carry potentially serious zoonotic viruses – Ebola Reston strain and Cercopithecine herpes virus type 1.

Based on current knowledge of zoonoses (see chapter 3), the greatest risk comes from primates, rodents and even-toed ungulates (mostly pigs and cows). Of these groups, primates are the most commonly eaten, and this is especially true if we consider the species that are popular (figure 4). Even-toed ungulates are mostly represented by species of deer, although the wild pig, *Sus scrofa* was recorded in all four surveys. Rodents are not eaten very widely, although one of the most popular mammal species is a rodent, the Chinese bamboo rat. Carnivores, the source of a significant 5% of direct zoonotic transfers worldwide are very widely consumed. Two mammal groups, the lagomorphs (rabbits/hares) and the anteaters, are reasonably popular as food and have no history of disease transfer.

It is important to stress that previous occurrence of zoonotic disease transfer is not necessarily a good predictor of future risk. Recent serious diseases such as hendraviruses, or SARS, have emerged from animal groups (bats and carnivores, respectively) with little history of disease transfer.

It is also important to stress that if the arboviruses had been included in this review, the prevalence of birds as natural hosts would have been greater. Crimean Congo haemorrhagic fever, West Nile fever and Sindbis virus are examples of well-known arboviruses carried by birds. While arboviruses cannot be caught directly from living animals, they can potentially be caught through contact with body fluids, for example from milk, or during butchering.

Although no zoonoses are known to have been transmitted or carried by reptiles, there is a suggestion in the media that the SARS virus may have been found in snakes (News24, 2003).

2 - Ecological Change

Large-scale ecological change is occurring in China, particularly deforestation, climate change and desertification. There is also evidence that populations of some wild rodents are increasing in China, as a result of various factors, including agricultural change and possibly hunting of predators. In the cases of deforestation, climate change and increasing rodent populations, there are direct links to the emergence of rodent-borne viral zoonoses in the scientific literature.

Deforestation

Deforestation has been a large problem in China for more than a century and continues to occur (Zhou, 1995; Rozelle, Huang *et al.*, 1997; Young and Wang, 2001; Houghton and Hackler, 2003; Liu, Liu *et al.*, 2003; Wang, Pitman *et al.*, 2003). This kind of habitat change directly affects wildlife communities. For example, deforestation in southern Ganus, China, resulted in a large increase in density of some rodent species, but a reduced number of species (Giraudoux, Quere *et al.*, 1998). Giradoux recently demonstrated that conversion of land from forest to grassland near the Qinghai-Tibet plateau region of China can lead to increased risk of a human zoonotic disease carried by carnivores (the pathogenic helminth *Echinococcus multilocularis*), through interaction with small mammal communities, which are an intermediate host (Giradoux, Craig *et al.*, 2003).

Climate change

Climate change is almost certainly affecting the annual mean temperature in China, as it is globally (Watson and Team, 2001) and in nearby Japan (Yue and Hashino, 2003). Whilst climate change is likely to result in water shortage in northern China, in southern China, it may even increase rainfall (Tao, Yokozawa *et al.*, 2003), an effect associated with the outbreak of hantaviruses in the Americas, due to the resultant increase in rodent food source (see case study four). Climate change also increases rodent numbers more directly, because it is cold in winter that reduces their numbers (Saul, 1996).

Desertification

Desertification is a serious problem in China (e.g. Runnstrom, 2000; Xu, Lin *et al.*, 2002; Zhao, Wu *et al.*, 2002), although mostly in the North and West of the country, so not in areas where consumption of wild animals is most popular. We can find no direct connection between desertification and disease transfers in the literature, but this degradative process is an ecological change that will put some wild species under stress.

Rodent populations

An explosive increase in rodent populations, particularly rats and mice, in China has been reported in the news (e.g. BBCi, 2001; Reuters, 2003). Rat populations are soaring in China, with an average of three or four rats per person, rising to 20 or 30 in Guangxi, according to Zhou Fang, a Chinese professor in zoology (Jian and Jun, 2003). This increase has been blamed on the removal of predators such as snakes and owls for consumption in restaurants (BBCi, 2001; Jian and Jun, 2003). In the 1990s, the snake trade in China saw an estimated 1000 tonnes of snake a year (Jian and Jun, 2003). It has now increased to at least 3000 tonnes a year, just in the southern city of Guangzhou, according to a Chinese government agency (ACAP, 2003). A survey by the China Wildlife Conservation Association in 2001 showed snake numbers had declined drastically in some provinces where they used to be common (BBCi, 2001) and Chinese farmers have been claiming huge crop losses to rodents in recent years (BBCi, 2001). In 1998 the Vietnamese Government blamed wildlife trade to China for a fall in populations of cats, and encouraged farmers to raise cats and enhance populations, in a Prime Ministerial Decree (number 09/1998/CT) (Singleton, Kenney *et al.*, 2003).

The scientific literature confirms there has been an increase in the frequency of outbreaks of rodents across Asia and Australia (Singleton, Hinds *et al.*, 2003). For example, serious outbreaks of Brandt's voles (*Microtus brandti*) in Inner Mongolia have increased from one every seven years in 1970 to one every 3 to 5 years (Zhang, Pech *et al.*, 2003). And there are suggestions that rodent numbers are increasing all over the world (Saul, 1996).

However, the allegation that hunting of predators is responsible is not corroborated by scientific literature. Experts from the CSIRO Rodent Research Group (see Appendix V) in Australia stress there are too many factors influencing the ecology of rodents to be sure of an influence of predator numbers (pers.comm. Singleton, 2003).

We could find no published evidence of medium-long term change in predator numbers in China. In the case of Brandt's voles, the study showed the main factor responsible to be the increase in livestock numbers leading to greater areas of the voles' favoured short grass habitat (Zhang, Pech *et al.*, 2003). Likewise in Vietnam, the most compelling evidence is that greater intensity of rice cropping is responsible for the increase in rodent impacts (Singleton, Kenney *et al.*, 2003). There is no unequivocal evidence that rodent populations are controlled by predators, and more research is required (Singleton, Kenney *et al.*, 2003).

Whatever the immediate cause, an increase in wild rodent populations could increase human contact with rodents and therefore increase the likelihood of disease transfers. The same effect is feared as a result of the spread of particularly virulent form of West Nile virus that has just arrived in Central America from North America. This arbovirus kills birds of prey and could lead to an increase in rodent numbers through lack of predators (Ananthaswamy, 2003). Rodents in these countries are known to carry deadly hantaviruses and bunyaviruses. In China, there is a theory that SARS is transmitted by rats (Ng, 2003). Research on wild rats, *Rattus norvegicus*, in the UK has shown that the more rodents there are, the greater number of diseases each animal carries (Webster and Macdonald, 1995). So higher rodent density not only increases contact with human, it increases the risk of disease transfer with each contact event.

All these ecological changes affect species in unpredictable ways. Ecological disturbance is a key factor implicated in the emergence of new viruses (see chapter 3). Populations of wild animals under stress may themselves carry more pathogens and come into increasing contact with humans due to habitat loss. China, and other governments around the world, should be taking steps to minimize direct contact between people and wildlife species, as well as to reverse the trends of habitat and energy over-use that are largely responsible for these changes.

3 - Immunosuppression Resulting from AIDS

AIDS is a growing epidemic in China. A million and a half Chinese people are now living with HIV and official estimates foresee a manifold increase in that number over the coming decade (BBCi, 2002; UNAIDS/WHO, 2002)

An immunosuppressed population represents ample opportunity for otherwise benign or harmless viruses to establish themselves and perhaps cause harm to humans (Sawitzky, 1997; Woolhouse, 2002; Ludwig, Kraus *et al.*, 2003). For example, the only known fatal case of the cowpox virus was in an 18-year-old man whose immune system was suppressed by steroid drugs (Czerny, Zeller-Lue *et al.*, 1997). He caught the virus from his cat, and it killed him.

4 - Selenium Deficiency

A team of scientists led by Melinda Beck at the University of North Carolina at Chapel Hill have argued that nutritional selenium deficiency in the population may be a factor in the risk of new virus strains emerging from China (Nelson, Shi *et al.*, 2001; Cyranoski, 2003). They have shown that both Coxsackievirus B3 and influenza A viruses mutate at higher rates and can produce virulent strains more quickly when they infect selenium-deficient mice (Beck, Shi *et al.*, 1995; Nelson, Shi *et al.*, 2001). Beck suspects this phenomenon might explain the high incidence of Keshan disease, a weakening of heart muscle, in some Chinese populations (Levander and Beck, 1997). This link is tentative and dismissed as speculation by other scientists (Pearson, Clarke *et al.*, 2003).

RECOMMENDATIONS

The risk of another previously unknown viral disease emerging in China as a result of direct contact between people and wildlife species is substantial. The following steps are recommended to reduce the risk.

1 Reduce hunting and consumption of wildlife, particularly primates, wild pigs and rodents. Li, Fuller *et al.* (1996) and Zhijun, Huojie *et al.* (1996) recommend strengthening enforcement of China's Wild Animal Protection Law (1989), particularly by training and deploying teams of wildlife inspectors in the southern port towns.

2 If overall consumption cannot be reduced, consider limiting wildlife consumption to a number of known species, reducing contact with novel species. Based on this review of past zoonotic virus transfers, it is best to eat rabbits and hares. However, such advice must be balanced by conservation considerations for these species.

3 Promote farm-based production of 'wildlife' species, and oblige farmers to have regular veterinary inspections for disease, as recommended by Stöhr and Meslin (1997).

4 Post health warnings in restaurants and wildlife markets, warning consumers and traders about the risk of contracting novel diseases from wild animals and their raw meat. The following is a suggested text:

76 different viruses can be caught directly from wild animals. Two-thirds of them are serious diseases that spread rapidly to other people, or kill. Experts warn there could be many more unknown viruses, waiting to infect and kill humans, especially in monkeys. Close contact with wild animals and their raw meat puts you at risk. Buying the meat of wild animals puts thousands of people at risk.

5 Encourage research to survey potentially zoonotic viruses in mammals, as recommended by Wain-Hobson and Meyerhans (1999) and Jemmi, Danuser *et al.* (2000). Begin with the three primate species most commonly eaten: the rhesus macaque (*Macaca mulatta*), the pigtail macaque (*Macaca nemestrina*), and the slow loris (*Nycticebus coucang*). Also include *Macaca fascicularis*, source of the Reston Ebola virus.

6 Encourage long term research to monitor wild rodent populations and the link with predator populations, to establish whether excessive hunting is causing an indirect risk of disease transfer by leading to high rodent densities.

APPENDIX I: Virus families containing human and animal viruses

Adapted from (Fields, 1996)

Virus family	Characteristics	Well-known examples of zoonoses
RNA Viruses		
Picornaviridae Caliciviridae Astroviridae	Single-stranded RNA Positive-sense Nonsegmented Non-enveloped	
Togaviridae Flaviviridae	Single-stranded RNA Positive-sense Nonsegmented Enveloped	
Coronaviridae	Single-stranded RNA Positive-sense Nonsegmented Enveloped Nested set transcription	SARS
Paramyxoviridae Rhabdoviridae Filoviridae	Single-stranded RNA Negative-sense Nonsegmented Enveloped	Hendra, Nipah Rabies Ebola
Orthomyxoviridae Bunyaviridae Arenaviridae	Single-stranded RNA Negative-sense (some ambisense genes) Segmented Enveloped	Influenza A Hantavirus and Lassa fever
Reoviridae Birnaviridae	Double-stranded RNA Positive-sense Segmented Non-enveloped	
Retroviridae	Single-stranded RNA Positive-sense DNA intermediate step in replication	HIV

DNA Viruses		
Hepadnaviridae	Double-stranded/single-stranded DNA Enveloped Retroid DNA step in replication	
Circoviridae Parvoviridae	Single-stranded DNA Non-enveloped	
Papovaviridae Adenoviridae	Double-stranded DNA Non-enveloped	
Herpesviridae Poxviridae Iridoviridae Unnamed family African Swine Fever	Double-stranded DNA Enveloped	Monkeypox
SUBVIRAL AGENTS		
Deltavirus	Single stranded RNA Negative sense Non-segmented Defective, satellite	
Prions – agents of spongiform encephalopathies	No known nucleic acid 'self-replicating' proteins	vCJD

APPENDIX II: Review of viral zoonoses without arthropod vectors

Viruses are listed alphabetically by family and grouped into genera where applicable. Emerging viruses, those that are new or increasing in the human populations in the last 20 years, are underlined. References for each family of viruses are given below the table. Diseases are classed as a public health problem if there have been one or more fatalities, *and/or* more than 100 people have been infected with the virus at one time.

Transmission routes are divided into three categories: **direct** contact (by fomites, droplets, aerosol, saliva, urine, fecal-oral route); **indirect** contact (virus can be carried in an environmental reservoir such as water or food); and **internal** contact (blood, tissue or other internal body fluid/sexual contact required). Blank cells imply that no information was found.

HF=haemorrhagic fever; HFRS=haemorrhagic fever with renal syndrome
HPS=hantavirus pulmonary syndrome
CJD=Creutzfeldt Jakob Disease

* = known to be natural reservoir; ϕ = suspected reservoir, little or no evidence.
∞ = disease known to be more commonly acquired from other humans than direct from animals.

Virus name	Disease	Virus family	Public health issue?	Animal host (*=known to be natural reservoir)	Distribution	Main transmission route	Human-human transmission?	Factors associated with zoonotic transfer
Guanarito virus	HF	Arenaviridae	Yes	Cotton rat* *Sigmodon alstoin*	Venezuela	Direct/ indirect	Rare	
Junin virus	HF	Arenaviridae	Yes	Voles* *Calomys musculinus, Calomys laucha, Akadon azarae*	Pampas, Argentina	Direct/ indirect	No	Agricultural change
Lassa virus	HF	Arenaviridae	Yes	Rat* *Mastomys natalensis*	W. Africa	Direct/ indirect	Yes ∞	Contact with domestic rodents
Lymphocytic choriomeningitis virus	flu-like/ meningitis	Arenaviridae	Yes	Domestic mouse* *Mus musculus*, other rodents	Worldwide	Direct	No	Contact with domestic rodents
Machupo virus	HF	Arenaviridae	Yes	Vole* *Calomys callosus*	Bolivia	Direct/ indirect	Low	Agricultural change
Sabia virus	HF	Arenaviridae	No	Rodentsϕ	Brazil		No	Laboratory contact
Borna virus	Psychiatric?	Bornaviridae	Maybe	Many vertebrates, esp. horses	Europe, Japan, USA	Unknown		

Virus name	Disease	Virus family	Public health issue?	Animal host (*=known to be natural reservoir)	Distribution	Main transmission route	Human-human transmission?	Factors associated with zoonotic transfer
Andes	HPS	Bunyaviridae	Yes	Rice rat* *Oligoryzomys* sp.	Argentina, Chile	Direct	Yes	increased forestry
Bayou virus	HPS	Bunyaviridae	Yes	Rice rat* *Oryzomys paluastris*	USA	Direct	Rare	Changes in rodent ecology/climate?
Bermejo	HPS	Bunyaviridae	Yes	*Oligoryzomys**	Bolivia	Direct	Rare	Changes in rodent ecology/climate?
Black Creek Canal virus	HPS	Bunyaviridae	Yes	Cotton rat* *Sigmodon hispidus*	USA	Direct	Rare	Changes in rodent ecology/climate?
Central Plata virus	HPS	Bunyaviridae	Yes	Yellow pygmy rice rat* *Oligoryzomys flavescens*,	Argentina, Uruguay	Direct	Rare	Changes in rodent ecology/climate?
Choclo	HPS	Bunyaviridae	Yes	Unknown (rodent*)	Panama	Direct	Rare	Changes in rodent ecology/climate?
Dobrava-Belgrade virus	HFRS	Bunyaviridae	Yes	Yellow-necked mouse* *Apodemus flavicollis*	Yugoslavia	Direct	Rare	
Hantaan virus	HFRS	Bunyaviridae	Yes	Field mouse* *Apodemus agrarius*	Asia, Europe, USA	Direct	Rare	
HU39694	HPS	Bunyaviridae	Yes	Unknown (rodent*)	Argentina	Direct	Rare	Changes in rodent ecology/climate?
Juquitiba	HPS	Bunyaviridae	Yes	Rodents*	Brazil	Direct	Rare	Changes in rodent ecology/climate?
Laguna negra	HPS	Bunyaviridae	Yes	Vesper mouse* *Calomys laucha*	Paraguay, Bolivia	Direct	Rare	Changes in rodent ecology/climate?
Lechiguanas	HPS	Bunyaviridae	Yes	Rodent*	Argentina	Direct	Rare	Changes in rodent ecology/climate?
Monongahela virus	HPS	Bunyaviridae	Yes	White-footed mouse* *Peromyscus leucopus*	USA, Canada	Direct	Rare	Changes in rodent ecology/climate?
New York virus	HPS	Bunyaviridae	Yes	White-footed mouse* *Peromyscus leucopus*	USA	Direct	Rare	Changes in rodent ecology/climate?
Oran virus	HPS	Bunyaviridae	Yes	Rodent*	Argentina	Direct	Rare	Changes in rodent ecology/climate?

Virus name	Disease	Virus family	Public health issue?	Animal host (*=known to be natural reservoir)	Distribution	Main transmission route	Human-human transmission?	Factors associated with zoonotic transfer
Puumala virus	HFRS	Bunyaviridae	Yes	Voles* *Clethrionomys*. House mouse *Mus musculus*	Europe, Asia	Direct	Rare	Changes in rodent ecology/climate?
Sin Nombre virus	HPS	Bunyaviridae	Yes	Deer mouse* *Peromyscus maniulcatus*	USA	Direct	Rare	Changes in rodent ecology/climate?
Soeul virus	HFRS	Bunyaviridae	Yes	Rats* *Rattus rattus, R. norvegicus*	Worldwide	Direct	Rare	
Kasokero virus	Flu-like	Bunyaviridae	No	Bats *Rousettus aegyptiacus*	Uganda		Yes	Laboratory contact
San Miguel sealion virus	Vesicles, flu-like	Calciviridae	No	Sealions*, pigs	USA	Direct	No	Laboratory contact
Human Coronavirus OC43	Common cold	Coronaviridae	Yes	Pigs	Worldwide in humans; pigs in Japan	Direct	Yes ∞	
SARS virus	Severe Acute Respiratory Syndrome	Coronoviridae	Yes	Several carnivore species*, possibly other mammals and reptiles	Asia, Europe, USA, Canada	Direct, possibly indirect?	Yes	Contact with wildlife?
Cote D'Ivoire Ebola virus	HF	Filoviridae	Yes	Monkeys; bats?*	W. Africa	Direct/ internal	Yes	Contact with sick chimpanzee
Marburg virus	HF	Filoviridae	Yes	Monkeys; bats?*	Africa, Europe	Internal	Yes	Imported lab. monkeys
Reston Ebola virus	None	Filoviridae	No	monkeys	USA, Philippines	Direct	No	Laboratory contact
Sudan Ebola virus	HF	Filoviridae	Yes	Monkeys; bats?*	Africa	Direct/ internal	Yes ∞	Hunting bushmeat?
Zaire Ebola virus	HF	Filoviridae	Yes	Monkeys; bats?*	Africa	Direct/ internal	Yes ∞	Hunting bushmeat?
Hepatitis B virus	Hepatitis	Hepadnaviridae	Yes	Chimpanzees	Worldwide	Internal	Yes ∞	Contact with wild chmpanzees?
Cercopitechine herpes virus 1	Encephalitis	Herpesviridae	Yes	Primates, mainly *Macaca* sp.*	Mostly old world tropics	Internal	Yes	Contact with laboratory monkeys

Virus name	Disease	Virus family	Public health issue?	Animal host (*=known to be natural reservoir)	Distribution	Main transmission route	Human-human transmission?	Factors associated with zoonotic transfer
Suid herpesvirus 1	Aujeszky's (rabies-like)	Herpesviridae	No	Pigs	Worldwide in pigs	Internal (bite)	No	Rare, unsubstantiated
Influenza A	Respiratory	Orthomyxoviridae	Yes	Wildfowl*, poultry, pigs	Worldwide	Direct	Yes ∞	Genetic change, pig/duck agriculture
Influenza B	Respiratory	Orthomyxoviridae	Yes	Seals	Worldwide	Direct	Yes ∞	
Influenza C	Respiratory	Orthomyxoviridae	Yes	Pigs	Worldwide	Direct	Yes ∞	
Hendra virus	Respiratory	Paramyxoviridae	Yes	Horses, fruit bats* (*Pteropus* sp.)	Australia	Direct	Yes	Pressure on bat ecology
Menangle virus	Mild fever, reproductive	Paramyxoviridae	No	Pigs, fruit bats* (*Pteropus* sp.)	Australia	Direct	No	Pressure on bat ecology
Nipah virus	Encephalitis	Paramyxoviridae	Yes	Pigs, fruit bats* (*Pteropus* sp.)	Malaysia, Singapore	Direct	Yes	Pressure on bat ecology/
Human parainfluenza virus 2	Respiratory	Paramyxoviridae	Yes	Dogs, monkeys?	Worldwide	Direct	Yes ∞	Contact in medical laboratories?
Newcastle disease virus	Conjunctivitis, flu-like	Paramyxoviridae	No	Birds	Worldwide	Direct	No	Contact with poultry
Human Respiratory Syncytial virus	Respiratory	Paramyxoviridae	Yes	Chimpanzees, cattle	Worldwide	Direct	Yes ∞	
Encephalomyocarditis virus	various	Picornaviridae	No	Includes ruminants, primates, rodents, chickens, insects	Worldwide	Uncertain	Unknown	
Foot and mouth disease virus	Vesicles/lesions	Picornaviridae	No	Hooved animals esp. pigs, cows	Worldwide	Direct/indirect	No	Contact with cows/pigs
Hepatitis A	Liver disease	Picornaviridae	Yes	Higher primates including chimpanzees	Worldwide	Direct	Yes ∞	
Swine vesicular disease virus	Various symptoms	Picornaviridae	No	Pigs	Europe, Hong Kong, Japan	Direct		Contact with infected pigs
Buffalopox virus	Hand lesions	Poxviridae	No	Buffalo *Bubalus bubalis*; rodents?*	India	Direct	Rare	Contact with infected animals

Virus name	Disease	Virus family	Public health issue?	Animal host (*=known to be natural reservoir)	Distribution	Main transmission route	Human-human transmission?	Factors associated with zoonotic transfer
Cowpox virus	Lesions	Poxviridae	No	Cattle, cats, rodents* (wild voles in UK)	Worldwide	Direct	Rare	Contact with infected cattle
Monkeypox virus	Lesions	Poxviridae	Yes	Squirrels* *Funiscuirus* sp. Monkeys	Africa, USA	Direct	Yes	Hunting bushmeat, imported pets (USA)
Bovine popular stomatitis virus	Lesions	Poxviridae	No	Cattle	Worldwide	Direct	Rare	Contact with infected cattle
Orf virus	Lesions	Poxviridae	No	Domestic sheep/goats	Worldwide	Direct	Rare	Contact with infected sheep
Pseudocowpox virus	Lesions	Poxviridae	No	Domestic cattle	Worldwide	Direct	Rare	Contact with infected cattle
Sealpox virus	Lesions	Poxviridae	No	Seals (various species)	USA, Canada, Europe	Direct	Rare	Contact with infected seals
Tanapox virus	Lesions/ fever	Poxviridae	No	Monkeys, reservoir unknown	Central Africa	Unknown	Rare	Associated with rivers
Yaba monkey tumour virus	Fibrous tomours	Poxviridae	No	Monkeys	Africa/USA	Unknown		Contact in medical laboratories
BSE agents	vCJD	Prions	Yes	Cattle	UK	Indirect (infected meat)	Yes	Bad husbandry and food processing
Rotavirus A	Gastroenter-tis	Reoviridae	Yes	Wide range mammals and birds, not rodents	Worldwide	Direct	Yes ∞	Contact with infected animal faeces
Rotavirus B	Gastroenter-tis	Reoviridae	Likely	Pigs, cows, rats	Worldwide	Direct	Yes ∞	Contact with infected animal faeces
Rotavirus C	Gastroenter-tis	Reoviridae	Likely	Cows	Worldwide	Direct	Yes ∞	Contact with infected animal faeces
Rotavirus D	Gastroenter-tis	Reoviridae	Likely	Wide range mammals	Worldwide	Direct	Yes ∞	Contact with infected animal faeces
Rotavirus E	Gastroenter-tis	Reoviridae	Likely	Wide range mammals	Worldwide	Direct	Yes ∞	Contact with infected animal faeces
Rotavirus F	Gastroenter-tis	Reoviridae	Likely	Wide range mammals	Worldwide	Direct	Yes ∞	Contact with infected animal faeces

Virus name	Disease	Virus family	Public health issue?	Animal host (*=known to be natural reservoir)	Distribution	Main transmission route	Human-human transmission?	Factors associated with zoonotic transfer
HIV-1	AIDS	Retroviridae	Yes	Chimpanzee *Pan troglodytes troglodytes*	Worldwide	Internal	Yes ∞	Hunting wildlife/ medical practise?
HIV-2	AIDS	Retroviridae	Yes	Sooty mangabey *Cerocebus atys*	West Africa	Internal	Yes ∞	Hunting wildlife
Human T-lymphotropic virus-1	Leukaemia, paralysis	Retroviridae	Yes	Primates	Worldwide	Internal	Yes ∞	
Rabies virus	Rabies	Rhabdoviridae	Yes	Mammals, small-medium sized omnivores, especially dogs	Almost worldwide	Internal (bite)	No	Bite from infected animal
Australian bat lyssavirus	Rabies-like	Rhabdoviridae	Yes	Fruit bats *Pteropus* sp.	Australia	Internal (bite)	No	Bite from infected animal
Duvenhage virus	Rabies-like	Rhabdoviridae	Yes	Bats	Worldwide	Internal (bite)	No	Bite from infected animal
European bat lyssavirus 1	Rabies-like	Rhabdoviridae	Yes	Insectivorous bats	Europe	Internal (bite)	No	Bite from infected animal
European bat lyssavirus 2	Rabies-like	Rhabdoviridae	Yes	Insectivorous bats (*Myotis* spp.)	Europe	Internal (bite)	No	Bite from infected animal
Mokola virus	Rabies-like	Rhabdoviridae	Yes	Dogs, cats, rodents	Africa	Internal (bite)	No	Bite from infected animal
Hepatitis E	Hepatitis	Unclassified (Caliciviridae?)	Yes	Many mammals, including primates, rodents, pigs.	Asia, Africa, Indian subcontinent	Indirect (water)	Yes ∞	

REFERENCES USED TO COMPILE REVIEW

General: (Beran, 1994; Palmer, Soulsby *et al.*, 1998; Granoff and Webster, 1999; Taylor, Latham *et al.*, 2001)

Specific to virus family/genus

Arenaviruses: (Monath, 1987; Salas, 1991; Childs, 1994; Coimbra, Nassar *et al.*, 1994; Howard, 1998)
Bornaviridae: (Hatalski, Lewis *et al.*, 1997; Boucher, Barbillon *et al.*, 1999)
Hantaviruses: (Lee, Lee *et al.*, 1978; Avsic-Zupanc, Xiao *et al.*, 1992; Nichol, Spiropoulou *et al.*, 1993; Chu, Rossi *et al.*, 1994; Diglisic, Xiao *et al.*, 1994; Peters, 1994; Song, Baek *et al.*, 1994; Morzunov, Feldmann *et al.*, 1995; Rollin, Ksiazek *et al.*, 1995; Levis, Rowe *et al.*, 1997; Williams, Bryan *et al.*, 1997; Clement, McKenna *et al.*, 1998; Johnson, de Souza *et al.*, 1999; Rhodes, Huang *et al.*, 2000; Vincent, Quiroz *et al.*, 2000; Della Valle, Edelstein *et al.*, 2002; Padula, Della Valle *et al.*, 2002; Delfraro, Clara *et al.*, 2003; Täger, Vial *et al.*, 2003)
Other Bunyaviridae: (Kalunda, Mukwaya *et al.*, 1986)
Coronaviridae: (Hirano, Suzuki *et al.*, 1999; Enserink, 2003; Normile and Enserink, 2003)
Caliciviridae: (Bankowski and Sawyer, 1994)
Filoviridae: (Peters, Jonhson *et al.*, 1993; McCormick and Fisher-Hoch, 1994; Lloyd, 1998; Monath, 1999)
Hepatitis B: (Bollyky, Rambaut *et al.*, 1997; Odemuyiwa, Mulders *et al.*, 2001)
Herpesviridae: (Brown, 1998; Meurens, Gallego *et al.*, 2002)
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Hendraviruses: (Chant, Chan *et al.*, 1998; Philbey, Kirkland *et al.*, 1998; Barclay and Paton, 2000; Chua, Bellini *et al.*, 2000; Field, Young *et al.*, 2001; Wang and Eaton, 2001; Wang, Chua *et al*, 2003)
Other Paramyxoviridae: (Hsiung and Chang, 1994; Khan, 1994; Lehmkuhl, 1994; Morgan-Capner and Bryden, 1998)
Picornoviridae: (Brown, Goodridge *et al.*, 1976; Morgan-Capner and Bryden, 1998)
Poxviridae: (Falk, 1978; Jezek and Fenner, 1988; Douglass, Richardson *et al.*, 1994; Reid, 1998; Chantrey, Meyer *et al.*, 1999; Pastoret, Bennett *et al.*, 2000; Lutz, 2003)
Prions: (Will, Ironside *et al.*, 1996)
Retroviruses: (Voevodin, Johnson *et al.*, 1997; Gao, Bailes *et al.*, 1999; Gessain and Mahieux, 1999; Hahn, Shaw *et al.*, 2000; Weiss and Weiss, 2001)
Rhabdoviridae: (King, 1998)

APPENDIX III: Wildlife species reported to have been consumed or sold in wildlife markets in China

Four systematic surveys of species traded in wildlife markets in southern China are summarized here. All were carried out in the late 90s. The first three are published in the scientific literature. The fourth was carried out by CWCA, and reported in the Chinese press.

Species are separated by class, into mammals, birds and reptiles. Mammals are further divided into orders, because of their greater relevance in disease transfer to humans. Within each taxonomic group, species are listed in alphabetical order for ease of reference. Common names are given where available. Where species were grouped into a genus in any one of the surveys, species identified from that genus in other surveys are placed in the same group.

Reference 1 (Zhijun, Huojie *et al.*, 1996) recorded live animals being imported through 6 ports in the Province of Yunnan from May 1998 to December 1999. These species could have been destined for consumption or for use as medicines or even pets. However, most of them were also observed being transferred directly to wildlife markets and restaurants. Number of ports (out of six) the species was recorded at is given.

Reference 2 (Li, Fuller *et al.*, 1996) is a survey of wildlife trade in Guangdon Province and Guangxi Zhuang Nationality Autonomous Region, in 1994. Trade markets, trade sites on the Vietnam border were monitored and wildlife and forestry officials were interviewed to compile a list of species being traded. Species presence across nine markets was recorded as rare (+), common (++) or in large quantities (+++). The highest rating is shown here.

Reference 3 (Li and Li, 1998) surveyed wildlife markets in towns near the China Vietnam border between 1993 and 1996, and inspected middle-high quality restaurants in Donxing, Pingxiang, Longzhou and Nanning. Twenty types of wildlife were found in restaurants. The highest percentage of restaurants serving these species in any of the three one-month survey periods is given, to nearest per cent. * = local or commercial name, species not identified.

Reference 4 (Anon., 2000) was a survey of wildlife eaten by people in China, published by CWCA in Chinese only. The survey was carried out from Septmber to December 1999, and surveyed restaurants, food stores and street markets in Beijing, Shanghai, Guangzhou, Nanning, Chongqing, Changsha, Fuzhou, Nanchang, Haikou, Guiyang, Kunming, Xi'an, Chengdu, Zhengzhou,Nanjing, Harbin, and Sanming, Quanzhou,Xiamen, Wuzhou and Guilin. EJF have obtained only a list of the most common species, from a brief report of the survey sent by Zhang Zhengwang, of Beijing Normal University.

♦ = Species not observed in markets or restaurants by any study, but seen traded at one port.

Class/Order	Species (common name)	Latin name	Quantity observed	Study
MAMMALIA: Primates	Hoolock gibbon	*Hylobates hoolock*	1/6 ports	1
	Gibbon	*Hylobates* sp.	3/6 ports	1
	Assam macaque	*Macaca assamensis*	+++	2, 3
	Crab-eating macaque	*Macaca fascicularis*	1/6 ports ++	1, 2, 3
	Rhesus macaque	*Macaca mulatta*	5/6 ports +++	1, 2, 3
	Pigtail macaque	*Macaca nemestrina*	2/6 ports +++	1, 2, 3
	Stump-tailed macaque	*Macacca arctioides*	++	2, 3
	Slow loris	*Nycticebus coucang*	4/6 ports +++	1, 2, 3
	Pygmy loris	*Nycticebus pygmaeus*	1/6 ports	1
	Sureli	*Presbytis* sp.	3/6 ports	1
	Tonkin snub-nosed monkey	*Pygathrix avunculus*		3
	Francois' leaf monkey	*Trachypithecus francoisi*	++	2, 3, 4
Carnivores	Owston's palm civet	*Chrotogale owstoni*	++	2
	Asian wild dog	*Cuon alpinus*	3/6 ports	1
	Leopard cat	*Felis bengalensis*	++ 2% rests.	2, 3
	Jungle cat	*Felis chaus*	5/6 ports	1
	Asiatic golden cat	*Felis temmincki*	3/6 ports	1
	Malayan sun bear	*Helarctos malayanus*	2/6 ports	1
	Crab-eating mongoose	*Herpestes urva*	++	2, 3
	Otter	*Lutra* sp.	5/6 ports	1
	Badger	*Meles meles*	+	2
	Chinese ferret badger	*Melogale moschata*	+ 3% rests.	2, 3
	Siberian weasel	*Mustela sibirica*	++	2
	Clouded leopard	*Neofelis nebulosa*	2/6 ports	1
	Masked palm civet	*Paguma larvata*	5/6 ports +++ 35% rests.	1,2,3,4
	Leopard	*Panthera pardus*	4/6 ports	1
	Tiger	*Panthera tigris*♦	1/6 ports	1
	Spotted linsang	*Prionodon pardicolor*	+++	2
	Asiatic black bear	*Selenarctos thibetanus*	5/6 ports ++	1, 2
	Brown bear	*Ursus arctos*	+	2
	Large Indian civet	*Viverra zibetha*	2/6 ports +++	1, 2, 3
	Small Indian civet	*Viverricula indica*	3/6 ports ++ 2% rests.	1, 2, 3
	Red fox	*Vulpes vulpes*	10% rests.	3

Even-toed ungulates	Roe deer	*Capreolus capreolus*		4
	Red deer	*Cervus elaphus*	+++	2
	Sika deer	*Cervus nippon*	++	2
	Sambar	*Cervus unicolor*	4/6 ports +++	1, 2
	Indian muntjac	*Muntiacus muntjak*	3/6 ports +++	1, 2
	Chinese muntjac	*Muntiacus reevesi*	+++	2, 4
	Saiga antelope	*Saiga tatarica*	+	2
	Wild pig	*Sus scrofa*	2/6 ports + 2% rests.	1, 2, 3, 4
Elephants	Asian elephant	*Elephas maximus*	2/6 ports	1
Anteaters	Pangolin	*Manis* sp. (mostly *pentidactyla*)	6/6 ports +++ 36% rests.	1, 2, 3
Rabbits and hares	Cape hare	*Lepus capensis*		4
	Chinese hare	*Lepus sinensis*	+++ 8% rests.	2
	Squirrel	*Callosciurus erythraeus*		3
Rodents	Malayan porcupine	*Hystrix Brachyura*	+	2
	Himalayan porcupine	*Hystrix hodgsoni*	4/6 ports	1
	Chinese mountain rat	*Niviventer coxingi*	+++	2
	Black Giant Squirrel	*Ratufa bicolor*	+++	2
	Chinese bamboo rat	*Rhizomys sinensis*	6/6 ports +++ 22% rests.	1, 2, 4
AVES: Birds	Hawks	*Accipiter* spp.	4/6 ports ++	1, 2, 3
	Mynas	*Acridotheres* spp.	6/6 ports	1
	Mandarin duck	*Aix galericulata*	++	2
	Common kingfisher	*Alcedo atthis*	++	2
	White-breasted water hen	*Amaurornis pheonicurus*	2/6 ports	1, 3
	Golden crested myna	*Ampeliceps coronatus*	4/6 ports	1
	Ducks	*Anas* spp.	1/6 ports +++ 2% rests.	1, 2, 3
	Bar-headed goose	*Anser indicus*	3/6 ports	1
	Malabar pied hornbill	*Anthracoceros coronatus*	2/6 ports	1
	Eagles	*Aquila* spp.	2/6 ports + 8% rests.	1, 2, 3
	Sichuan partridge	*Arbophila rufipectus*	+	2
	Green-legged hill partridge	*Arborophila chloropus*	1/6 ports	1
	Grey heron	*Ardea cinerea*	1/6 ports	1
	Purple heron	*Ardea pupurea*	3/6 ports	1
	Long-eared owl	*Asio otus*	++	2
	Black baza	*Aviceda leuphotes*♦	1/6 ports	1
	Mountain Bamboo-partridge	*Bambusicola fytchii*	++	2

	Chinese Bamboo-partridge	*Bambusicola thoracica*	++	2, 4
	Eurasian eagle-owl	*Bubo bubo*	++	2, 3
		Bubo niaplensis	1/6 ports	1
	Greater coucal	*Centropus sinensis*	1/6 ports	1, 3
	Emerald dove	*Chalcophaps indica*	3/6 ports	1
	Lady Amherst pheasant	*Chrysolophus amherstiae*	4/6 ports	1
	Golden pheasant	*Chrysolophus pictus*		
		Contunix spp.		4
	Oriental magpie robin	*Copsychus saularis*	2/6 ports	1
	Whooper swan	*Cygnus cygnus*	2% rests.	3
	Lesser whistling duck	*Dendrocygna javanica*	1/6 ports	1
	Mountain imperial pigeon	*Ducula badia*	2/6 ports	1
	Yellow-breasted bunting	*Emberiza aureola*	3% rests.	3
	Avadavat	*Estrilda amandava*	1/6 ports	1
	Falcons	*Falco* spp.	3/6 ports ++	1, 2
	Chinese francolin	*Francolinus pintadaenus*	4/6 ports	1, 3, 4
	Barred rail	*Gallus gallus*	6/6 ports	1
	Hwamei	*Garrulax canorus*	1/6 ports +++	1, 2
	Black-throated laughingthrush	*Garrulax chinensis*	3/6 ports	1
	White-crested laughingthrush	*Garrulax leucolophus*	2/6 ports	1
	Spot-breasted laughingthrush	*Garrulax merulinus*	1/6 ports	1
	Lesser necklaced laughingthrush	*Garrulax monileger*	1/6 ports	1
	Greater necklaced laughingthrush	*Garrulax pectoralis*	1/6 ports	1
	White-browed laughingthrush	*Garrulax sannio*	++	2
	Asian barred owlet	*Glaucidium cucloides*	++	2
	Eurasian pygmy-owl	*Glaucidium passerinum*	++	2
	Common hill myna	*Gracula religiosa*	6/6 ports	1
	Griffon vulture	*Gyps fulvus*	3/6 ports	1
	Kingfishers	*Halcyon* spp.	++	2
	Silver-eared mesia	*Leiothrix argentauris*	++	2
	Silver-eared mesia	*Leiothrix argentauris*	3/6 ports	1
	Red-billed leiothrix	*Leiothrix lutea*	++	2
	Red-faced liocichla	*Liocichla phoenicea*	1/6 ports	1
	Edward's pheasant	*Lophura edwardsi*	1/6 ports	1
	Silver pheasant	*Lophura nycthemera*	1/6 ports ++	1, 2
	Black kite	*Milvus migrans*	++	2
	Brown hawk owl	*Ninox scutulata*	3/6 ports	1
	Orioles	*Oriolus* spp.	+++	2
	Tree sparrow	*Passer montanus*	1/6 ports	1, 4
	Green peafowl	*Pavo muticus*	4/6 ports	1
	Scarlet minivet	*Pericrocotus flammeus*	++	2
	Common pheasant	*Phasianus colchicus*	3/6 ports 10% rests.	1,3,4
	Asian bay owl	*Phodilus badius*	1/6 ports	1

	Magpie	*Pica pica*		4
	Grey peacock pheasant	*Polyplectron bicalcaratum*	5/6 ports	1
	Coral-billed scimitar babbler	*Pomatorhinus ferruginosus*	1/6 ports	1
	Large scimitar babbler	*Pomatorhinus hypoleucos*	1/6 ports	1
	Purple gallinule	*Porphyrio porphyrio*	5/6 ports	1
	Long-tailed broadbill	*Psarisomus dalhousiae*	++	2
	Moustached parakeet	*Psittacula alexandri*	4/6 ports	1, 3
	Plum-headed parakeet	*Psittacula cyanocephala*	1/6 ports ++	1, 2
	Derbyan parakeet	*Psittacula derbiana*	2/6 ports	1
	Rose-ringed parakeet	*Psittacula krameri*	1/6 ports +++	1, 2
	Blue-breasted banded rail	*Rallus striatus*	2/6 ports	1
	Silver breasted broadbill	*Serilophus lunatus*	++	2
	Crested serpent eagle	*Spilornis cheela*	2/6 ports	1
	Wallace's hawk eagle	*Spizaetus nanus*	1/6 ports	1
	Crested finchbill	*Spizixos canifrons*	++	2
	Collared finchbill	*Spizixos semitorques*	++	2
	Spotted dove	*Streptopelia chinensis*	1/6 ports +++	1, 2, 4
	Oriental turtle-dove	*Streptopelia orientalis*	1/6 ports +++	1, 2, 4
	Red collared-dove	*Streptopelia tranquebarica*	1/6 ports +++	1, 2, 4
	Starlings	*Sturnus* sp.	6/6 ports	1
	Bar-tailed pheasant	*Syrmaticus humiae*	2/6 ports	1
	Pin-tailed green pigeon	*Treron apicauda*	4/6 ports	1
	Wedge-tailed green pigeon	*Treron sphenura*	2/6 ports	1
	Yellow-legged button quail	*Turnix tanki*	2/6 ports	1
	African grass owl	*Tyto capensis*	2/6 ports	1, 3
	Houtouying	Tytonidae		3
	Japanese white-eye	*Zosterops japonica*	1/6 ports	1
	Oriental white-eye	*Zosterops palpebrosa*	2/6 ports	1
REPTILIA	Mountain horned dragon	*Acanthosaura armata*	4/6 ports	1
	Hundred-pace pit viper	*Agkistrodon acutus*	2/6 ports	1
	Vipers	*Agkistrodon* spp.	1/6 ports +++	1, 2, 3
	Fea's viper	*Azemiops feae*	2/6 ports	1
	Banded krait	*Bungarus fasciatus*	4/6 ports +++	1, 2, 3
	Many-banded krait	*Bungarus multicinctus*	4/6 ports +++	1, 2, 3
	Common garden lizard	*Calotes versicolor*	+++ 2% rests.	2, 3
	Loggerhead turtle	*Caretta caretta*		3
	Chinese broad-headed pond turtle	*Chinemys megalocephala*	+++	2
	Chinese three-keeled pond turtle	*Chinemys reevesii*	++++	2, 3
	Spotted terrapin	*Clemmys bealei*	3/6 ports	1

	Four-eyed turtle	*Clemmys quadriocellata*	3/6 ports	1
	Snake-eating turtle	*Cuora hainanensis*	3/6 ports	1
	Chinese three-striped box turtle	*Cuora trifasciata*	+++	2, 3
	Yunnan box turtle	*Cuora yunnanensis*	++	2, 3
	Asian leaf turtle	*Cyclemys dentata*	+++	2
	Keeled box turtle	*Cyclemys mouhotii*	3/6 ports	1
	Yellow-margined box turtle	*Cystoclemmys flavomarginata*	++	2
	Sharp-nosed viper	Deinagkistrodon acutus	+++	2
	Leatherback	*Dermochelys coriacea*	+++	2
	Yellow banded wolf snake	*Dinodon flavozonatum*	3/6 ports	1
	Mandarin rat snake	*Elaphe mandarina*	3/6 ports	1
	Moellendorff's rat snake	*Elaphe moellendorffi*	4/6 ports +++	1, 2, 3
	Copperhaed trincket snake	*Elaphe radiata*	4/6 ports +++	1,2, 3
	Taiwan beauty snake	*Elaphe taeniurus*	4/6 ports	1, 3
	Mangrove water snake	*Enhydris bennetti*	3/6 ports	1
	Rainbow water snake	*Enhydris enhydris*	3/6 ports	1
	Asian green snake	*Entechinus major*	4/6 ports	1
	Hawksbill turtle	*Eretmochelys imbricata*	+++	2
	Tokay	*Gekko gecko*	4/6 ports +++ 40% rests.	1, 2, 3
	Geckos	*Gekko spp.*	+++	2
	Black breasted leaf turtle	*Geoemyda spengleri*	+++ 4/6 ports	1, 2, 3
	Crowned river turtle	*Hardella thurjii*	++	2
	Elongated tortoise	*Indotestudo elongata*	+++	2
	Olive Ridley sea turtle	*Lepidochelys olivacea*		3
	Wolf snake	*Lycodon laoensis*	1/6 ports	1
	Impressed tortoise	*Manouria impressa*	+++	2
	Asian yellow pond turtle	*Mauremys mutica*	3/6 ports +++	1, 2
	Common small-headed sea snake	*Microcephalophis gracilis*		3
	Asian cobra	*Naja naja*	4/6 ports +++	1, 2, 3
	Chinese stripe-necked turtle	*Ocadia sinensis*	4/6 ports	1, 3
	Greater green snake	*Opheodrys major*		3
	King cobra	*Ophiophagus hannah*	4/6 ports +++	1, 2, 3
	Chinese slug snake	*Pareas chinensis*	1/6 ports	1
	Chinese slug snake	*Pareas hamptoni*	3/6 ports	1
	Asian giant softshell turtle	*Pelochelys bibroni*	+++	2
	Asian water dragon	*Physignathus cocincinus*	++	2
	Chinese water dragon	*Physignathus cocincinus*	4/6 ports	1,3
		Plagiopholis chinensis	1/6 ports	1
	Assamese mountain snake	*Plagiopholis nuchalis*	2/6 ports	1

	Big-headed turtle	*Platysternon megacephalum*	3/6 ports	1,3
	Bamboo snake	*Pseudoxenodon bambusicola*	4/6 ports	1
	Indochinese rat snake	*Ptyas korros*	4/6 ports	1, 3
	Common rat snake	*Ptyas mucosus*	3/6 ports +++	1, 2, 3
	Burmese python	*Python molurus*	4/6 ports +++	1, 2, 3
		Rhabdophis leonardi	2/6 ports	1
	Oriental long-tailed lizard	*Takydromus sexlineatus*	++	2
	Coahuilan box turtle	*Terrapene coahuila*	++	2
	Elongated tortoise	*Testudo elongata*	2/6 ports	1
	Central Asian tortoise	*Testudo horsfieldii*	+++	2
	Impressed tortoise	*Testudo impressa*	2/6 ports	1
	Yagui*	Testudoformes		3
	Zhenggui*	Testudoformes		3
	White-lipped pit viper	*Trimeresurus albolabris*	4/6 ports	1
	Jerdon's pit viper	*Trimeresurus jerdonii*	4/6 ports	1
		Trimeresurus mucrosquamatus	4/6 ports	1
	Stejneger's pit viper	*Trimeresurus stejnegeri*	4/6 ports +++	1, 2
		Trionyx impressa	3/6 ports	1
	Chinese softshell turtle	*Trionyx sinensis*	4/6 ports +++ 49% rests.	1, 2, 3
	Wattle-necked softshell turtle	*Trionyx steindachneri*	4/6 ports ++	1, 2, 3
	Water skink	*Tropidophorus berdmorei*	3/6 ports	1
	Common worm snake	*Typhlops braminus*	+++	2
	Yellow monitor	*Varanus flavescens*	+++	2
	Sepik monitor	*Varanus jobiensis*	+++	2
	Water monitor	*Varanus salvator*	4/6 ports +++ 37% rests.	1, 2, 3
	Russell's Viper	*Vipera russelli*	+++	2
		Xenopeltis hainanensis	3/6 ports	1
		Xenopeltis unicolor	3/6 ports	1
	Chinese rat snake	*Zaocys dhumnades*	1/6 ports +++	1, 2
		Zaocys dhumnades	2/6 ports	1
AMPHIBIA	Chinese giant salamander	*Andrias davidianus*	+++	2
	Toads	*Bufo* spp.	+++	2
	Boulenger's Toad	*Rana boulengeri*	+++	2
		Rana japonica	++	2
		Rana nigromaculata		3
	Tiger frog	*Rana tigerina*	+++	2

APPENDIX IV: List of arboviruses

This is an alphabetical list of viruses known to cause disease in humans that are transmitted by arthropod vectors. The list is derived from an electronic appendix to (Taylor, Latham *et al.*, 2001). The majority are carried by mosquitos, ticks or sand-flies. In some cases, such as Apoi virus and Phnom-Penh bat virus, the vector is not yet identified. Emerging viruses are underlined. All are zoonotic.

- Apoi virus
- Bagaza virus
- Bangui virus
- Banna virus
- Banzi virus
- Barmah Forest virus
- Batkon virus
- Bebaru virus
- Bhanja virus
- Bovine ephemeral fever virus
- Bunyamwera virus
- Bussuquara virus
- Bwamba virus
- California encephalitis virus
- Candiru virus complex
- Caraparu virus
- Catu virus
- Chandipura virus
- Changuinola virus
- Chikungunya virus
- Chim virus
- Colorado tick fever virus
- Crimean Congo haemorrhagic fever virus
- Dakar bat virus
- Dengue virus
- Dhori virus
- Dugbe vius
- Eastern equine encephalitis virus
- Edge Hill virus
- European tick-borne encephalitis virus
- Everglades virus
- Eyach virus
- Far Eastern tick-borne encephalitis virus
- Gan gan virus
- Getah virus
- Guama virus
- Guarea virus
- Hughes virus
- Igbo-ora virus
- Ilheus virus
- Issyk Kul virus
- Japanese encephalitis virus
- Kairi virus
- Kedougou virus
- Kemerovo virus
- Kokobera virus
- Koutango virus
- Kyasanur forest disease virus
- Lanjan virus
- Lebombo virus
- Louping ill virus
- Madrid virus
- Marituba virus
- Mayaro virus
- Mucambo virus
- Murray Valley encephalitis virus
- Nyando virus
- Ockelbo virus
- Omsk haemorrhagic fever virus
- O'nyong-nyong virus
- Oriboca virus
- Oropouche virus
- Orungo virus
- Phnom-Penh bat virus
- Piry virus
- Powassan virus
- Punta Toro virus
- Quaranfil virus
- Rift Valley Fever virus
- Rocio virus
- Ross river virus
- Royal Farm virus
- Salehabad virus
- Sandfly fever Naples virus
- Sandfly fevervirus group
- Saumarez Reef virus
- Semliki Forest virus
- Sepik virus
- Sindbis virus
- St. Louis encephalitis virus
- Tacaiuma virus
- Tamdy virus
- Tataguine virus
- Thogoto virus
- Trubanaman virus
- Tyuleniy virus
- Usutu virus
- Venezuelan equine encephalitis virus
- Vesicular stomatitis virus
- Wad medani virus
- Wanowrie virus
- Wesselsbron virus
- West Nile virus
- Western equine encephalitis virus
- Wyeomyia virus
- Yellow fever virus
- Yogue virus
- Zika virus

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