

Literature review



A concise review on certain important veterinary viruses in the Americas

Sebastian Giraldo-Ramirez^{1 💴} M.Sc; Santiago Rendon-Marin^{1 💴} IB; Julian Ruiz-Saenz^{1*} 💴 Ph.D.

¹Universidad Cooperativa de Colombia, sede Bucaramanga. Facultad de Medicina Veterinaria y Zootecnia. Grupo de Investigación en Ciencias Animales - GRICA. Bucaramanga, Colombia. *Correspondencia: julian.ruizs@campusucc.edu.co

Received: May 2020; Accepted: November 2020; Published: April 2021.

ABSTRACT

Animals have become an essential member for our society, with roles related to company, human well-being and therapy for some diseases, and as a source of food in many populations around the world. Animals intended for human consumption like pigs and cattle, as well as companion animals, specifically cats and dogs, are constantly threatened by multiple viral agents. This puts at risk pet owners and threatens food security in the region. Considering that control or eradication is a complex problem that involves several aspects, there is a limited success in this regard for viral diseases such as foot-and-mouth disease, rabies and classical or African swine fever, this review aims to show the most important characteristics, in the epidemiological context, from farm animals virus, re-emerging viruses affecting companion animals, and emerging and re-emerging zoonotic viruses. Since viral pathogens affect animal populations and human well-being, there is a need to increase efforts to control, monitor and eradicate them from livestock and companion animals. The following sections contribute to improve the understanding of these viral agents and orchestrate actions of control entities in the Americas.

Keywords: Animal viruses; companion animals; farm animals; livestock; re-emerging diseases; zoonotic diseases (Source: MeSH).

RESUMEN

Los animales se han convertido en miembros esenciales de nuestra Sociedad, con roles que incluyen compañía, bienestar y terapia para algunas enfermedades, así como fuente de alimento para muchas poblaciones alrededor del mundo. Los animales destinados para el consumo humano como cerdos y bovinos, así como los animales de compañía, especialmente los gatos y perros están constantemente amenazados por múltiples agentes virales, lo cual pone en riesgo a los propietarios de mascotas y amenaza la seguridad alimentaria en las regiones. Sabiendo que el control o la erradicación es un problema complejo que involucra diversos aspectos, existe un éxito limitado respecto a esto para enfermedades virales tales como la fiebre aftosa, rabia, la peste porcina

How to cite (Vancouver).

Giraldo-Ramirez S, Rendon-Marin S, Ruiz-Saenz J. A concise review on important veterinary viruses in the Americas. Rev MVZ Cordoba. 2021; 26(2):e1965. https:// doi.org/10.21897/rmvz.1965



©The Author(s), Journal MVZ Cordoba 2021. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by-nc-sa/4.0/), lets others remix, tweak, and build upon your work non-commercially, as long as they credit sa you and license their new creations under the identical terms.

clásica o africana. Esta revisión tiene como objetivo mostrar las características más importantes, en el contexto epidemiológico, de virus de animales de producción, virus reemergentes que afectan animales de compañía y virus zoonóticos emergentes y reemergentes. Debido a que los patógenos virales afectan poblaciones animales y el bienestar humano, existe la necesidad de incrementar los esfuerzos en el control, monitoreo y erradicación de estos tanto de los animales de producción como en los animales de compañía. Por lo cual, las siguientes secciones contribuyen a mejorar el entendimiento de estos agentes virales y diseñar acciones de control en las Américas.

Palabras clave: Virus animales; animales de compañía; animales de granja; ganado; enfermedades reemergentes; enfermedades zoonóticas (*Fuente: MeSH*).

INTRODUCTION

Historically, animals have played crucial roles in human lives; from company and well-being to food resource, animals are important members of our society and they are heavily besieged by different viral agents (1). Because of the human activity expansion, wildlife is getting in touch with human productive systems. Wildlife plays an important role as a reservoir of virus-based human diseases (2), as well as it does in farm and companion animals, which have also become a relevant reservoir of different viruses, includes dogs, cats, ferrets, guinea pigs, reptiles, birds and some ornamental fish and food production animal species, such as domestic pigs. Viral infections in animals pose not only a risk to pet ownership and animal conservation, but also to the region's food security and potentially endanger the public health (3). The aim of this review is to characterize veterinary viruses affecting livestock and companion animals in the Americas. Although, the importance of animals in human society is well established, there are still research gaps related to animals as sources of zoonotic viruses. The following sections will present three main groups of pathogens. Firstly, viruses that affect animal production systems, putting at risk the food safety of populations; secondly, re-emerging viruses of companion animals and their challenges in pet's internationalization and transportation; and finally, viruses that could have reservoirs in animal populations and are zoonotic

Viruses from livestock and farm animals

Foot and Mouth Disease Virus (FMDV). This agent is considered one of the most economically important veterinary viruses due to its extremely infectious nature, a wide range of host, and its capacity to cause persistent infections. FMDV causes the Foot-and-Mouth Disease (FMD) and

it is the prototype member of the *Aphthovirus* genus, which affects a vast array of domestic livestock such as pigs, sheeps, goats, and cattle (i.e. members of the order *Artiodactyla*) (4). Countries where disease is present possess trade restrictions (4). The FMDV is transmitted through a variety of excretions and secretions such as saliva, urine, milk and semen, by which large amounts of viruses are eliminated and infect other animals by respiratory and oral route. In addition, FMDV could also be spread by fomites that are contaminated by infected animal excretions and secretion (4).

The infection of livestock regularly results in significant loss of milk yield in dairy cattle, reduction in the growth rate of animals used for meat production, temporary loss of draught power with working buffalo and cattle, reductions in fertility, and death in younger animals. Additionally, the FMD incidence has as consequence the slaughter of unprotected and chronically infected animals, which could generates loss of income and valuable breeding stock, and also disturbance of programs that aim the livestock improvement (5).

In the Americas, the FMDV has been known the nineteenth century; since however, nowadays there is almost no presence of this virus in most of the continent. North America, Central America and the Caribbean countries are exempt from this disease, whereas countries in South America are working together to eradicate FMDV (6). For this aim, the FAO/OIE Global Framework for the Progressive Control of Transboundary Animal Diseases has established FMDV eradication as a common regard and a world public good. The main objective is helping to mitigate poverty and improve not only the current situation in developing countries but also to improve world and regional trade for animals and their products.

Although FMDV has been regulated in most of the South American countries (Table 1), control and effective eradication remains as a challenge in the region due to there are countries such as Venezuela and the Amazonian region of Brazil in which there are no effective control of the virus (7). It is important to highlight that countries or regions recognized as FMD free with vaccination must strength their surveillance systems for achieving signs early recognition, or to evidence infection through antigen, antibody or viral particles detection (8). Also, it is important to avoid transboundary virus transmission trough empowerment of international surveillance systems, especially in countries like Colombia, Peru and Brazil which share border to non-controlled areas (9) (Figure 1). A full list research needs for the region has been recently published elsewhere by the Global FMD Research Alliance (7).

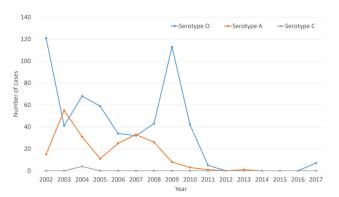


Figure 1. Timeline of FMDV cases reported in the PANAFTOSA eradication program of between 2002 and 2017. Adapted from PAHO (10).

FMD is not considered a zoonotic disease by the World Health Organization (WHO), thus, it is not a threat to human health. However, some cases has been reported, mainly among people who are in contact with infected animals or samples such as farm workers and research laboratory users (11).

Avian Influenza Virus (AIVs). Influenza A viruses belong to the *Orthomyxoviridae* family. The avian influenza, commonly termed as bird flu, is an extremely contagious acute viral disease that is able to occur as an epidemic and cross-border forms in poultry (12). Up to sixteen of the eighteen discovered hemagglutinin subtypes (H1-H16) and 9 of the described neuraminidase (N1-N9) subtypes have been distinguished as avian species (12).

Moreover, those viruses are able to infect a vast array of mammal species, which include humans, horses, pigs, cats, dogs, and even some marine species (13, 14). Besides, new influenza A viruses have been recently identified in yellow shouldered bats from Guatemala, which is compatible for genetic exchange with human influenza (15). Moreover, a novel influenza A virus was identified in Peruvian fruit bats. It was found that Influenza virus in bats had a big genetic diversity suggesting a longstanding host-virus association. Bats could play an important role in the spread of Influenza virus for another species even poultry (16). In the Americas, it has been reported the genomic reassortment of American and Eurasian genes in an influenza A virus H13N2, isolated from a great black-backed gull, a specie that moves between these two regions (17).

Table 1. Health status of FMDV-free countries in the Americas.

| , | incus. | | | | |
|-----------|--------|----|------|-----|------------------------|
| Country | FWV | FW | FZWV | FZV | Last case reported* |
| Argentina | | | Х | Х | 2006 serotype O |
| Bolivia | | | Х | Х | 2007 serotype O |
| Brazil | | | Х | Х | 2006 serotype O |
| Chile | Х | | | | 1987 serotype O |
| Colombia | | | Х | | 2017 serotype O |
| Ecuador | | | Х | х | 2011 serotype O |
| Peru | Х | | | | 2004 serotype O |
| Paraguay | | х | | | 2001 serotype O |
| Uruguay | | х | | | 2001 serotype A |
| Venezuela | | | | | 2011 serotype A |

FWV: Free without vaccination; FW: Free with vaccination; FZWV: Free zones without vaccination; FZV: Free zones with vaccination. *Adapted from PAHO (10)

From a pathogenicity point of view, AIVs have been classified as highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI) viruses. Currently, only the H5 and H7 subtypes have been demonstrated to be HPAI viruses, however not all H5 and H7 viruses are considered HPAI viruses (18). Either LPAI H5 or H7 viruses could become HPAI viruses due to mutations accumulation that occurs after infection of one poultry (19). It is estimated that HPAI viruses have contributed to avian health and poultry production worldwide. More than 500 million poultry deaths have been related to avian influenza infections (20) which provoke repercussion in economic, political and/or sociocultural aspects (21).

Further, the AIVs has an important incidence in human health, it has been involved in sporicidal pandemic events as those occurred in 1918 (H1N1), 1957 (H2N2) and 1968 (H3N2) (22). The most recent outbreak of infecting-humans AIVs, occurred in 2003 in Asian countries. This outbreak was related to a highly pathogenic influenza H5N1 and were reported more than one hundred cases in four countries (Thailand, Cambodia, Indonesia and Viet Nam) with 57 human deaths (23). In 2009 Influenza A H1N1 virus become pandemic and caused around 200.000 human deaths in the first twelve months. This virus is a swine-origin influenza, but it has been demonstrated that shares genetic information with human and avian strains (24).

Latin America and Caribbean produces 20.40% of poultry at global level, that is why poultry has an important role in livestock of the region (25), and the risk of a continent-wide outbreak of AIVs has become greater. There is a wide range of animals and their products that are interchanged inside and between Latin-American countries. A HPAI outbreak in Mexico in 2012-2013 caused the slaughter of 30 million of chickens, and in United States an outbreak in 2014-2015 led to the losing of 48 million of domestic birds and five billion dollars in total losses (26).

In Latin America, it has been reported around 14 subtypes of influenza viruses in birds, including LPAI and HPAI strains. The most common AIVs that has been isolated is the LPAI H5N2 (27,28), reported to firstly appear in Mexico, Guatemala, El Salvador, and Honduras. Mexico and Chile has suffer the presence of HPAI; however LPAI H7N3 viruses were originally isolated and through time, it became HPAI viruses as the result of its genome drift (29). Phylogenetic analyses of AIVs in Latin America has proven the relationships between North American AIVs and the South American viruses. These facts suggest that there is viral transmission between the Americas continent probably due to the migratory flyways, which are not possible to control (27). Regarding the circulation of other AIVs in the Americas, whole genome sequencing studies enables to determine circulating variants in the Americas (27). H7N9 was first detected in China in 2013 as a LPAI virus, with the ability to infect humans, causing more than 1600 infections. In 2017, this virus mutated and became a HPAI strains virus that spreads to other regions of China, affecting poultry. In 2015, a new H5N1 virus rearranged in poultry was reported in the United States and Canada and, finally, in 2018, outbreaks of HPAI strain H7N3 were reported in Mexico. Subtypes of LPAI reported in America between 2013 and 2018 are H5N1, H5N2, H5N8, H7N3, H7N8 (30).

The OIE has proposed strategies for the management of infected birds, including the removal of dead bodies, feces and wastes, surveillance and monitoring of potentially infected or exposed poultry, quarantine and control of bird movement, personnel and possibly contaminated vehicles, decontamination of infected establishments, a waiting period of not less than 21 days before restocking (30). Vaccination is important in endemic areas, where it seeks to generate population protection (31).

Due to this scenario of AIVs circulation in the Americas, it is imperative to perform an accurate diagnostic of the disease and mortality cases in reservoirs, looking for rapid detection of AIVs (32). Thus, it is crucial to reinforce AIVs surveillance systems by a cooperative work either by non-governmental or governmental entities (33). Moreover, it is relevant to develop diverse strategies to prevent and respond to AIVs outbreaks. If biosecurity training at poultry industry and backyard poultry production could be helpful to reduce the risk of transmission of AIVs between wildlife (natural reservoirs) and poultry (susceptible hosts) (34).

Classic Swine Fever Virus (CSFV). It belongs to the Flaviviridae family and causes the Classic Swine Fever (CSF), also named as "hog cholera", which is a contagious viral disease which affects domestic and wild pigs, boars and peccaries (35). Its transmission is mostly through saliva, urine, feces and nasal fluid from an infected animal to a healthy one pig (36). Additionally, indirect contact with food, surfaces and objects contaminated with these secretions also represents an important source of virus transmission. Animals with chronic disease can excrete viral particles in feces for months and transplacental transmission is present. It has great impact on animal health and pig industry, and even though CSFV is not considered a zoonotic pathogen, infected animals are banned from the human consumer chain, causing restrictions on animal production and international trade (37). In areas where CSFV is enzootic, vaccination represents the main means of disease prevention. However, an

efficient reporting system, strict import policies for live animals or their products, effective identification of sick animals and adequate hygiene measures for pens must help in disease control (36).

Countries as Canada, USA, Chile, Belize, Costa Rica, Panama, and Mexico, where 13 of 32 States are disease free, have given importance to the control and possible eradication of CSF. However, in other American countries, the disease appears under control, as is the case of the five countries of the Andean Region and the 12 northern States of Brazil. In South America, Chile, Uruguay and 13 States in Brazil are disease free and Argentina has developed a national campaign being in the process of eradicating the disease (37). In order to achieve the complete control and eradication of CSFV, the FAO has led the "Continental Plan for the Eradication of CSF in the Americas" which has as a main goal the complete eradication of the virus in the Americas by 2020 (37). However, the last OIE report in 2019 of the presence of CSF in Latin America, shows this disease is present in four countries; Colombia, Brazil, Ecuador and Peru (38). This situation makes it difficult to achieve the CSF eradication for 2020.

The main challenges for fulfilling this goal reside in the difficulty to define signs of clinical CSF, since some of the virus strains that circulates in the Americas seem to have moderate virulence producing subacute or chronic infection. Moreover, the movement of piglets immunotolerant to the CSFV constitute the source of infection for other animals due mainly to those animals do not respond efficaciously to vaccination. However, the efficacy of a live attenuated vaccine in postnatally persistently infected pigs has been proven, enabling a sort of new prevention strategy(39). Finally, stricter border controls in free countries are needed to maintain their status. Practices such as the illegal movement of pigs, the incorporation of new animals without control to other herds, the mismanagement of vaccines and their deficient application, breaches of biosafety, among others, contribute to spread the disease and must be avoided in order to achieve the CSFV eradication in near future (36).

Important re-emerging viruses for companion animals

Canine parvovirus (CPV-2), a Parvoviridae member and Canine morbillivirus (CDV), formerly "Canine distemper virus", which belongs to the *Paramyxoviridae* family, both are the etiological agents of the most infectious diseases affecting domestic dogs. Nowadays CDV is also known as a highly prevalent virus in wildlife, becoming in an important hazard for conservation of endangered species around the world (40). CDV and CPV-2 have high substitution rates, and even though live attenuated vaccines have been used since more than 40 years to control the diseases, those viruses continue causing outbreaks in naïve and even fully vaccinated domestic and wild animals in different areas of the American continent.

The high genome diversity of CPV-2 and CDV in the South American continent has raised an important concern about the role of those viruses in animal health, mainly because outbreaks of clinical disease by CDV and CPV-2 in vaccinated animals and potentially susceptible wildlife are becoming more frequent. In the Americas, it has been reported the circulation of at least, eight CDV genetic lineages, becoming the continent with the higher number of described linages to date. The emergence of new strains could be due to the high genetic diversity of CDV circulating strains, besides the current vaccination failure worldwide (41, 42).

Moreover, the circulation of the three known variants has been described for the CPV-2, and a possible new variant of CPV-2a has recently been reported (43). This wide circulation of different viruses in the region (Table 2), added to the constant international transit of pets could be the reason of the emergence or reemergence of new viral variants that circulate from the south to the northern region of the continent. Those facts lead to the presentation of new endemic cases, which causes economic losses and damages in quality of life of the owners since its constant circulation in 1980's decade in the America and worldwide (44).

| Table 2. | Presence of different antigenic CPV variants |
|----------|--|
| | and CDV lineages by country in America. |

| | 5 , | , |
|---------------------|-----------------------|--|
| Country | CPV detection | CDV lineages |
| Argentina | 2a, 2b, 2c | South America - 2, Europe/South America 1 |
| Uruguay | 2a, 2c | Europe/South America 1 |
| Chile | Serological detection | NR |
| Paraguay | 2c | NR |
| Brazil | 2a, 2b, 2c | South America - 2 |
| Peru | 2a, 2c | NR |
| Ecuador | 2a, 2b, 2c | South America - 4 |
| Bolivia | Serological detection | NR |
| Colombia | 2a, 2b | South America – 3; South America - 4 |
| Nicaragua | Serological detection | NR |
| Galapagos island | Serological detection | NR |
| Cuba | 2 | NR |
| St. Kitts Island | 2a | NR |
| Mexico | 2c | NR |
| USA | 2a, 2b, 2c | North America 1 - 4 |
| Canada | 2a, 2b, 2c | America -2 |
| | | |

NR: Never reported.

Considering that CDV can affect a vast array of species, including domestic and wildlife animals, it has been proposed its potential cross-species transmission to humans, due to appearance of diverse different linages (45). Even though, to date, there is no evidence of human infection by CDV, the virus has been isolated *in vivo* from non-human primates and *in vitro* in human cell lines, highlighting the possibility of a zoonotic jump to humans in the absence of Measles virus immunity (46,47).

Important measures and control must be taken in country borders for pets travelling, in order to prevent the dissemination of viruses from one region to another. Furthermore, it must be ensured endorsed vaccination schemes internationally, applied in different countries where there is pet transit among them (48). In addition, future research may address the dynamics of transmission, evolution and evasion of the immune response by new viral variants in the region should to ensure control on time these agents and reduce the chances of new epidemics.

Emerging And Re-Emerging Zoonotic Viruses

Rabies Virus (RABV). Rabies is a fatal progressive viral encephalomyelitis that affects mammals. It is transmitted to humans through domestic or wild animals through bites or scratches, via saliva (49). It is caused by a Lyssavirus, Family Rhabdoviridae and it is estimated to cause 59.000 human deaths annually worldwide, mostly in Asia and Africa and over 3.7 million disability-adjusted life years (DALYs) lost every year (50). Rabies transmission occurs in two epidemiological forms: a) urban form, with dogs as the main reservoir and transmitter, and b) wildlife form, with bats, foxes, and wolves as main reservoirs and transmitters and cats as just transmitters (51). It is important to mention that although bat rabies in livestock industry has a productive impact, its role in transmitting this zoonosis from cattle to humans is low (52)

Although a reduction of ninety-five percent of the cases of human rabies transmitted by dogs in Latin America has been achieved (53), there are still cases of dog transmitted rabies in only six countries in 2015, and three in 2016 (52). In addition to this scenario, in the last decade, bat rabies has become an important limitation for livestock production and has become the main cause of lethal human rabies outbreaks in the Americas (54, 55) (Table 3). Due to the presence of the virus in bat populations throughout the region, it is important to consider the role of wildlife in the disease control. The main efforts to control RABV have been made at controlling those reservoir species and vaccinating the livestock, considering it as a possible source of spread to humans (56).

To efficiently control the spread of the virus from potential reservoirs (domestic and wild animals) to human populations and susceptible livestock, rabies control strategies must focus on reinforcing the regional programs for vaccinations of domestic animals and understand the role of wildlife in the epidemiology of the disease. The most recent cases of human rabies in the US and Mexico has been associated to wildlife (57), highlighting an urgent need to stablish international standard protocols to control rabies in wildlife and to avoid transmission of wild viral variants from wildlife to humans (58), considering that human activity as deforestation, agriculture, hunting and animla domestication play an important role in the emergence and reemergence of viral pathigens, due to the proximity with animals facilites this potential scenario.

| Country | 2018 | Species |
|---|---------|---|
| Anguila | NI | |
| Antigua and Barbuda | NI | |
| Argentina | Present | Bov, equi, wild |
| Aruba | NI | |
| Bahamas | NI | |
| Barbados | NR | |
| Belize | Present | Bov, equi, sheep, wild |
| Bermudas | NI | |
| Bolivia | Present | Can, fel, bov, equi, lep, goat |
| Brazil | Present | Fel, sheep, sui, bov, buf, can, goat, equi, wild, cml |
| British Virgin Islands | NI | |
| Canada | Present | Wild, can, goat, fel, bov |
| Cayman Islands | NI | , ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, |
| Chile | Present | Wild |
| Colombia | Present | Bov, buf, goat, equi, sheep, sui |
| Costa Rica | Present | Bov, can, equi |
| Cuba | Present | Can, fel, wild |
| Dominica | NI | |
| Dominican Republic | Present | Can, fel, wild, equi |
| Ecuador | Present | Bov, equi, sui |
| El salvador | NI | 201, 644, 64 |
| Falkland Islands (Malvinas) | NR | |
| French Guiana | Present | Bov, buf, can, goat, equi, fel, sheep |
| Grenada | NI | |
| Guadaloupe | NR | |
| Guatemala | NI | |
| Guyana | NI | |
| Haití | Present | Can |
| Honduras | Absent | Cun |
| Jamaica | NR | |
| Martinique | NR | |
| Martinque | Present | Bov, buf, wild, equi, sheep, fel |
| Montserrat | NI | bov, bul, wild, equi, sheep, lei |
| Netherlands Antilles | NI | |
| Nicaragua | Present | Bov, goat, equi, sheep, can, sui, fel |
| 5 | Present | |
| Panama | Present | Bov, buf, can, goat, equi, fel, bovi, sui Can, bovi, equi, sheep, goat, wild |
| Paraguay Perú | Present | Bovi, goat, equi, sheep, sui, buf, can, fel, lep, cml |
| Peru Puerto Rico & US Virgin Islands | NI | Bovi, goat, equi, sneep, sui, bui, can, iei, lep, chii |
| St. Kitts and Nevis | NI | |
| St. Lucía | | |
| | NI | |
| St. Pierre and Miquelón | NI | |
| St. Vincent and the Granadines | NR | |
| buth Georgia and the south Sandwich Islands | NI | |
| Suriname | Absent | |
| Trinidad and Tobago | Absent | |
| Turks and Caicos Islands | NI | |
| US Virgin Islands | NI | |
| United States minor Outlying islands | NI | |
| United States of America | Present | Bov, can, equi, fel, fau |
| Uruguay | Present | Wild |
| Venezuela | Present | Bov, buf, goat, equi, sheep, sui, wild |

Table 3. Rabies circulation status in the Americas by 2018.

NI: No information. NR: Never reported. Bov: Bovine. Equi: Equine. Can: canine. Fel: Feline. Lep: Leporid. Buf: Buffalo. Sui: suine. Cml: Camelidae. Data from WAHIS/OIE.

Venezuelan Equine Encephalitis Virus (VEEV). It is one of the most important veterinary and medically viruses due to its zoonotic potential, which belongs to the Togaviridae Family, which is characterized for transmitting through the bite of infected mosquitoes (59). Currently, there are no licensed human vaccines for the VEEV; however, live attenuated and formalin-inactivated vaccines are currently employed in USA under US Food and Drug Administration (FDA) surveillance developed by the United States Army Medical Research Institute of Infectious Disease (60). VEEV has been associated with equine and human diseases, and it is classified in subtypes: IAB, IC, ID, and IE. IAB and IC viruses include epizootic/epidemic viruses related to equine outbreaks, which result in severe disease in equids and substantial transmission to humans. Subtypes ID and IE encompass enzootic/ endemic viruses that circulates in forests and swamps of northern countries of South America, Central America and Mexico, causing endemic diseases with direct spillover (61).

Enzootic mosquito vectors have been identified for four VEEV variants: i) Culex (Melanoconion) transmits Mucambo (VEE portesi virus complex subtype IIIA) in Trinidad, ii) Culex (Melanoconion) cedecei transmits Everglades virus (VEE complex subtype II) in southern Florida, iii) Culex (Melanoconion) aikeniisensu lato transmits subtype ID VEEV in Panama, and 4) Culex (Melanoconion) taeniopus is the primaryenzootic vector of subtype IE VEEV in Guatemala. These mosquitoes are the principal vectors of most or all enzootic VEE complex strains. However, in Colombia, it has been identified Culex (Melanoconion) vomerifer, pedroi, and adamesi as natural enzootic vectors of subtype ID (62).

The last important VEEV epidemic outbreak in the Americas happened in 1995 in the northern region of Venezuelan and northeastern Colombia producing \approx 75,000–100,000 human cases with \approx 300 deaths and a higher number of equines reported that were infected or dead (63). After a prolonged period of epidemiological inactivity of the VEEV in the region, it is important to explore if these viruses continued being a threat for humans and animals in the Americas (Figure 2).

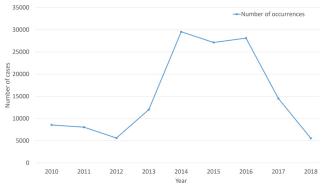


Figure 2. Timeline of VEEV cases reported by the OIE in America between 2010 and 2018. Data form WAHIS/OIE.

Different aspects must be evaluated to understand the possible risk of a new epidemic of VEEV in the Americas. We already know that there has been circulation of VEEV virus in horses, cattle and vectors in Colombia and Venezuela for the last few years (64) Moreover, it has been confirmed the post-epizootic persistence of IAB and IC VEEV viruses in Venezuela (64) and the continuous circulation of endemic ID subtypes in Colombia (65), Bolivia, Ecuador and Peru (61). Furthermore, fatal endemic ID subtype cases has been reported in Panama (66), highlighting the role of endemic VEEV as a significant, but usually neglected arboviral disease the Americas. Thus, it is a necessity to stablish an agenda of priorities to diminish the impact of a possible re-emergence of the VEEV.

Important international efforts must be done to understand the risk of dissemination of VEEV across the continent as seen in the last few years for other arboviral emerging diseases such as West Nile virus. Wide regional epidemiological surveillance studies must be conducted to establish the abundance of VEEV vector populations, serological studies to determine the availability of susceptible nonequine mammals acting as reservoirs and the vaccine coverage in equines as a source of virus amplification for humans. Finally, continuous virologic surveillance must be done to establish the presence of endemic viruses and the emergence of epizootic viral subtypes to set early control measures and international trade restrictions that avoid virus expansion to the region.

This review summarizes the key features, in the epidemiological context, of certain important viral pathogens that affect companion animals, livestock and farm animals in the Americas. Reducing the risk of emergence or re-emergence of animal viruses must be accomplished to keep safe animal and human populations. Measures to control and eradicate zoonotic viral agents are urgent, to safeguard human health, food safety and well-being.

Since, the epidemiological situation of a particular country could potentially affect the entire region, there is a need to implement interregional integrated prevention and control policies in order to ensure animal health and food security of the region.

It is also important to take into account that regional problems demand continental responses reinforcing the inter-institutional cooperation not only at the regional but also at the transnational level to better comprehend the dynamics of transmission and distribution of animal viral diseases. It is necessary to strengthen the role of standardized diagnostic, prevention and control measures for mentioned viral diseases, so all countries talk the same "control and eradiation language". Better understanding and control of relevant viral diseases will improve animal and human health and well-being of our populations.

Conflict of interest

There was no conflict of interest with respect to this manuscript.

Acknowledgements

We would like to thank to Dr. Edward McSweegan from the Global Virus Network and Dr. Mike Bray, editor of Antiviral Research for their helpful corrections. In addition, we would like to thank the Colombian Society for Virology for promote the virology in our country.

REFERENCES

- 1. Walsh F. Human-animal bonds I: the relational significance of companion animals. Fam Process. 2009; 48(4):462-480. <u>https://doi.org/10.1111/j.1545-5300.2009.01296.x</u>
- Christou L. The global burden of bacterial and viral zoonotic infections. Clin Microbiol Infect. 2011; 17(3):326-330. <u>https://doi. org/10.1111/j.1469-0691.2010.03441.x</u>
- Reperant L, Brown I, Haenen O, de Jong M, Osterhaus AD, Papa A, et al. Companion Animals as a Source of Viruses for Human Beings and Food Production Animals. Journal of Comparative Pathology. 2016; 155(1):S41-S53. <u>https://doi.org/10.1016/j.jcpa.2016.07.006</u>
- Ruiz-Saenz J, Goez Y, Tabares W, Lopez-Herrera A. Cellular receptors for foot and mouth disease virus. Intervirology. 2009; 52(4):201-212. <u>https://doi.org/10.1159/000226121</u>

- Robinson L, Knight-Jones TJ, Charleston B, Rodriguez LL, Gay CG, Sumption KJ, et al. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 7 - Pathogenesis and Molecular Biology. Transbound Emerg Dis. 2016; 63(Suppl 1):63-71. <u>https://doi. org/10.1111/tbed.12520</u>
- Clavijo A, Sanchez-Vazquez MJ, Buzanovsky LP, Martini M, Pompei JC, Cosivi O. Current Status and Future Prospects to Achieve Foot-and-Mouth Disease Eradication in South America. Transbound Emerg Dis. 2017; 64(1):31-36. <u>https://doi.org/10.1111/tbed.12345</u>
- Knight-Jones TJ, Robinson L, Charleston B, Rodriguez LL, Gay CG, Sumption KJ, et al. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 1 - Overview of Global Status and Research Needs. Transbound Emerg Dis. 2016; 63(Suppl 1):3-13. <u>https://doi.org/10.1111/</u> tbed.12528

- Knight-Jones TJ, Robinson L, Charleston B, Rodriguez LL, Gay CG, Sumption KJ, et al. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 4 - Diagnostics. Transbound Emerg Dis. 2016; 63(Suppl 1):42-48. <u>https://doi.org/10.1111/ tbed.12523</u>
- Knight-Jones TJ, Robinson L, Charleston B, Rodriguez LL, Gay CG, Sumption KJ, et al. Global Foot-and-Mouth Disease Research Update and Gap Analysis: 2 - Epidemiology, Wildlife and Economics. Transbound Emerg Dis. 2016; 63(Suppl 1):14-29. <u>https://doi. org/10.1111/tbed.12522</u>
- PAHO. Informe de situación de los programas de erradicación de la fiebre aftosa en Sudamérica y Panamá, año 2018. Rio de Janeiro, Brazil: Pan American Health Organization; 2019.
- 11. Prempeh H, Smith R, Muller B. Foot and mouth disease: the human consequences. The health consequences are slight, the economic ones huge. BMJ. 2001; 322(7286):565-566. <u>https://doi.org/10.1136/bmj.322.7286.565</u>
- 12. Maclachlan NJ, Dubovi EJ. Fenner's veterinary virology: Academic press; London, UK; 2010.
- Chan JF, To KK, Chen H, Yuen KY. Crossspecies transmission and emergence of novel viruses from birds. Current Opinion in Virology. 2015; 10:63-69. <u>https://doi. org/10.1016/j.coviro.2015.01.006</u>
- 14. Parrish CR, Murcia PR, Holmes EC. Influenza virus reservoirs and intermediate hosts: dogs, horses, and new possibilities for influenza virus exposure of humans. Journal of Virology. 2015; 89(6):2990-2994. https://doi.org/10.1128/JVI.03146-14
- Tong S, Li Y, Rivailler P, Conrardy C, Castillo DA, Chen LM, et al. A distinct lineage of influenza A virus from bats. Proc Natl Acad Sci U S A. 2012; 109(11):4269-4274. <u>https:// doi.org/10.1073/pnas.1116200109</u>
- Tong S, Zhu X, Li Y, Shi M, Zhang J, Bourgeois M, et al. New world bats harbor diverse influenza A viruses. PLoS Pathog. 2013; 9(10):e1003657. <u>https://doi. org/10.1371/journal.ppat.1003657</u>

- 17. Wille M, Robertson GJ, Whitney H, Ojkic D, Lang AS. Reassortment of American and Eurasian genes in an influenza A virus isolated from a great black-backed gull (Larus marinus), a species demonstrated to move between these regions. Arch Virol. 2011; 156(1):107-115. <u>https://doi.org/10.1007/s00705-010-0839-1</u>
- 18. Alexander DJ. An overview of the epidemiology of avian influenza. Vaccine. 2007; 25(30):5637-5644. <u>https://doi.org/10.1016/j.vaccine.2006.10.051</u>
- 19. Abdelwhab EM, Hafez HM. An overview of the epidemic of highly pathogenic H5N1 avian influenza virus in Egypt: epidemiology and control challenges. Epidemiol Infect. 2011; 139(5):647-657. https://doi.org/10.1017/S0950268810003122
- Setiawaty V, Dharmayanti NL, Misriyah, Pawestri HA, Azhar M, Tallis G, et al. Avian Influenza A(H5N1) Virus Outbreak Investigation: Application of the FAO-OIE-WHO Four-way Linking Framework in Indonesia. Zoonoses and public health; 2014. https://doi.org/10.1111/zph.12158
- 21. WHO. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2019. París: World Health Organization: WHO; 2019. https://www.who.int/influenza/human animal interface/H5N1 cumulative table archives/en/
- 22. Kilbourne ED. Influenza pandemics of the 20th century. Emerg Infect Dis. 2006; 12(1):9-14. <u>https://doi.org/10.3201/</u> <u>eid1201.051254</u>
- 23. de Jong MD, Hien TT. Avian influenza A (H5N1). J Clin Virol. 2006; 35(1):2-13. https://doi.org/10.1016/j.jcv.2005.09.002
- 24. Dawood FS, Iuliano AD, Reed C, Meltzer MI, Shay DK, Cheng PY, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis. 2012; 12(9):687-695. <u>https://</u> doi.org/10.1016/S1473-3099(12)70121-4
- 25. Williams GW, Anderson DP. The Latin American Livestock Industry: Growth and Challenges. Choices. 2020; 34(316-2020-617):1-11. <u>https://www.choicesmagazine.</u> <u>org/choices-magazine/submitted-articles/</u> <u>the-latin-american-livestock-industry-</u> <u>growth-and-challenges</u>

- 26. Marquez MA. Control and prevention of Avian Influenza, a Latin American perspective. AviNews International Magazine. 2020. <u>https://avicultura.info/ en/control-and-prevention-of-avianinfluenza-a-latin-american-perspective/</u>
- Afanador-Villamizar A, Gomez-Romero C, Diaz A, Ruiz-Saenz J. Avian influenza in Latin America: A systematic review of serological and molecular studies from 2000-2015. PLoS One. 2017; 12(6):e0179573. <u>https:// doi.org/10.1371/journal.pone.0179573</u>
- 28. Senne DA. Avian influenza in North and South America, 2002-2005. Avian diseases. 2007; 51(S1):167-173. <u>https:// doi.org/10.1637/7621-042606R1.1</u>
- 29. Suarez DL, Senne DA, Banks J, Brown IH, Essen SC, Lee C-W, et al. Recombination resulting in virulence shift in avian influenza outbreak, Chile. Emerg Infect Dis. 2004; 10(4):693-699. <u>https://dx.doi.</u> org/10.3201%2Feid1004.030396
- 30. OIE. OIE Situation Report for Highly Pathogenic Avian Influenza: World Organisation for Animal Health; 2020. <u>https://www.oie.int/en/animalhealth-in-the-world/update-on-avianinfluenza/2020/</u>
- 31. Mishra A, Vijayakumar P, Raut AA. Emerging avian influenza infections: Current understanding of innate immune response and molecular pathogenesis. Int Rev Immunol. 2017; 36(2):89-107. <u>https://doi.org/10.1080/08830185.2017.</u> 1291640
- Wainwright S, Trevennec C, Claes F, Vargas-Terán M, Martin V, Lubrotha J. Highly pathogenic avian influenza in Mexico (H7N3). Food and Agriculture Organization; 2012. <u>http://www.fao.org/docrep/016/ an395e/an395e.pdf</u>
- Beldomenico PM, Uhart M. Ecoepidemiología de los virus de influenza aviar. FAVE Sección Ciencias Veterinarias. 2008; 7(1/2):23-40. <u>https://doi.org/10.14409/favecv.v7i1/2</u>
- 34. Pepin KM, Spackman E, Brown JD, Pabilonia KL, Garber LP, Weaver JT, Riley S. Using quantitative disease dynamics as a tool for guiding response to avian influenza in poultry in the United States of America. Prev Vet Med. 2014; 113(4):376-397. <u>https://dx.doi.org/10.1016%2Fj. prevetmed.2013.11.011</u>

- 35. Kleiboeker SB. Swine fever: classical swine fever and African swine fever. Vet Clin North Am Food Anim Pract. 2002; 18(3):431-451. <u>https://doi.org/10.1016/</u> <u>s0749-0720(02)00028-2</u>
- 36. Blome S, Staubach C, Henke J, Carlson J, Beer M. Classical Swine Fever-An Updated Review. Viruses. 2017; 9(4):86. <u>https:// doi.org/10.3390/v9040086</u>
- 37. Vargas Teran M, Calcagno Ferrat N, Lubroth J. Situation of classical swine fever and the epidemiologic and ecologic aspects affecting its distribution in the American continent. Ann N Y Acad Sci. 2004; 1026:54-64. <u>https://doi.org/10.1196/annals.1307.007</u>
- 38. OIE. OIE Official disease status Classical Swine Fever. World Organisation for Animal Health; 2020. <u>https://www.oie.</u> <u>int/en/animal-health-in-the-world/officialdisease-status/</u>
- Munoz-Gonzalez S, Perez-Simo M, Munoz M, Bohorquez JA, Rosell R, Summerfield A, et al. Efficacy of a live attenuated vaccine in classical swine fever virus postnatally persistently infected pigs. Vet Res. 2015; 46:78. <u>https://doi.org/10.1186/s13567-015-0209-9</u>
- 40. Martinez-Gutierrez M, Ruiz-Saenz J. Diversity of susceptible hosts in canine distemper virus infection: a systematic review and data synthesis. BMC Vet Res. 2016; 12:78. <u>https://doi.org/10.1186/</u> <u>s12917-016-0702-z</u>
- 41. Espinal MA, Diaz FJ, Ruiz-Saenz J. Phylogenetic evidence of a new canine distemper virus lineage among dogs in Colombia, domestic South America. Vet Microbiol. 2014; 172(1-2):168-176. https://doi.org/10.1016/j. vetmic.2014.05.019
- 42. Duque-Valencia J, Diaz FJ, Ruiz-Saenz J. Phylogenomic Analysis of Two Co-Circulating Canine Distemper Virus Lineages in Colombia. Pathogens. 2020; 9(1):26. <u>https://doi.org/10.3390/</u> pathogens9010026
- 43. Duque-Garcia Y, Echeverri-Zuluaga M, Trejos-Suarez J, Ruiz-Saenz J. Prevalence and molecular epidemiology of Canine parvovirus 2 in diarrheic dogs in Colombia, South America: A possible new CPV-2a is emerging? Vet Microbiol. 2017;201:56-61. <u>https://doi.org/10.1016/j.vetmic.2016.12.039</u>

- 44. Zhou P, Zeng W, Zhang X, Li S. The genetic evolution of canine parvovirus
 A new perspective. PLoS One. 2017; 12(3):e0175035. <u>https://doi.org/10.1371/journal.pone.0175035</u>
- 45. Rendon-Marin S, da Fontoura Budaszewski R, Canal CW, Ruiz-Saenz J. Tropism and molecular pathogenesis of canine distemper virus. Virol J. 2019; 16(1):30. <u>https://doi. org/10.1186/s12985-019-1136-6</u>
- 46. Otsuki N, Nakatsu Y, Kubota T, Sekizuka T, Seki F, Sakai K, et al. The V protein of canine distemper virus is required for virus replication in human epithelial cells. PloS one. 2013; 8(12):e82343. <u>https://doi.org/10.1371/journal.pone.0082343</u>
- 47. Quintero-Gil C, Rendon-Marin S, Martinez-Gutierrez M, Ruiz-Saenz J. Origin of Canine Distemper Virus: Consolidating Evidence to Understand Potential Zoonoses. Front Microbiol. 2019; 10:1982. <u>https://doi.org/10.3389/fmicb.2019.01982</u>
- 48. Day MJ, Horzinek MC, Schultz RD, Squires RA, Vaccination Guidelines Group of the World Small Animal Veterinary A. WSAVA Guidelines for the vaccination of dogs and cats. J Small Anim Pract. 2016; 57(1):E1-E45. <u>https://doi.org/10.1111/jsap.2_12431</u>
- 49. WHO. WHO Expert Consultation on Rabies: second report: World Health Organization; Geneva, Switzerland. 2013. <u>https://apps.</u> who.int/iris/handle/10665/85346
- 50. WHO. WHO Expert Consultation on Rabies: Third report: World Health Organization; Geneva, Switzerland. 2018. <u>https://apps.who.int/iris/handle/10665/272364</u>
- 51. Páez A, Hernández C, Escobar H, Zapata JJ, Méndez J, Rey-Benito G. Evaluación de la seroconversión como respuesta a la vacunación antirrabica en perros en el departamento del Valle del Cauca, Colombia, 2009. Biomédica: Revista del Instituto Nacional de Salud. 2011; 31(4):474-484. <u>https://doi.org/10.7705/ biomedica.v31i4.395</u>
- 52. Del Rio Vilas VJ, Freire de Carvalho MJ, Vigilato MA, Rocha F, Vokaty A, Pompei JA, et al. Tribulations of the Last Mile: Sides from a Regional Program. Front Vet Sci. 2017; 4:4. <u>https://doi.org/10.3389/</u> <u>fvets.2017.00004</u>

- 53. Freire de Carvalho M, Vigilato MAN, Pompei JA, Rocha F, Vokaty A, Molina-Flores B, et al. Rabies in the Americas: 1998-2014. PLoS Negl Trop Dis. 2018; 12(3):e0006271. <u>https://doi.org/10.1371/</u> journal.pntd.0006271
- 54. Escobar LE, Peterson AT, Favi M, Yung V, Medina-Vogel G. Bat-borne rabies in Latin America. Rev Inst Med Trop Sao Paulo. 2015; 57(1):63-72. <u>https://doi.org/10.1590/S0036-46652015000100009</u>
- 55. Streicker DG, Winternitz JC, Satterfield DA, Condori-Condori RE, Broos A, Tello C, et al. Host-pathogen evolutionary signatures reveal dynamics and future invasions of vampire bat rabies. Proc Natl Acad Sci U S A. 2016; 113(39):10926-109231. <u>https:// doi.org/10.1073/pnas.1606587113</u>
- 56. Johnson N, Montano Hirose JA. The impact of paralytic bovine rabies transmitted by vampire bats in Latin America and the Caribbean. Rev Sci Tech. 2018; 37(2):451-459. <u>https://doi.org/10.20506/</u> rst.37.2.2814
- 57. Birhane MG, Cleaton JM, Monroe BP, Wadhwa A, Orciari LA, Yager P, et al. Rabies surveillance in the United States during 2015. J Am Vet Med Assoc. 2017; 250(10):1117-1130. <u>https://doi. org/10.2460/javma.250.10.1117</u>
- 58. Favoretto SR, de Mattos CC, de Mattos CA, Campos AC, Sacramento DR, Durigon EL. The emergence of wildlife species as a source of human rabies infection in Brazil. Epidemiol Infect. 2013; 141(7):1552-1561. <u>https://doi.org/10.1017/</u> S0950268813000198
- 59. Arechiga-Ceballos N, Aguilar-Setien A. Alphaviral equine encephalomyelitis (Eastern, Western and Venezuelan). Rev Sci Tech. 2015; 34(2):491-501. <u>https:// doi.org/10.20506/rst.34.2.2374</u>
- 60. Dupuy LC, Richards MJ, Livingston BD, Hannaman D, Schmaljohn CS. A Multiagent Alphavirus DNA Vaccine Delivered by Intramuscular Electroporation Elicits Robust and Durable Virus-Specific Immune Responses in Mice and Rabbits and Completely Protects Mice against Lethal Venezuelan, Western, and Eastern Equine Encephalitis Virus Aerosol Challenges. J Immunol Res. 2018; 2018:8521060. https://doi.org/10.1155/2018/8521060

- 61. Aguilar PV, Adams AP, Suarez V, Beingolea L, Vargas J, Manock S, et al. Genetic characterization of Venezuelan equine encephalitis virus from Bolivia, Ecuador and Peru: identification of a new subtype ID lineage. PLoS Negl Trop Dis. 2009; 3(9):e514. <u>https://doi.org/10.1371/</u> journal.pntd.0000514
- 62. Ferro C, Boshell J, Moncayo AC, Gonzalez M, Ahumada ML, Kang W, et al. Natural enzootic vectors of Venezuelan equine encephalitis virus, Magdalena Valley, Colombia. Emerg Infect Dis. 2003; 9(1):49-54. <u>https://doi.org/10.3201/eid0901.020136</u>
- 63. Weaver SC, Ferro C, Barrera R, Boshell J, Navarro JC. Venezuelan equine encephalitis. Annu Rev Entomol. 2004; 49:141-174. <u>https://doi.org/10.1146/annurev.ento.49.061802.123422</u>

- 64. Navarro JC, Medina G, Vasquez C, Coffey LL, Wang E, Suarez A, et al. Postepizootic persistence of Venezuelan equine encephalitis virus, Venezuela. Emerg Infect Dis. 2005; 11(12):1907-1915. <u>https://doi.org/10.3201/eid1112.050533</u>
- 65. Ferro C, De las Salas J, González M, Díaz A, Cabrera C, Flórez Z, et al. Do some conditions contribute to the reemergence of the Venezuelan equine encephalitis virus in the Colombian Alta Guajira? Biomédica. 2015; 35(1):62-72. <u>http://doi.org/10.7705/biomedica.v35i1.2212</u>
- 66. Quiroz E, Aguilar PV, Cisneros J, Tesh RB, Weaver SC. Venezuelan equine encephalitis in Panama: fatal endemic disease and genetic diversity of etiologic viral strains. PLoS Negl Trop Dis. 2009; 3(6):e472. <u>https://doi.org/10.1371/</u> journal.pntd.0000472