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Companion Animals as a Source of Viruses for Human Beings and Food Production Animals

L. A. Reperant[*], I. H. Brown[†], O. L. Haenen[‡], M. D. de Jong[§], A. D. M. E. Osterhaus[*], A. Papa[¶], E. Rimstad[||], J.-F. Valarcher[#] and T. Kuiken[*]

[*] Department of Viroscience, Erasmus Medical Centre, PO Box 2040, 3000 CA Rotterdam, The Netherlands, [†] Animal and Plant Health Agency Weybridge, New Haw, Addlestone, Surrey, UK, [‡] National Reference Laboratory for Fish, Shellfish and Crustacean Diseases, Central Veterinary Institute of Wageningen UR, PO Box 65, 8200 AB Lelystad, [§] Department of Medical Microbiology, Academic Medical Centre, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands, [¶] Department of Microbiology, Medical School Aristotle University of Thessaloniki, Thessaloniki, Greece, [||] Department of Food Safety and Infection Biology, University of Life Sciences, Oslo, Norway and [#] Department of Virology, Immunology, and Parasitology, National Veterinary Institute, Uppsala, Sweden

Summary

Companion animals comprise a wide variety of species, including dogs, cats, horses, ferrets, guinea pigs, reptiles, birds and ornamental fish, as well as food production animal species, such as domestic pigs, kept as companion animals. Despite their prominent place in human society, little is known about the role of companion animals as sources of viruses for people and food production animals. Therefore, we reviewed the literature for accounts of infections of companion animals by zoonotic viruses and viruses of food production animals, and prioritized these viruses in terms of human health and economic importance. In total, 138 virus species reportedly capable of infecting companion animals were of concern for human and food production animal health: 59 of these viruses were infectious for human beings, 135 were infectious for food production mammals and birds, and 22 were infectious for food production fishes. Viruses of highest concern for human health included hantaviruses, Tahyna virus, rabies virus, West Nile virus, tick-borne encephalitis virus, Crimean–Congo haemorrhagic fever virus, Aichi virus, European bat lyssavirus, hepatitis E virus, cowpox virus, G5 rotavirus, influenza A virus and lymphocytic choriomeningitis virus. Viruses of highest concern for food production mammals and birds included bluetongue virus, African swine fever virus, foot-and-mouth disease virus, lumpy skin disease virus, Rift Valley fever virus, porcine circovirus, classical swine fever virus, equine herpesvirus 9, peste des petits ruminants virus and equine infectious anaemia virus. Viruses of highest concern for food production fishes included cyprinid herpesvirus 3 (koi herpesvirus), viral haemorrhagic septicaemia virus and infectious pancreatic necrosis virus. Of particular concern as sources of zoonotic or food production animal viruses were domestic carnivores, rodents and food production animals kept as companion animals. The current list of viruses provides an objective basis for more in-depth analysis of the risk of companion animals as sources of viruses for human and food production animal health.

Keywords: companion animal; livestock; virus; zoonosis

Contents

Correspondence to: T. Kuiken (e-mail: t.kuiken@erasmusmc.nl).

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Introduction

Little is known about the role of companion animals in the transmission of pathogens, in particular viruses, to man or to livestock. A plethora of viruses have zoonotic potential (Gortazar *et al.*, 2014) or are of economic importance as they infect food production animals (Morgan and Prakash, 2006). Studies aiming at inventorying viruses with zoonotic potential have revealed their expanding diversity with an average of three to four new zoonotic pathogens identified each year (Woolhouse *et al.*, 2012). Wild animal species commonly are the source of these novel or newly identified pathogens. New virus species, and sometimes even new virus genera, have been reported increasingly in wild animal species, such as bats or rodents (Drexler *et al.*, 2012, 2013).

Viruses of economic importance, because of their ability to infect and cause disease in food production animal species (and therefore their ability to undergo transboundary spread), have long been listed by international organizations, such as the Office International des Epizooties (OIE; World Organisation for Animal Health; www.oie.int), with associated regulatory phytosanitary measures. In addition, as for zoonotic pathogens, new pathogens are recognized occasionally to infect food production animals. Wild animal species are likewise often implicated in the transmission of such newly discovered pathogens, both to human beings and to livestock species (Field *et al.*, 2007; Raj *et al.*, 2014).

Companion animals, in particular domestic carnivores, also are hosts of an expanding diversity of viruses. For example, canine parvovirus, now a major pathogen of domestic dogs worldwide, emerged in the 1970s (Parrish, 1999). Influenza A viruses that appear to be maintained in domestic dog populations have only recently emerged (Dubovi, 2010). However, populations of companion animal species are expanding both in size and diversity, in particular in industrialized countries. In this review, companion animals are defined as any domesticated, domestic-bred or wild-caught animals, permanently living in human communities and kept by people for company, amusement, work (e.g. support for blind or deaf people, police or military dogs) or psychological support. These include dogs, cats, horses, rabbits, ferrets, guinea pigs, reptiles, birds and ornamental fish, but also food production animals, such as domestic pigs, kept as companion animals. These changes in populations of companion animals have so far not been matched with an assessment of the role of these animals as a source of zoonotic viruses and viruses of economic importance in livestock. Here, we review the literature on the occurrence of infections of companion animal species by zoonotic viruses and viruses of food production animals in order to establish a complete list of viruses that could possibly be transmitted from companion animals to man or livestock, based on published records of cross-species transmission. We further prioritize these viruses semiquantitatively, in terms of health and economic importance, by ranking the likelihood that companion animals act as relevant sources for the cross-species transmission of the listed viruses, and associated potential impact, with a special focus on Europe.

Materials and Methods

Literature Search

We retrieved articles published before 1st July 2012 in PubMed to identify and list mammalian, avian and fish viruses that have proven ability to cross the species barriers between companion animals and man or between companion animals and food production animals. To this end, PubMed was searched for combinations of terms belonging to the following general categories: 'virus' AND 'companion animal' AND 'food production animal' OR 'human' (Supplementary Tables 1a and 1b). Viruses of food production animals (without report of infection in companion animals) were also included, to account for the risk posed by viruses transmitted from ruminants, pigs and poultry kept as companion animals to people or food production animals. Zoonotic viruses and viruses of food production animals were considered capable of infecting companion animals, based on published positive polymerase chain reaction (PCR) data, viral isolation or serology in the latter. Accordingly, a total of 170 viruses or virus groups at or below genus level were included (Supplementary Table 2).

Semiquantitative Prioritization

Based on a set of priority criteria (Supplementary Table 3a), these viruses were ranked for the likelihood that they could be transmitted from companion animals to man or food production animals, and the associated potential impact of such transmission. Particular attention was given to possible demographic changes that are currently occurring or that may occur in the near future, and which may increase the likelihood of cross-species transmission of viruses from companion animals to man or food production animals. For example, expanding populations of a particular companion animal species, or emergence of a particular virus, may translate into increased likelihood of cross-species transmission.

The prioritization criteria included the trends in the companion animal populations that are putatively the source of the particular virus, its host range, the level of environmental resistance, the clinical impact in man or food production animals and, for viruses transmitted to food production animal species, the population size of the food production animal species, and whether the virus is on the OIE list of notifiable terrestrial and aquatic animal diseases. We further classified the current epidemiological situation for each virus in Europe as absent, endemic or emerging.

As mentioned earlier, expanding populations of a companion animal species may favour cross-species transmission of the pathogens it may host. Populations of companion animals were categorized into either stable, increasing or booming. Pathogens with a wide host range are considered more likely to cross species barriers than more species-specific pathogens. Accordingly, we categorized the listed viruses into viruses infecting less than or more than four different host species. Viruses that may survive in the environment can rely on indirect transmission, which may increase the likelihood of cross-species transmission. We categorized the viruses into labile or resistant, based on the presence or absence of a lipid envelope, respectively. In order to assess the potential impact of the listed viruses, the severity of the resulting clinical disease was categorized into four categories, from no disease to severe disease. Viruses that can infect food production animals were further divided into those listed and those not listed as notifiable by the OIE, and their clinical impact was weighted by the size of the food production animal populations, categorized semiquantitatively into three classes.

The rank was calculated based on the sum of all criteria and weighted by the epidemiological situation in Europe (Supplementary Table 3b). The ranks were calculated separately for viruses transmitted from companion animals to man, for viruses transmitted from companion animals to mammalian and avian food production animals and for viruses transmitted from ornamental fish to food production fish species. They were standardized on a unit scale for comparison purposes.

The semiquantitative scores of all viruses and of viruses of relevance to Europe were compared, using the non-parametric Mann–Whitney test. Differences were considered significant when $P < 0.05$. The distributions of viruses were represented by Venn diagrams produced in 'R' using the Venneuler package.

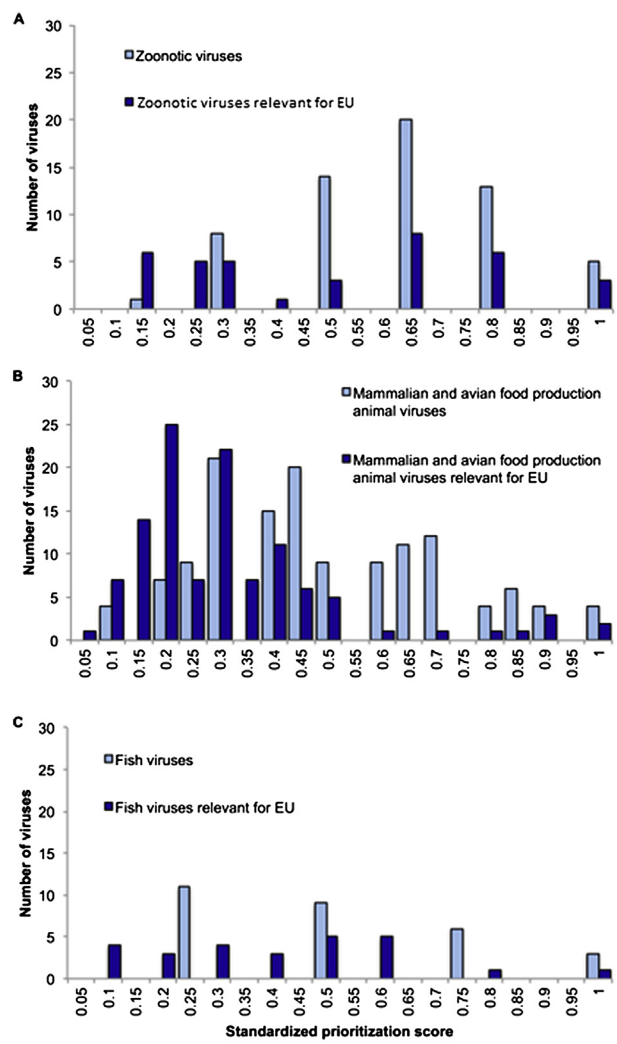

Fig. 1. Semiquantitative prioritization scores. (A) Zoonotic viruses. (B) Viruses of mammalian and avian food production animals. (C) Viruses of fish. Scores of all listed viruses are represented by light blue bars; scores of viruses that are present or with emerging potential in Europe are represented by dark blue bars.

Table 1
List of viruses with highest prioritization scores that may be transmitted from companion animals to man and/or food production animals

Family	*Virus*	*Zoonotic*	*Food production animals*	*Vector-borne*	*Selected references*
Adenoviridae	Avian adenoviruses		X		McFerran and Smyth (2000)
Arteriviridae	Porcine reproductive and respiratory syndrome virus		X		Cho and Dee (2006)
Asfarviridae	African swine fever virus		X	V	Marshall *et al.* (2007), Sipos *et al.* (2007), Costard *et al.* (2009)
Birnaviridae	Infectious bursal disease virus		X		Mahgoub *et al.* (2012)
	Infectious pancreatic necrosis virus		X		Dobos (1995), Munro and Midtlyng (2011)
Bunyaviridae	Rift Valley fever virus	X	X	V	Gerdes (2004)
	Hantaviruses	X			Desmyter *et al.* (1983), Vapalahti *et al.* (2003), Heyman *et al.* (2009), Olsson *et al.* (2010), Zhang *et al.* (2010), Dobly *et al.* (2012), Papa (2012)
	Dobrava–Belgrade virus	X			Heyman *et al.* 2009), Papa (2012)
	Crimean–Congo haemorrhagic fever virus	X		V	Shepherd *et al.* (1987), Capua (1998), Whitehouse (2004), Ergonul (2006)
Caliciviridae	Vesicular exanthema virus		X		Lin and Kitching (2000)
Circoviridae	Chicken infectious anaemia virus		X		Schat (2009)
	Porcine circovirus		X		Li *et al.* (2010), Grau-Roma *et al.* (2011), Baekbo *et al.* (2012)
Coronaviridae	Avian bronchitis virus		X		Sjaak de Wit *et al.* (2011), Cook *et al.* (2012)
	Swine transmissible gastroenteritis virus		X		Wood (1979)
Flaviviridae	Bovine viral diarrhoea disease virus		X		Lindberg *et al.* (2006), Walz *et al.* (2010)
	Powassan virus	X		V	Charrel *et al.* (2004)
	Japanese encephalitis virus	X	X	V	Mackenzie *et al.* (2004)
	Classical swine fever virus		X		Moennig *et al.* (2003)
	West Nile virus	X	X	V	Hubalek and Halouzka (1999), Campbell *et al.* (2002), Austgen *et al.* (2004), Zeller and Schuffenecker (2004), Crespo *et al.* (2009), Danis *et al.* (2011)
	Tick-borne encephalitis virus	X		V	Gritsun *et al.* (2003), Gover *et al.* (2011), Pfeffer and Dobler (2011), Hubalek and Rudolf (2012)

(*Continued*)

Table 1 (*continued*)

Family	*Virus*	*Zoonotic*	*Food production animals*	*Vector-borne*	*Selected references*
Hepeviridae	Hepatitis E virus	X			Kuno *et al.* (2003), Renou *et al.* (2007), Vasickova *et al.* (2007), de Deus *et al.* (2008), Schielke *et al.* (2009), Lewis *et al.* (2010), Meng (2010), Pavio *et al.* (2010), Rutjes *et al.* (2010), Kamar *et al.* (2012)
Herpesviridae	Gallid herpesvirus 1 (laryngotracheitis virus)		X		Bagust *et al.* (2000), Fuchs *et al.* (2007)
	Ovine herpesvirus 2 (malignant catarrhal fever virus)		X		Russell *et al.* (2009)
	Suid herpesvirus 1 (pseudorabies/ Aujeszky virus)		X		Tischer and Osterrieder (2010), Muller *et al.* (2011)
	Equine herpesvirus 9		X		Schrenzel *et al.* (2008), Osterrieder and Van de Walle (2010)
	Cyprinid herpesvirus 3 (koi herpesvirus)		X		Hedrick *et al.* (2000), Haenen *et al.* (2004), Haenen and Hedrick (2006), Perelberg *et al.* (2008), Way (2009)
Iridoviridae	Infectious spleen and kidney necrosis virus		X		Jeong *et al.* (2008)
	European catfish virus		X		Whittington *et al.* (2010)
	Lymphocystis disease virus		X		Paperna *et al.* (2001), Hossain *et al.* (2008)
Nodaviridae	Viral nervous necrosis virus		X		Hegde *et al.* (2003), Furusawa *et al.* (2007), Mazelet *et al.* (2011)
Orthomyxoviridae	Infectious salmon anaemia virus		X		Cottet *et al.* (2011), Rimstad *et al.* (2011)
	Influenza A virus	X	X		Olsen (2000), Myers *et al.* (2007), Thiry *et al.* (2007), Peiris (2009), Harder and Vahlenkamp (2010), Swenson *et al.* (2010), Reperant *et al.* (2012)
Paramyxoviridae	Newcastle disease virus (APMV 1)		X		Alexander (2011), Alexander *et al.* (2012)
	Nipah virus	X	X		Luby and Gurley (2012), Clayton *et al.* (2013)
	Hendra virus	X	X		
Picornaviridae	Encephalomyocarditis virus		X		Carocci and Bakkali-Kassimi (2012)
	Foot-and-mouth disease virus	X	X		USDA (1994) Anonymous (2006), Marshall *et al.* (2007), Valarcher *et al.* (2008)
	Avian encephalomyelitis virus		X		Welchman Dde *et al.* (2009)
	Aichi virus	X			Le Guyader *et al.* (2008), Li *et al.* (2011), Phan *et al.* (2011), Reuter *et al.* (2011)

(*Continued*)

Table 1 *(continued)*

Family	*Virus*	*Zoonotic*	*Food production animals*	*Vector-borne*	*Selected references*
Polyomaviridae	Avian polyomaviruses		X		Johne *et al.* (2006)
Poxviridae	Monkeypox virus	X			Reed *et al.* (2004), Tack and Reynolds (2011)
	Lumpy skin disease virus		X		Babiuk *et al.* (2008), Bowden *et al.* (2009), Tuppurainen and Oura (2012)
	Salmon gill poxvirus		X		Nylund *et al.* (2008)
Reoviridae	Bluetongue virus		X	V	Akita *et al.* (1994), Alexander *et al.* (1994), Brown *et al.* (1996), Mellor and Wittmann (2002), Oura and El Harrak (2011)
	Piscine reovirus		X		Palacios *et al.* (2010)
	G5 rotavirus	X			Esona *et al.* (2004), Santos and Hoshino (2005), Ahmed *et al.* (2007), Duan *et al.* (2007), Midgley *et al.* (2012), Mladenova *et al.* (2012)
Rhabdoviridae	Spring viraemia of carp virus		X		Haenen and Davidse (1993), Ahne *et al.* (2002), Gomez-Casado *et al.* (2011)
	Viral haemorrhagic septicaemia virus		X		Skall *et al.* (2005), Smail and Snow (2011)
	Vesicular stomatitis virus		X		Schmitt (2002)
	Rabies virus	X	X		Rupprecht *et al.* (2001), De Benedictis *et al.* (2008), Capello *et al.* (2010)
Togaviridae	Western equine encephalitis virus	X		V	Zacks and Paessler (2010)
	Eastern equine encephalitis virus	X		V	Zacks and Paessler (2010)
	Salmon pancreas disease virus (salmonid alphavirus)		X		McLoughlin and Graham (2007)

Highlighted rows are viruses relevant for Europe. Relevance for zoonotic transmission and transmission to food productions animals is indicated by X; vector-borne viruses are indicated by V.

Results

The list of viruses reportedly capable of infecting companion animal species and man or food production animal species comprises 138 virus species, of which 26 are vector borne, and 32 groups of virus species at the genus level or below (Supplementary Table 2). 'Vector borne' refers here to biological rather than mechanical transmission by arthropod vectors. Fifty-nine virus species or groups of species have zoonotic potential, of which 17 are vector borne; 135 infect mammalian or avian food production animal species, of which 24 are vector borne, and 22 infect food production fish species. Of the fish viruses, only six species have been demonstrated in ornamental fish. The distributions of standardized semiquantitative positive prioritization scores are presented in Fig. 1. The scores are significantly lower for zoonotic viruses and viruses of mammalian and avian food production animals relevant to Europe than those considered in the global list ($Z = 2.21$, $P = 0.02$ and $Z = 6.82$, $P < 0.0001$, respectively). Although a similar trend was observed for fish viruses, this difference was not significant.

Viruses that received scores >0.5 are highlighted in Supplementary Table 2. Viruses with the highest prioritization scores, hence those which may be at the highest risk for cross-species transmission from companion animals to man and/or food production animals, are listed in Table 1. Additional virus species with high prioritization scores and of relevance to Europe include European bat lyssavirus (Fooks *et al*., 2003; van der Poel *et al*., 2006; Dacheux *et al*., 2009), cowpox virus (Baxby *et al*., 1994; Baxby and Bennett, 1997; Pfeffer *et al*., 2002; Wolfs *et al*., 2002; Tack, 2011; von Bomhard *et al*., 2011), lymphocytic choriomeningitis virus (Gregg, 1975; Rousseau *et al*., 1997; Barton and Mets, 2001; Amman *et al*., 2007), Puumala virus (Vapalahti *et al*., 2003; Heyman *et al*., 2009; Olsson *et al*., 2010), Tahyna virus (Hubalek *et al*., 2005; Hubalek, 2008) and peste des petits ruminants virus (Banyard *et al*., 2010).

Companion animals were categorized subsequently into domestic carnivores, small mammals, horses, birds and food production animals kept as companion animals. These harbored, respectively, 42, 54, 40, 40 and 91 viruses with zoonotic potential or of economic importance. The distribution of viruses with zoonotic potential, of economic importance for food production animals, and those transmitted by arthropod vectors are shown in Fig. 2.

The companion animal sources of viruses that can infect man and/or food production animals are shown in Fig. 3. Viruses with zoonotic potential have the greatest diversity in companion animal sources, with more limited overlap between host species. So far, there are no reports of fish as a source of zoonotic viruses. Because ruminants, pigs, horses, rabbits and poultry have companion animal counterparts, viruses infecting these species may originate from food production animals kept as companion animals. Small mammals, in particular rodents, are hosts to the second largest number of viruses of economic importance that may infect food production animals.

Discussion

The present study is an initial attempt to delineate the importance of companion animals in the transmission of viruses to man and food production

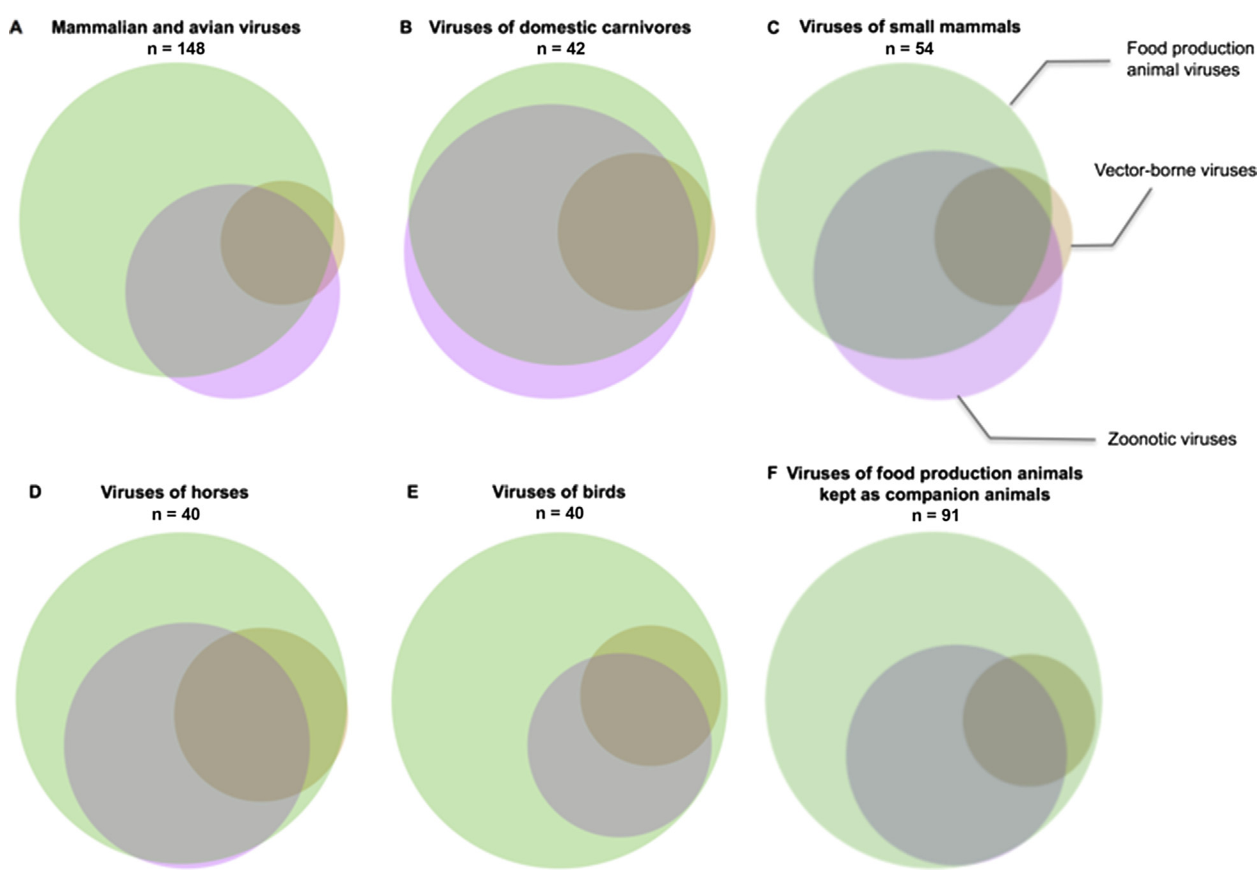

Fig. 2. Distribution of zoonotic viruses, viruses of mammalian and avian food production animals and vector-borne viruses in companion animal species. (A) All listed viruses. (B) Viruses of domestic carnivores (i.e. dogs, cats and ferrets). (C) Viruses of small mammals (i.e. rodents and rabbits). (D) Viruses of horses. (E) Viruses of birds (i.e. ornamental birds and poultry kept as companion animals). (F) Viruses of mammalian food production animals kept as companion animals (i.e. cattle, sheep, goats and pigs).

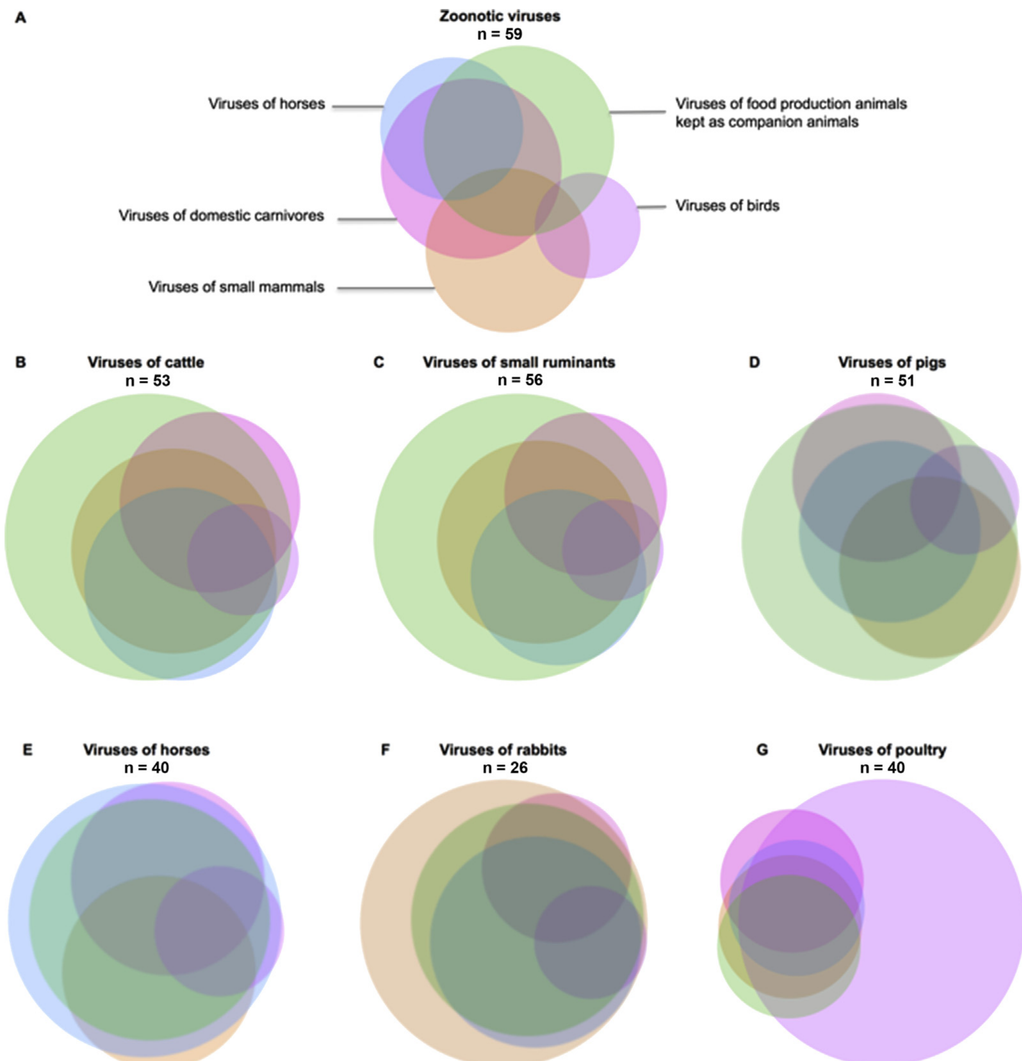

Fig. 3. Distribution of viruses of companion animal species in man and in mammalian and avian food production animals. (A) Zoonotic viruses. (B) Viruses of cattle. (C) Viruses of small ruminants (i.e. sheep and goats). (D) Viruses of pigs. (E) Viruses of horses. (F) Viruses of rabbits. (G) Viruses of poultry.

animals. The resulting list of viruses potentially transmitted by companion animals likely is conservative, as reports of actual cross-species transmission events from companion animals to man or food production animals remain rare and non-systematic. Viruses were included based on reports of actual infection in both companion animals and man or food production animals, irrespective of the direction of cross-species transmission. For example, there is no direct evidence to date that companion animals play a role in the transmission of vector-borne viruses to man or food production animals. However, 10 vector-borne virus species cumulated high prioritization scores, suggesting a potential for such cross-species transmission.

Nonetheless, our use of a systematic and objective selection method to assess the potential importance of companion animal viruses for human health and food production brings a number of advantages compared with the sole reliance on expert opinion. Expert opinion is undeniably valuable, but has the inherent risk of becoming a self-fulfilling prophecy: if pathogen testing is limited to those considered important by experts, the results will be limited to those pathogens. In contrast, the current list includes some pathogens that most experts would not have scored highly (e.g. Aichi virus and G5 rotavirus as zoonotic viruses, and lumpy skin disease virus and equine herpesvirus 9 as viruses of food production animals). Of note, the recent incursions of lumpy skin disease in cattle in Europe (Cyprus, Greece) and neighbouring countries (Turkey and Russia), as reported by Promed, support the need to expect the unexpected.

Due to their population size, in particular in industrialized countries, domestic carnivores and rodents are among the most important companion animal sources of zoonotic viruses. On the other hand, expanding populations of food production animals kept as companion animals (e.g. domestic pigs, Sipos *et al*., 2007) may also result in the cross-species transmission of zoonotic viruses, which represent about half of the viruses they harbour. Rodents also harbour a large number of viruses of economic importance that can infect food production animals.

The present analysis does not include the potential for direct or indirect contact necessary for cross-species transmission between host species, since data for such an assessment are largely lacking. While the current list of viruses potentially transmitted from companion animals thus has its limitations, it represents a solid and objectively constructed basis for more in-depth risk assessment analyses.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jcpa.2016.07.006.

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