
EDITORIAL REVIEW

Bats and human emerging diseases

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Recently, two independent research teams reported evidence of infection with SARS-like coronaviruses in insectivorous horseshoe bats (genus *Rhinolophus*) in China [1, 2]. SARS emerged in China in 2002, and eventually infected over 8000 people around the world, killing about 10% of them. Early epidemiological studies suggested that the human disease may have originated in Chinese live-animal food markets, and the hunt for a source of the virus quickly identified apparently healthy Himalayan palm civets (*Paguma larvata*) as prime suspects [3]. Other studies, however, failed to find any evidence of widespread infection in civets [4] or a variety of other animals traditionally used as food in China. Rather, palm civets, like human beings, seem to be only accidental hosts of the virus, becoming infected, again like people, when mixed with other species in markets. More structured hunts for the reservoir continued, although not before thousands of palm civets had been slaughtered.

The most recent studies examined samples from a range of Chinese wildlife. Neither study managed to isolate virus in cell culture, but both found antibody and detected SARS viruses by PCR. Lau *et al.* [1] sampled 127 bats, 60 rodents and 20 monkeys from the Hong Kong area, and identified three different coronaviruses by PCR in 29 bats: of these, 23 samples from Chinese horseshoe bats (*R. sinicus*) had *pol*-gene nucleotide sequences 88% identical to the SARS coronavirus. Antibody to recombinant nucleocapsid protein, derived from the bat SARS virus, was detected in over 80% of *R. sinicus* tested, and

virus-neutralizing antibody to human SARS virus in just over 40%. Li *et al.* [2] concentrated their study entirely on bats, but from a wider area of China. They sampled 408 bats, and detected antibody to the SARS coronavirus in three species: *R. pearsoni* (Pearson's horseshoe bat), *R. pussilus* (least horseshoe bat) and *R. macrotis* (big-eared horseshoe bat). They also obtained PCR positive faecal samples from *R. pearsoni*, *R. macrotis* and *R. ferrumequinum* (greater horseshoe bat). These bats are found mainly in S.E. Asia and India, apart from the greater horseshoe bat, which is found in temperate areas from Japan to Great Britain, although several geographically separate subspecies exist.

Both groups used PCR to derive complete genome sequences from positive samples. Lau *et al.* [1] produced such sequences from three samples, with overall 88% nucleotide (93% amino acid) identity to SARS coronaviruses. Li *et al.* [2] obtained a complete sequence from one of their *R. pearsoni* samples, and found it to have overall 92% nucleotide identity to that of a human SARS coronavirus. Li *et al.* also compared the N-gene sequences obtained from several bat samples, and found greater variation amongst the bat viruses than among human SARS virus isolates and some evidence for recombination between bat viruses (a feature seen in other coronaviruses). Furthermore, both groups found their bat virus genomes to have features found in viruses isolated from palm civets and early human cases of SARS but not in human isolates from later in the SARS epidemic, suggesting that selection and adaptation of the SARS virus occurred during transmission between human beings.

Why is it that bats suddenly find themselves to be such fashionable hosts for emerging infectious

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diseases? The more people look, the more lyssaviruses are found in bats around the world. Indeed lyssaviruses are now regarded as essentially bat viruses, with the more familiar carnivore-based rabies virus a rather anomalous, evolutionarily recent adaptation to a new host [5]. Hendra, Menangle and Nipah viruses are all recently emerged zoonotic paramyxoviruses in south Asia and Australia, with fruit bats of the genus *Pteropus* as reservoirs [6, 7]. And very recently, after a long search for possible reservoir hosts, Ebola virus has been detected in central Africa in the fruit bats *Hypsignathus monstrosus*, *Epomops franqueti* and *Myonycteris torquata* by both serology and PCR [8].

Of course, there is no reason why bats should not be the source of many potentially zoonotic infections. Probably because they are nocturnal and we are not, bats were, until recently, not even considered in studies of wildlife disease, and remarkably little is still known about the pathogenesis and transmission of any virus, even lyssaviruses, in bats. Yet, based simply on counting the number of species, bats represent almost 20% of all mammalian biodiversity, second only to rodents (50% of all mammal species), and, like rodents, they are found on every continent apart from Antarctica. Furthermore, many bats live in large colonies with close contact between individuals, life-history traits that might select for endemic infections. Therefore, perhaps all that has happened is that opportunities for transmission have increased: humans moving into the bats' environments, and bats having to adapt to sharing (or being brought into) man-made environments are common themes of all these new, bat-derived human diseases.

Another common factor in their emergence is liaison hosts. The bat SARS viruses were most likely amplified in palm civets rather than being directly transmitted from bats to people, while Nipah, Menangle and Hendra are usually amplified through pigs or horses, and Ebola, perhaps, through non-human primates. Even carnivores, now hosts of epidemic rabies, can, over evolutionary time, be regarded as liaison hosts between bats and human beings. The concept of liaison hosts is an important one, and by no means limited to emerging zoonoses from bats, yet it is often ignored in discussions about reservoir hosts, and adds an extra complication (and, perhaps, opportunity) to the design of disease control measures.

It is also striking that filoviruses, rhabdoviruses (the family to which the lyssaviruses belong) and paramyxoviruses (though not coronaviruses) are all members of the order Mononegavirales, making it

tempting to ask whether these viruses and bats share some co-evolutionary paths. However, these virus families often have wide host ranges (in the case of the Rhabdoviridae, including plants) so it may simply be that aspects of the life histories of both bats and these viruses lend themselves to co-existence. All the same, perhaps we should investigate bats as potential reservoir hosts of the remaining group in the Mononegavirales, the bornaviruses, for which the endemic hosts have not yet been determined.

The next step, though, should be to learn more about the ecology of these infections in their natural hosts: what are the roles of the various bat species in the maintenance of coronavirus infections? Are all these bats endemic hosts, or are some spillover hosts? And does the diversity of bat coronaviruses correspond to the diversity of *Rhinolophus* species and subspecies, not just in China, but worldwide? Are there further potentially zoonotic paramyxoviruses in other *Pteropus* bats around the Pacific and Indian Ocean, and more filoviruses to be found in other African flying foxes? These emerging infections from bats should remind us that human beings are still part of a global ecosystem that includes many as yet undiscovered infectious agents that can infect us, given the transmission opportunity, while SARS particularly should remind us that some of these, perhaps even a third of emerging zoonoses [9], will have the potential for human-to-human transmission.

DECLARATION OF INTEREST

None.

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