

Editorials

Zoonoses

Humans have enjoyed a long and intimate relationship with other animals. Some animals are reared to provide food, milk or clothing, some for recreational purposes and others are brought into the home for companionship or to act as guards. Most often those interactions are decidedly to human benefit. In their interaction with wild animals humans are also usually in the ascendant. However, there are occasional disadvantages to humans including transmission of infection. Such infections are usually called zoonoses. A Joint Expert Committee of the WHO and FAO has defined zoonoses as those diseases and infections naturally transmitted between vertebrate animals and humans.¹ There are well over 500 different pathogens, (viruses, bacteria, fungi, protozoa, multi-cellular parasites and insects), that are transmitted to humans from animals. The range of pathogens has increased with recent epidemiological and protein sequence data linking the prion proteins that cause bovine spongiform encephalopathy (BSE) and new variant Creutzfeldt-Jakob disease, (CJD).^{2,3} Although it is clear that zoonoses occur, it is difficult to estimate their overall impact on human health. Undoubtedly the most numerous of the zoonoses are infections with non-typhoidal salmonellae (NTS), *Campylobacter spp*, *Cryptosporidium parvum* and with the recently emerged enterohaemorrhagic *Escherichia coli* 0157.⁴ Even though each is notifiable as a cause of food poisoning the national figures are undoubtedly an underestimate. The picture is further clouded by the fact that each of the above pathogens is also transmissible person to person as well as being zoonotic.

There are a number of ways in which zoonoses can be classified, none of which is ideal. An approach based on the organ system involved can be clinically useful. However, zoonotic causes of for example pneumonia, (for example, *Chlamydia psittaci*) or meningitis (for example, *Streptococcus suis*) usually fall at the end of a series of differential diagnoses and this will inevitably lead to underdiagnosis. Classification based on animal species of origin can also be problematic, firstly because the patient may not recall the contact animals and secondly because several animal species may harbour the same zoonotic pathogen, (for example, *Cryptosporidium parvum*, *Campylobacter spp* and NTS in cattle, sheep, pigs, cats and dogs). Recognition of the source of a zoonosis can be difficult too, because with a few exceptions, (for example, rabies, orf, *Francisella tularensis*, *Burkholderia mallei*) the zoonotic pathogen is well adapted to its animal host and rarely produces disease.

Another classification scheme is based on mode of transmission.⁴ Thus zoonoses may be acquired by direct contact through cuts, scratches or abrasions, (for example, cowpox virus, *Bartonella henselae*, *Clostridium tetani*, *Micro-*

sporum canis or *Tunga penetrans*) or through animals bites, (for example, rabies, *Capnocytophaga canimorsus* or *Spirillum minor*). Arthropods may act as biological vectors transferring zoonotic pathogens from their natural or multiplier hosts, (for example, *Culex* and *Anopheles* transmitting Japanese B encephalitis virus from pigs, or, ixodid ticks transferring *Borrelia burgdorferi* and the agent of human granulocytic ehrlichiosis from rodents and deer). A number of zoonotic pathogens, (for example, hantavirus, *Coxiella burnetii*, or *Cryptococcus neoformans*), are acquired via the respiratory route. Finally they may be acquired by ingestion either by faeco-oral contamination directly or in water, (for example, *Campylobacter spp*, *Cyclospora cayentanensis* or *Dracunculus medinensis*) or by ingestion of meat, fish, shellfish, eggs or dairy products, (for example, *Brucella abortus*, *E coli* 0157, *Toxoplasma gondii* or *Trichinella spiralis*). In reality a combination of each of these three classification schemes is the most useful.

An alternative view is to group zoonoses according to their likely evolutionary history (table 1). Viewed from this perspective, many human infectious diseases seem to have originated as zoonoses.⁵⁻⁹ Examples of human infections that were probably zoonoses in the historically distant, (but recent in evolutionary terms), past include measles and the common cold. Both are acute viral infections provoking good immunity and maintained in the host population by rapid transmission from infected to susceptible hosts. Thus neither can be maintained in human populations below a threshold size sufficient to generate a supply of new susceptibles. As few human populations reached the threshold size required to maintain measles until around 6000 years ago, measles must be a relatively new human disease. The simplest explanation of their appearance is that they are derived originally from infections of non-human animals—that is, they were zoonoses. Their precise animal source is impossible to determine but it seems likely that measles might be derived from the closely related morbilliviruses of cattle (rinderpest) or dogs, (canine distemper virus or CDV). Certainly CDV has a wide host range that might include humans.¹⁰⁻¹²

A topical example of a recent zoonosis that has become established as a human disease is HIV/AIDS. It now seems most likely that HIV-2 originated in the sooty mangabey (*Cercocebus atys*)¹³ and recent data have indicated that HIV-1 originated in a subspecies of the chimpanzee, (*Pan troglodytes troglodytes*) found in central equatorial Africa.¹⁴ These viruses have probably been transmitted to humans sporadically over the centuries and it is interesting to speculate that it may be recent changes in socioeconomic factors and human behaviour, such as the development of pan-African road systems and worldwide air travel, that

Table 1 Classification scheme for zoonoses based on likely history

Old zoonoses	Epidemic and endemic human specific infections with a temporally distant non-human source. (for example, measles, common cold, smallpox).
Recent zoonoses	New or emerging human epidemic or endemic infections with a recent non-human source. (for example, HIV).
Established zoonoses	Infectious diseases with a non-human reservoir host that are occasionally transmitted to humans. (for example, rabies, monkeypox, NTS)
New and emerging zoonoses	Infectious diseases with a non-human reservoir host that have only recently (or observed to) spread to humans, (for example, hantaviruses, ebola virus, hendra-like virus (Nipah), ehrlichiosis)
Parazoonoses	Infectious disease epidemic or endemic in humans but that change in virulence periodically after an input of genes from non-human pathogens. (for example, antibiotic resistance transferred from animal to human bacteria or, genomic reassortment (antigenic shift) in influenza A virus or rotavirus.

have enabled their widespread establishment in human populations for the first time.

It is in the area of emerging infectious diseases that zoonoses have exerted their greatest impact. *E coli* 0157, which causes haemorrhagic colitis and haemolytic uraemic syndrome, is excreted asymptotically by cattle, sheep and a number of other animal species.¹⁵ It seems to be a newly evolved bacterial pathogen as it is not found in any collections of enteric *E coli* strains before 1980. Other examples of zoonoses with fatal consequences include the filoviruses, (Ebola and Marburg) and arenaviruses, (Lassa, Sabia, Guarano), that cause viral haemorrhagic fevers. In each case the virus causes little to no disease in its natural host, (for example, bats for Ebola, multimammate rat for Lassa fever). In 1993 a "new" and frequently fatal disease of hantavirus pulmonary syndrome was described attributable to Sin Nombre virus, which again is excreted asymptotically by its reservoir host the deer mouse, (*Peromyscus maniculatus*) and acquired either when the deer mouse enters human's habitat or vice versa.¹⁶ The most recent zoonosis to have emerged is an outbreak of febrile encephalitis that began in September 1998 and still continues. This began in Perak State in Malaysia but other clusters of infection have occurred in other states, (Negri Sembilan and Selangor), and in Singapore.¹⁷ The infective agent is a Hendra-like paramyxovirus (now named Nipah virus), which seems to be associated with pigs as most of those affected have been pig farmers and abattoir workers. The pigs have also developed respiratory and neurological disease so it is unlikely that they are the reservoir host. The reservoir for Hendra virus is the fruit bat (*Pteropus spp*), which is found in south east Asia.¹⁸ This outbreak has thus far resulted in 229 cases of febrile encephalitis, 111 (48%) of which were fatal.

Much of this review has concentrated on classic zoonotic pathogens. However, it is now clear that animal pathogens can transfer part of their genetic make up to contribute to the virulence of established human pathogens or even to human commensals. Examples of this are the acquisition of virulence or antibiotic resistance genes transferred by plasmids, transposons, integrons or bacteriophages (bacterial viruses), to bacteria,^{19, 20} and genetic reassortment when two influenza A viruses simultaneously infect the same avian host, leading to the emergence of a new "flu" virus as occurred with Influenza A H5N1 in Hong Kong,²¹ and is currently occurring with H9N2.

Clearly the emergence of new zoonotic pathogens requires us to be increasingly vigilant. Neither should we neglect the classic zoonoses.

C A HART

Department of Medical Microbiology and Genitourinary Medicine, Centre for Comparative Infectious Diseases, University of Liverpool

M BENNETT

Department of Veterinary Pathology, Centre for Comparative Infectious Diseases, University of Liverpool

M E BEGON

School of Biological Sciences, Centre for Comparative Infectious Diseases, University of Liverpool

Correspondence to: Professor C A Hart, Department of Medical Microbiology and Genitourinary Medicine, PO Box 147, Liverpool L69 3GA.

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