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Viral zoonotic diseases of horses

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Abstract

This literature review provides a comprehensive overview and analysis of the epidemiology of equine zoonotic viruses. It focuses on the critical question of which viruses have and will continue to play significant roles in the relationship between humans and equids due to current trends such as globalization and climate change. To accomplish this, an extensive review of scientific papers and books, as well as general supporting reports, spanning from 1978 to 2023, was done. This work comprises a literature review, an analysis of the current field, a discussion, and a conclusion.

List of Abbreviations

BFV Barmah Forest Virus

BoDV Borna Disease Virus

CFT Complement fixation test

COCV Cocal Virus

CSF cerebrospinal fluid

DNA Deoxyribonucleic acid

EEEV Eastern Equine Encephalitis Virus

EIV Equine Influenza Virus

ELISA Enzyme-linked Immunosorbent Assay

EqPPV Equine Parapoxvirus

ERAV Equine Rhinitis A Virus

ERBV Equine Rhinitis B Virus

ERV Equine Rhinitis Virus

FAT Fluorescence Antibody test

FMD Foot-and-Mouth disease

GETV Getah Virus

HeV Hendra Virus

HEV Hepatitis E Virus

HI Hemagglutination inhibition

HJV Highlands J Virus

IHC Immunohistochemistry

ILHV Ilheus Virus

IND Vesicular Stomatitis Indiana Virus

JEV Japanese Encephalitis Virus

LIV Louping Ill Virus

MADV Madariaga virus

MIDV Middleburg Virus

MVEV Murray Valley Virus

NiV Nipah Virus

NJ Vesicular Stomatitis New Jersey Virus

PBV Picobirnavirus

PCR Polymerase chain reaction

POWV Powassan Virus

PPV Parapoxvirus

PRNT Plaque reduction neutralization test

RABV Rabies Virus

RNA Ribonucleic acid

RRV Ross River Virus

RT-PCR reverse transcriptase Polymerase chain reaction

rtRT-PCR real-time RT-PCR

SINV Sindbis Virus

SLEV St. Louis Encephalitis Virus

SVD Swine Vesicular disease

TBEV Tick-borne Encephalitis Virus

USUV Usutu Virus

VACV Vaccinia Virus

VEEV Venezuelan Equine Encephalitis Virus

VN Virus neutralization tes

VSIV Vesicular Stomatitis Indiana Virus

VSV Vesicular Stomatitis Virus

WEEV Western Equine Encephalitis Virus

WNV West Nile Virus

1. Introduction

Since the onset of the 2019 Coronavirus pandemic, there has been an unprecedented rise in interest and research focused on the study of viruses. Especially the interest in zoonotic agents has increased. This heightened awareness comes from the realization that factors such as climate change, globalization, and the rapid adaptability of viruses have led to shifts in their distribution and the emergence of new viruses. The close contact between humans and animals elevates the importance of understanding and managing zoonotic diseases through a One Health perspective [1].

The primary objective of this literature review is to get an overview and focus on the epidemiology of equine zoonotic viruses. It is intended to address the question of which viruses already have and will play a significant role in the relationship between humans and equids as a result of current trends like globalization and climate change, which have changed the viral dynamics.

This thesis is based on reports and scientific papers available from 1978 to 2023. The listing of the viruses follows the order established by the International Committee on Taxonomy of Viruses as of November 2023.

The literature review will serve as the foundation of the later conducted analysis. It will include the epidemiological context of equine zoonotic viruses and the most important clinical signs. The analysis will be a comprehensive assessment of the present landscape, focusing on the current continental distribution of equine zoonotic viruses. The discussion will merge with the analysis of the findings, focusing on the current situation and a short prospect for the future. Finally, a conclusion is drawn.

By having a better understanding and broadening our knowledge in this field, effective strategies can be developed for the future on how to prevent and intervene in prospective future epidemics.

2. The Viruses

In the following section, a broad overview of the epidemiology of equine zoonotic viruses is given. In many cases, clinical signs and further important topics are being discussed.

2.1 Hepeviridae

The family *Hepeviridae* consists of two general *Orthohepevirus* and *Piscihepevirus*. *Piscihepevirus* natural hosts are fish. The viruses have a positive single-stranded RNA without an envelope. *Orthohepeviruses* are further divided into four species, *Orthohepevirus* A-D, the natural hosts are birds and mammals including humans [2].
Avihepevirus infects birds, *Chirohepevirus* bats, *Rocahepevirus* rats, and carnivores, and *Paslahepevirus* infects humans and other mammals. *Paslahepevirus* is further divided into Hepatitis E virus (HEV) from 1 to 8. 1 and 2 only infect humans, 3 and 4 are zoonotic and have a broad host range including horses and pigs, 5 and 6 only infect wild boar in Japan, 7 and 8 infect camels with one reported spillover to humans from HEV-7 [3].

2.1.1 Hepatitis E Virus

Worldwide, the Hepatitis E virus (HEV) is a major cause of viral hepatitis in humans. HEV belongs to the genus *Orthophepevirus* within the family of *Hepeviridae* [2]. First discovered in 1983, pigs and rodents are now known to be the primary reservoir for HEV [3, 4]. The infection mostly happens through the fecal-oral route but contact with reservoir hosts or infected people and ingestion of raw or undercooked meat and shellfish can cause disease in humans and other animals [3, 4].
Already known to be a human pathogen, spillovers to equids have been reported. Several studies have shown antibodies in horses in Egypt, Korea, Spain, or Bulgaria [3–6], with racehorses having an increased risk [4]. It is thought that exposure to reservoir hosts like rats can increase the risk of being infected. Since only antibodies and no current infection have been proven, it is not possible to report any clinical signs in horses. In humans, infection can be asymptomatic or cause hepatitis with clinical signs like fever, myalgia, nausea and

jaundice [7]. The detection of HEV or antibodies can be done with PCR and ELISA [4]. Since 2012, a vaccine has been licensed in China, this vaccine is so far the only vaccine on the market [2].

2.2 Togaviridae

Togaviridae are enveloped viruses with a positive-sense single-stranded RNA and icosahedral symmetry [8]. The envelope has glycoprotein spikes for the attachment in the host cell that is responsible for the agglutinating properties in duck and chicken erythrocytes. The viruses are sensitive to pH changes, detergents, and disinfectants but can also be inactivated by heat or organic solvents.

The family of *Togaviridae* consists of the *Alphavirus* genus. The *Alphavirus* genus has over 25 different species with important animal and zoonotic pathogens. Based on genomic composition, antigenically related groups can be identified like the Venezuelan equine encephalitis virus complex, the Eastern equine encephalitis virus complex, or the Western equine encephalitis complex as well as the Semliki Forest virus complex or Middleburg virus complex. These viruses have cytolytic properties in vertebrate hosts, that can act as amplifying, reservoir, or dead-end hosts, and non-cytolytic in invertebrate, vectoring hosts. This property is important since *Alphaviruses* are arthropod-borne viruses, they primarily infect and are being transmitted by mosquitoes [9]. Furthermore, the *Alphavirus* genus can be divided into New-World viruses, causing neurological symptoms, and Old-World viruses, causing arthralgia and fever [10].

2.2.1 Eastern Equine Encephalitis Virus Complex

The Eastern equine encephalitis complex is composed of several strains and occurs in North and South America. The following section includes viruses belonging to that complex.

2.2.1.1 Eastern Equine Encephalitis Virus

The Eastern equine encephalitis virus (EEEV) occurs in the western hemisphere, mainly in the Atlantic coastal area of North America as well as in Michigan, near the Canadian border, the Caribbean Islands, and South America [9].-Formerly, the North (Group I) and the South American viruses (Group II, III, IV) were thought to have two different lines and therefore differences in antigens and genetics. Recently, groups II, III, and IV were identified as separate species. This new virus strain, named Madriaga virus, infects humans less frequently and is less virulent [9, 11].

The EEEV is an arbovirus, transmitted by mosquitoes (*Culiseta melanura, Aedes spp., Coquillettidia perturbans*), but also chicken lice and chicken mites of the *Dermanyssus* genus and assassin bugs can be infected [11]. Passerine birds and other wild birds that frequent freshwater swamps in eastern North America, Caribbean islands and parts of South America are endemically infected and are a constant reservoir for mosquitoes, but also rodents are thought to be a reservoir. Within a tight population, for example in captivated birds like pheasants, infection by oral route has been proven [11]. Infected equids and humans are mostly dead-end hosts; however, some horses reached a high enough viremic titer to infect mosquitoes, and horse-to-horse transmission was shown in laboratory conditions. It is possible for the virus to also infect domesticated ruminants, companion animals, rodents, bats, reptiles and amphibians [11]. Despite this, caution should be paid during post-mortem examination and handling of bigger amounts of blood or cerebrospinal fluids as this way of getting infected cannot be ruled out [12]. Because the EEEV is an arbovirus transmitted through mosquitoes, an increase in infections follows high humidity and heavy rainfalls in the late summer. On the other hand, if it is very dry or very cold and the vectors cannot multiply, a decrease in infections is seen [9].

If infected, the virus will replicate in the nearest lymph nodes to the entry site and cause viremia in different ranges along with fever. In severe cases, the virus enters the central nervous system and necrotizes the neurons as well as causing perivascular lymphoid cuffing. The incubation period is between 5 to 14 days and clinical signs appear for 4 to 9 days [11]. The clinical signs can be mild fever and depression as well as colic-like symptoms, fatal febrile encephalomyelitis accompanied by photophobia, blindness, head pressing, circling, ataxia and inability to swallow. In horses with severe depression, a wide stance and low head can be observed. Recumbency and convulsions can be seen before death. The fatality rate

lies at 90% [9]. In the postmortem examination, congestion of the brain and meninges can be seen along with severe inflammation of the grey matter, neuronal degeneration and hemorrhages in the brain [11].

An EEEV infection can only be diagnosed clearly with a laboratory exam, however, previous regional cases and the clinical signs can be indicative. The antibodies can be demonstrated with Enzyme-linked Immunosorbent Assay (ELISA), Plaque reduction neutralization test (PRNT), Hemagglutination inhibition (HI) and complement fixation test (CFT). After the death of the animal, the virus can be detected from the brain and sometimes from the liver and spleen and can be propagated in cell lines from vertebrates or mosquitoes. Furthermore, Immunohistochemistry (IHC) and reverse transcriptase polymerase chain reaction (RT-PCR) can be used for the demonstration. The differentiation between the EEEV and the Madriaga virus is difficult and cannot be done in a common laboratory [11]. For the prevention of the disease, it is important to mention that inactivated whole virus vaccines are available [13], and measures to reduce the mosquito population must be taken [9].

2.2.1.2 Madariaga Virus

The Madariaga virus (MADV) belongs to the eastern equine encephalitis virus complex and occurs in Central and South America, mostly near the Gulf Coast. The virus is suspected to be less virulent than EEEV but can still cause severe illness. In an epidemic between 2007 and 2008 in Brazil, over 200 horses were affected with a fatality rate of 73%. The clinical signs in horses are similar to an infection with EEEV. In humans, rash, fever, conjunctivitis and central nervous symptoms can be observed [14, 15]. *Culex* spp. seems to be the primary vector for MADV, and small mammals might play a role as reservoirs, making up a sylvatic cycle. But like EEEV, other arthropod vectors, and birds as reservoirs cannot be excluded [14]. Also, antibodies of MADV have been found in bats and lizards in Panama [15]. Humans and equids but also other mammals can get infected. The differentiation between EEEV and Madariaga virus is based on special diagnostic tests that cannot be performed in basic laboratories [11]. Further investigations must be made to build a clearer picture of this virus.

2.2.2 Venezuelan Equine Encephalitis Complex

The Venezuelan equine encephalitis complex has several strains, endemic and epidemic, and occurs primarily in South America.

2.2.2.1 Venezuelan Equine Encephalitis Virus

The Venezuelan equine encephalitis virus (VEEV) is found in Central and South America and is the cause of major illness and encephalitis outbreaks in equids and humans in 10-to-20-year intervals [9]. The virus builds a complex and has 6 subtypes (I-VI). Subtype I is divided into five further antigenic variants which are designated from AB-F. Different subtypes are named differently: Mosso das Pedras virus (I-F), Everglades virus (II), Mucambo virus (III-A, III-C, III-D), Tonate virus (III-B), Pixuna virus (IV), Cabassou virus (V) and Rio Negro virus (VI) [11]. Within these subtypes, enzootic and epizootic subtypes could be identified. I-AB and I-C are epizootic and highly virulent, leaving the other subtypes in the group of the enzootic types. The enzootic strains are normally not pathogenic for equids, only produce a low viremia titer, and are restricted to a geographic area. However, in an outbreak in Mexico in the 1990s, the enzootic subtype I-E was responsible for severe neurological symptoms in horses. The epidemic strains only cause sporadic but significant outbreaks affecting equids and humans [9, 11].

The epizootic subtypes are suspected to be mutated enzootic strains with a significant increase in infectivity for mosquitoes as well as causing an increased titer of viremia in equids. This increase in titer leads equids to act as amplifying hosts and the possibility to infect mosquitoes feeding on them is increased [9, 13].

From 1962 to 1972, frequent epizootic outbreaks occurred in South and Central America. It is assumed, that these outbreaks happened after vaccination with formalin-inactivated whole virus vaccines, in which the viruses were not completely inactivated [9].

The VEEV is being maintained by a sylvatic rodent-mosquito-rodent cycle, mainly by *Culex* spp. mosquitoes in swampy regions [9]. But also, *Aedes, Anopheles, Mansonia, Psorophora* and *Deinocerites* of the family *Culicidae* can transmit the virus, and mites and blackflies can play a role in mechanical transmission. Additionally, ticks like *Amblyomma cajennense* and *Hyalomma truncatum* have been identified to carry enzootic and epizootic strains. In

epidemics in equids, the virus can be shed in body fluids, posing a risk to the handler and animals with close contact possibilities, although no horse-to-human or horse-to-horse transmission has been described. Humans have been infected under laboratory conditions in accidents or after handling laboratory animals infected with VEEV. Also, no human-to-human transmission was reported, but the possibility stays open since the virus was found in pharyngeal secrets in infected personnel. Also, vertical infection in humans is possible [11]. The usual reservoirs are wild rodents, but pet rodents and laboratory animals are susceptible, along with companion animals and bats. In enzootic strains, no cases of illness are reported. Differently in epizootic strains, where an infection in wild and pet rodents can cause severe disease and they do not have a reservoir function. Humans, sometimes swine, cattle, and dogs, reach sufficient viremia to infect mosquitoes. Livestock, companion animals, and some birds mostly have a subclinical course if infected [11].

The clinical signs in epidemic strains show after an incubation period of up to 9 days, with neurological symptoms mostly starting around day 5 [9, 11]. Viremia, fever, tachycardia, anorexia and depression can be followed by more severe signs and the invasion of the central nervous system with the possibility of fatal encephalomyelitis. The signs can be photophobia, blindness, head pressing, inability to swallow, ataxia, recumbency, coma, convulsions and death. Also, colic-like signs can be possible or even sudden death [9]. The endemic strains often go unnoticed with a subclinical course or only mild signs, the outbreak in Mexico with encephalitis and high mortality (30-50%) being the only exemption [11]. The prognosis after infection is poor, the fatality rate lies between 50-80%, depending on the virulence of the infective strain. In the postmortem examination, hemorrhages, lymphoid cuffing, neuronal necrosis, necrotic foci in the pancreas, liver and heart, along with severe inflammation of grey matter and neuron degeneration have been described [9]. But also, no lesions in the central nervous system are possible [11].

Humans can also show diverse but milder signs, mostly flu-like with fever, malaise, headache and myalgia, as well as nausea with vomitus and diarrhea are reported. Rarely, an infection can result in encephalitis and death. The possibility of the virus crossing the placenta can result in fetal encephalitis, damage of the placenta, abortion, or fetal congenital anomalies [11].

The VEEV can be isolated from whole blood or serum in the viremic phase of the infection, but mostly brain or cerebrospinal fluid from deceased animals is used. For RT-PCR, immunofluorescence (IF) or PRNT, tissues of the affected animals or mosquitoes can be

used. For serology, virus neutralization (VN) can be done by PRNT as well as ELISA, CFT or HI. Problematic for the differentiation is the occurrence of antibodies from vaccines and cross-reactions from enzootic VEEV strains [11]. The differentiation between pathogenic and non-pathogenic strains happens based on the use of monoclonal antibodies or nucleic acid sequencing [9].
Unfortunately, only symptomatic treatment is possible but inactivated whole virus vaccines are available [11, 13]. It is important for humans and animals to be protected from mosquitoes and to reduce their population with adequate measures [9].

2.2.3 Western Equine Encephalitis Virus Complex

In North and South America and Africa, the Eastern equine encephalitis complex occurs. The following section includes viruses belonging to that complex.

2.2.3.1 Western Equine Encephalitis Virus

The Western equine encephalitis virus (WEEV) occurs in the western hemisphere, like the Eastern equine encephalitis virus. Originally it was more common in the USA, on the western side of the Mississippi, but has now spread to more parts of North America as well as northern parts of South America, Mexico and to Canada. It is suspected that the virus is a recombination of the eastern equine encephalitis virus and the Sindbis-like virus and started to occur around 1 300-1 900 years ago [9]. Proven outbreaks have been recorded since 1847. Larger ones were in 1930 (about 6,000 equine and mules in California), 1937 and 1938 (264 000 equids in the USA and Canada), 1941 (300 000 equids and 3 336 humans infected in the USA and Canada), and after that a decline could be seen. In the 1970s, 209 human cases have been recorded, followed by 87 in the 1980s. After that, in the 1990s, 4 cases in humans, and since 1998 no more cases have been reported. Also, the virus has not been found in a larger population of mosquitoes in the United States since 2008. However, cases from Central and Southern America have been reported, with the last outbreak in Brazil in 2007 and serological investigation that demonstrated a low prevalence of the virus in countries like Brazil, Uruguay, Costa Rica, and Bolivia [13]. The decline in infections is being brought

in connection with changes in selective pressure that altered the course of WEEV evolution with a different serotype becoming more prominent as well as changes in the fitness, circulation, and virulence of the virus [13, 16].

The WEEV is mostly transmitted by *Culex tarsalis,* other *Culex spp.,* and *Aedes spp.* which infect passerine birds, that are widespread on the American continent, and which are a constant reservoir for the virus. The Blacktail Jackrabbit is also suspected to be a possible reservoir for the virus along with reptiles in the wintertime. The probability of a sylvatic cycle between these rabbits and *Aedes* mosquitoes has been reported [11]. For horses and humans being dead-end hosts, it is quite uncommon to have a high enough viremic titers to be infectious to mosquitoes. Further susceptible animals are emus, turkeys, and pheasants, where clinical signs can also occur. Receptive are also cattle, rodents, hares, snails, tortoises, and frogs [11]. Rarely, epizootic strains occur, and these are mostly mutated enzootic strains [9].

The incubation period is between 5 to 14 days and of sudden onset with no specific signs in humans [11]. Fever, headache, nausea, vomiting, anorexia and signs of meningeal irritation can be seen. In severe cases, patients will develop stiffness of the neck, confusion, seizures, somnolence and coma, followed by death. The fatality for human infection lies at 5 to 15%. The virus can cross the placenta and infect fetuses. In horses, fever, inappetence, and lethargy can be observed, followed by excitation and drowsiness stages which go into paresis, seizures and coma within 5 to 10 days in the course of the infection. Colic-like symptoms have also been reported. The mortality rate is between 20 and 30%. Like WEEV, the postmortem lesions are congestion of the brain and meninges, severe inflammation of the grey matter, neuronal degeneration and hemorrhages [9, 11].

Infections are suspected to be milder than infections with the EEEV in horses and humans. After infection through a bite by a mosquito, the virus will spread from the site of entry to the nearest lymph node, multiply, and cause viremia. As mentioned, an infection will be milder, meaning that an exceptionally low percentage of people will develop neurological symptoms. Mostly young or old patients develop encephalitis, which might be fatal or cause permanent brain damage [9].

Infections with WEEV can be diagnosed with the detection of the virus. Only for a brief time the virus is found in the blood, so it is recommended to use the brain for virus detection in case of death. Rarely, the virus can also be found in the liver or spleen. Virus isolation is infrequently successful in western equine encephalitis viruses, therefore IHC and RT-PCR

are recommended. The virus isolation can be done in vertebrate and mosquito cell lines. In the living animal, a previous infection can be identified with the ELISA test, PRNT, HI or CFT [11]. The treatment in case of an infection can only be supportive; however, inactivated whole virus vaccinations are available to prevent a fatal outcome [13] and it is highly encouraged to vaccinate horses in affected areas with the start of the arbovirus season [9].

2.2.3.2. Highlands J virus

In the eastern part of North America, the Highlands J virus (HJV) was found and it belongs to the Western equine encephalitis complex [9]. First isolated in Florida in 1960 and thought to be an eastern variant of WEEV, four different lineages have now been identified. Lineage 1 is the least infective, and 2 and 4 have higher infection rates [17]. HJV, mainly being an avian pathogen, infects wild birds and is amplified in them. Although, rare infections of horses and humans have been reported [11, 18]. Vectored by *Culiseta melanura* [11, 17], but also by other mosquitoes like *Aedes*, *Culiseta* and *Culex*, sporadic cases of encephalitis in horses can be attributed to this virus [9, 11]. Further investigations have to be done because serious zoonotic potential exists.

2.2.3.3 Sindbis Virus

Like HJV, Sindbis virus (SINV) belongs to the WEEV complex and is associated with acute or fatal neurological disease in equids and wildlife in South Africa [10, 19]. The virus was first isolated in 1952 in *Culex univitattus* in Africa but is now found in Eurasia, Africa, and Australia [10]. Studies have shown that the virus has become endemic in Northern Europe. The SINV is suspected of having migrated with birds to Europe in the 1920s [19]. The virus has 6 genotypes, with SINV-1 being the most prevalent one and causing disease in humans in Africa, Finland, and Sweden. SINV II and SINV VI neutralizing antibodies have been found in equids in Australia and neutralizing antibodies of SINV V in New Zealand [19]. *Culex* spp. are suspected to be transmitting the disease and passerine birds are thought to be the natural and amplifying host for the virus [10]. Normally, mosquito-borne viruses show

seasonality (late summer to late fall), but in this case, the seasonality is questionable [10]. The virus was identified in nestlings in early summer [19].
The disease can cause fever and arthritis, lasting from weeks to years in humans [19]. Further symptoms are rashes, myalgia and fatigue [10]. In horses, SINV can be asymptomatic or cause febrile illness, with or without neurological signs, accompanied by colic signs, dysphagia, recumbency, muscle weakness, depression, icterus, nasal discharge and possible death [19]. Neurological symptoms may include circling or paddling, facial nerve paralysis, seizures, and tongue paralysis [10].

2.2.4 Semliki Forest Virus Complex

The below-mentioned viruses primarily appear in Asia, Australia, and Europe and form the Semliki Forest Virus Complex.

2.2.4.1 Getah Virus

In 1955, the Getah virus (GETV) was isolated for the first time from *Culex* mosquitoes in Malaysia [8]. Since the first isolation, further investigations have shown that the GETV is found in Eurasia and Australasia and keeps geographically expanding [20, 21]. The virus moved from rather tropical regions into temperate or even cold regions. Four diverse groups have been identified with over 170 different strains [8]. The strain causing the first outbreak belongs to Group I. Group III nowadays has the most different strains with the most diversity in hosts and vectors and will probably stay predominant [21]. The GETV belongs to the Semliki Forest virus complex.
Mosquitoes of the Culicidae family like *Aedes, Culex, Anopheles,* and *Mansonia* can transmit the virus but midges in Eurasia have been found to be an appropriate vector. The prevalence of different mosquitoes in different geographic regions plays a role in the detection of the virus in these insects. For example, *Culex* spp. is the most important vector in southern regions, and *Aedes* spp. in eastern Japan and Russia [20]. Depending on the season, an increased number of cases occurs. In the summer and autumn time, most mosquitoes are active in high numbers [20]. Different mammals like equids, swine, and

cattle but also rodents and lagomorphs can get infected, and even act as amplifying hosts, but in most cases, the infection stays subclinical. Antibodies of GETV have been found in humans, monkeys, equids, cattle, swine, domesticated birds and other mammals like foxes, pandas and kangaroos. In wild birds and reptiles, antibodies have also been found, but less frequent [8, 20, 21]. Investigations of swine showed a rather high prevalence of antibodies with occasional cases of abortion. The GETV is thought to be mostly pathogenic for pregnant sows and a subclinical course is to be expected in other swine [20].

The first outbreak in horses was reported in 1978 in Japan when racehorses showed signs of infection with clinical signs like fever, urticarial rash, lymphadenitis, and edema on the hindlimbs. The diseased animals recovered within a rather brief time without fatalities [21]. To this date, six major outbreaks in horses have been reported. The first one was in 1978 as stated and later five more in Japan in 1979,1983,2014 and 2015, one outbreak was in India in 1990 [8]. In later experimental inoculation of horses, further symptoms could be identified as well as the possibility of transmission with aerosols [20]. Nasal discharge and in more virulent strains, swelling of the submandibular lymph nodes was demonstrated along with mild icterus, stiff gait, abdominal pain, and scrotal edema. The postmortem lesions could only be examined after euthanasia of some of the experimental infected horses. Lesions were enlarged lymph nodes in the entire body with lymphoid follicular hyperplasia, enlargement of the spleen and liver, glomerular congestion in the kidneys, congestion and swelling of the pia mater, edematous subcutaneous tissue, and thickened blood vessels as well as hemorrhagic foci [20].

Although no cases linked to GETV in humans have been described, serological investigations in Asia and Australia of fever and healthy patients demonstrated the existence of antibodies. Professional personnel working closely with livestock are at risk for infection and should be closely monitored. Mutations of the virus could pose a future threat to humans and cause epidemics [20, 21].

The propagation of the virus is possible in equine and mosquito cell cultures but also others [20]. An infection with the virus can be diagnosed from nasal swabs, saliva, blood, parenchymal organs, and spinal cord samples. The virus can be demonstrated by RT-PCR and virus neutralization test. Serologically, CFT, HI, and ELISA are being used, with ELISA being the most frequent test [20, 21]. Only symptomatic treatment can be done since no specific medication is available.

Preventative methods like vaccines for horses and pigs can be used. Since 1979, a formalin-inactivated whole-virus vaccine exists for horses [8, 20]. Previously having a high protection, recently small breakthroughs have been reported, meaning, that the vaccine cannot completely protect from new strains. In swine, an oil emulsion inactivated vaccine was tested and showed high protective capabilities [21]. Furthermore, humans and animals should be protected from mosquitoes to prevent an infection.

2.2.4.2 Ross River Virus

The Ross River virus (RRV) belongs to the Semliki Forest virus complex and is present in Australia and the Pacific Islands [22]. It causes inflammation in the joints of humans and equids [19]. First isolated from mosquitoes around 1950, it had been identified in horses and humans in the late 1970s. It is the most common arboviral infection in humans with around 5 000 cases every year and is also called ‘Ross River fever’ or ‘epidemic polyarthritis’. Over 40 different mosquito species have been identified transmitting the virus in a marsupial-mosquito cycle, with kangaroos and wallabies as reservoir hosts. But also, human-to-human transmission cannot be excluded. [23]. Although equids can be infected, they just show a low infectability whereas humans have moderate to high infectability [22].

The clinical signs in humans, after an incubation period of 3 to 21 days, are arthralgia, lethargy, stiffness in the joints, myalgia, rashes, fever and flu-like signs that can last up to years. Also, cases of encephalitis have been reported. In equids, lethargy, fever, tachycardia and tachypnoea, muscle pain, stiffness and lameness, limb edema as well as colic and neurological signs like ataxia were seen. In both humans and horses, chronic long-term arthritis can be the result of an infection. Human and equine vaccines are on trial, but not on the market yet [23].

2.2.5 Barmah Forest Virus Complex

The Barmah Forest virus (BFV) is also current in Australia. Seropositivity was seen in humans, horses, dogs, and cats, but so far, no clinical disease in equids has been proven. For humans, it is the second most common arboviral disease causing similar symptoms to the Ross River virus. The epidemiology of this virus is suspected to be similar to RRV [24].

2.2.6 Middleburg Virus Complex

In Middleburg in South Africa, in 1957 the Middleburg virus (MIDV) was first isolated from mosquitoes (*Aedes caballus* and *Aedes Banksinella sp.*). The virus causes febrile acute or fatal central nervous disease in humans, equids and wildlife. The virus belongs to the Middleburg virus complex and occurs in late summer and autumn due to being an arbovirus [10].

The epidemiology is not completely clear, however, MIDV was isolated with Polymerase chain reaction (PCR) from horse blood 21 days after the onset of clinical signs. The long replication time might support theories, in which the horse might act as an amplifying host for the virus. The antibodies and infections have been reported in a broad range of mammals and birds, showing the versatility of this virus [10].

The first case of an infection in a horse with fever and icterus was described in South Africa in 1974. Another horse in Zimbabwe, that died in 1993, had tachycardia, fever, pulmonary signs and edema. Furthermore, the virus was found in the placenta and brain of an aborted fetus, showing the capability of the virus to cross the placenta and the blood-brain barrier. Fever, stiffness, swollen limbs and depression were noted in less severe cases. In further cases with central nervous system signs, ataxia, paresis, recumbency, paralysis, tremors, seizures, icterus anorexia and paleness were identified. The possibility of simultaneous infection, with for example the West Nile virus, might increase the fatality rate in equids. Coinfections in humans might have the same result [10].

2.3 Flaviviridae

The viruses of the family *Flaviviridae* are small, enveloped, and have a positive-sense single-stranded RNA. The virus replicates in the cytoplasm and the virion is spherical shaped and has a lipid envelope with two envelope proteins. Most viruses in this family are pathogenic, host-specific, and of importance for humans and animals. Within the family are four genera, *Flavivirus*, *Pestivirus*, *Hepacivirus,* and *Pegivirus*. Found worldwide, the *Flavivirus* genus is known for many diseases in humans like dengue virus or yellow fever virus, but mammals as well as birds can get infected [9, 25]. Within the genus, over 70 different species are found, most of them transmitted by arthropods. The arthropod-borne viruses can be further divided into three groups: viruses vectored by mosquitoes, by ticks, and by an unidentified vector [26]. Infections can be asymptomatic, severe, fatal, with hemorrhagic fever or with neurological symptoms [9, 27]. In the following section, my focus will lie on the *Flavivirus* genus with its different viruses causing disease in horses and humans like the West Nile virus or Tick-borne encephalitis virus.

2.3.1 Japanese Encephalitis Serocomplex

Vectored by mosquitoes, the Japanese Encephalitis serocomplex has a wide variety of equine zoonotic viruses which are mentioned in the following segment.

2.3.1.1 Japanese Encephalitis Virus

The Japanese encephalitis virus (JEV) affects mainly humans but also swine, equids, and cattle within a wide geographic distribution in Southeast Asia and Oceania [26]. The first outbreak happened in 1871 in Japan, therefore the name ‘Japanese encephalitis virus’. With the St. Louis encephalitis virus, Murray Valley encephalitis virus, West Nile virus, Kunjin virus, Usutu virus, Kokobera virus and Alfuy virus, the Japanese encephalitis virus builds the Japanese encephalitis serocomplex. These viruses are similar in their structure and can either provide cross-immunity or worsen the course of a disease. The JEV has at least five genotypes with a changing geographic prevalence. Genotype I is found in Korea, China,

Japan, Cambodia, Vietnam and Thailand, and is predominant in humans. Genotype II causes endemic disease in tropical regions in Asia, Australia, and Korea. In temperate zones in Asia, Genotype III is found and is also endemic and predominant in humans. Genotype IV is found in Indonesia and Australia and Genotype V is a resurfaced strain in Asia and causes human encephalitis. Currently, Genotype I is the most dominant worldwide [26]. In 1997 and 2000, JEV RNA was found in dead birds in Italy, and in 2010 the virus was found in mosquitoes there. So far, no human or livestock cases have been reported in that region.

The virus is being vectored by mosquitoes of the *Culex* genus and maintained by a mosquitoes-aquatic bird cycle (especially herons and egrets), but also pigs are seen as reservoirs, and both birds and swine act as amplifying hosts [28–30]. Humans, horses, and cattle are dead-end hosts [9]. Due to the vector being mosquitoes, the main time for infections is during summer and autumn, when local epidemics can be seen [29].

Apart from arthropod infection, boar semen can carry the virus and an infection can also cause reproduction failure in sows like abortion, stillbirth, mummification or weak piglets [9]. In humans, transmission through mucous membranes, small wounds in the skin, or iatrogenic infection has been reported. Fever, headache, vomiting and neuralgia are displayed in case of an infection, but asymptomatic cases have been reported in humans as well [26, 30]. About 30% of infected and diseased humans show neurological signs like seizures, flaccid paralysis, facial paralysis, encephalitis, meningitis, coma and death [25, 26]. The mortality lies at 30% and even in recovered people, the consequences of the infection can be seen. About 68 000 cases are being reported annually [26, 29].

In horses, the incubation period lies between four to 14 days, and the infection is usually asymptomatic but fever, decreased appetite, jaundice, rigidity of legs, hypersensitivity, photophobia, muscle tremor, ataxia, recumbency, convulsions, circling, depression and disorientation are seen in case of a clinical manifestation. Death follows within 2 weeks in case of severe neurological signs [29, 30]. In the postmortem examination, focal and perivascular accumulation of lymphocytes as well as petechial hemorrhages in the brain, and congestion of the blood vessels, paired with neuronal swelling, necrosis and glial cell proliferation can be seen [29].

The direct detection of a virus infection happens based on virus isolation or detection of viral RNA by RT-PCR. Indirectly the virus can be demonstrated by specific antibody demonstration with ELISA and HI. As mentioned earlier, cross-reactions with other *Flaviviruses* can occur [9, 29].

For the prevention of the disease, inactivated and live attenuated vaccines are in use for horses and swine. So far, no vaccines for humans and cattle exist. Therefore, prevention is important and is based on restriction of the vectors and moving pig farms further away from civilization [9, 25, 29].

2.3.1.2 West Nile Virus

The West Nile virus (WNV) is one of the most widespread *Flaviviruses* today and belongs to the Japanese encephalitis serocomplex [9, 26, 31]. 1937 first isolated in Uganda, now found globally, it became a constant threat for neurological disease in birds, humans, and horses [25]. For example, in 1999 the virus became permanent in the USA, and since 2018 cases in Germany have been reported with increasing case numbers annually [31].
The virus has nine different lineages with lineage 1 being the most prevalent one. Lineage 1 is divided into 1a and 1b, and they are found as follows: 1a in Europe, Africa, America, and Asia and 1b Kunjin virus in Australia. In Africa and Madagascar lineage 2 is found but also associated with avian mortality in Europe. Lineages 3 and 4 are found in Europe and Russia and Lineage 5, previously described as 1c, in India. Lineage 6 is prevalent in Spain and Lineage 7 in Africa, Malaysia, and Senegal. Also in Senegal, Lineage 8 is found. Lastly, Lineage 9 is present in Austria [26]. Lineage 1 is thought to be the underlying cause of most West Nile virus epidemics happening nowadays [9]. Global warming and changes in migration routes of birds as well as the possibility for mosquitoes to overwinter in former colder areas support the upcoming of the virus.
The virus is transmitted mainly by *Culex* mosquitoes (primary transmission cycle), but also *Aedes* species (secondary transmission cycle) have a transmission part. Especially in late summer, increased case numbers can be seen. In warm humid weather, the mosquitoes thrive and reproduce. Apart from mosquitoes, a case has been reported, where the WNV was isolated from a tick [26]. Furthermore, organ transplantation and blood transfusions as well as cases of transmission during lactation have been described [26, 32]. Not only humans and horses can develop clinical signs but crows, ravens, jays, geese and birds of prey as well [9, 31]. These highly susceptible birds develop severe clinical signs including encephalitis and sudden death. Thus, an increased number of dead birds can be a sign of an increased number of mosquitoes carrying the WNV. However, other birds are not as susceptible and only

develop subclinical infection, causing an enzootic cycle between birds and mosquitoes. Humans and horses are only accidental hosts [31].

About 80% of infections in humans are subclinical [25]. If clinical signs show, there can be a differentiation between a mild and a severe course of the disease. Mild signs in humans are flu-like, including myalgia, arthralgia and rashes. Severe clinical signs show the high neurotropic characteristic of the WNV. Meningoencephalitis and meningitis, acute flaccid paralysis and death can be the result of infection [25, 26]. In horses, clinical signs vary as well. Although only a small percentage of infected animals develop clinical signs, anorexia, depression, ataxia, circling, head pressing, convulsions as well as paralysis, coma and death in approximately 30% of cases are observed [9].

For the diagnosis of infection in live animals and humans, samples can be taken from blood, saliva, and excretes. The processing of the samples should happen on biosecurity level 3. In dead birds, the whole tissue of the carcass can be used for the detection of the virus, and in horses, samples of the brain and spinal cord [9]. It is possible to propagate the virus in an appropriate cell culture. The antigens of the virus can be shown with Immunoassays and IHC. The genome of the virus can be identified by RT-PCR. For indirect detection, ELISA and PRNT are being used with the latter being the most specific assay. It is important to note that cross-reactions with other *Flaviviruses* can occur [9].

Vaccines for horses are available and can reduce viremia as well as clinical signs and economic losses. Different types of vaccines like canarypox-vectored, DNA, or a chimeric vaccine that is based on the yellow fever virus in humans, exist [9]. No human vaccines exist, which makes it particularly important to prevent infection with the vaccination of horses and the reduction and protection of and from vectors. Also, wild bird monitoring programs show the relation between an increased number of dead birds and an increase in WNV cases [31].

2.3.1.3 St. Louis Encephalitis Virus

The St. Louis encephalitis virus (SLEV) was detected in 1933 in St. Louis, United States of America, and is now found from Canada to Argentina. A close relationship between SLEV, Japanese encephalitis virus, and West Nile Virus exists. The SLEV is an arbovirus and is transmitted by mosquitoes (*Aedes* spp., *Culex* spp.) to mainly horses and birds. However, it

can also affect other vertebrates including humans. During epidemics in Texas, the virus was isolated from birds like blue jays, mockingbirds, pigeons, house sparrows and domestic geese [33]. These birds happen to be the reservoir of the SLEV. With the development of severe viremia, they can transmit the virus to other mosquitoes feeding on them [34]. There is a seasonality in the infection happening in late summer and fall due to the increased upcoming of mosquitoes, in more temperate regions infections happen all year [34, 35]. Humans and horses are dead-end hosts as they do not develop a significant enough viremia to transmit the virus further to mosquitoes. However, transmission with blood transfusions is possible [34]. The infections with the SLEV have significantly decreased since the upcoming of the West Nile Virus, but it is unknown whether the two pathogens are competing for prevalence in the vectors or if there are other unidentified reasons [33].

After being bitten by an infected mosquito, the virus replicates near the site of infection and the local lymph nodes. The incubation period is between 5 and 15 days. The clinical symptoms in humans may be flu-like with fever, fatigue, headache, nausea, vomiting and myalgia but also asymptomatic infections have been recorded. Mostly, recovery follows spontaneously without the development of encephalitis. In more severe cases, when the virus can cross the blood-brain barrier, neurological symptoms occur like disorientation, agitation, confusion, delirium, stupor, tremors and coma following the flu-like symptoms. Severe symptoms like meningitis and encephalitis mostly occur in elderly patients. The fatality lies between 5 and 15% [33, 34].

For horses, the infection can be asymptomatic but neurological signs have been reported like incoordination, depression and flaccid paralysis of the hind limbs [36].

Diagnosis is done with ELISA to detect IgM antibodies in the cerebrospinal fluid (CSF) as well as PCR from CSF to exclude other similar manifesting infections with Enteroviruses or Herpesviruses [34]. Only supportive treatment and no vaccinations are available. The control of the mosquito population and self-protection with repellants are key points in the prevention of the disease [33].

2.3.1.4 Murray Valley Virus

The Murray Valley virus (MVEV) belongs to the JEV serocomplex and is endemic in Australia [37]. *Culex* spp. and waterbirds act in a bird-mosquito cycle. Especially egrets are an amplifying host for the virus [38]. In humans and horses, encephalitis with depression, weakness, hypermetria and incoordination can occur [37]. In an outbreak in Australia 2022-2023, the case fatality was up to 83% in humans [38].

2.3.1.5 Usutu Virus

Also belonging to the JEV antigenic complex, the Usutu virus (USUV) has eight genetic lineages with two major groups in Africa and Europe. *Culex* spp. mosquitoes are vectors and birds act as amplifiers, co-circulation with the WNV can occur. In humans and horses, fever, meningitis, encephalitis and acute flaccid paralysis as well as sudden death can occur [39, 40].

2.3.1.6 Ilheus Virus

The Ilheus virus (ILHV) is related to the Japanese encephalitis serocomplex and was first described in 1944 in Brazil. It has spread over Central and South America and is being transmitted by mosquitoes. The ILHV persists in a bird-mosquito cycle and has been isolated from *Aedes* spp. and *Culex* spp. mosquitoes, birds, monkeys, and humans [39, 41]. Also, antibodies have been found in horses, but no clinical signs have been reported. Sporadic infections in humans can cause febrile symptoms and encephalitis [39].

2.3.2 Tick-borne Encephalitis Serocomplex

The tick-borne encephalitis serocomplex consists of *Flaviviruses* that can cause neurological signs in mammals and birds. The following section addresses the most important tick-borne viruses of said group, that can infect both humans and equids.

2.3.2.1 Tick-borne Encephalitis Virus

The tick-borne encephalitis virus (TBEV) belongs to the tick-borne encephalitis antigenic group which is composed of viruses like the Omsk hemorrhagic fever virus, Looping Ill virus, or Powassan virus, and others [26]. The TBEV causes encephalitis in humans and some mammals, and can infect a broad range of wildlife, companion animals, livestock and birds [42]. It is the most important tick-borne viral infection in Europe [43, 44]. The TBEV is endemic from Europe to Asia and has five different subtypes: TBEV-Eu, the European subtype, TBEV-Sib, the Siberian subtype, TBEV-Fe, the East Asian subtype, TBEV-Him, the Himalayan subtype, and TBEV-Bkl, the Baikalian subtype [42].

The virus is transmitted mainly by the *Ixodes* ticks but can also be received with dairy products of infected ruminants [42]. Within ticks, the virus is transmitted transovarial and transstadial, and while co-feeding on the same host. The reservoirs for the virus are rodents, insectivores, and small carnivores like foxes. These animals develop long-term viremia if infected. Livestock ruminants like sheep, goats and cattle only have a short viremic phase, are frequently asymptomatic, and are therefore seen as indicator hosts to determine the regional prevalence of the virus [43].

In horses, antibodies have been found but only very few clinical cases have been described. The symptoms include fever, tachypnea, change in behavior, depression, disorientation, ataxia, recumbency, paralysis of the neck and shoulder muscles and convulsions [43, 44]. Postmortem, no gross lesions were found but lymphocytic encephalomyelitis. Because of the similarity to other neurological infections like with the WNV, and the Borna Disease virus, laboratory investigation is necessary [43, 44]. Humans suffer from biphasic fever, headache, malaise, myalgia, and viremia. High fever with severe headache, nausea, and changes in sensory perception can hint at a neurological course of disease that can persist after recovery or even be fatal [43, 44].

The identification of the virus is based on RT-PCR, IHC or virus isolation. Serologically, ELISA and PRNT can be used. Cross-reactions with other *Flaviviruses* can occur, therefore VN is necessary to confirm the results [43, 44].
Whole virus formalin-inactivated vaccines are available and highly effective and safe in the prevention of infection for humans and horses [25]. Further prevention should include the control of reservoir hosts like rodents and general protection from ticks. Also, milk should be pasteurized before consumption [42].

2.3.2.2 Louping Ill Virus

The Louping Ill Virus (LIV) is found in most of Great Britain and Ireland, but also in other regions like Norway, Spain, Bulgaria, Russia and Turkey. Turkey and Spain each have a different strain, and these strains are also different from the strain current in Great Britain and Ireland [9, 45]. Within Great Britain, four geographically different lineages have been discovered [45]. The LIV belongs to the mammalian tick-borne encephalitis complex, which viruses are mostly human pathogens. This virus however, infects primarily sheep and causes encephalitis. But it can also infect humans, equids, other mammals and birds. In particular, the red grouse is highly susceptible, the mortality can rise to 80% in endemic regions. The LIV is maintained in endemic regions in a sheep-tick cycle, but mountain hares can act as reservoirs for the virus [9].
The ticks of the genus *Ixodes* are the main transmission vector in Europe. The most active time for these ticks is between late summer and early autumn, causing LIV infections to occur seasonally. An infection in humans and horses is rarely seen [9]. Apart from transmission by ticks, humans can also be infected by close contact with diseased sheep or in laboratory misconduct [45]. If infected, humans experience flu-like and mild neurological symptoms. Biphasic encephalitis, poliomyelitis-like illness and hemorrhagic fever have been described [45]. In horses, neurological symptoms like ataxia, muscle tremors, depression and photophobia were recorded. Also, excitation, fever and anorexia occurred [46].
An indicator of the occurrence of the virus can be the death of sheep during tick activity. The postmortem lesions are restricted to the central nervous system and can be non-suppurative encephalomyelitis with neuronal degeneration and necrosis, and perivascular

cuffing [9, 45]. Further diagnostics can be done with RT-PCR, CFT, HI, and gel diffusion tests for the detection of IgM antibodies in an acute infection [9, 46].
For sheep, inactivated vaccines have been used, but these are now discontinued [45]. Ectoparasiticides against ticks can be used for the prevention of the disease, but resistances can develop [45]. In humans, repellants along with proper clothing and thorough examination after exposure are recommended.

2.3.2.3 Powassan Virus

The Powassan virus (POWV) belongs to the tick-borne encephalitis group. It is prevalent in North America and Eastern Europe and has two genetic lineages [39]. The POWV can cause encephalitis and meningoencephalitis in humans and horses [47]. Transmitted by *Ixodes* ticks, the clinical signs in humans include fever, myalgia, malaise, headache, sore throat, nausea, vomitus, rash, confusion, decreased conscience, seizures and paralysis [47]. In horses, muscle tremors, increased chewing, depression, stiffness, disorientation, ataxia, recumbency and hyperexcitability have been recorded [48]. The main reservoir and amplifier are rodents, lagomorphs and deer.

2.4 Bornaviridae

Bornaviridae can be found in equids, humans, and birds. The following section is dedicated to the Borna Disease Virus, which causes encephalitis in both humans and equids.

2.4.1 Borna Disease Virus

The Borna Disease Virus (BoDV) is named after the city of Borna in Saxony, Germany. The virus was discovered in 1885 after causing death to a high number of horses in that area. The BoDV occurs in Central Europe and belongs to the *Bornaviridae* family. The Borna Disease Virus is an enveloped single-stranded RNA virus. It is most likely transmitted via small rodents. The shrew (*Crocidura leucodon, Sorex araneus*) could be identified for infections

caused in horses in 2015 and 2016 in Austria. After these BoDV infections, shrews have been collected to demonstrate the possibility of being a reservoir host for the virus. It was proven that these shrews did have infections with the BoDV as well as a high amount of viral antigen [49]. Shrews excrete the virus with urine, excrements and saliva [50].

Affected by the infection are mostly horses and sheep, but other mammals like cats [9] as well as humans can be affected [51]. It is being suggested that the virus is introduced into the body through the oronasal cavity as signs of inflammation and edema have been observed in horses [51]. The incubation period can last from a few weeks up to months [50, 51].

In horses, the severity of the clinical signs might be connected to the age, immune status, and the virulence of the strain [9]. Fever, anorexia as well as inflammation and edema in the nasal cavity have been observed in the early stages of the infection. Neurologically, excitability or depression have been reported at the beginning of the course of the disease. These signs are followed by ataxia, pharyngeal paralysis, hyperesthesia, severe excitability, aggressiveness or lethargy, circling, paresis, paralysis, stupor, and coma over 3-4 weeks. Blindness and colic may also appear. Often the outcome is lethal, sometimes mortality is up to 100%. If not lethal, the horse may have permanent damage to the central nervous system and therefore neurological disturbances. However, the infection may go without clinical signs [9, 51].

For human infection only a few data are available. The incubation time varies from a few weeks to several months, like in equids. After the onset of the clinical signs, unspecific flu-like symptoms may appear like depression, headache, increased temperature and a decrease in leisure. After that, neurological symptoms start to show. These can be disorientation, myoclonus, dysphagia, nystagmus, ataxia, polyradiculitis, radiculopathy, paresis of the brain nerves, seizures and coma. Almost all diseased individuals died after a short but intense course of infection [50].

The Borna Disease Virus can be diagnosed by demonstrating the existence of eosinophilic intranuclear inclusion bodies, Joest-Degen bodies, in infected tissue. The viral antigens as well as antibodies in serum or cerebrospinal fluid can be observed in case of an infection with indirect immunofluorescence, immunoblotting, or ELISA as well as RT-PCR to detect the RNA of the virus. The treatment for infected horses and humans is supportive. For humans, antiviral drugs can be used [50].

2.5 Paramyxoviridae

Paramyxoviridae belongs to the order *Mononegavirales* and are pleomorphic, enveloped viruses with a negative-sense single-stranded RNA and a helical nucleotide. They have six major proteins: the nucleocapsid protein (N), the phosphoprotein (P), the matrix protein (M), the fusion protein (F), the glycoprotein (G) and the large protein (L). Due to their envelope, *Paramyxoviridae* are sensitive to heat, desiccation, and disinfectants.
They have a narrow host range and are known to cause diseases like Rinderpest or canine distemper. The transmission occurs by close contact as well as aerosols. After infection, the primary replication site is in the respiratory tract. The *Paramyxoviridae* family can be further divided into *Pneumovirinae* and *Paramyxovirinae*. Within the subfamily of the *Paramyxovirinae* are the Hendra and the Nipah virus which belong to the *Henipavirus* genus [9, 52].

2.5.1 Hendra Virus

The Hendra virus (HeV) was isolated for the first time in 1994 during a massive outbreak in Brisbane, Australia, and was initially called equine morbillivirus. During the later genetic investigation however, it could be excluded that it was a part of the *Morbillivirus* genus, and a new classification came up, the *Henipavirus* genus. Now the genus is made up of the Hendra virus and the Nipah virus. Since then, more *Henipaviruses* have been discovered, mostly with unknown etiology and unknown impact. In the 1994 outbreak, 20 horses were infected, and 14 horses died as well as a trainer working closely with the infected animals. In further outbreaks, seven humans have been infected resulting in the death of four, which totals a mortality of 57%. So far, only infections in Australia have been recognized [9, 52, 53].
The virus is being carried by flying foxes of the *Pteropus* genus, which are fruit-eating bats. They shed HeV with feces, urine, and saliva and the virus can survive for days in these excretes. The antibodies of HeV have been recognized in all four existing species of flying foxes in Australia. The infections, mostly in horses, happen with the contact or inhalation of these infectious fluids. But also, horse-to-horse transmission is described as well as horse-to-human transmission. The horse acts as an amplifying host for the HeV. Humans mostly

get infected with close contact with these infected horses in stables or veterinary clinics, if they do not protect themselves properly from the infectious body fluids of the horses. The incubation period lies between a few days and can last up to two weeks. The clinical symptoms in horses include sudden death, high fever, severe respiratory difficulties with extensive nasal discharge, central nervous signs like loss of vision, circling, ataxia and myoclonus, as well as colic-like signs. In humans, acute encephalitis has been described. The postmortem lesions are mostly unspecific and result from the degeneration of small blood vessels in the organs. Mostly, dilated pulmonary vessels, pulmonary edema, and congestion can be seen [9, 52–54].

The virus can be identified by the propagation in cell culture and with immunostaining of the infected cells. Fixed samples can be used in places where the safe handling of the samples cannot be guaranteed. RT-PCR as well as qRT-PCR are being used with samples from blood, nasal, oral, or rectal swabs. Tissue and parenchymal organ samples should be used in dead animals. The serology is done with ELISA and with VNT as confirmation and reference. Cross-reactions with the Nipah virus are possible, therefore it is recommended to use the VNT for both HeV and NiV in places other than Australia or Malaysia. Samples should be processed in Biosafety level 4 due to the highly contagious properties of these viruses [52, 53, 55].

Vaccination for horses has existed in Australia since November 2012 but can only be carried out by a specialized veterinarian. So far, this is the most advanced and safest method for the prevention of the disease in horses. The subunit vaccine is based on an artificially produced G protein of the virus. However, tests with ferrets show that not all infected animals develop antibodies to all antigens, which makes it possible to have a false negative result. This means, that the serology of an unvaccinated animal can look like the serology of a vaccinated one. For further prevention, the drinking water of horses in the stable should be covered, and pastures near fruit trees should be avoided. Thorough hygiene should be enforced to prevent the infection of horses as well as the infection of humans. Removing, quarantining, and testing sick horses should become a standard [52, 53].

2.5.2 Nipah Virus

The Nipah virus (NiV) is closely related to the Hendra virus and was first isolated in a mass outbreak of pigs and humans in 1998/1999 in Malaysia and Singapore. At first, it was thought to be an unusual presentation of the JEV but was later identified as a virus of the Henipavirus genus. The virus is named after 'Sungai Nipah', the village where the first cases occurred. Over one million pigs had to be slaughtered in the effort to contain the outbreak that followed over 100 human fatalities. Nowadays the virus' antibodies are found in fruit bats of the *Pteropus* genus in Malaysia, Cambodia, Indonesia, Madagascar, Vietnam, and Thailand and indicate the persistent presence of NiV. It must be mentioned, that in serological investigation 39% of the straw-colored fruit bats of the genus *Eidolon helvum* in Ghana, Africa have been found to carry NiV antibodies. But so far, no human cases have been reported. Since 2001, cases have been reported from Bangladesh and India with a different strain than the original Nipah virus found in Malaysia. In 2012 the first outbreak that could be tracked back to infected horses occurred. Horses with signs of acute encephalitis were slaughtered for human consumption resulting in 17 human cases with 9 fatalities. This was the only reported outbreak with horses but shows the potential for future infections [9, 52, 54, 55].

Like HeV, flying foxes of the *Pteropus* genus are considered to be the natural host of the virus. Pigs are extremely susceptible and act as an amplifying host but also humans and companion animals like horses, cats, dogs, and goats can get infected. The infection of pigs happens through the ingestion of bat excretions, followed by severe respiratory signs as well as neurological symptoms with febrile encephalitis. Humans get infected through the ingestion of palm sap sugar or fruit, that is contaminated with infectious bat excretes, as well as contaminated meat or contact with the excretes of infected swine. But also, human-to-human transmission is possible, as seen in the Bangladesh strain of 2001. The incubation period lies between one to two weeks. In humans, febrile encephalitis with signs of general central nervous disease and general malaise as well as respiratory disease have been described. Respiratory symptoms were more frequent in the Bangladesh strain than in the Malaysian strain. The only possible treatment remains supportive care and the mortality in humans lies at 57% [52, 54, 55].

For the processing of samples, Biosecurity level 4 is required, because the virus is highly pathogenic to humans, just like the Hendra virus. The identification of the NiV is similar to

the HeV. The virus can be propagated in living cell cultures and can be identified by immunostaining, RT-PCR, and qRT-PCR. Also, Immunohistochemistry of the antigens in formalin-fixed tissue is possible. Serologically, the virus can be detected with ELISA and the results can be confirmed by the Virus Neutralization test. Again, it is important to screen for both HeV and NiV since cross-reactions are possible and very frequent, and a clear identification of the virus is needed [52, 55].

So far, neither vaccines for humans nor for animals are on the market, but experimental vaccines for humans exist based on recombinant vesicular stomatitis virus. Prevention in the region is being done by strict surveillance of pigs, seropositive animals should be culled. Furthermore, stables should be distanced from fruit trees and procedures must be done to ensure that animals and humans cannot get in contact with the infectious material of the bats. Humans should cover and boil any palm tree sap to inactivate the virus as well as wash and peel fruit thoroughly and avoid any vegetables and fruits with bite marks on them [55].

2.6 Rhabdoviridae

The *Rhabdoviridae* belong to the order *Mononegales* which also includes *Bornaviridae* and *Paramyxoviridae*. They have a linear single-stranded negative-sense RNA with helical symmetry. Six genera belong to *Rhabdoviridae*: the *Vesiculovirus, Lyssavirus, Ephemerovirus, Cytorhabdovirus, Novirhabdovirus,* and *Nucleorhabdovieus.* Surface glycoprotein (G), RNA polymerase (L), matrix protein (M) nucleoprotein (N), and viral polymerase (P) are the five major proteins of these viruses. The G interacts with the host cell and induces cell-mediated immunity and virus-neutralizing antibodies. The viral replication takes place in the cytoplasm. Of the six genera, three can infect vertebrates, the *Vesiculovirus,* the *Lyssavirus,* and the *Ephemerovirus*. The infection happens through bites, arthropods, direct contact or even environmental contamination [9].

2.6.1 Vesicular Stomatitis Virus

The Vesicular Stomatitis virus (VSV) belongs to the genus *Vesiculovirus* in the *Rhabdoviridae* family and is a zoonotic virus causing vesicular lesions, and has low mortality [56]. Different serotypes can be identified. Vesicular Stomatitis Indiana virus (IND), which has three subtypes, and Vesicular Stomatitis New Jersey virus (NJ). Subtype 1, Vesicular Stomatitis Indiana virus (VSIV), can infect cattle, equids, swine, and humans in North and South America and is also named 'classical' vesicular stomatitis virus. Subtype 2 is named Cocal virus (COCV). It also infects humans, equids, and cattle in South America. Lastly, subtype 3, Alagoa virus, is current in Brazil and other South American countries and infects equids, cattle, and humans. The Vesicular Stomatitis New Jersey virus (NJ) is more virulent than the IND viruses and infects humans, equids, cattle, and swine in North and South America. The VSV is endemic in Central America and some regions in North and South America [9]. Since 1886 several outbreaks have also been reported in Africa and after 1915 also in France [56].

In tropical and subtropical regions, every two to three years outbreaks occur. They mostly happen at the end of the rainy season and at the beginning of the dry season. During summer, a fast spread from endemic regions to non-endemic regions can occur. In an interval of five to ten years, outbreaks in temperate zones appear but find a sudden end at the beginning of winter. The transmission of the VSV is not fully understood, but direct contact and insect vectors are thought to play a significant role. In infected animals, the virus can be shed in the saliva and ruptured vesicles, contaminating water and food sources. The seasonality of the viral infections is attributed to insect vectors due to the timing and clusters near rivers and bigger water sources. Furthermore, the RNA was isolated in insect species like mosquitoes, sandflies, blackflies, and houseflies. In domestic animals, no viremic phase was detected, but small mammals are suspected to be the reservoir host of VSV [9, 56].

The infection of mammals mostly happens through insect bites or small lesions in the skin or mucous membranes. After that, vesicles develop that spread locally at the site of infection, and that can fuse together in the course of the disease. The clinical signs start up to five days post infection, but subclinical infection is also possible. The clinical signs include fever, anorexia, lethargy, and vesicles on the tongue and oral mucous membranes, causing increased salivation. Further vesicles can show on the coronary band and teats and can cause lameness and mastitis, even severe, if a secondary bacterial infection ensues [9, 56]. Without

a secondary infection, the lesions can heal with symptomatic treatment within two weeks. In humans, similar lesions have been described. Influenza-like symptoms with nausea, vomitus, headache, myalgia, malaise, and pharyngitis, but also oral lesions and vesicles on the tongue, oral mucosa, and pharynx as well as lymphadenitis were reported. Rarely, encephalitis in children can occur [56].

After infection, high levels of antibodies have been found, however no cross-protection between the IND and NJ serotypes exists [9, 56].

Due to the similarity between VSV, Foot-and-Mouth disease (FMD) and swine vesicular disease (SVD), fast laboratory confirmation is needed. For samples, the epithelium from the vesicles and vesicular fluid is being examined with CFT and ELISA for antigens of the virus. RT-PCR, virus isolation, Fluorescence antibody test (FAT), and VN are further diagnostic measures, used for the identification of the virus. The antibodies in the animals can be detected with ELISA, CFT, and VN. Since no specific treatment is possible, prevention of secondary infection is important to support a fast course and recovery of the infection [9].

If the suspicion of the eruption of the disease arises, movement restrictions must be made and the establishment in question must be taken under quarantine. The prevention is mostly just possible through avoidance of insects. Vaccines for livestock in Latin America exist [9, 56].

2.6.2 Rabies Virus

Belonging to the *Lyssavirus* genus, the rabies virus (RABV) is considered to be one of the deadliest zoonoses worldwide [13]. The virus can be found globally with several countries claiming to be free like some European countries, Iceland, Greenland, New Zealand, and Australia. Different genotypes can be differentiated. With the possibility of infecting all mammals and the prospect of causing fatal encephalitis, different susceptibility between mammals was discovered [9].

The *Lyssavirus* genus consists of over 17 different species, with thr RABV being the only one reported in the New World [57]. The virus is transmitted mainly through bites of infected animals, but also scratching or licking can cause an infection [9]. The main reservoirs and amplifier hosts are bats and carnivores. In these animals, the susceptibility is remarkably high. Humans and domestic animals are only moderately susceptible. Urban and sylvatic

cycles were established. In urban cycles, dogs, and cats, and in sylvatic cycles, wildlife, like raccoons, foxes, or bats, act as a reservoir for the RABV.

After being inoculated into the tissue, the virus enters the peripheral nerve endings and makes its way into the central nervous system, where it causes neuronal damage and further infects different tissues like the salivary glands. The incubation period is very variable, depending on the site of entry, the amount of virus, and the virulence of the strain. One week to one year is possible, and the virus is excreted in the saliva before the onset of clinical signs [56]. Although rare, infections in equids have been reported, also with the possibility of infecting contact humans [13, 56].

The clinical signs can be diverse. In furious rabies, an increase in aggression, hyperexcitability, biting of inanimate objects or other animals, and traveling long distances can be seen in companion animals, especially cats. Dumb rabies is the other form of the disease. Here, animals show muscle weakness, difficulties swallowing due to pharyngeal paralysis, increased salivation, and jaw-dropping. Equids mostly develop the ‘dumb’ form with further clinical signs like fever, ataxia and hindleg paresis, recumbency and colic. Two to five days after the onset of clinical signs, death follows due to cardio- and respiratory failure [56].

Clinical features in humans include fever, malaise, headache, pain, pruritus and sensory alterations. Hyperexcitability, but also paralysis can be a neurological symptom; death follows two to ten days after the onset of the clinical signs. In humans, emergency vaccination can be performed to alter the course of the disease [56].

In the postmortem exam of the brain, non-suppurative encephalitis with perivascular lymphoid cuffing and intracytoplasmic inclusion bodies (Negri bodies) can be observed [9]. Other lyssaviruses can cause indistinguishable clinical symptoms, therefore laboratory investigations for clear identification are necessary. Mostly, the diagnostic is done postmortem, only in humans PCR of the saliva is performed after exposure to a probable rabid animal. The diagnostic is based on the clinical signs of animals, examination of the brain, and the occurrence of rabies in the region. Direct immunofluorescence test (FAT) is a fast and specific test but can be false negative in autolyzed brain tissue. RT-PCR and ELISA can be performed on brain tissue as well. Serology is rarely used for confirmation but for the detection of antibodies after vaccination [9].

For the control of the disease, vaccination programs are implemented in several countries. In urban areas, the stray dog population is being vaccinated and sometimes even reduced

[9]. Inactivated whole virus vaccines are used for humans, equids, and dogs, and recombinant canary pox vaccine for cats [9, 13]. In disease-free countries, quarantine and serological tests for animals can be required before entering. In sylvatic rabies, baits with live oral vaccines are distributed to wildlife [9].
It is important to mention, that further *Lyssaviruses*, like the Australian bat virus, are zoonotic and have the potential to infect both humans and equids [58].

2.7 Peribunyaviridae

Peribunyaviridae belong to the order *Bunyavirales*. Within the *Peribunyaviridae* family, we can find the genus *Orthobunyavirus.* These viruses are spherical, enveloped, and have a negative-sense single-stranded RNA. Over 18 serogroups with over 170 *Orthobunyaviruses* have been identified worldwide so far. Most of these viruses are vectored by arthropods (mosquitoes, biting midges, black flies) [59, 60]. Infections with *Orthobunyaviruses* are frequently connected to central nervous disease in vertebrates, especially humans. Different virus species within the genus can infect both humans and equids. Examples are the La Crosse virus (North America, West Europe), the California encephalitis virus (North America, West Europe), the Snowshoe hare virus (North America, East Asia), the Main Drain virus (North America), the Bunyamwera virus (Africa), the Jamestown Canyon virus (North America, West Europe), and the Shuni virus (Africa). These viruses can cause congenital diseases, like hydrocephaly in humans and horses, as well as encephalitis, meningoencephalitis, and encephalomyelitis, but also general signs including fever [59, 61–64].

2.8 Orthomyxoviridae

The viruses of the *Orthomyxoviridae* are linear negative-sense single-stranded RNA viruses, have spherical or pleomorphic morphology, and replicate in the nucleus of the host cell. The hemagglutinin proteins (H) bind to the cell receptors and the neuraminidase proteins (N) are found in the envelope. Seven different genera were identified, the *Alphainfluenzavirus, Betainfluenzavirus, Gammainfluenzavirus, Deltainfluenzavirus, Isavirus, Quaranjavirus,*

and the *Thogotoviurs.* The species Influenza A of the *Alphainfluenzavirus* genus occurs in humans, birds, swine, and equids. 16 H proteins have been identified as well as 9 N proteins. Due to the segmented genome of the virus reassortment, building new subtypes, and point mutations, creating variations in subtypes, are very frequent [9].

2.8.1 Equine Influenza Virus

The Equine Influenza virus (EIV) belongs to the Influenza A species and the subtypes H7N7 and H3N8 have been recorded to circle in the equine population [65]. These subtypes are closely related to Avian Influenza, with H3N8 being the most prevalent worldwide, with the exclusion of New Zealand and Australia. Within H3N8, different strains have been identified in the United States, Europe, and Eurasia, that were also able to occasionally recombine [9]. The virus is very contagious, causing respiratory disease with high morbidity and high mortality [65]. Records as early as 1892 suggest spillover events from equids to humans. Three weeks after respiratory disease in horses, flu-like symptoms have been recorded in humans [56].

The transmission occurs based on the shedding of the virus in aerosols during coughing, but also indirect transmission with fomites is possible. The incubation is between one and three days, depending on the infective dose. Fever, cough, nasal discharge, anorexia, and depression are seen, but also limb edema, conjunctivitis, and stiffness. Secondary bacterial infection can enable a more severe course of disease [9].

The diagnosis is possible with nasopharyngeal swab samples in the acute phase of the infection. It is important to examine the sample for antigenic drift. For a fast detection of an infection, commercial diagnostic kits for human influenza virus A can be used. RT-PCR and real-time RT-PCR (rtRT-PCR) can also be used. The treatment is based on the symptoms.

The infection can be reduced in severity using vaccines in horses. These vaccinations for equids are updated frequently, but still failure is seen due to the high mutation rate within the strains. In Australia, a recombinant canarypox vaccine was used for the successful eradication of the virus during an outbreak in 2007 [9]. The reassortment with other Influenza A strains, like human influenza, cannot be dismissed and can be a cause for future epidemics [65].

2.9 Picobirnaviridae

The Picobirnaviruses (PBV) are non-enveloped RNA viruses that are bi-segmented and double-stranded. They can infect a broad range of vertebrate hosts worldwide and can cause gastroenteritis or remain asymptomatic. It is a scarcely investigated pathogen; therefore, information is limited. However, a close relationship between animal strains was established, and the possibility of genetic reassortment due to the segmented genome exists. Horse PBV strains are very closely related to human PBV strains, this carries the potential for future zoonotic outbreaks [58, 66].

2.10 Picornaviridae

Picornaviridae are of icosahedral symmetry, not enveloped, and have a positive-sense single-stranded RNA. They have major proteins, VP 1 to 4, and replicate in the cytoplasm of the host cell. They are very resistant viruses and have eight genera that are mostly limited to one host species: *Aphtovirus., Enterovirus, Cardiovirus, Hepatovirus, Parechovirus, Erbovirus, Kobuvirus, Teschovirus, Tremovirus, Sapelovirus, Senecavirus* and *Avihepatovirus.* However, the Foot-and-Mouth disease (*Aphtovirus* genus) and Encephalomyocarditis (*Cardiovirus* genus) for example, are susceptible to a broader host range and zoonotic agents. Usually, transmission happens via the fecal-oral route, but infection with fomites and aerosol is possible [9].

2.10.1 Equine Rhinitis Virus

The Equine Rhinitis virus (ERV) was found worldwide and has four different stereotypes. The Equine Rhinitis A virus (ERAV) is closely related to the FMD virus and belongs to the *Aphtovirus* genus. The Equine Rhinitis B virus (ERBV) has three serotypes, ERBV-1 to -3, and is part of the *Erbovirus* genus. The ERV is a worldwide quite common infection of equids, to which horses are exposed very early in life [9]. The ERBV-1 is the most frequent in Europe [67]. It can cause mild to severe acute upper respiratory disease [9, 67]. 1962, the ERAV was first isolated in the UK, and in 1973, the ERBV1 [67]. Infected horses have fever,

anorexia, dry cough, and mucopurulent nasal discharge. The transmission happens through horse-to-horse contact, droplet infection, indirect infection or with feces or urine [68].
In ERAV infection, prolonged viremia occurs and shed in urine and faces is increased [9, 67]. Also, *in vitro,* a broad host range has been demonstrated, including human cells. The first infection of a human was reported in 1962 during an experimental intranasal inoculation of ERAV. The infected person had fever, pharyngitis, lymphadenitis, and confirmed viremia [67]. Studies have been undertaken in Austria to determine the seroprevalence for antibodies of ERAV and ERBV-1 in horses and veterinarians. As expected, horses had a high seroprevalence, but also humans showed, even if low, that they had been exposed to and infected with ERV. The low prevalence in humans shows the zoonotic potential for further infections [67].

2.11. Poxviridae

Poxviridae are enveloped linear double-stranded DNA viruses that replicate in the cytoplasm and that are stable in the environment. Two major subfamilies have been established with 18 genera in the *Chordopoxviridae* subfamily and 4 genera in the *Entomopoxviridae*. Genetic recombination, cross-reaction, and cross-protection within the genera are possible [9].

2.11.1 Vaccinia Virus

Orthopoxvirus is the genus of the Vaccinia virus (VACV). Infections have been described in mammals including equids and humans. Papular lesions can occur on the teats of horses, like equine papular dermatitis or horsepox. In humans, fever and pustular eruptions can occur [69]. VACV is found globally [70].

2.11.2 Equine Parapoxvirus

The genus of *Parapoxviruses* (PPV) frequently causes zoonotic diseases of veterinary importance. Recently, PPV strains infecting humans and horses (EqPPV) emerged. Between

2013 and 2022, cases have been reported in Finland as well as the United States. The infected horses showed signs of dermatitis [71]. Due to the given characteristics of EqPPV, the zoonotic potential cannot be underestimated for humans [58].

3. Analysis and discussion

Based on the research in section 2, a continental guide was developed. In the following table, the continents are on the x-axis, and the viruses are on the y-axis in alphabetical order.

	Africa	Asia	Australia	Europe	North America	South America
BFV			x			
BoDV				x		
EEEV					x	x
EIV	x	x		x	x	x
EqPPV				x	x	
ERV	x	x	x	x	x	x
GETV		x	x	x		
HeV			x			
HEV	x	x		x		
HJV					x	
ILHV						x
JEV		x	x	(x)		
LIV		x		x		
MADV						x
MIDV	x					
MVEV			x			
NiV	x	x				
PBV	x	x	x	x	x	x
Peribunyav.	x	x		x	x	
POWV				x	x	
RABV	x	x	x	x	x	x
RRV		(x)	x			
SINV	x	x	x	x		
SLEV					x	x
TBEV		x		x		
USUV	x			x		
VACV	x	x	x	x	x	x
VEEV						x
VSV	(x)			(x)	x	x
WEEV					x	x
WNV	x	x	x	x	x	x

Observations from the table highlight that more viruses have been reported in Europe compared to other continents. Several factors could contribute to this phenomenon, including greater availability of funding for medical research, leading to increased discoveries of infectious agents. Global warming plays a role, as most arboviral diseases are traditionally found in tropical and subtropical regions. However, rising temperatures and climate change have created favorable conditions for vectors, such as mosquitoes, in regions previously considered not ideal for those.
The distribution of discussed viruses across continents is detailed in the table, with Antarctica excluded as no research suggests the presence of equine zoonotic viruses in this area. ERV, PBV, VACV, and WNV are globally distributed, but establishing a common pattern is challenging due to their diverse transmission methods and virus families. Apart from WNV, these viruses are transmitted through both direct and indirect contact, highlighting potential hygiene issues, and emphasizing the close interaction between humans and equids. This could also indicate a lack of awareness regarding the virus' ability to infect both humans and equids, stressing the need to raise awareness and promote better hygiene practices in the horse industry.

The WNV, as an arbovirus, has been documented in numerous regions, primarily due to global warming altering bird migration routes and providing an environment for mosquitoes to overwinter in warmer northern countries. Humid weather, increased rainfall during the summer months, and mild winters further facilitate vector reproduction. Seasonal patterns and the rising incidence of the virus have been confirmed through studies conducted by the Friedrich-Löffler-Institute in Germany. The National Reference Laboratory for West Nile Virus reported that positive WNV samples in birds were first detected in Germany in August 2018, with over 100 cases in birds, five in humans, and evidence of overwintering in mosquitoes in 2019. Subsequently, cases began to appear earlier in the summer, affecting birds, equids, and humans [31]. These developments emphasize the significance and rapid spread of WNV, concluding that this is also possible for other viruses.

In contrast, viruses such as BFV, HeV, ILHV, and MVEV are confined to a single continent. While these infections can lead to severe diseases, their relevance is limited to a relatively small affected portion of the global population.

Observations from the table highlight that more viruses have been reported in Europe compared to other continents. Several factors could contribute to this phenomenon, including greater availability of funding for medical research, leading to increased discoveries of infectious agents. The two main factors are, first, globalization, characterized by the movement of people and horses, which may also heighten the risk of disease and vector importation. And, secondly, global warming, as most arboviral diseases are traditionally found in tropical and subtropical regions. However, rising temperatures and climate change have created favorable conditions for disease vectors, in regions previously considered not ideal for those. It is hard to predict what viruses will cause epidemics in the future, the more important it is to focus now on the investigation and the understanding of those.

As highlighted in the previous sections, these pathogens pose a significant threat to both human and animal health. Recent studies have highlighted the alarming fact that zoonotic viruses are more widespread and affect a wider range of animal species than previously assumed. Several key factors contribute to this expanding reach. Climate change is influencing the behavior and distribution of both viruses and their hosts. This can have a profound impact on the prevalence and geographic spread of zoonotic diseases. For instance, West Nile Virus serves as a strong example, as seen in the previously mentioned study [31]. Vector-borne diseases are on the rise due to numerous factors, including climate change and the movement of vectors themselves. The distribution and activity of these vectors are no longer restricted to their traditional habitats. Consequently, the risk of zoonotic viruses being transmitted across geographic and species boundaries has increased.
Furthermore, the migration of birds plays a vital role in the global spread of zoonotic viruses as well as vectors. As avian species travel far distances, they become potential carriers of these viruses and vectors, facilitating their introduction into new regions. In combination with climate change and the result of changing routes, the spread can be facilitated even more.

Many of these equine zoonotic viruses result in severe neurological signs in both humans and animals. Infections can be fatal and often leave individuals with persistent symptoms even after recovery. This emphasizes the seriousness of these infections and the need for effective prevention and treatment strategies. Beyond health concerns, there are economic

consequences associated with equine zoonotic viruses. The equine industry faces substantial losses due to the impact of these diseases on the health and productivity of horses. Considering these recent dynamics, it is imperative to intensify research efforts to better understand the ecology and epidemiology of zoonotic viruses. This includes identifying reservoirs, amplifying hosts, and vectors, as well as monitoring their movements and prevalence.

4. Conclusion

Following the research question of which viruses already have and will play a significant role in the relationship between humans and equids as a result of current trends like globalization and climate change, it can be summarized that due to the complexity and variety of viruses, it is difficult to predict what viruses will cause epidemics in the future. It is important to focus on further investigation and prioritize ongoing research, prevention, and intervention strategies to ease their impact.

5. Summary

The thesis outlines the distribution and implications of equine zoonotic viruses across the continents. It emphasizes the global reach of viruses with challenges due to not yet acquired knowledge. The broader context underlines the expanding reach of zoonotic viruses due to climate change, vector-borne diseases on the rise, and the role of host migration in the global spread. The severe health and economic consequences of these viruses are emphasized, imposing intensified research efforts for better understanding and prevention.
In conclusion, the complex interplay of factors emphasizes the urgency of comprehensive research and interventions to address the threat of equine zoonotic viruses effectively.

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Thesis progress report for veterinary students

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Department: Department of Microbiology and Infectious Diseases

Thesis title: Viral zoonotic diseases of horses

Consultation – 1st semester

	Timing			Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2023.	03.	1.	Consultation about the topic of the thesis.	[redacted]
2.	2023.	03.	21.	Consultation about the topic of the thesis	[redacted]
3.	2023.	04.	18.	Consultation about the draft.	[redacted]
4.	2023.	05.	09.	Consultation about the draft.	[redacted]
5.	2023.	06.	13.	Consultation about the draft.	[redacted]

Grade achieved at the end of the first semester: 5 (excellent).

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1.	2023.	09	06.	Correction of the first version.	[redacted]
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The thesis meets the requirements of the Study and Examination Rules of the University and the Guide to Thesis Writing.

I accept the thesis and found suitable to defence,

[redacted]
signature of the supervisor

Signature of the student: Hannah Klaus

Signature of the secretary of the department: .....

Date of handing the thesis in..... .....

I hereby confirm that I am familiar with the content of the thesis entitled

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which I deem suitable for submission and defence.

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