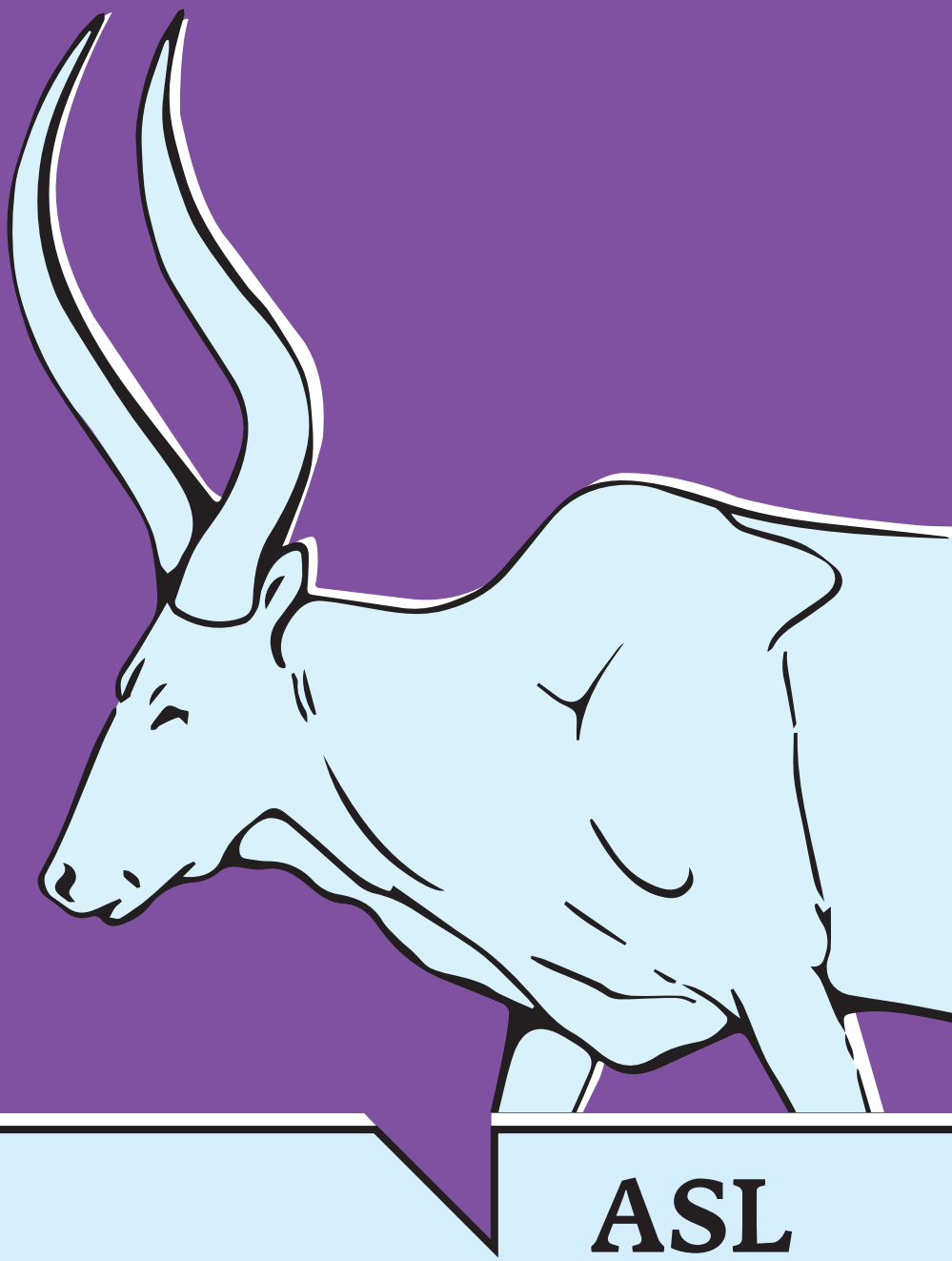
Food and Agriculture Organization of the United Nations

AFRICA SUSTAINABLE LIVESTOCK 2050

Livestock and viral emerging infectious zoonotic diseases



USAID FROM THE AMERICAN PEOPLE

Financial support provided by the United States Agency for International Development (USAID)

ASL 2050

Required citation:
Otte, J., Heilmann, M. & Pica-Ciamarra, U. 2022. *Livestock and viral emerging infectious diseases. Africa Sustainable Livestock, 2050*. Rome, FAO. https://doi.org/10.4060/cc2160en

Contents

Abstract

A majority of virus species capable of infecting humans are zoonotic and have wildlife and/or arthropod reservoirs. The current narrative on preventing the next pandemic thus stresses the role of wildlife in the emergence of human infectious diseases. The emphasis on wildlife, while warranted, appears to underappreciate the role livestock plays in the emergence and spread of virus diseases affecting humans. Although livestock are reservoir hosts for a minority of the zoonotic virus species, they may be susceptible to infection and thereby act as bridge-hosts. Given the frequency of livestock-wildlife and subsequent livestock-human interactions, indirect transmission of zoonotic viruses from wildlife to humans via livestock provides and important pathway for disease emergence. This paper examines extent to which mammalian livestock have been found to be susceptible to infection with zoonotic viruses and thereby have the potential to contribute to within and cross species virus propagation. Evidence of infection in mammalian genera representing the main livestock species could be found for close to half (46.1 percent) of the 267 zoonotic virus species in our dataset. A better understanding of multi-host virus sharing pathways is needed to support efforts to mitigate EIZD threats.

September 2022. This paper was drafted by Joachim Otte (FAO), Martin Heilmann (FAO) and Ugo Pica-Ciamarra (FAO).

Introduction

The on-going COVID-19 pandemic clearly illustrates the threat posed by emerging infectious diseases (EIDs), particularly those caused by highly transmissible viruses. In a seminal paper on "Global trends in emerging infectious diseases" covering the period from 1940 to 2004, Jones *et al.* (2008) estimated that 72 percent of zoonotic EIDs (EIZDs) originated in wildlife. Consequently, the current narrative on preventing the next pandemic (Daszak, 2020; Dobson *et al*., 2020; Kahn, 202; UNEP & ILRI, 2020; US Senate, 2021) stresses the role of wildlife in the emergence of human infectious diseases with substantial amounts of resources being devoted to the identification of wildlife reservoirs and associated emergence hotspots.

The emphasis on wildlife, while warranted, appears to underappreciate the role livestock plays in the emergence and spread of diseases affecting humans. Livestock are a recognized source of a considerable share of human diseases of evolutionary and historical significance (Wolfe, Dunavan and Diamond, 2007). Viruses carried by domestic species are 1.8 times as likely to be zoonotic than those from wildlife (Wells *et al*., 2020). Nearly 40 percent of the EIZD events recorded by Jones *at al*. (2008) have been associated with food animals, the latter either acting as reservoir or amplifying hosts (Otte & Pica-Ciamarra, 2021). Livestock are associated with four of WHO's ten priority diseases requiring urgent R&D attention, namely CCHF, MERS, Nipah and RVF[1]. Humans occupationally exposed to livestock (and/or commercial poultry) are more likely to carry antibodies against zoonotic viruses than less/non-exposed controls (e.g. Giangaspero *et al*., 1988; Kayali *et al*., 2011; White *et al*., 2016).

To date, more than 200 virus species capable of infecting humans have been identified (e.g. Olival *et al*., 2017, Rosenberg *et al*., 2013, Zhang *et al*., 2020), a majority of which are zoonotic and have (known or unknown) wildlife and/or arthropod reservoirs. Although livestock are frequently not reservoir hosts for these virus species, they may be susceptible to infection and thereby act as bridge-hosts. Given livestock-wildlife and livestock-human interactions are probably more frequent than wildlife-human interactions, indirect transmission of zoonotic viruses from wildlife to humans via livestock (as for instance the case for MERS-CoV and Nipah virus) should be considered in EIZD risk assessments. The purpose of this paper is to provide an overview of the extent to which livestock have been found to be susceptible to infection with zoonotic viruses and thereby can potentially contribute to within and cross species virus propagation. The review focusses on the five major mammalian livestock groups, namely large ruminants (genera *Bos* and *Bubalus*), small ruminants (genera *Capra* and *Ovis*), camelids (genera *Camelus*, *Lama* and *Vicugna*), swine (genus *Sus*), and equines (genus *Equus*).

Methods

The most recent list of virus species affecting humans compiled by Otte, Heilmann and Pica-Ciamarra (submitted) contains 267 ICTV-recognized zoonotic species from 24 virus families. Peer-reviewed publications and the CDC catalogue of arboviruses[2] were searched for evidence of infection (natural and/or experimental exposure) with any of these virus species in mammals of the genera *Bos, Bubalus, Camelus, Capra, Equus, Lama, Ovis, Sus,* and *Vicugna*. Both, positive molecular (virus isolation, detection of viral R/DNA or antigen) as well as serologic findings were accepted as evidence for a species to have undergone infection and all domestic species within the affected genus were considered potential hosts for the particular virus species (e.g. all species of the genus *Bos* were considered as potential hosts of a virus species even if the evidence of infection was only available for *Bos taurus*). We base this assumption of host potential of all domestic species within a genus given infection detected in one species on the results of Johnson *et al*. (2020) that 81.3 percent (113/139) of zoonotic viruses were found to infect mammalian species from at least two genera (excl. humans), which suggests that host-specificity of zoonotic virus species is generally low.

[1] www.who.int/topics/zoonoses/en

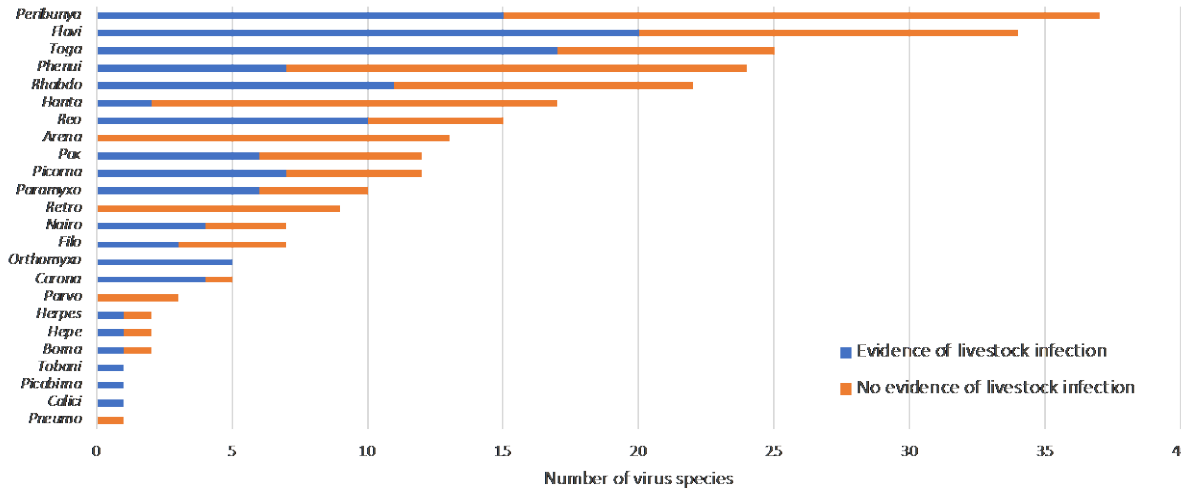
[2] wwwn.cdc.gov/arbocat

Results

Evidence of infection of mammals belonging to the nine genera representing the main livestock species could be found for nearly half (123/267, 46.1 percent) of the 267 zoonotic virus species in our dataset. All but five of the reported infections were of natural occurrence. The five experimental infections involved swine exposed to Hendra virus (Li, Embury-Hyatt and Weingartl, 2010), SARS-CoV (Weingartl *et al*., 2004), SARS-CoV-2 (Pickering *et al.* 2021), Tioman virus (Yaiw *et al*., 2008) and Zaire ebola virus (Kobinger *et al.*, 2011). Of the 123 zoonotic virus species found in mammalian livestock 115 (93 percent) are RNA viruses and 77 (63 percent) are transmitted by arthropod vectors.

The largest number of zoonotic virus species capable of infecting livestock belongs to the *Flavi-* (20), *Toga-* (17), *Peribunya-* (15), *Rhabdo-* (11) and *Reoviridae* (10) (Figure 1), the vast majority thereof being transmitted by arthropod vectors. A significant share of virus species from families responsible for major human health crises in the recent past are capable of infecting livestock: 4/5 zoonotic Corona virus species, 3/7 Filo virus species, 5/5 Orthomyxo virus species and 6/10 Paramyxo virus species. No reports of infection of mammalian livestock could be found for zoonotic virus species of the *Arena-, Parvo-, Pneumo- and Retroviridae*.

Figure 1. Number of zoonotic virus species with and without evidence of the ability to infect mammalian livestock by virus family

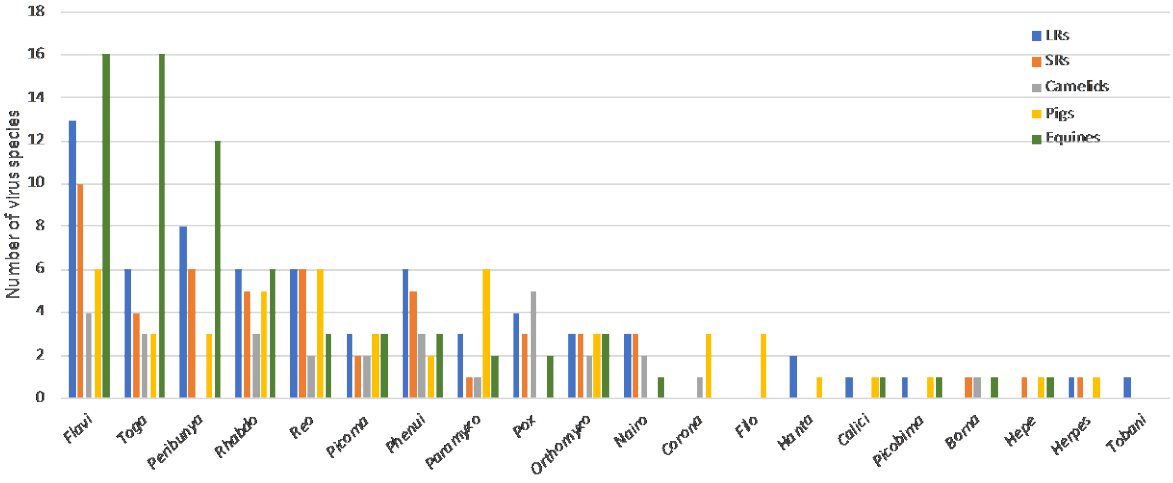


Source: authors' calculations.

Eight virus families contain zoonotic species with the ability to infect genera of any of the five livestock groups (large ruminants, small ruminants, camelids, swine, and equines) (Figure 2). Of virus families with 10 or more zoonotic species, no zoonotic species of the *Peribunyaviridae* has so far been detected in camelids, for zoonotic species of *Hantaviridae* evidence of infection has only been reported in cattle (Danes *et al*., 1992) and swine (Yang *et al*., 2004), and, as mentioned previously, no infection with any of the currently recognized 53 species of *Arenaviridae* (ICTV2020v.1 list[3]) has so far been reported in any of the assessed livestock genera. On the other hand, no zoonotic species of the *Arteriviridae*, *Asfarviridae* and *Circoviridae*, which comprise important livestock pathogens, has been recorded to date.

[3] https://talk.ictvonline.org/files/master-species-lists/m/msl/12314

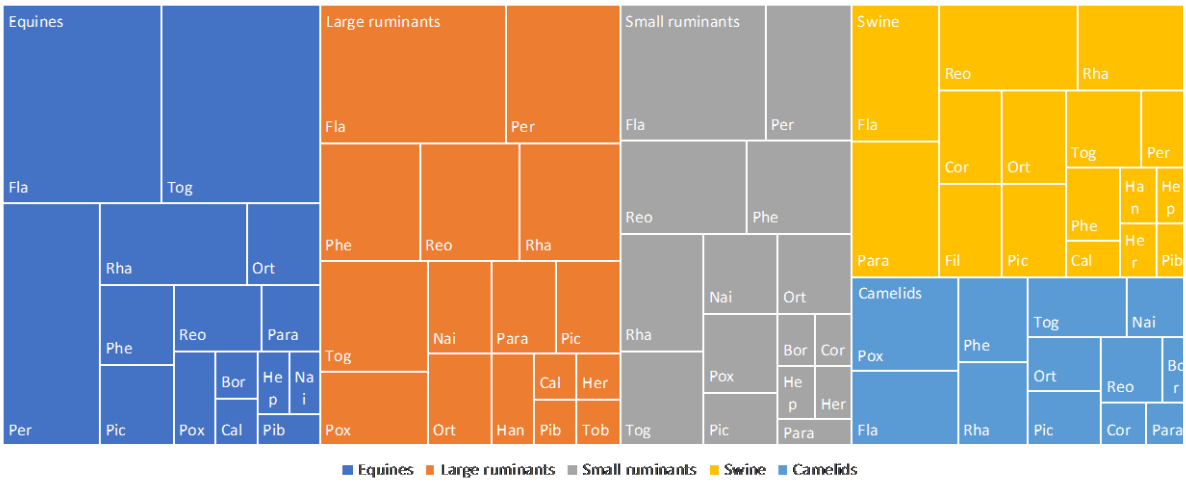
Figure 2. Number of zoonotic virus species capable of infecting livestock groups (large ruminants (LRs), small ruminants (SRs), camelids, swine and equines) by virus family



Source: authors' calculations

Within the five major mammalian livestock groups, equines are host to the largest number of zoonotic virus species (71) followed by large ruminants (67), small ruminants (51), swine (48) and camelids (29) (Figure 3). Combined, small and large ruminant livestock are susceptible to infection with a total of 81 zoonotic virus species. Flavi-, Toga- and Peribunyaviruses comprise the most common zoonotic virus species detected in equines (>50 percent of all zoonotic species). Togaviruses are less prominent in large and small ruminants with Flavi- and Peribunyaviruses contributing the largest number of zoonotic virus species. In swine, by contrast, species of the *Reo*, *Paramyxo*- and *Rhabdoviridae*, in addition to *Flaviviridae*, comprise close to half of the zoonotic virus species. In camelids, the *Poxviridae* contribute the largest number of zoonotic virus species.

Figure 3. Zoonotic virus species richness and diversity of viruses associated with major livestock host groups. Each rectangle represents livestock–virus family combination, with size corresponding to the number of zoonotic virus species.



Source: authors' calculations. Virus families are abbreviated as follows: Cal = Caliciviridae, Bor = Bornaviridae, Cor = Coronaviridae, Fil = Filoviridae, Fla = Flaviviridae, Han = Hantaviridae, Hep = Hepeviridae, Her = Herpesviridae, Nai = Nairoviridae, Ort = Orthomyxoviridae, Para = Paramyxoviridae, Per = Peribunyaviridae, Phe = Phenuiviridae, Pib = Picobirnaviridae, Pic = Picornaviridae, Pox = Poxviridae, Reo = Reoviridae, Rha = Rhabdoviridae, Tob = Tobaniviridae, and Tog = Togaviridae.

Seventeen zoonotic virus species are capable of infecting mammalian species from five or more of the genera included in this study. Equines exhibit the largest number and proportion of zoonotic virus species only recorded in equine livestock (23 percent, 32.4 percent) followed by pigs (12 percent, 25.0 percent) while the number and share of 'unique' virus species in ruminant livestock is considerably lower (9, 13.4 percent in large and 6, 11.8 percent in small ruminants) (Table 1). A large share of zoonotic virus species detected in camels (>75 percent) have also been found in large and small ruminants while the reverse shares are considerably lower (34.3 and 43.1 percent respectively).

Table 1. Number (percent) of zoonotic virus species reported to be able to infect large ruminants (LRs), small ruminants (SRs), camelids, pigs and equines and number (percent) found in pairs of livestock groups.

	LRs	SRs	Camelids	Swine	Equines
Total	67 (100)	51 (100)	29 (100)	48 (100)	71 (100)
Unique[1]	9 (13.4)	6 (11.8)	2 (6.9)	12 (25.0)	23 (32.4)
Pairwise occurrence					
LRs	--	37 (72.5)	23 (79.3)	33 (68.8)	36 (50.7)
SRs	37 (55.2)	--	22 (75.9)	17 (35.4)	29 (40.8)
Camelids	23 (34.3)	22 (43.1)	--	8 (16.7)	15 (21.1)
Swine	33 (49.3)	17 (33.3)	8 (27.6)	--	22 (31.0)
Equines	36 (53.7)	29 (56.9)	15 (51.7)	22 (45.8)	--

Source: Authors' calculations

[1] Evidence of infection only in specific livestock group

Discussion

Molecular techniques are regarded to be more specific in the identification of viruses in host species, while serological techniques, although regarded as less specific, are more sensitive as they can detect previous infection for some time even after virus elimination. Peer-reviewed publications of virus infection determined by serology involve review of the evidence that the serologic test has been optimized to detect the specified virus or a very close relative (Johnson *et al*., 2020). Given the limited systematic research efforts *vis-à-vis* the large potential number of zoonotic virus-livestock host associations (≈250 zoonotic virus species and >15 mammalian livestock species in the genera included) 'under-reporting' of virus-livestock host associations is more likely than reports of false positive associations. Because the purpose of this study was to estimate the potential of mammalian livestock species to serve as host for zoonotic virus species, false negatives are just as, if not more important. We therefore included all virus-livestock host associations reported in the literature, regardless of the method used to detect the virus.

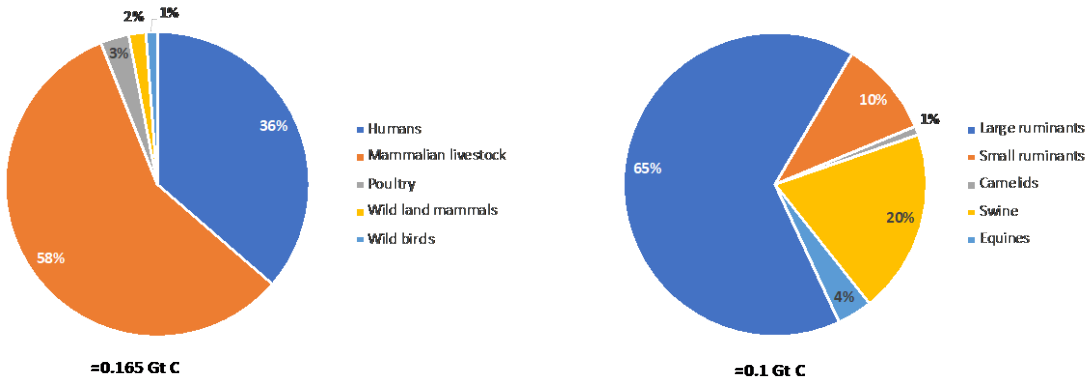
We acknowledge the potential for misclassification in cases determined by methods other than virus isolation. However, the main weakness of this and other studies of host-virus relationships is that specimens are usually collected opportunistically with no systematic surveys over the spectrum of domestic and wild species in a particular environment (Morand, McIntyre and Baylis, 2014). The relatively large asymmetries in the share of virus species common to pairs of livestock groups, e.g. that 72 percent of zoonotic virus species found in small ruminants have also been detected in large ruminants but that only 55 percent of those found in large ruminants have been found in small ruminants, and that, for instance, large ruminants share almost as many zoonotic virus species with equines as with small ruminants, suggests that search effort and/or exposure are uneven across the selected livestock groups. The virome of camelids, for example, has so far received much less attention than that of bovines or equines, which is likely one of the reasons for the comparatively small number of reported zoonotic virus species. The emergence of Middle East Respiratory Coronavirus (MERS-CoV) linked to dromedaries (*Camelus dromedaries*) in 2012 has boosted interest in the search of novel viruses in dromedaries and recent metagenomic studies of respiratory and fecal samples from camels

have revealed a large diversity of viruses (Woo *et al*., 2014; Li *et al*., 2017). The notion that sampling efforts impact the topography of currently known mammal-virus networks is supported by the much broader and deeper analysis of virus-host relationships between 1 785 virus species and 725 mammalian host species[4] by Wells *et al*. (2020).

In their study, Wells *et al.* (2020) found that wild mammalian host species were *c*. 4.2 times (odds ratio 4.9–5.5) more likely to share virus species with domestic animals (not limited to livestock but including dogs, cats and peri-domestic rodents) than with any other wild species and that any pair of domestic species was *c*. 70 times (odds ratio 49.4–102.5) more likely to share viruses than any pair of two wildlife species. They thus conclude that "*acknowledging the role of domestic species in addition to host and virus traits in patterns of virus sharing is necessary to improve our understanding of virus spread and spillover in times of global change*."

The importance of livestock in virus networks involving humans is clearly a result of the longstanding and close relationship between humans as livestock and the related ubiquity and abundance of livestock species *vis-à-vis* wild mammals. Bar-On, Phillips and Milo (2018) estimate that mammalian livestock and poultry constitute around 60 percent of the total biomass of terrestrial mammals and birds which is 20-fold their estimate for wild terrestrial mammals and birds (Figure 4).

Figure 4. Composition of global biomass (expressed in Gt C) of terrestrial mammals and birds (left) and of mammalian livestock (right)



Source: Bar-On, Phillips and Milo., 2018

Large and small ruminants represent around three quarters the global livestock biomass, have a standing population totaling more than 4 billion head, can be found on all continents except Antarctica, and have adapted to a wide range of climates and ecosystems. Similarly, equines, although far less abundant (approximately 120 million head), are used by humans across the globe in very diverse environments. The large number of zoonotic viruses shared between humans and their livestock is thus to a large extent an expression of common exposure to a wide range of virus species across time and space and to some extent possibly also due to the larger research effort directed at pathogens affecting livestock relative to wildlife. The sheer size of the human-livestock interface and the extensive movement of livestock - official cross-border livestock trade alone amounted to an annual average of 75 million head of live exports over the period 2011 to 2020 (FOSTAT) - warrants consideration of livestock in the study of virus-host networks involving humans even if livestock are neither reservoir nor particularly permissive hosts. Additionally, more research and collaboration across natural and social science are required to better understand the cultural aspects of human-livestock relationships that are naturally closer than those with wild animals. While evidence suggest that occupations such as veterinarians, culling personnel, slaughterhouse workers and farmers are at

[4] The Mammal Diversity Database lists 6 399 currently living mammalian species (Burgin *et al.*, 2018).

higher risk, little is known about the intensity and type of contact patterns between livestock and humans that can result in disease transmission (Klous *et al.*, 2016). Such information however is required to strengthen occupational health and biosecurity especially in livestock systems with closer contact between humans and animals (e.g. extensive, backyard, urban, etc.). Box 1 and Figure 5 illustrate the above using CCHF as an example.

Box 1. The role of livestock in the maintenance and spread of Crimean-Congo hemorrhagic fever virus

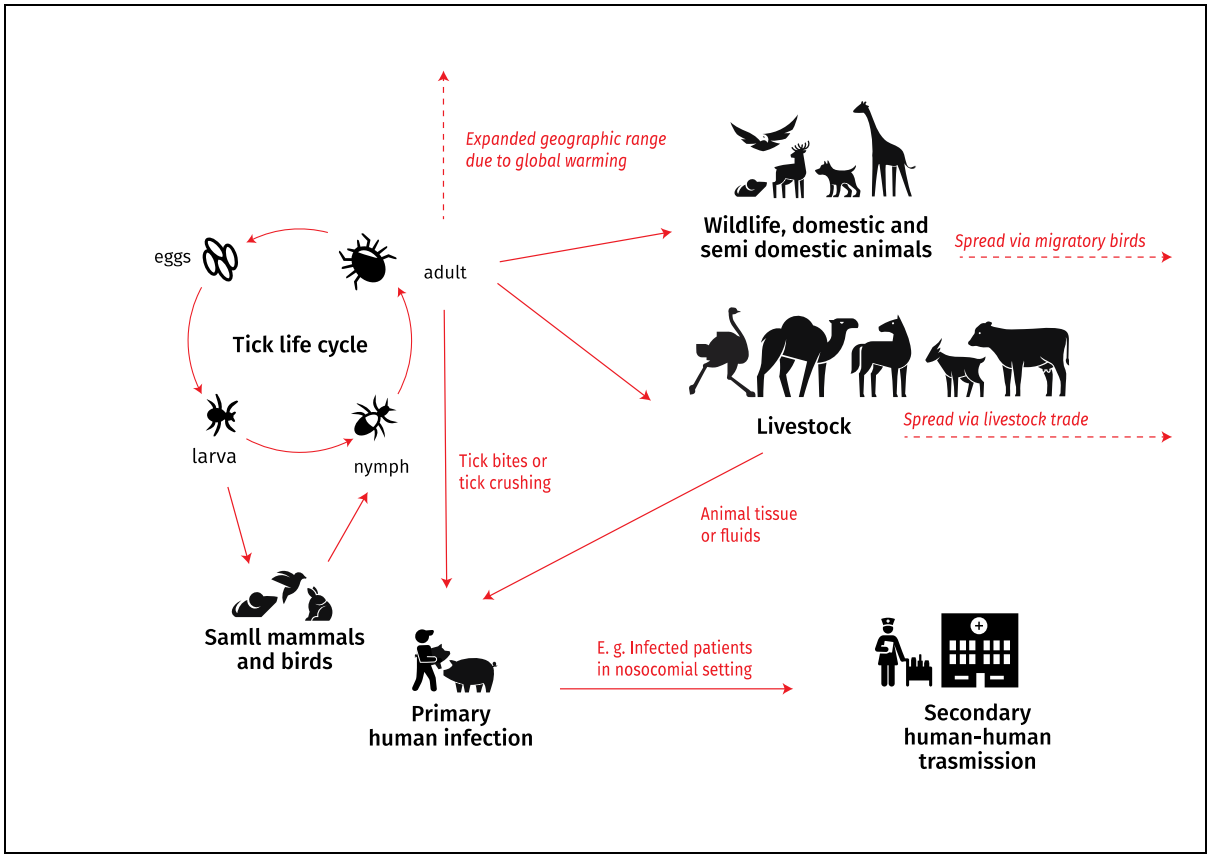
This box illustrates the complex role of livestock in the emergence of viral diseases affecting humans using Crimean-Congo hemorrhagic fever virus (CCHFV) as an example. CCHFV is an RNA virus of the Nairoviridae family listed in Figure 1. It is endemic in Africa, the Middle East, and parts of Asia and Europe. The virus circulates in a tick–vertebrate–tick cycle where vertebrate hosts can include wildlife as well as livestock species. A particular feature of the infection is that it causes viremia without any clinical signs in animals whereas humans suffer from severe and life-threatening disease with a case fatality rate of 10–40 percent. This feature of asymptomatic animals has three important implications in regard to livestock: (i) infected livestock may contribute to maintenance and spread of the virus, (ii) livestock producers may be unaware of the virus affecting their livestock, and (iii) infected livestock may become a 'silent' source of infection to humans. In fact, studies have shown that slaughterhouse workers, butchers, veterinarians, health-care workers and livestock handlers are at high-risk of infection(1). The virus can be transmitted to humans either through tick bites, crushing of engorged ticks, or direct contact with infected livestock and livestock organs and tissues during slaughter(2). Human-to-human transmission is less frequent but can occur in nosocomial contexts through contact with skin, mucus membranes and body fluids of infected patients or contaminated tissues during surgery and medical equipment(3).

The important role of livestock in CCHFV ecology is reflected in the high levels of reported species-specific CCHFV antibody prevalence in affected regions (between 20 and 30 percent in ruminant livestock)(4). An important factor is the ecologic link between livestock, the multi-host tick vectors and peri-domestic animals (e.g. mice or rats), which are susceptible to CCHFV. Given the wide distribution of livestock (also in terms of biomass as highlighted in Fig. 4), they provide not only a susceptible host for the virus but also a feeding source to ticks. International trade of livestock has been identified as a potential route of dissemination of CCHFV(5). The impact of climate trends on tick abundance, which has been linked to CCHF outbreaks(6), is likely to also enhance its geographic distribution.

The above illustrates some of the livestock related aspects that contribute to CCHF being classified as a priority disease requiring more research and development (WHO). Many of the interactions between human, wildlife, livestock and environmental factors remain to be investigated applying a holistic One Health approach(7).

Sources: (1) Mostafavi *et al*., 2017; (2) Ergönül, 2006; (3) Nasirian, 2020; (4) Spengler, Bergeron and Rollin, 2016; (5) Heyman *et al*., (6) Estrada-Peña, Aillon and De La Fuente, 2012; (7) Sorvillo *et al.,* 2020.

Figure 5. Transmission and dispersal of Crimean-Congo hemorrhagic fever virus



Clearly, non-livestock mammalian species, more than half of which are either rodents (40 percent) or bats (23 percent) (Williams *et al.*, 2021), maintain the bulk of potentially zoonotic virus species, but the ecology of specific viruses within their ecosystems mostly remains undetermined. The majority of zoonotic virus species, which are predominantly RNA viruses (Zhang *et al*., 2020) exhibits a fairly wide wildlife host range (Johnson *et al.,* 2020; Pandit *et al.*, 2018). Furthermore, RNA viruses generally have high rates of mutation (Drake & Holland 1999) resulting in populations of heterogenous virions ('quasispecies'), which enhances the potential to adapt to novel host species. A notable example of this process is provided by the recently emerged SARS-CoV-2, for which free-ranging white-tailed deer (*Odocoileus virginianus*) are capable of sustaining transmission in nature (Hale *et al*., 2021).

In conclusion, EIZD risk assessments should systematically examine the potential role of livestock as reservoir, amplifying or dead-end hosts and their position in wildlife-human interfaces. For zoonotic viruses transmitted by arthropods this would include assessment of the ability to produce a level of viremia that is likely to propagate transmission and feeding habits of the associated arthropod vectors. A better understanding of multi-host virus sharing pathways would bolster efforts to mitigate EIZD threats.

References

Bar-On Y.M., Philipps R., Milo R. 2018. The biomass distribution on Earth. *PNAS* 115(29): 6502–6511. doi:10.1073/pnas.1711842115

Burgin C.J., Colella J.P., Kahn P.L., Upham N.S. 2018. How many species of mammals are there? *J Mammalogy* 99(1): 1–14. doi:10.1093/jmammal/gyx147

Danes L., Pejcoch M., Bukovjan K., Veleba J., Halackova M. 1992. [Antibodies against hantaviruses in game and domestic oxen in the Czech Republic]. *Cesk Epidemiol Mikrobiol Imunol* 41: 15–18.

Daszak P. 2020. We are entering an era of pandemics – it will end only when we protect the rainforest. Opinion, The Guardian, 28 July 2020

Dobson A.P., Stuart L.P., Lee H., Kaufman L., Ahumada J.A., Ando A.W., Bernstein A. *et al*. 2020. Ecology and economics of pandemic prevention. *Science* 369 (6502): 379–381. doi: 10.1126/science.abc3189

Drake J.W., Holland J.J. 1999. Mutation rates among RNA viruses. 1999. *PNAS* 94(24): 13910–13913.

Ergönül O. 2006. Crimean-Congo haemorrhagic fever. *The Lancet. Infectious diseases* 6(4): 203–214. doi: 10.1016/S1473-3099(06)70435-2

Estrada-Peña A., Ayllon N., De La Fuente J. 2012. Impact of Climate Trends on Tick-Borne Pathogen Transmission. *Frontiers in Physiology* 3. DOI: 10.3389/fphys.2012.00064

Giangaspero M., Wellemans G., Vanopdenbosch E., Belloli A., Verhulst A. 1988. Bovine viral diarrhoea. *Lancet* 2(8602): 110.

Hale V.L., Dennis P.M., McBride D.S., Nolting J.M., Madden C., Huey D., Ehrlich M. *et al.* 2021. SARS-CoV-2 infection in free-ranging white-tailed deer. *Nature* doi:10.1038/s41586-021-04353-x

Heyman P., Cochez C., Hofhuis A., van der Gleeson J., Sprong H., Porter S.P., Losson B. *et al*. 2010. A clear and present danger: tick-borne diseases in Europe. *Expert Rev Anti Infect Ther* 8: 33–50. DOI: 10.1586/eri.09.118

Johnson C.K., Hitchens P.L., Pandit P.P., Rushmore J., Evans T.S., Young C.C.W., Doyle M.M. 2020. Global shifts in mammalian population trends reveal key predictors of virus spillover risk. *Proc R Soc B* 287: 20192736. doi:10.1098/rspb.2019.2736

Jones K.E., Patel N.G., Levy M.A., Storeygard A., Balk D., Gittleman J.L., Daszak P. 2008. Global trends in emerging infectious diseases. *Nature* 451(21): 990–994. doi:10.1038/nature06536

Kahn J. 2020. How Scientists Could Stop the Next Pandemic Before It Starts. Feature. New York Times Magazine, 21 April 2020.

Kayali G., Ortiz E.J., Chorazy M.L., Nagaraja K.V., DeBeauchamp J., Webbey R.J., Gray G.C. 2011. Serologic evidence of avian metapneumovirus infection among adults occupationally exposed to Turkeys. *Vector Borne Zoonotic Dis* 11(11): 1453–58.

Klous G., Huss A., Heederik D.J.J., Coutinho R.A. 2016. Human-livestock contacts and their relationship to transmission of zoonotic pathogens, a systematic review of the literature. *One Health* 2: 65–76. doi: 10.1016/j.onehlt.2016.03.001

Kobinger G.P., Leung A., Neufeld J., Richardson J.S., Falzarano D., Smith G., Tierney K., Patel A., Weingartl H.M. 2011. Replication, Pathogenicity, Shedding, and Transmission of Zaire ebolavirus in Pigs. *JID* 204: 200–208. doi:10.1093/infdis/jir077

Li M., Embury-Hyatt C., Weingartl H.M. 2010. Experimental inoculation study indicates swine as a potential host for Hendra virus. *Vet Res* 41(3): 33–45. doi:10.1051/vetres/2010005

Li Y., Khalafalla A.I., Paden C.R., Yusof M.F., Eltahir Y.M., Al Hammadi Z.M., Tao Y. *et al*. 2017. Identification of diverse viruses in upper respiratory samples in dromedary camels from United Arab Emirates. *PLoS ONE* 12(9): e0184718. doi:10.1371/journal.pone.0184718

Morand S., McIntyre K.M., Baylis M. 2014. Domesticated animals and human infectious diseases of zoonotic origins: Domestication time matters. Infection, Genetics and Evolution 24: 76–81. doi:10.1016/j.meegid.2014.02.013

Mostafavi E., Pourhossein B., Esmaeili S., Bagheri Amiri F., Khakifirouz S., Shah-Hosseini N., Tabatabaei S.M. 2017. Seroepidemiology and risk factors of Crimean-Congo Hemorrhagic Fever among butchers and slaughterhouse workers in southeastern Iran. *Int J Infect Dis* 64: 85–89. doi: 10.1016/j.ijid.2017.09.008. Epub 2017 Sep 19. PMID: 28935247.

Nasirian H. 2020. New aspects about Crimean-Congo hemorrhagic fever (CCHF) cases and associated fatality trends: A global systematic review and meta-analysis. *Comp Immunol Microbiol Infect Dis* 69: 101429. doi: 10.1016/j.cimid.2020.101429. Epub 2020 Feb 5. PMID: 32062190.

Olival K.J., Hosseini P.R., Zambrana-Torrelio C., Ross N., Bogich T.L., Daszak P. 2017. Host and viral traits predict zoonotic spillover from mammals. *Nature* 546: 646–650. doi:10.1038/nature22975

Otte J., Pica-Ciamarra U. 2021. Emerging infectious zoonotic diseases: The neglected role of food animals. *One Health* 13: 100323. Epub 2021/09/16. doi: 10.1016/j.onehlt.2021.100323. PubMed PMID: 34522761; PubMed Central PMCID: PMCPMC8426280.

Otte J., Heilmann M., Pica-Ciamarra U. Submitted. Virus discovery in humans does not support a rise in zoonotic spillover. Submitted.

Pandit P.P., Doyle M.M., Smart K.M., Young C.C.W., Drape G.W., Johnson C.K. 2018. Predicting wildlife reservoirs and global vulnerability to zoonotic *Flaviviruses*. *Nature Communications* 9: 5425. doi:10.1038/s41467-018-07896-2

Pickering B.S., Smith G., Pinette M.P., Embury-Hyatt C., Moffat E., Marszal P., Lewis C.E. 2021. Susceptibility of Domestic Swine to Experimental Infection with Severe Acute Respiratory Syndrome Coronavirus 2. *EID* 27(1): 104–112. doi:10.3201/eid2701.203399

Rosenberg R., Johansson M.A., Powers A.M., Miller B.R. 2013. Search strategy has influenced the discovery rate of human viruses. *PNAS* 110(34): 13961–13964. doi:10.1073/pnas.1307243110

Sorvillo T.E., Rodriguez S.E., Hudson P., Carey M., Rodriguez L.L., Spiropoulou C.F., Bird B.H., Spengler J.R., Bente D.A. 2020. Towards a Sustainable One Health Approach to Crimean-Congo Hemorrhagic Fever Prevention: Focus Areas and Gaps in Knowledge. *Trop Med Infect Dis* 5(3): 113. doi: 10.3390/tropicalmed5030113. PMID: 32645889; PMCID: PMC7558268.

Spengler J.R., Bergeron É., Rollin P.E. 2016. Seroepidemiological Studies of Crimean-Congo Hemorrhagic Fever Virus in Domestic and Wild Animals. *PLoS neglected tropical diseases* 10(1), e0004210. https://doi.org/10.1371/journal.pntd.0004210

United Nations Environment Programme and International Livestock Research Institute. 2020. *Preventing the Next Pandemic: Zoonotic diseases and how to break the chain of transmission*. Nairobi, Kenya, pp.74.

Weingartl H.M., Copps J., Drebot M.A., Marszal P., Smith G., Gren J., Andonova M., Pasick J., Kitching P., Czub M. 2004. Susceptibility of Pigs and Chickens to SARS Coronavirus. *EID* 10(2): 179-183.

Wells K., Morand S., Wardeh M., Baylis M. 2020. Distinct spread of DNA and RNA viruses among mammals amid prominent role of domestic species. *Global Ecol Biogeogr* 29: 470–481. doi:10.1111/geb.13045

White S.K., Ma W., McDaniel C.J., Gray C.G., Lednicky J.A. 2016. Serologic evidence of exposure to influenza D virus among persons with occupational contact with cattle. *J Clin Virol* 81: 31–33.

Williams E., Spruill-Harrell B., Taylor M., Lee J., Nywening A.V., Yang Z., Nichols J.H. *et al*. 2021. Common Themes in Zoonotic Spillover and Disease Emergence: Lessons Learned from Bat- and Rodent-Borne RNA Viruses. *Viruses* 13: 1509. doi:10.3390/v13081509

Wolfe N.D., Dunavan C.P., Diamond J. 2007. Origins of major human infectious diseases. *Nature* 447: 279–283.

Woo P.C., Lau S.K., Teng J.L., Tsang A.K., Joseph M., Yong E.Y.M., Tang Y. *et al*. 2014. Metagenomic analysis of viromes of dromedary camel fecal samples reveals large number and high diversity of circoviruses and picobirnaviruses. *Virology* 471–473: 117–125. Epub 2014/12/03. doi:10.1016/j.virol.2014.09.020 PMID: 25461537

Yaiw K.C., Bingham J., Crameri G., Mungall B., Hyatt A., Yu M., Eaton B. *et al*. 2008. Tioman Virus, a Paramyxovirus of Bat Origin, Causes Mild Disease in Pigs and Has a Predilection for Lymphoid Tissues. *J Virol* 82(1): 565–568. doi:10.1128/JVI.01660-07

Yang Z.Q., Yu S.Y., Nie J., Chen Q., Li Z.F., Liu Y., Zhang J.I. *et al*. 2004. [Prevalence of hemorrhagic fever with renal syndrome virus in domestic pigs: an epidemiological investigation in Shandong province]. *Di Yi Jun Yi Da Xue Xue Bao* 24: 1283–1286

Zhang F., Chase-Topping M., Guo C-G., van Bunnik B.A.D., Brierley L., Woolhouse M.E.J. 2020. Global discovery of human-infective RNA viruses: A modelling analysis. *PLoS Pathog* 16(11): e1009079. doi:10.1371/journal. ppat.1009079

CC2160EN/1/11.22