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Emerging zoonotic viral diseases

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Summary
Zoonotic diseases are infectious diseases that are naturally transmitted from vertebrate animals to humans and vice versa. They are caused by all types of pathogenic agents, including bacteria, parasites, fungi, viruses and prions. Although they have been recognised for many centuries, their impact on public health has increased in the last few decades due to a combination of the success in reducing the spread of human infectious diseases through vaccination and effective therapies and the emergence of novel zoonotic diseases. It is being increasingly recognised that a One Health approach at the human–animal–ecosystem interface is needed for effective investigation, prevention and control of any emerging zoonotic disease. Here, the authors will review the drivers for emergence, highlight some of the high-impact emerging zoonotic diseases of the last two decades and provide examples of novel One Health approaches for disease investigation, prevention and control. Although this review focuses on emerging zoonotic viral diseases, the authors consider that the discussions presented in this paper will be equally applicable to emerging zoonotic diseases of other pathogen types.

Keywords
Ebola virus – Emerging infectious disease – Hendra virus – Middle East respiratory syndrome coronavirus – Nipah virus – One Health – Severe acute respiratory syndrome coronavirus – Vaccine – West Nile virus – Zoonosis.

Introduction

The World Health Organization (WHO)/Food and Agriculture Organization of the United Nations (FAO)/ World Organisation for Animal Health (OIE) joint consultation on emerging zoonotic diseases held in Geneva, May 2004, defined an emerging zoonosis as 'a zoonosis that is newly recognised or newly evolved, or that has occurred previously but shows an increase in incidence or expansion in geographical, host or vector range' (1). Emerging zoonotic diseases have potentially serious human health and economic impacts and their current upwards trend is likely to continue. The last 30 years have seen a rise in emerging infectious diseases in humans and of these over 70% are zoonotic (2, 3). Zoonotic infections are not new. They have always featured among the wide range of human diseases and most, e.g. anthrax, tuberculosis, plague, yellow fever and influenza, have come from domestic animals, poultry and livestock. However, with changes in the environment, human behaviour and habitat, increasingly these infections are emerging from wildlife species.

The WHO and most infectious disease experts agree that the source of the next human pandemic is likely to be zoonotic, and wildlife is emerging as the primary source. Many zoonoses from wildlife, including avian influenza and rabies, are well established, while others have only recently emerged or have only recently been linked to wildlife reservoir species. One example of the latter is the Ebola virus, which, after decades of research, was recently linked to cave-dwelling bats in Africa. Similarly, the severe acute respiratory syndrome (SARS) coronavirus, which claimed over 800 lives and cost over 60 billion dollars globally, emerged from bats to civets before ultimately affecting humans in the wet markets and restaurants of southern China (4, 5).

The current emergence of the Middle East respiratory syndrome (MERS) (6) reminds us that while we need to be vigilant to those known pathogens of pandemic potential it is possible that the next deadly pandemic may be the result of a currently unknown zoonotic agent or one of the thousands of genetically identified agents of currently unknown pathogenic potential. The identification and cataloguing of infectious agents from wildlife has been

exceptional over the past ten years. While we can group some of them with known agents of pathogenic potential, there is little understanding of the genetic factors that elicit pathogenicity once the agents switch hosts.

Emerging zoonoses on the rise

It is clear that there is an increased recognition of the emergence of zoonotic infections. This increase is a result of both the increase in the rate of emerging zoonotic infections across the globe and our enhanced ability to detect and identify agents. New technologies have expanded the sensitivity and scope of our detection and diagnostic capability. However, a pathogen may still go undetected if it does not cause a significant disease outbreak. The causative agent of Hendra virus (HeV) disease in Australia, for example, may never have been identified had it not been for the scale and temporal cluster of the primary outbreak in 1994. Twenty horses and two humans were affected in two weeks, prompting lead authorities and scientists to carry out an in-depth investigation (7). Hendra virus, its close relative Nipah virus (NiV) (8) and many other emerging zoonotic viruses are highly pathogenic, but their transmissibility in humans and non-reservoir species is low compared to many agents resident and circulating in the human population. It may be that many unknown agents emerge from their wildlife reservoir – causing a certain amount of disease or death in other animals, including humans – but do not become established in their new host species and, thus, go unrecognised. Had HeV not been mechanically transmitted between such an unusually high number of horses and humans during that first outbreak, the virus may well have remained one of those unrecognised pathogens, and the infection may still have been unknown today.

Interspecies transmission of zoonotic agents from their natural reservoir host is still an unusual event and for most zoonoses human-to-human transmission is rare. However, increased spillover events will increase the chances of the emergence of an adapted virus that will be highly transmissible.

One Health in the context of zoonoses

The One Health Initiative (www.onehealthinitiative.com) defines One Health as 'the collaborative efforts of multiple disciplines working locally, nationally and globally to attain optimal health for people, animals, plants and our environment'. In the context of emerging zoonoses from wildlife, the disciplines that must work together are those of human and veterinary medicine. Emerging transboundary zoonoses require improved collaboration between these sectors to develop control strategies and implement surveillance and response activities at the animal–human interface. But, just as importantly, to establish control strategies we must also consider the interactions of humans and animals with ecosystems and the environment.

Drivers for the emergence of zoonotic diseases

Many factors lead to the emergence of zoonotic diseases. The environments associated with pathogens and their reservoir hosts are constantly changing and the rate of change is increasing. The drivers of change include the modernisation of farming practices, particularly in the developing world, habitat destruction, human encroachment and climate change (3, 9, 10). It is critical to evaluate and understand the impacts of these changes on the interactions between pathogens and their hosts and between the host and other species, including other wildlife, livestock and humans. These interactions are at the core of disease emergence, understanding these drivers and impacts will allow the development of mitigation strategies and enable an effective and timely response.

Agricultural drivers are significant and include major changes such as new agricultural practices, modernisation and intensification of farming systems, and habitat clearing for cropping and grazing. These changes have a number of effects, including driving diverse wildlife species together and pushing wildlife and livestock into overlapping environments, thus facilitating the transfer of novel agents into naive and susceptible species. Bushmeat (obtained from either hunting or farming wildlife species) is a significant traditional and growing food source in many cultures. Increasing trade in bushmeat can heighten the risk of transmission if live animals are transported to centralised markets where diverse species are forced into close contact. It is believed the initial transmission of the SARS coronavirus from a currently unidentified bat species to the amplifying hosts, including the civet cat, occurred due to such farming and trading activities (11, 12).

Climate and habitat changes have a significant effect on vector distribution, introducing formerly geographically restricted pathogens into naive populations of potentially susceptible animals and humans. The geographical ranges of zoonotic pathogens such as West Nile virus (WNV), chikungunya virus (CHIKV) and dengue virus are expanding, with the movement of vectors into newly established habitats. This causes the mixing of previously isolated vectors and introduces the agents to new potential vectors (13).

It should be emphasised that the emergence of a zoonotic disease is a multifactorial event; it may involve changes in, among others, human behaviour, farming and trading practices, vector distribution and the genetics of microbes. It is equally important to recognise that different drivers play distinct roles in the emergence of different viruses, which can be the case even for viruses from the same family (14).

Emerging zoonotic viruses of bat origin

Bats in the order Chiroptera are the second most species-rich mammalian order, with over 1,200 species spread across almost every part of the world (15). Since the discovery of bats in Australia as the natural reservoir of HeV, there has been a significant surge of research interest in bats as the reservoir of other important known and unknown zoonotic viruses. Publications in the area of bats and viruses have more than doubled in the last decade and there is at least one new publication per week on bat viruses in the literature. In many respects, bats represent an ideal reservoir for pathogens. Their flight ability allows them to disseminate and acquire pathogens over a wide geographical range; they live in large colonies or roosts (sometimes in the millions); and they enjoy remarkable longevity for their body size (16, 17, 18).

The number and diversity of viruses identified in bats is extraordinary and is the subject of many recent reviews (14, 16, 19). Here, the authors will provide a brief review of the most significant bat zoonotic viruses which have had a major impact on public health in different parts of the world over the past two decades.

Paramyxoviruses

Hendra virus

Although the virus appears to have been circulating in Australian flying foxes for a long time, the first detection of HeV emergence was in 1994. In two independent spillover events, this previously unknown paramyxovirus claimed the lives of 15 horses and two humans who had close contact with infected horses (20). Over the last few years, the incidence of HeV spillover events in Australia has drastically increased, peaking in 2011 with 18 independent outbreaks in horses in Queensland and New South Wales (21). In total, 89 horses have died of HeV infection from 49 independent spillovers. Out of seven human infections, four were fatal. All human infections can be traced back to close contact with infected horses and there is no evidence of human-to-human infection so far (20, 21).

Nipah virus

In 1998, another related paramyxovirus emerged in Malaysia. Named Nipah virus, this highly infectious virus was first detected in humans and commercially farmed pigs exhibiting respiratory and neurological disease (8, 22). Between September 1998 and April 1999 NiV caused the deaths of 105 humans and the culling of over 1 million pigs in Malaysia and Singapore. A slightly different NiV emerged in Bangladesh and India in 2001 and continues to cause regular outbreaks of fatal encephalitis in humans, with evidence of direct bat-to-human and human-to-human transmission and mortality of between 70% and 100% (21, 23).

Coronaviruses

Severe acute respiratory syndrome virus

Severe acute respiratory syndrome emerged in late 2002 and represents one of the most high-profile examples of infectious disease emergence. The global epidemic caused more than 8,000 confirmed infections and ultimately resulted in the deaths of approximately 800 people. Although palm civets were shown to be infected with SARS virus in live animal markets and restaurants in the Guangdong province in southern China, extensive epidemiological and surveillance studies demonstrated that civets were probably an amplifying and/or adaptation host and that the true reservoir of the SARS and SARS-like coronaviruses was bats of the genus *Rhinolophus* (5, 24).

Middle East respiratory syndrome virus

Recently, another coronavirus responsible for an acute respiratory disease (which has been named Middle East respiratory syndrome, MERS) has emerged (6). To date, more than 160 cases of human infection by the MERS coronavirus (CoV) have been reported in the Middle East, Europe and Africa. The fatality rate is between 40% and 50%. Genome sequencing has demonstrated that this virus is most closely related to coronaviruses in bats in different parts of the world, including bats in Asia and South Africa, indicating that bats are likely natural hosts of MERS or MERS-like viruses and that the emergence of similar viruses in other parts of the world is a significant possibility. This hypothesis was further supported when a small polymerase chain reaction (PCR) fragment with a sequence which was identical to that of a human MERS-CoV isolate was detected in the Egyptian tomb bat (*Taphozous perforates*) in Saudi Arabia (25). The route of introduction into the human population remains unknown. A serological study detected neutralising antibodies in camels from the Middle East and Spain (26). In November 2013, a 43-year-old male patient from Saudi Arabia was confirmed as having MERS infection. He had no travel history before disease onset, but had significant contact with animals. Interestingly, camels owned by the patient were symptomatic (fever and

rhinorrhoea) and tested positive for MERS-CoV by PCR (27). The exact role of camels (or other animals) in MERS-CoV transmission to humans is yet to be established.

Filoviruses

Ebola and Marburg viruses are among the most deadly viruses known to humankind and Ebola has caused massive die-offs of great apes in Central Africa. The transmission of filoviruses to humans is believed to occur mainly through 'bushmeat' activities, i.e. the capture and slaughtering of wild animals, including non-human primates (28). After decades of research into the potential reservoir host of filoviruses, recent data indicated that bats could be the potential natural hosts of Ebola and Marburg viruses in Africa (4, 29, 30). Filovirus RNA has been identified in a number of fruit bat species from Gabon and the Democratic Republic of Congo. It has also been shown that the incidence of Marburg haemorrhagic fever in mine workers in southern Uganda could be attributed to possible transmission from infected bats (*Rousettus aegyptiacus*) that had colonised the mine. Genetic analysis demonstrated that the Marburg virus isolated from the infected mine workers was highly similar to those circulating in the *R. aegyptiacus* population (30).

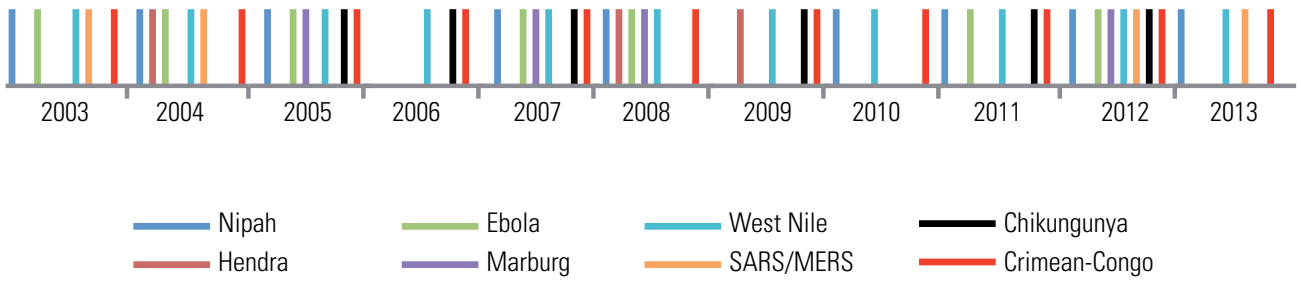
Ebola Reston virus was first identified in the United States of America (USA) in macaques which were imported from the Philippines. This virus has recently emerged in the pig population in the Philippines, posing a significant potential threat to public health and the livestock industry in the region (31). The discovery of Ebola Reston was made during a disease outbreak in pig farms in the Philippines, but further investigation revealed that at least six people were infected by Ebola Reston, as indicated by the presence of virus-specific antibodies in their serum samples (31). Since the diseased pigs were also co-infected with porcine circovirus 2, experimental inoculation of Ebola Reston in pigs was conducted to assess its pathogenic potential. It was shown that Ebola Reston challenge resulted in asymptomatic infection in pigs. But virus shedding was observed in infected pigs, demonstrating a potential risk for farm and abattoir workers (32). Detection of Ebola-Reston-specific antibodies in *R. amplexicudatus* bats suggests that bats may also be the natural host of Ebola Reston virus (33).

Other bat-borne viruses

In addition to those 'high-profile' bat zoonotic viruses discussed above, there have been a large number of previously unknown viruses discovered in the last two decades. These include viruses of known zoonotic transmission, such as the Menangle virus in Australia and the related Tioman and Melaka viruses in Malaysia, and many other related bat reoviruses (34, 35). Bat viruses related to known human pathogens have also been detected in large numbers, including bat lyssaviruses, parainfluenza viruses, hantaviruses, hepaciviruses and pegiviruses (36, 37). In addition, a large number of other paramyxoviruses, coronaviruses, astroviruses, adenoviruses and herpesviruses have been reported (38, 39, 40). The public health threat of these viruses is unknown, but it would be prudent to place these viruses under a close watch for potential spillover.

Emerging zoonotic viruses from other sources

It should be emphasised that, while bat viruses represent one of the most important sources of recent emergence, there are many other important zoonotic viruses with a significant impact on public health that have emerged or re-emerged. As shown in Figure 1, the frequency of major zoonotic virus outbreaks in the last decade is very high. Here, the authors provide a brief review of three examples of emerging zoonotic viruses of non-bat origin.



MERS: Middle East respiratory syndrome
SARS: severe acute respiratory syndrome

Fig. 1

Schematic summary of zoonotic viral disease outbreaks in the last decade

The colour bars above the line indicate the different disease events whereas the small bars below the line define the boundary of each calendar year

West Nile virus

West Nile virus is a member of the family *Flaviviridae* (41). It is a neurotropic flavivirus that is endemic in many parts of the world. As an arbovirus, WNV is transmitted by mosquitoes between birds and mammals. More than 100 different mammalian species, including many species of bats, have been shown to be susceptible to WNV infection (42), further increasing the risk of emergence via the close proximity of animal and human populations.

First isolated from a febrile patient in Uganda in 1937, it was introduced into North America in 1999, resulting in a large outbreak and rapid spread from the East Coast to the West Coast in a very short period. Although most (~80%) human infections are subclinical, symptomatic infections range from a self-limiting fever to severe neurological disease, long-term sequelae and death (41). The year 2012 saw a new wave of WNV outbreaks in the USA, with the second-highest number of WNV cases on record (43). High numbers of WNV cases were also reported in Europe in the same year, with 224 cases in the European Union and 538 additional cases in neighbouring countries (43). Epidemiologists suspect that a combination of the presence of wild birds, increased mosquito populations and favourable weather conditions in the USA and Europe are the key drivers for these outbreaks.

The Kunjun virus in Australia is a strain of WNV (WNV_{KUN}) (44). In 2011, a total of 982 cases of arboviral disease were reported in horses across Australia between January and June, mainly in the south-east of the country. It was the largest epidemic of equine arboviral disease in the history of Australia. The three major mosquito-borne viruses, Murray Valley encephalitis virus, WNV_{KUN} and Ross River virus, were involved in this epidemic (45). Two interesting observations were made after the 2011 epidemic. First, until 2011 these three viruses were rarely associated with diseases in horses. Second, despite the large number of equine cases, very few human WNV_{KUN} cases were reported in areas of intense viral activity. It was suggested that the two likely drivers for this unusual epidemic were the unusual weather pattern prior to the epidemic and the emergence of a new variant of WNV_{KUN} (46).

Chikungunya virus

Chikungunya virus was first isolated from a febrile patient in Tanzania in 1952. It is a member of the genus *Alphavirus*, family *Togaviridae*. It is an enzootic virus found in tropical and subtropical regions of Africa, in Indian Ocean Islands and in some parts of Asia (47). In Africa, the virus is maintained between non-human primates, small mammals (such as bats) and *Aedes* mosquitoes. Serological and virus isolation studies confirm that non-human primates are the host in CHIKV transmission and *Aedes* mosquitos are the main vectors.

Before 2000, it was rare to have large outbreaks of CHIKV. Since 2000, large CHIKV outbreaks have become more frequent. There is emerging genetic evidence to suggest that the virus has acquired multiple mechanisms for evolutionary adaptation to the vector. After several decades of 'hiding', the re-emergence of CHIKV was dramatic: in the Democratic Republic of Congo in 2000, Indonesia between 2001 and 2003, Kenya in 2004, the Comoros Islands from 2005 to 2007, and India from 2006. The virus was detected for the first time in the Maldives in 2006 and in Singapore in 2008 (47).

To a large degree, CHIKV infections have been limited to endemic areas of Africa and South-East Asia and to travellers returning to Europe, Australia and the USA from these areas. However, there was a report of local CHIKV transmission in northern Italy in 2007, resulting in approximately 250 locally acquired infections (48). With the increasing impact of climate change on mosquito distribution and evolution, CHIKV will remain an important zoonotic virus to be monitored by the international community for further spread and future outbreaks.

Crimean-Congo haemorrhagic fever virus

Crimean-Congo haemorrhagic fever virus (CCHFV) is a member of the genus *Nairovirus,* family *Bunyaviridae*. Ticks of the genus *Hyalomma* are considered to be both the main vector and the natural reservoir (49). These ticks are present on the ground and can infest a number of small and large mammals. Most infected animals can carry the virus without showing symptoms, providing a source of virus in their blood for further transmission to other animals and/or humans. Although tick bites are the main route of transmission to humans, direct contact with the body fluids, tissue or blood of infected animals can also lead to human infections.

Since its first recognition in 1944, human CCHFV infections have been documented in over 30 countries in Asia, the Middle East, South-Eastern Europe and Africa. Although most infections with CCHFV lead to a mild and non-specific febrile illness, some patients develop severe haemorrhagic disease, as suggested by its name. The fatality rate of CCHFV infection in humans can vary from 5% to 30% depending on the virus strain, the location and the public health infrastructure associated with outbreaks.

Climate change could be the risk factor that has the greatest potential to cause an expansion in the geographical distribution of CCHFV. *Hyalomma* ticks prefer warm summers and mild winters. Concerns have been raised that the trend towards warmer weather in Central and Northern Europe could allow CCHFV to spread outside its current range. This could be achieved through different mechanisms, including the direct introduction of infected

Hyalomma ticks by migratory birds or by international trade in livestock. Another route of introduction could be the switch of CCHFV to ticks other than its current vectors, such as the various ixodid ticks which have already played a role in transmitting tick-borne encephalitis in Central Europe and Russia (50).

Responses to Hendra virus outbreaks: a One Health success story

As discussed above, the emergence of HeV in Australia in 1994 was a major milestone in our efforts to improve our understanding of, and response to, emerging zoonotic viruses of bat origin. Tremendous progress has been made during the last two decades, from the rapid identification of the agent, proof of the causality of the agent and discovery of its natural reservoir host to the development of novel diagnostics, therapeutics and a recombinant subunit vaccine. Many of these achievements were made possible by applying the One Health strategy, as discussed below.

Outbreak investigation

On 22 September 1994, health authorities in Queensland, Australia, were notified of a mysterious outbreak of disease in horses in the Brisbane suburb of Hendra. Eleven horses had died and the horse trainer was extremely sick from what was suspected to be the same cause (51). This triggered a nationwide emergency response to identify the source of the outbreak. A taskforce was formed with participants from state public health and animal health agencies, as well as the Commonwealth Scientific and Industrial Research Organisation (CSIRO) Australian Animal Health Laboratory, which was commissioned to respond to exotic and emergent disease outbreaks.

The One Health team (consisting of virologists, diagnosticians and public and animal health experts) worked effectively and cooperatively, sharing epidemiological and laboratory findings. This led to the rapid identification of the agent responsible for this explosive outbreak (initially called equine morbillivirus, later renamed Hendra virus). By the fourth day of the outbreak investigation, suspicions about a viral pathogen were confirmed when the CSIRO team isolated a virus from tissues of diseased horses (7). By the seventh day, an antibody test had been developed for monitoring infection in both humans and animals in the vicinity of the outbreak; within two weeks it was confirmed that the horse trainer was infected with the same virus and a virus challenge experiment was completed in horses, which proved that this novel viral agent was responsible for the death of the horses, thus fulfilling Koch's postulates (7, 52).

The speed with which this detective story unfolded was unprecedented and the efforts of the research team were widely praised. 'Excellent' and 'absolutely superb' were the words used to describe their work by Frederick Murphy, a world leader in emerging viruses, then at the University of California, Davis (53). The success was largely due to the seamless collaboration between the public health and animal health agencies at both the state and federal level.

Tracing the origin of Hendra virus

The collaboration of the One Health team led to another major discovery less than two years after the outbreak, i.e. that bats were the natural host of HeV. To pursue the theory that HeV originated from a wildlife source, the team led by the Animal Research Institute in Queensland tested 5,264 sera from 46 species, but all were negative. The retrospective confirmation of another HeV case in a horse in Mackay, 800 km north of Brisbane, prompted the team to focus on the following criteria:

– the species should be present in both locations

– it should be capable of migrating between these two locations

– there is opportunity for contact with horses.

Birds and flying foxes came into focus for further investigation. In the first testing, 9% of 224 bat samples had neutralising antibodies to HeV, suggesting that flying foxes could be the natural host of HeV. This was later confirmed by direct isolation of HeV from various bat tissues (54).

At the same time, the public health team in Queensland tested human sera for HeV-specific antibodies. Sera from 60 people from the outbreak areas were all negative (51). A further 128 bat carers were tested and none of them had HeV-specific antibodies (55). Similarly, testing of more than 2,000 horse sera revealed no pre-existing antibodies in the horse population (56). Taken together, these studies support the hypothesis that bats are the likely natural reservoir host and that there is no persistent circulation of the virus in either human or horse populations. The data also indicated that direct bat-to-human transmission is a very rare if not impossible event, since some of the bat carers in this area have had almost daily contact with bats for up to 36 years and have never become infected (55).

Breaking the transmission chain by using a One Health vaccine

Finally, the One Health approach was vividly demonstrated in the strategic development of countermeasures to prevent HeV infection in humans. Three different scenarios exist for human infection by henipaviruses (Fig. 2). For HeV, human infection has only been documented from exposure to sick

horses. For NiV-Malaysia, the source of human infection was pigs. NiV-Bangladesh is the only henipavirus which has proven bat-to-human transmission (23, 57).

In the context of human HeV prevention in Australia, there have been many ideas proposed, from culling all the bats to vaccinating bats or humans. These proposals are either impractical or very expensive. So a two-pronged One Health approach was developed, comprising an equine vaccine to break the only known transmission route between bats and humans and a therapeutic human monoclonal antibody for post-exposure treatment (Fig. 2). Animal challenge model studies indicated that a subunit vaccine based on the recombinant HeV surface glycoprotein was efficacious in protecting cats and ferrets from lethal virus challenge (58). Further testing in horses indicated that the same recombinant protein formulated with a proprietary equine adjuvant was able to provide sterile immunity (D. Middleton and J. Pallister, personal communications). This vaccine has been licensed for field use by a commercial partner under the trade name Equivac®HeV (59). As far as the authors are aware, this is the first vaccine licensed for use against any Biosafety Level-4 agent. This is an excellent example of what a One Health approach can achieve in the fight against emerging zoonotic disease.

One Health approach to other emerging zoonotic diseases

With the increasing recognition of wildlife as a major source of emerging zoonotic diseases, more and more attention is being directed to the One Health approach for disease investigation and prevention. Here are some further examples of recent successes demonstrating the power of the One Health strategy.

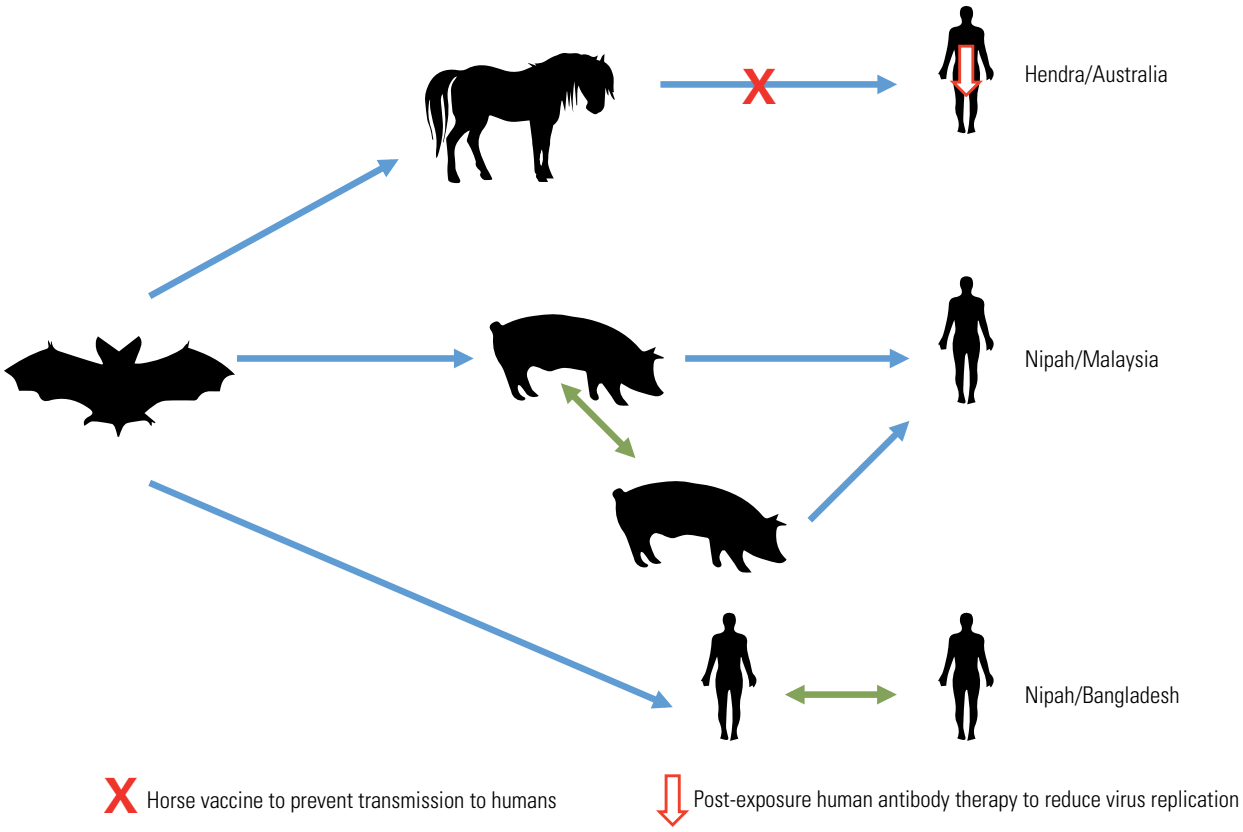


Fig. 2
One Health strategy for the control and prevention of Hendra virus outbreaks in Australia: a comparative summary of the main transmission routes for the three known pathogenic henipaviruses
Blue arrows indicate transmission between different species of animals while the green two-headed arrows indicate confirmed transmission between different individuals of the same species

Epidemiological investigation of severe acute respiratory syndrome and Middle East respiratory syndrome

After the discovery of SARS-CoV it took less than two years to identify civets and bats as the transmitting host and natural host, respectively, of the novel coronaviruses, which had never been detected prior to the 2002/2003 outbreaks. By any standard, this is a great achievement and outcome. It was made possible by the close collaboration of scientists in public health, animal health and wildlife ecology. For example, the identification of civets as the main transmitting host was achieved by a group with extensive previous experience in investigating avian influenza virus at the human–animal interface (60). Similarly, the identification of horseshoe bats as the natural host of SARS-like coronaviruses was made possible by two independent groups of virologists, zoologists, veterinarians, ecologists and epidemiologists, each of which had extensive experience of tracing the origin of zoonotic pathogens (5, 61). These studies provided the foundation for effective prevention measures, such as the banning of live civet trading and mixing of bats and other mammals in live animal markets; this seems to have played a role in preventing the re-emergence of SARS.

The emergence of MERS presented a new challenge for One Health expertise. Although the exact origin and transmission route of this newly emergent virus remain unknown, recent studies have provided encouraging clues to unravel its mystery. A recent study conducted by scientists from both public health and animal health institutes demonstrated the presence of antibodies to MERS or related virus(es) in camels (26). The role of camels in MERS emergence is yet to be determined since this study failed to detect any animals shedding the virus.

Control of Nipah virus infection in Malaysia and Bangladesh

One Health measures have also contributed to the prevention and/or reduction of Nipah virus outbreaks. In Malaysia, locating pig farms in areas without fruit trees (to reduce the direct contact of pigs with bats or bat excretions) was believed to be a major factor in the prevention of any subsequent outbreaks after the emergence of Nipah virus in 1998 (62). In Bangladesh, the prevention measures involved a combination of multidisciplinary approaches. Social scientists played an important role in educating people in high-risk areas about the importance of avoiding direct contact with bats or bat secretions. Covering date palm juice collecting pots with bamboo mats (known as bamboo 'skirts') has proven to be another simple, yet effective, way to prevent Nipah virus transmission from bats to humans (63).

Association of a new tick bunyavirus with an emerging haemorrhagic fever

In June 2009 an outbreak of a mysterious infectious disease occurred in rural areas of Hubei Province, China, resulting in 17 cases of human infection, five of which were fatal (64). The principal clinical presentation was severe fever with thrombocytopenia. A multidisciplinary team involving rickettsiologists, virologists and public and animal health agencies was assembled under the auspices of the Chinese Center for Disease Control and Prevention (China CDC) to investigate the cause of this outbreak. Eventually, a novel bunyavirus, named severe fever with thrombocytopenia syndrome virus (SFTSV), was isolated from the blood of a patient (64). Reports of other patients infected with this virus have since been confirmed in at least 16 different provinces of East China (64). Importantly, this One Health team was able to rapidly trace the source of the virus to ticks (*Haemaphysalis longicornis* and *Boophilus microplus*) collected from domestic animals in outbreak areas, including cattle, goats and dogs. Furthermore, serosurveillance for SFTSV has confirmed the presence of the antibody to the agent in cattle, goats, dogs, pigs and, to a lesser degree, in chickens and rats (64). A small proportion of the animals studied (1.7% to 5.5%) also carried low levels of viral RNA, suggesting that these animals may act as amplifying hosts that infect the ticks that feed on them, thus enabling them to spread the virus to humans. The potential role of wildlife as reservoir or amplifying hosts is yet to be determined.

Interestingly, almost at the same time in June 2009, two men from two geographically distant farms in north-western Missouri, USA, were admitted to hospital with fever, fatigue, diarrhoea, thrombocytopenia and leucopoenia. Both had been bitten by ticks five to seven days before disease onset. Viruses were isolated from the leucocytes of both patients and were later identified by next-generation sequencing as two isolates of the same virus, a novel bunyavirus (named Heartland virus), which is most closely related to the Chinese SFTSV (65).

Since these disease events in China and the USA, human infection with SFTSV has also been reported in Japan, with four fatal cases (66), and in South Korea, where there have been eight deaths (67). Considering that these similar viruses and human infections have been detected in two well-separated continents, Asia and North America, it is tempting to hypothesise that similar bunyaviruses with zoonotic potential may also exist in tick populations in other continents.

Concluding remarks

In this review, the authors have presented the increasing trend of zoonotic virus emergence in the last few decades

and demonstrated the role that the One Health approach has played in almost every aspect of outbreak investigation, control and prevention. This is only the beginning of the One Health era. It is imperative that governments, health workers and scientists at every level and in every nation work together to further nurture and maximise One Health practices so that we can be more effective in our future fight against emerging and re-emerging zoonotic diseases.

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Les maladies zoonotiques virales émergentes

L.-F. Wang & G. Crameri

Résumé

Les zoonoses sont des maladies infectieuses qui se transmettent naturellement des vertébrés à l'homme et vice-versa. Toutes les catégories d'agents pathogènes sont représentées, y compris les bactéries, les parasites, les champignons, les virus et les prions. Bien que les zoonoses soient connues depuis des siècles, leur impact sur la santé publique s'est intensifié au cours des dernières décennies par l'effet conjugué du succès de la lutte contre la propagation des maladies infectieuses humaines grâce à la vaccination et au recours à des thérapies efficaces et de l'émergence de nouvelles maladies zoonotiques. Il est désormais bien établi que les activités de recherche, de prévention et de contrôle entreprises pour lutter contre les zoonoses émergentes sont plus efficaces lorsqu'elles sont conduites dans le cadre d'une démarche « Une seule santé » à l'interface homme–animal–écosystèmes. Les auteurs examinent les facteurs à l'origine de l'émergence de ces maladies, mettent en avant certaines maladies zoonotiques émergentes à fort impact apparues au cours des vingt dernières années et présentent des exemples d'approches innovantes « Une seule santé » utilisées pour la recherche, la prévention et la lutte contre ces maladies. Bien que cet examen porte principalement sur les maladies zoonotiques d'origine virale, les auteurs estiment que les éléments de discussion présentés s'appliquent également aux zoonoses émergentes causées par d'autres types d'agents pathogènes.

Mots-clés

Coronavirus responsable du syndrome respiratoire aigu sévère – Coronavirus responsable du syndrome respiratoire du Moyen-Orient – Maladie infectieuse émergente – Une seule santé – Vaccin – Virus Ebola – Virus Hendra – Virus Nipah – Virus West Nile – Zoonose.

Enfermedades zoonóticas emergentes de origen vírico

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Resumen

Las enfermedades zoonóticas son enfermedades infecciosas que se transmiten de forma natural de animales vertebrados al ser humano, y viceversa. Tienen su origen en agentes patógenos de todo tipo: bacterias, parásitos, hongos, virus o priones. Aunque hace muchos siglos que son conocidas, sus repercusiones en la salud pública han ido en aumento en los últimos decenios, debido al efecto combinado de los éxitos obtenidos contra la propagación de enfermedades infecciosas en el hombre (gracias a las vacunas y a tratamientos eficaces), por un lado, y de la aparición de nuevas enfermedades zoonóticas, por el otro. Cada vez está más claro que para resultar eficaz toda labor de investigación, prevención y control de una enfermedad zoonótica emergente debe abordarse aplicando los planteamientos de «Una sola salud» en la interfaz entre personas, animales y ecosistemas. Los autores pasan revista a los factores que alimentan la aparición de enfermedades zoonóticas emergentes, deteniéndose en algunas de las que más consecuencias han tenido en los últimos dos decenios y ofreciendo ejemplos de nuevos métodos en clave de «Una sola salud» para investigar, prevenir y controlar esas enfermedades. Aunque en este artículo se centran especialmente en las enfermedades zoonóticas emergentes de origen vírico, los autores entienden que las reflexiones aquí presentadas se aplican igualmente a enfermedades zoonóticas emergentes causadas por otros tipos de patógeno.

Palabras clave

Coronavirus del síndrome respiratorio agudo severo – Coronavirus del síndrome respiratorio de Oriente Medio – Enfermedad infecciosa emergente – Una sola salud – Vacuna – Virus Ebola – Virus Hendra – Virus Nipah – Virus West Nile – Zoonosis.

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