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Review Article

Synanthropic rodents as virus reservoirs and transmitters

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Abstract

This review focuses on reports of hepatitis E virus, hantavirus, rotavirus, coronavirus, and arenavirus in synanthropic rodents (*Rattus rattus*, *Rattus norvegicus*, and *Mus musculus*) within urban environments. Despite their potential impact on human health, relatively few studies have addressed the monitoring of these viruses in rodents. Comprehensive control and preventive activities should include actions such as the elimination or reduction of rat and mouse populations, sanitary education, reduction of shelters for the animals, and restriction of the access of rodents to residences, water, and food supplies.

Keywords: Viruses. One health. Urban environment. Rat.

INTRODUCTION

Rodents (Order: Rodentia) are distributed on all continents except for Antarctica[1]. Their heterogeneous and cosmopolitan distribution expands as their interaction with humans increases[2]. Some species are better able to adapt to urban environments (synanthropism).

In a study conducted in Buenos Aires (Argentina), black rats (*Rattus rattus*) were found in residential and industrial areas, while house mice (*Mus musculus*) and brown rats (*Rattus norvegicus*) were captured in green areas and shantytowns[3], where their presence was favored by easy access, availability of shelter, and large food supply[4].

These animals are natural reservoirs of infectious diseases[5,6], and are involved in the emergence and dissemination of viruses, bacteria, and protozoa. The transmission of these agents can occur through both direct (bite, contact) and indirect (urine, feces) means, through vectors (ticks, fleas, and mites) that infest rodents, or when they are predated by other species[1,7,8].

Although little information is currently available on the size of the population of synanthropic rats, some indicators allow the subjective estimation of their presence, such as the presence of excrement, marks on walls, trails on the ground, food sources, or the visual observation of rodents and/or the damage caused by them[9-11].

To evaluate the size of rodent populations, the concept of the 'minimum known number' is used[12], where individuals have to be captured and recaptured to estimate the infestation rate. This statistical formula can be simplified by multiplying the number of animals caught in a trap in a single catch by 100[11,13].

A survey carried out in 1529 dwellings in a low-income region of São Paulo (Brazil) showed an initial synanthropic rodent infestation rate of 40%, which was reduced to 14.4% after the implementation of sanitary education and pest control[13]. Similarly, in Pau de Lima (Bahia, Brazil), 62% of households (137/221) presented signs of active rodent infestations[14].

Besides synanthropic species, other rodents can cocirculate in rural environments and wild and urban interface areas, where they contact other animals and people[10,15]. Wild rodents are reservoirs for hantavirus, vaccinia virus, and *Lassa virus*, among others[16-19].

Fernandes et al. (2019)[20] investigated rural settlements in Goiás (Brazil), and found 2.57% (n=12) positive rate for *Orthohantavirus*, equally distributed between women and men (n=6). In contrast, similar studies showed higher frequency in middle-aged men due to their risk behaviors[21,22].

Refugee camps accommodate large number of people and consequently there is accumulation of food and residues, attracting rodents (synanthropic and wild). In Africa, studies have revealed the circulation of *Mastomys natalensis* infected by *Lassa virus* in

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these camps, which is facilitated by the dissemination routes of the virus (urine, fomites, consumption of rodents as food)[23]. Bonner et al. (2007)[24] investigated communities of up to 9,000 people and determined that the quality of housing, external hygiene, and the visualization of rodent burrows were the main epidemiological factors associated with the spread of *Lassa virus*.

Aircrafts and ships may also contribute to the introduction of rodents and even dissemination of diseases in new areas[25,26]. Consequently, the World Health Organization (WHO) has implemented rodent control measures at airports and ports, including periodic surveys to verify the absence of rodents onboard vessels. According to reports, 24.7% (270/1093) of moored ships at the port of Shanwei (China) were infested with rats[25]. In Heilongjian, another Chinese port area, 4.47% of the 649 collected rats tested positive for hantavirus[27].

Therefore, this article aims to review important viral agents disseminated by synanthropic rodents (*M. musculus*, *R. rattus*, and *R. norvegicus*), and thereby contribute to a better understanding of disease epidemiology and prevention.

SEARCH STRATEGY AND SELECTION CRITERIA

Scientific texts in English and Portuguese were retrieved from the PubMed, Scopus, Web of Science, and Scielo research platforms using the search term "virus" in combination with "disease" and "rat or rodent or murine". Additionally, a second more refined research was performed with the terms "Hepatitis E," "Hantavirus," "Rotavirus," "Coronavirus", or "Arenavirus" associated with "rat or rodent or murine."

Among the resulting, studies mainly related to synanthropic rodents (*M. musculus*; *R. rattus*; *R. norvegicus*) collected in the field were selected, excluding the studies restricted to animal experimentation.

Thus, hepatitis E, hantavirus, rotavirus, coronavirus, and arenavirus are the focus of this review, as they are neglected diseases transmitted by rodents.

HEPATITIS E (HEV)

The hepatitis E virus (HEV) has a single-stranded RNA genome of approximately 7 kb length[28]. As a member of the *Hepeviridae* family, the genus *Orthohepevirus* has four species (from *A* to *D*)[29], among which *Orthohepevirus A* and *C* have already been described in rodents[30].

Infection occurs via the fecal-oral route through the consumption of water contaminated with excrement or the consumption of raw/undercooked meat and the viscera of infected animals[31]. The prevalence rate in humans reaches 40% in industrialized countries, and the virus has been detected in blood banks[32]. Socially vulnerable people may be an important epidemiological group at risk, along with patients who depend on blood transfusions[33,34].

The virus shows tropism to digestive system and is eliminated in stool after 4 to 23 days of infection[35], remaining in this state for additional 5 weeks[36,37].

The symptoms are mainly nonspecific, and include fever, headaches, abdominal pain, but these infections may also be asymptomatic (depending on the HEV dose to which the patient was exposed), hindering the detection, and potentiating the agent's spread[38-40].

Mortality rates are higher among infected people presenting previous liver disease, immunocompromised patients, and pregnant women, as they present higher chances of renal failure leading to death[33,41,42].

The role of black rats (*R. rattus*) and brown rats (*R. norvegicus*) as reservoirs and transmitters of this viral agent and its prevalence rate remains unknown[30].

Orthohepevirus A has seven different genotypes (HEV1-7) defined by the concatenated amino acid distance between the open reading frames of ORF1 (nonstructural proteins) and ORF2 (capsid proteins)[43]. HEV-1 and HEV-2 occur only in humans; HEV-3 has been isolated from humans and several animal species; HEV-4 has been isolated from humans and pigs; HEV-5 and HEV-6 have been identified only in wild boars; and HEV-7 has only been found in camels[44].

The presence of anti-HEV IgG[30,45], and the detection of viral particles in the feces of these rodents (with or without seroconversion) have been demonstrated[37,46,47]. However, only a single study has shown similarities between rodent (*R. norvegicus*) strains with regard to the HEV-3 genotype, which is most closely related to the genotypes found in rabbits[37].

On the other hand, *rat* HEV (genotype C1), belonging to the *Orthohepevirus C* group, has been reported in *R. norvegicus* and *R. rattus*, although its potential to cause disease in humans is still questioned[37,47].

In Vietnam, animals captured at bus stations and hospitals have tested positive for *rat* HEV[48]. These findings are supported by serological evidence from domestic animals and rodents in other studies[45,49,50].

Detection methods for HEV include serological (specific IgG), histopathological, and molecular (RT-PCR) techniques[41]. Commercially, there are no specific prophylatic measures available on the market, although Chinese researchers have developed the HEV p239 vaccine from the HEV1 genotype[51]. Its efficacy is considered high (> 90%), requiring three doses (0,.1 and 6 months), and it may be used even in pregnant women[52].

HANTAVIRUS (HV)

Hantaviruses, belonging to the *Hantaviridae* family, are divided into four genera: *Loanvirus*, *Mobatvirus*, *Thottimvirus*, and *Orthohantavirus*[53]. These enveloped viruses have a negative-sense RNA genome segmented into three fragments: Large - L (6.8-12 kb), Middle - M (3.2-4.9 kb), and Small - S (1-3 kb). They encode four proteins; the L segment encodes viral polymerase, while the M and S segments encode the precursor (GPC) of two viral surface glycoproteins (G1 and G2, alternatively called Gn and Gc), and the nucleocapsid (N) protein, respectively[54].

More than 50 species of hantaviruses have been reported worldwide[55]; however, some of them do not cause diseases, including the *Prospect Hill* virus[56]. Rodents, bats, and moles are

reservoirs of these agents[57]; transmission occurs through bites (saliva), and especially via the inhalation of viral particles from the feces and urine of these animals[58]. Despite a report of transmission between humans, this form is rare[59].

The *Orthohantavirus* genus includes the greatest number of pathogenic species of public health importance[60]. Its presence is associated with the geographic distribution of rodents (*Murinae, Avicolinae, and Sigmodontinae families), which can harbor distinct forms of the disease.*

The earliest reports of hemorrhagic fever with renal syndrome (HFRS), caused by viruses known as Old World hantaviruses (Europe and Asia), come from Chinese writings dating from 960 BC. Later, in the Korean War (1951-1954), these diseases caused the death of over 3,000 soldiers[61]. The *Hantaan* virus (HTNV) species was related to this outbreak. HTNV was isolated for the first time in 1978[62] and was linked to the rodent *Apodemus agrarius*; the virus was detected in blood, urine, feces, and respiratory tract samples. In humans, this species causes a severe form of HFRS, which has thus far been restricted to rural areas of China, Korea, and Russia[63,64].

Dobrava virus (DOBV) is also associated with HFRS syndrome, for which men are accidental hosts[65]. Mortality rates vary according to the genotype, ranging from 0.5% (DOBV - *Kurkino*) to 12% (DOBV - *Dobrava* and DOBV - *Sochi*)[66,67].

The most commonly detected viral agent of this group in Western Europe, *Puumala* virus (PUUV), is disseminated by *Myodes glareolus,* whose proliferation is favored by the underbrush vegetation of this region, and the spread of the virus is further affected by virus-host coevolution[68]. In humans, it causes moderate nephropathy, and can lead to subclinical infections[69].

Seoul virus usually causes mild infections and without medical care the mortality rates reach 1%. The host of this virus (*R. norvegicus*) is found in urban areas, leading to a cosmopolitan distribution of the disease, in contrast to those caused by other Old World hantaviruses[60,70]. The incubation period varies from 2-3 weeks, and the endothelial cell tropism of the virus[71] produces nonspecific symptomatology (fever, headaches, muscle pain, nausea, vomiting), in addition to respiratory problems, dizziness, and diarrhea. Thrombocytopenia entails the development of petechias, and decreased blood pressure affects kidney function, causing renal failure followed by disseminated intravascular coagulation[72].

Hantavirus cardiopulmonary syndrome (HCPS) is another pathology associated with agents of the genus New World hantaviruses (Americas), and appears to be related to climatic phenomena such as *El Niño*[58].

The first report of hantavirus in Brazil dates from 1993, when *Juquitiba* virus, transmitted by *Oligoryzomys nigripes,* was detected by Silva et al. (1997)[73]. To date, the following viruses have been identified in the country: (a) *Araraquara* virus (transmitted by *Necromys lasiurus* rodents*);* (b) *Castelo dos Sonhos* virus (*Oligoryzomys utiaritensis*); (c) *Laguna Negra* virus (*Calomys callidus*); (d) *Anajatuba* virus (*Oligoryzomys mattogrossae*); and *Rio Mamore* virus (*Oligoryzomys microtis*), among others[20].

The incubation period of HCPS ranges between 16-24 days, with initial nonspecific HFRS-like symptomatology differentiated by pulmonary edema and lymphoid organ impairment[74], which may cause cardiovascular shock and death[72]. Studies indicate that this pulmonary phase lasts approximately 1 week, but long-lasting sequelae have been reported, such as dyspnea and weakness[61]. According to available data from the Brazilian Ministry of Health, 2061 people had been infected in the country as of 2017, with a lethality rate of 40.1%[75].

In rodents, this virus causes a chronic infection with mild symptomatology such as decreased growth[76] and renal problems[77], although it is usually asymptomatic. This can be explained by the coevolution of rodents with the virus over millions of years[78]. Hantavirus can be diagnosed by associating the patient's history with the presence of wild or synanthropic rodents. Tests for hantavirus include specific serological detection using ELISA (IgM or IgG) or viral detection using RT-PCR or real-time PCR[79].

The occurrence of HFRS has not yet been reported in Brazil, despite serologically positive human and rodent samples[80]. For example, in an urban area in Salvador, Brazil, *Seoul* virus antibodies were found in *R. norvegicus* serum samples[81]. A molecular survey conducted in Madagascar detected the *Anjozorobe* virus (Thailand *Orthohantavirus*) strain in *R. rattus* and *M. musculus*, suggesting viral spillover[82].

To our knowledge, there is no licensed vaccine available on the market that prevents hantavirus infections. Several clinical trials at different stages are ongoing to test inactivated (monovalent and bivalent), DNA, and live attenuated vaccines for both HFRS and HCPS, with effectiveness of approximately 93.77-100% being reported[83-85]. Additionally, studies have demonstrated that the use of antiviral ribavirin increases the survival rate in hantavirus-infected rats[86-88].

ROTAVIRUS (RV)

Rotavirus (RV) belongs to the *Rotavirus* genus within the *Sedoreovirinae* subfamily of the *Reoviridae* family[53]. These nonenveloped viruses have a double-stranded RNA genome of approximately 18550 bp in length, fragmented into 11 segments. The genome encodes six structural (VP1, VP2, VP3, VP4, VP6, and VP7) and six nonstructural (NSP1, NSP2, NSP3, NSP4, and NSP5/6) proteins, as the NSP5/6 gene is bicistronic[89,90].

Myriad mechanisms of viral variability occur in RVs, such as point mutations, rearrangements, reassortments, and intragenic recombination, conferring great genetic diversity[91,92]. This genus is divided into nine different groups (RVA-RVI) based on the antigenic properties and nucleotide sequences of the VP6 protein[89,93,94], and there is a potential candidate tenth group, RVJ[95].

For the RVA group, it is necessary to adopt the notation of Gx-P[x]-Ix-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx, which considers all the variability presented by the coding genes of the VP7-VP4-VP1-VP2-VP3-NSP1-NSP2-NSP3-NSP4-NSP5/6 proteins, respectively[96]. To date, this group has at least 36 known G genotypes and 51 known P genotypes in humans and animals[93,97-99].

Although rotaviruses are considered species-specific, heterologous infections may occur[100]. Wa-like and DS1-like (RVA)

strains primarily cause disease in humans, and infections caused by genotypes and serotypes common to animals have also been documented[100,101].

Synanthropic rodents are usually not associated with RVs, however, their efficiency in disease transmission and their close contact with other animals and people highlight their importance to the epidemiology of these viruses[101,102].

Transmission initially occurs through the fecal-oral route, via particles present in the soil and water, causing diarrhea due to the loss of absorptive capacity of injured intestinal cells during viral replication[103]. Diarrhea is a leading cause of infant mortality worldwide, and rotavirus infections are responsible for more than 35% of these cases[104].

RVs are widely distributed in Brazil, and have been described in animals (both young and adults) such as cattle[105], birds[106], and pigs[107,108]. In rodents, there is a single report of RVA associated with swine production[109].

A metagenomic analysis of *R. norvegicus* in Germany characterized a sample of RVA, revealing close identity between the identified strain and other animal and human strains, namely, genotypes G3, P[3], and N2[110].

In Italy, 40 fecal samples from *R. rattus* collected on swine farms were analyzed, and a sample of RVA was characterized (G3-P[3]-I1-R11-C11-M10-A22-N18-T14-E18-H13), demonstrating an atypical combination of genotypes[102].

As the associated symptomatology is mainly nonspecific, the diagnosis can easily be misleading[111]. Commercial ELISA kits, RT-PCR (single or multiplex), and qPCR assays[99,102,110] are available for the detection of these infections.

To control this disease, animal vaccination (swine and cattle) should be carried out, mainly in females in the late gestation period. In production animals, prevalence rates may be higher than 90% in adults[103]. For humans, two vaccines are authorized by the WHO: (a) Rotarix® (GlaxoSmithKline Biologicals, Rixensart, Belgium, an attenuated strain of G1P [8] RVA) and (b) RotaTeq® (Merck & Co., Whitehouse Station, NJ, with five strains of genotypes G1P [5], G2P [5], G3P [5], G4P [5] and G6P [8]).

CORONAVIRUS (COV)

Coronaviruses are enveloped, nonsegmented, positive, single-stranded RNA viruses associated with the structural N-phosphoprotein in a nucleocapsid with helical symmetry[112,113]. They are found in a wide variety of animals causing respiratory, enteric, hepatic, and neurological diseases of varying severity[114]. According to the International Committee on Taxonomy of Viruses, two subfamilies belong to the *Coronaviridae* family; *Letovirinae*, which has one subgenus, *Milecovirus*, found only in frogs and a sea hare thus far[115], and *Orthocoronavirinae*, which is found in birds and mammals, and is divided into four genera due to the antigenic and genetic characteristics of the viruses[53,116].

Phylogenetic studies indicate that bats are the gene source for *Alpha* and *Betacoronaviruses,* while birds are the gene source for *Gama and Deltacoronaviruses*[117]. Thus, *Alpha* and *Betacoronaviruses* are found mainly in mammals, such as humans, dogs, cats, pigs, bats, mice, rats, horses, and cattle[114,118-123], while *Gama* and *Deltacoronaviruses* infect mainly birds, with exceptions such as the white whale *Gamacoronavirus* (*Delphinapterus leucas*)[124] and the porcine *Deltacoronavirus*[125].

Among the *Alpha* and *Betacoronaviruses*, six are of public health importance, causing mild (HCoV-229E, NL63, OC43, and HKV1) to severe respiratory syndromes (SARS and MERS)[120,126,127].

Despite the many uncertainties about the epidemiology and reservoirs of severe acute respiratory syndrome (SARS) and Middle Eastern respiratory syndrome (MERS), bats have been identified as the most likely reservoirs, while palm civets (*Paguma larvata*)[128] and dromedary camels (*Camelus dromedarius*)[129,130] act as intermediary hosts before dissemination to humans[120,131,132]. Both diseases have caused worldwide health problems, affecting 27 countries and causing hundreds of deaths in 2002 (SARS) and 2012 (MERS), aggravated by nosocomial transmission or transmission by family members[126].

In general, the virion contains at least three proteins: the spike (S), membrane (M), and envelope (E) proteins. In addition, some coronaviruses include hemagglutinin esterase (HE)[133]. Proteins M and E are related to viral assembly[134], while the S protein show hemagglutinating activity and is the main target for neutralizing antibodies[135].

The S protein, which shows great variability, is responsible for host specificity because its S1 and S2 subunits are used for binding the virus to host cell receptors, and are associated with the antigenicity and pathogenicity of the virus[112,136].

Many similarities exist between the CoVs of rats and bats[119,120,140,141], suggesting that rodents could act as important reservoirs[142]. A survey conducted on 330 intestinal content samples from rodents (*Apodemus sp*., *Myodes glareolus*, *Arvicola terrestris*, and *Microtus sp*.), collected between 2014 and 2016 in different regions of France[121], revealed positivity of 6.3% (21 samples), all belonging to *Alphacoronavirus* groups. This study also revealed *Alpha* and *Betacoronavirus* in bats, rabbits, and hedgehogs from the same area[121].

An investigation conducted in China[120], analyzed 177 rodent intestinal samples from three different species (*Apodemus chevrieri*, *Apodemus ilex*, and *Eothenomys fidelis*), and found *Alpha* and *Betacoronavirus* in 13% (23 samples).

Besides field investigations, rodent CoV also has an important role as Murine hepatitis virus (MHV)[(137)], and has been used for experimental infections, mostly for the identification of potential viruses showing interspecies transmission[119]. Although there is little information about the prevalence and diversity CoV in rodents[138,139], many new species of *Alpha* and *Betacoronaviruses* (LRNV, LAMV, LRLV, and HKU24) have been identified in rodents in China and Europe[119,120,140,141].

Some vaccine candidates are being developed only for MERS-CoV, including whole-virus, vectored virus, DNA, and protein-based vaccines, however, lack of investment is delaying their development[143].

ARENAVIRUS (AV)

Arenaviruses (genus *Arenavirus*, family *Arenaviridae*) are enveloped viruses with an RNA genome segmented in two ambisense single stranded molecules: small (S) and large (L)[53]. The S portion encodes nucleocapsid protein and envelope glycoproteins, while L segment contains RNA dependent RNA polymerase (RdRp) and zinc-binding protein genes. Both S and L intergenic regions may potentially form one or more hairpins, which regulate mRNA transcription[53,144-146].

This viral family has four genera, based on phylogenetic analysis involving pairwise sequence comparisons (PASC) of complete genomes[53,147]. *Antennavirus* genus includes viruses that infect frogfish[148], *Hartmanivirus* and *Reptarenavirus* infect snakes, and *Mammarenavirus*, which have been reported in bats, ticks, rodents, and primates, including humans[146,147].

*Mammarenavirus*es are correlated to the geographical location where their hosts are found[147]; currently classified as: (a) Old World (OW) (*Lassa* virus, *Lujo* virus, among others), and found mainly in Africa in rodents of the *Murinae* family as natural hosts[149]. Although *Lymphocytic choriomeningitis* virus (LCMV) belongs to this category, it circulates globally[146]. Approximately 5% of the human population have been exposed to LCMV, due to the ubiquity of the virus host, *M. musculus*[150]; (b) New World (NW), found in the American continent, are divided into four clades (A-D)[151]. Examples of NW viruses are *Junin* virus - Argentina[152], *Machupo* virus - Bolívia[153], *Sabiá* virus - Brazil[154], and *Guanarito* virus - Venezuela[155]. *Sigmodontinae* rodents are the main hosts of this class, even though *Tacaribe* virus has already been described in bats[156] and *Amblyomma americanum* ticks[157].

Members of both OW and NW arenaviruses can cause hemorrhagic fever and severe human diseases affecting the central nervous system[158]. Zoonotic transmission is through contact with rodents' urine or feces, and human-to-human transmission is possible[146]. Because of their impact on human health and rapid spread, they are potential bioterrorism agents[159].

In Colombia, a study conducted with *M. musculus*, collected from residential areas, detected 10% (8/80) of positives in serological analysis for LCMV. When brain samples of the same animals were submitted to RT-PCR, serologically negative individuals showed positive results in this second analysis, highlighting the importance of parallel diagnosis[160]. It can be justified by the vertical transmission among rodents that may deactivate cytotoxic T- lymphocytes, generating immune-complexes that may lead to misdiagnosis of ELISA reactions[160].

A research conducted in French Guiana sampled 37 animals (*M. musculus*) of which two were positive for LCMV by hemi-nested PCR (from lung and kidney samples)[161]; another inquiry in Argentina reported that 9.4% of the mice collected were positive for arenavirus, and the serological rate was 4.6% and 2.6% for men and women, respectively[162]. In Baltimore (USA), 9% of the mice were seropositive for LCMV[163], and 4.7% of the people were analyzed[164]. In Brazil, to our knowledge, there are no serological records on the prevalence of LCMV in rodents or humans.

Lassa virus (OW) is endemic in African countries, with seroprevalence reaching about 50% of the human population; this disease causes about 5,000 deaths every year[165]. *Mastomys natalensis* is considered the main reservoir of the virus[166], but it can also be found in *Hylomyscus pamfi* and *Mastomys erythroleucus*[167].

Surveys conducted in Nigeria reported positive animals for *Lassa virus* in *M. natalensis* and *M. erythroleucus*, *R. rattus*[168], and *M. musculus*[169]. In China, RT-PCRs performed in organs of *R. rattus* and *R. norvegicus* showed positive rates of 75% and 17%, respectively, and a new viral species, the *Wenzhou* virus, was isolated[145].

Junin virus is considered endemic in Argentina[170] and sporadic outbreaks have been reported[171]. There are several promising vaccinal prototypes being developed for this virus, most are in the preclinical stage[172] and one, based on plasmidial DNA, has already reached human test phase[173].

In Brazil, the most remarkable arenavirus is *Sabiá* virus, reported in São Paulo (Brazil) in 1994. Initial symptoms were described as flu-like (fever, sickness, headaches, and lethargy), quickly leading to hemorrhage and death (within 3 days)[154,174]. There have been two reports of this virus, caused by occupational exposure in a laboratory environment, one in Pará (Brazil) and the other in Connecticut (USA), both with non-fatal courses[175,176]. The 4th case was described in São Paulo (Brazil) in 1999[177] and the 5th, on January 2020 in Sorocaba (São Paulo, Brazil)[178] as a natural infection with lethal outcome.

A new arenavirus, namely *Pinhal* virus, has been characterized as a New World arenavirus (line C), first isolated from vesper mice (*Calomys tener*) in São Paulo (Brazil), but there is still no evidence that this viral strain causes disease to humans[177,179]. Besides *Pinhal* virus, other arenaviruses have been reported in Brazil: *Xapuri* virus was recently isolated from rodents (*Neacomys musseri*); *Amaparí* virus (*Neacomys guianae*); *Cupixi* virus (*Oryzomys megacephalus*); *Flexal* virus (unidentified *Oryzomyini* rodent); *Oliveros* virus (*Necromys lasiurus*); *Latino* virus (*Calomys callosus* and *Calomys callidus*) and *Aporé* virus (*Oligoryzomys mattogrossae*)[180].

Arenaviruses can be diagnosed using: (a) RT-PCR (fluids, feces, and tissues) followed by viral RNA sequencing for differentiation; (b) serology, through detection of specific IgG and IgM employing immunofluorescence and/or ELISA tests; (c) viral isolation in cell culture.

Recommended treatment is support therapy that can be combined with the antiviral ribavirin, which should be administered during the first 7-10 days after infection. Despite its efficacy, there are significant side effects, such as hemolytic anemia, progressive weight loss, respiratory difficulty, insomnia, and dermatitis, among others[180-182]. Alternative drugs with less side effects have been tested, such as favipiravir[183] and triarylmethane clotrimazole[184]. Cocktails using multiple antiviral drugs that target different steps of the viral life cycle appear to be the best strategy to limit viral multiplication with lower risk of drug resistance[185].

In literature we find description of viral rodent-infections, usually from within the context of biological models or experimentation. In this review, we focus on rodents within an urban environment, especially *R. rattus*, *R. norvegicus*, and *M. musculus*, although with the advancement of human populations, the interaction with

wild rodents increases, and different viruses can emerge. There are relatively few studies addressing the monitoring of viruses in these hosts, favoring the occurrence of outbreaks.

Control and preventive activities should go beyond the elimination or reduction of the populations of these hosts and involve sanitary education to aid the human population in the reduction of shelters for the hosts, the restriction of rodent access to residences, and the reduction of their water and food supply. Basic sanitation actions are a generic but effective measure in the reduction of rodents and, consequently, the propagation of diseases.

AUTHORS' CONTRIBUTION

MLG and FG: revision design, participated in data analysis, discussion, writing draft and review; **CMB and RMS:** participated in data analysis, discussion, writing draft and review.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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REFERENCES

1. Meerburg BG, Singleton GR, Kijlstra A. Rodent-borne diseases and their risks for public health. Crit Rev Microbiol. 2009;35(3):221-70.
2. Costa F, Carvalho-Pereira T, Begon M, Riley L, Childs J. Zoonotic and Vector-Borne Diseases in Urban Slums: Opportunities for Intervention. Trends Parasitol. 2017;33(9):660-2.
3. Cavia R, Cueto GR, Suárez OV. Changes in rodent communities according to the landscape structure in an urban ecosystem. Landsc Urban Plan. 2009;90(1-2):11-9.
4. Johnston RF. Synanthropic birds of North America. *In*: Marzluff JM, Bowman R, Donnelly R. Avian ecology and conservation in an urbanizing world. Boston: Springer; 2001.49-67.
5. McFarlane R, Sleigh A, McMichael T. Synanthropy of wild mammals as a determinant of emerging infectious diseases in the Asian-Australasian region. EcoHealth. 2012;9(1):24-35.
6. Chagas CRF, Gonzalez IHL, Favoretto SM, Ramos PL. Parasitological surveillance in a rat (*Rattus norvegicus*) colony in São Paulo Zoo animal house. Ann Parasitol. 2017;63(4):291-7.
7. Firth C, Bhat M, Firth MA, Williams SH, Frye MJ, Simmonds P, et al. Detection of Zoonotic Pathogens and Characterization of Novel Viruses Carried by Commensal *Rattus norvegicus* in New York City. Mbio. 2014;5(5):1-16.
8. Rabiee MH, Mahmoudi A, Siahsarvie R, Krystufek B, Mostafavi E. Rodent-borne diseases and their public health importance in Iran. Plos Negl Trop Dis. 2018;12(4):e0006256.
9. Reis RB, Ribeiro GS, Felzemburgh RDM, Santana FS, Mohr S, Melendez AXTO, et al. Impact of Environment and Social Gradient on Leptospira Infection in Urban Slums. PLoS Negl Trop Dis. 2008;2(4):e228.
10. Cavia R, Cueto GR, Suárez OV. Techniques to Estimate Abundance and Monitoring Rodent Pests in Urban Environments. In: Larramendy ML & Soloneski S, Integrated pest management and pest control - current and future tactics. Croatia: InTech; 2012.147-72.
11. Panti-May JA, Carvalho-Pereira TSA, Serrano S, Pedra GG, Taylor J, Pertile AC, Minter A, Airam V, et al. A Two-Year Ecological Study of Norway Rats (*Rattus norvegicus*) in a Brazilian Urban Slum. PLoS ONE. 2016;11(3):e0152511.
12. Krebs CJ. Demographic changes in fluctuating populations of *Microtus californicus*. Ecol Monograph. 1966;36(3):239-73.
13. Masi E, Vilac¸a PJ, Razzolini MTP. Environmental factors and rodent infestation in Campo Limpo District, São Paulo, Brazil. Int J Environ Health Res. 2009;19(1):1-16.
14. Santos NJ, Sousa E, Reis MG, Ko AI, Costa F. Rat infestation associated with environmental deficiencies in an urban slum community with high risk of leptospirosis transmission. Cad Saúde Pública. 2017;33(2):1-13.
15. Garden J, McAlpine C, Peterson A, Jones D, Possingham H. Review of the ecology of Australian urban fauna: a focus on spatially explicit processes. Austral Ecol. 2006;31(2):126-48.
16. Amaral CD, Costa GB, Souza WM, Alves PA, Borges IA, Tolardo AL, et al. Silent *Orthohantavirus* circulation among humans and small mammals from Central Minas Gerais, Brazil. EcoHealth. 2018;15(3):577-89.
17. Oliveira JS, Figueiredo PO, Costa GB, Assis FL, Drumond BP, Fonseca FG, et al. *Vaccinia* Virus Natural Infections in Brazil: The Good, the Bad, and the Ugly. Viruses 2017;9(11):340.
18. Saez AM, Haidara MC, Camara A, Kourouma F, Sage M, Magassouba NF, et al. Rodent control to fight Lassa fever: Evaluation and lessons learned from a 4-year study in Upper Guinea. PLoS Negl Trop Dis. 2018;12(11):e0006829.
19. Vadell MV, Villafañe IEG. Environmental Variables Associated with Hantavirus Reservoirs and Other Small Rodent Species in Two National Parks in the Paraná Delta, Argentina: Implications for Disease Prevention. EcoHealth. 2016;13(2):248-60.
20. Fernandes J, Oliveira RC, Coelho TA, Martins RMB, Caetano KAA, Horta MAP, et al. Rodent-borne viruses survey in rural settlers from Central Brazil. Mem Inst Oswaldo Cruz. 2019;114:e180448.
21. Olsson GE, Dalerum F, Hörnfeldt B, Elgh F, Palo TR, Juto P, et al. Human hantavirus infections, Sweden. Emerg Infect Dis. 2003;9(11):1395-401.
22. Santos IO, Figueirdo GG, Figueiredo LT, Azevedo MR, Novo NF, Vaz CA. Serologic survey of hantavirus in a rural population from the northern State of Mato Grosso, Brazil. Rev Soc Bras Med Trop. 2013;46(1):30-3.
23. Fair J, Jentes E, Inapogui A, Kourouma K, Goba A, Bah A, et al. Lassa Virus-Infected Rodents in Refugee Camps in Guinea: A Looming Threat to Public Health in a Politically Unstable Region. Vector Borne Zoonotic Dis. 2007;7(2):167-71.
24. Bonner PC, Schmidt W-P, Belmain SR, Oshin B, Baglole D, Borchert M. Poor housing quality increases risk of rodent infestation and Lassa Fever in refugee camps of Sierra Leone. Am J Trop Med Hyg. 2007;77(1):169-75.
25. Song M, Wang B, Liu J, Gratz N. Insect Vectors and Rodents Arriving in China Aboard International Transport. J Travel Med. 2003;10(4):241-4.
26. Mouchtouri VA, Anagnostopoulou R, Samanidou-Voyadjoglou A, Theodoridou K, Hatzoglou C, Kremastinou J, et al. Surveillance study of vector species on board passenger ships, Risk factors related to infestations. BMC Public Health. 2008;8:100.
27. Cao S, Ma J, Cheng C, Ju W, Wang Y. Genetic characterization of hantaviruses isolated from rodents in the port cities of Heilongjiang, China, in 2014. BMC Vet Res. 2016;12:69.
28. Koonin EV, Gorbalenya AE, Purdy MA, Rozanov MN, Reyes GR, Bradley DW. Computer-assisted assignment of functional domains in

the non-structural polyprotein of *hepatitis E* virus: Delineation of an additional group of positive-strand RNA plant and animal viruses. Proc Natl Acad Sci USA. 1992;89(17):8259-63.

29. Purdy MA, Harrison TJ, Jameel S, Meng X-J, Okamoto H, Van der Poel WHM, et al and ICTV Report Consortium. ICTV Virus Taxonomy Profile: *Hepeviridae*. J Gen Virol. 2017; 98:2645-6.

30. Simanavicius M, Juskaite K, Verbickaite A, Jasiulionis M, Tamosiunas PL, Petraityte-Burneikiene R, et al. Detection of rat hepatitis E virus, but not human pathogenic *hepatitis E* virus genotype 1-4 infections in wild rats from Lithuania. Vet Microbiol. 2018,221:129-33.

31. Li TC, Chijiwa K, Sera N, Ishibashi T, Etoh Y, Shinohara Y, et al. *Hepatitis E* Virus Transmission from Wild Boar Meat. Emerg Infect Dis. 2005;11(12):1958-60.

32. Marrone G, Biolato M, Mercurio G, Capobianchi MR, Garbuglia AR, Liguori A, et al. Acute HEV hepatitis: clinical and laboratory diagnosis. Eur Rev Med Pharmacol Sci. 2019;23(2):764-70.

33. Howard CM, Handzel T, Hill VR, Grytdal SP, Blanton C, Kamili S, et al. Novel Risk Factors Associated with *Hepatitis E* virus Infection in a Large Outbreak in Northern Uganda: Results from a Case-Control Study and Environmental Analysis. Am J Trop Med Hyg. 2010;83(5):1170-3.

34. Vollmer T, Diekmann J, Johne R, Eberhardt M, Knabbe C, Dreier J. A novel approach for the detection of *Hepatitis E* virus infection in German blood donors. J Clin Microbiol. 2012;50(8):2708-13.

35. Karetnyĭ IUV, Dzhumalieva DI, Usmanov RK, Titova IP, Litvak IAI, Balaian MS. The possible involvement of rodents in the spread of viral *hepatitis E*. Zh Microbiol Epidemiol Immunobiol. 1993;(4):52-6.

36. Chauhan A, Jameel S, Dilawari JB, Chawla YK, Kaur U, Ganguly NK. Hepatitis E virus transmission to a volunteer. Lancet. 1993;341:149-150.

37. Ryll R, Bernstein S, Heuser E, Schlegel M, Dremsek P, Zumpe M, et al. Detection of rat *Hepatitis E* virus in wild Norway rats (*Rattus norvegicus*) and Black rats (*Rattus rattus*) from 11 European countries. Vet Microbiol. 2017;208:58-68.

38. Jothikumar N, Cromeans TL, Robertson BH, Meng XJ, Hill VR. A broadly reactive one-step real-time RT-PCR assay for rapid and sensitive detection of *Hepatitis E* virus. J Virol Method. 2006;131(1):65-71.

39. Johne R, Dremsek P, Kindler E, Schielke A, Plenge-Bönig A, Gregersen H, et al. Rat *Hepatitis E* virus: geographical clustering within Germany and serological detection in wild Norway rats (*Rattus norvegicus*). Infect Genet Evol. 2012;12(5):947-56.

40. Li W, Guan D, Su J, Takeda N, Wakita T, Li TC, et al. High prevalence of rat hepatitis E virus in wild rats in China. Vet Microbiol. 2013;165(3-4):275-80.

41. Lenggenhager D, Weber A. An Update on the Clinicopathologic Features and Pathologic Diagnosis of *Hepatitis E* in Liver Specimens. Adv Anat Pathol. 2018;25(4):273-81.

42. Gupta E, Agarwala P. *Hepatitis E* virus infection: An old virus with a new story! Zoonoses Public Health. 2018;36(3):317-23.

43. Smith DB, Simmonds P, Izopet J, Oliveira-Filho EF, Ulrich RG, Johne R, et al. Proposed reference sequences for *Hepatitis E* virus subtypes. J Gen Virol. 2016;97(3):537-42.

44. Park WJ, Park BJ, Ahn HS, Lee JB, Park SY, Song CS, et al. *Hepatitis E* virus as an emerging zoonotic pathogen. J Vet Sci. 2016;17(1):1-11.

45. Vitral CL, Pinto MA, Lewis-Ximenez LL, Khudyakov YE, dos Santos DR, Gaspar AMC. Serological evidence of *Hepatitis E* virus infection in different animal species from the Southeast of Brazil. Mem Inst Oswaldo Cruz. 2005;100(2):117-22.

46. Johne R, Heckel G, Plenge-Bönig A, Kindler E, Maresch C, Reetz J, et al. Novel *Hepatitis E* virus genotype in Norway rats. Ger. Emerg Infect Dis. 2010;16(9):1452-5.

47. Johne R, Plenge-Bönig A, Hess M, Ulrich RG, Reetz J, Schielke A. Detection of a novel *Hepatitis E-like* virus in faeces of wild rats using a nested broadspectrum RT-PCR. J Gen Virol. 2010;91(3):750-8.

48. Obana S, Shimizu K, Yoshimatsu K, Hasebe F, Hotta K, Isozumi R, et al. Epizootiological study of rodent-borne *Hepatitis E* virus HEV-C1 in small mammals in Hanoi, Vietnam. J Vet Med Sci. 2017;79(1):76-81.

49. Huang F, Li Y, Yu W, Jing S, Wang J, Long F, et al. Excretion of infectious *Hepatitis E* virus into milk in cows imposes high risks of zoonosis. Hepatology. 2016,64(2):350-8.

50. Zeng MY, Gao H, Yan XX, Qu WJ, Sun YK, Fu GW, et al. High *Hepatitis E* virus antibody positive rates in dogs and humans exposed to dogs in the south-west of China. Zoonoses Public Health. 2017;64(8):684-8.

51. Zhao T, Wang X, Wei H, Yang M, Zeng F, Zhou H. Molecular and functional characterization of grass carp squint/nodal-related 1: a potential regulator of activin signaling in teleost pituitary cells. Domest Anim Endocrinol. 2012;42(4):239-48.

52. Cooper BS, White LJ, SiddiquI R. Reactive and pre-emptive vaccination strategies to control hepatitis E infection in emergency and refugee settings: A modelling study. PLoS Negl Trop Dis. 2018;12(9):e0006807

53. International Committee on Taxonomy of Viruses (ICTV). International Committee on Taxonomy of Viruses (ICTV) [Internet]. 2019 [cited 2019 Oct 10]. Available from: https://talk.ictvonline.org/.

54. Muyangwa M, Martynova EV, Khaiboullina SF, Morzunov SP, Rizvanov AA. Hantaviral proteins: structure, functions, and role in *Hantavirus* infection. Front Microbiol. 2015;6:1326.

55. Zuo S-Q, Fang L-Q, Zhan L, Zhang P-H, Jiang J-F, Wang L-P, et al. Geo-spatial hotspots of hemorrhagic fever with renal syndrome and genetic characterization of *Seoul* Variants in Beijing, China. PLoS Negl Trop Dis. 2011;5(1):e945.

56. Spiropoulou CF, Albarino CG, Ksiazek TG, Rollin PE. *Andes* and *Prospect Hill* hantaviruses differ in early induction of interferon although both can downregulate interferon signaling. J Virol. 2007;81(6):2769-76.

57. Oliveira RC, Guterres A, Fernandes J, D'Andrea OS, Bonvicino CR, Lemos ERS. Hantavirus reservoirs: current status with an emphasis on data from Brazil. Viruses. 2014;6(5):1929-73.

58. Guterres A, Lemos ERS. Hantaviruses and a neglected environmental determinant. One Health. 2018;5:27-33.

59. Wells RM, Sosa ES, Yadon ZE, Enria D, Padula P, Pini N, et al. An unusual hantavirus outbreak in southern Argentina: person-to-person transmission? Emerg Infect Dis. 1997;3(2):171-4.

60. Kim HC, Kim WK, No JS, Lee SH, Gu SH, Chong ST, et al. Urban rodent surveillance, climatic association, and genomic characterization of *Seoul* virus collected at US. Army Garrison, Seoul, Republic of Korea, 2006 - 2010. Am J Trop Med Hyg. 2018;99(2):470-6.

61. Hjelle B, Torres-Pérez F. Hantaviruses in the Americas and Their Role as Emerging Pathogens. Viruses. 2010;2(12):2559-86.

62. Lee HW, Lee PW, Baek LJ, Song CK, Seong IW. Intraspecific transmission of *Hantaan virus,* etiologic agent of Korean hemorrhagic fever, in the rodent *Apodemus agrarius*. Am J Trop Med Hyg. 1981;30(5):1106-12.

63. Yu X-J, Tesh RB. The role of mites in the transmission and maintenance of *Hantaan* Virus (Hantavirus: *Bunyaviridae*). J Infect Dis. 2014;210(11):1693-9.

64. Hansen A, Cameron S, Liu Q, Sun Y, Weinstein P, Williams C, et al. Transmission of Haemorrhagic Fever with Renal Syndrome in China and the role of climate factors: a review. Int J Infect Dis. 2015;33:212-8.

65. Gozalan A, Kalaycioglu H, Uyar Y, Sevindi DF, Turkyilmaz B, Çakir V, et al. Human *Puumala* and *Dobrava* Hantavirus infections in the Black

Sea region of Turkey: a cross-sectional study. Vector Borne Zoonotic Dis. 2013;13(2):111-8.

66. Hofmann J, Meier M, Enders M, Führer A, Ettinger J, Klempa B, et al. Hantavirus disease in Germany due to infection with *Dobrava-Belgrade* virus genotype Kurkino. Clin Microbiol Infect. 2010;20(10):O648-55.

67. Witkowski PT, Bourquain D, Bankov K, Auste B, Dabrowski PW, Nitsche A, et al. Infection of human airway epithelial cells by different subtypes of *Dobrava-Belgrade* virus reveals gene expression patterns corresponding to their virulence potential. Virology. 2016;493:189-201.

68. Laenen L, Vergote V, Vanmechelen B, Tersago K, Baele G, Lemey P, et al. Identifying the patterns and drivers of *Puumala* hantavirus enzootic dynamics using reservoir sampling. Virus Evolution. 2019;5(1):vez009.

69. Reil D, Rosenfeld UM, Imholt C, Schmidt S, Ulrich RG, Eccard JA, et al. *Puumala* hantavirus infections in bank vole populations: host and virus dynamics in Central Europe. BMC Ecol. 2017;17(1):9.

70. Ling J, Verner-Carlsson J, Eriksson P, Plyusnina A, Löhmus M, Järhult JD, et al. Genetic analyses of *Seoul* hantavirus genome recovered from rats (*Rattus norvegicus*) in the Netherlands unveils diverse routes of spread into Europe. J Med Virol. 2019;91(5):724-30.

71. Krautkrämer E, Zeier M. Old World hantaviruses: aspects of pathogenesis and clinical course of acute renal failure. Virus Res. 2014;187:59-64.

72. Jiang H, Zheng X, Wang L, Du H, Wang P, Bai X. Hantavirus infection: a global zoonotic challenge. Virol Sin. 2017;32(1):32-43.

73. Silva MV, Vasconcelos MJ, Hidalgo NTR, Veiga APR, Canzian M, Marotto PCF, et al. Hantavirus pulmonary syndrome: Report of the first three cases in São Paulo, Brazil. Rev Inst Med Trop S Paulo. 1997;39(4):231-4.

74. Ferres M, Vial P, Marco C, Yanez L, Godoy P, Castillo C, et al. *Andes virus household contacts study group*. Prospective evaluation of household contacts of persons with Hantavirus Cardiopulmonary Syndrome in Chile. J Infect Dis 2007;195(11):1563-71.

75. Ministério da Saúde [Internet]. Brasil: Ministério da Saúde. INC. Situação epidemiológica - dados hantavirose. [update 2019 Sep 15; cited 2019 Oct 01]. Available from: http://portalms.saude.gov.br/saude-de-a-z/hantavirose/11304-situacao-epidemiologica-dados.

76. Childs JE, Glass GE, Korch GW, Leduc JW. Effects of hantaviral infection on survival, growth and fertility in wild rat (*Rattus norvegicus*) populations of Baltimore, Maryland. J Wildl Dis. 1989;25(4):69-76.

77. Yanagihara R, Goldgaber D, Gajdusek DC. Propagation of nephropathia epidemica virus in Mongolian gerbils. J Virol. 1985;55(3):973-5.

78. Plyusnin A, Vapalahti O, Vaheri A. Hantaviruses: genome structure, expression and evolution. J Gen Virol. 1996;77(11):2677-87.

79. Jonsson CB, Figueiredo LT, Vapalahti O. A global perspective on hantavirus ecology, epidemiology, and disease. Clin Microbiol Rev. 2010;23(2):412-41.

80. de Oliveira RC, Guterres A, Fernandes J, D'Andrea PS, Bonvicino CR, de Lemos ERS. Hantavirus Reservoirs: Current Status with an Emphasis on Data from Brazil. Viruses. 2014;6(5):1929-73.

81. Costa F, Porter FH, Rodrigues G, Farias H, de Faria MT, Wunder EA, et al. Infections by *Leptospira interrogans*, *Seoul* virus, and *Bartonella spp*. Among Norway rats (*Rattus norvegicus*) from the urban slum environment in Brazil. Vector Borne Zoonotic Dis. 2014;14(1):33-40.

82. Raharinosy V, Olive MM, Andriamiarimanana FM, Andriamandimby SF, Ravalohery JP, Andriamamonjy S, et al. Geographical distribution and relative risk of *Anjozorobe* virus (Thailand *orthohantavirus*) infection in black rats (*Rattus rattus*) in Madagascar. Virol J. 2018;15(1):83.

83. Maes P, Clement J, Van Ranst M. Recent approaches in Hantavirus vaccine development. Expert Rev Vaccines. 2009;8(1):67-76.

84. Kruger DH, Schonrich G, Klempa B. Human pathogenic hantaviruses and prevention of infection. Hum Vaccin. 2011;7(6):685-93.

85. Valdivieso F, Gonzalez C, Najera M, Olea A, Cuiza A, Aguilera X, et al. Knowledge, attitudes, and practices regarding hantavirus disease and acceptance of a vaccine trial in rural communities of southern Chile. Hum Vaccin Immunother. 2017;13(4):808-15.

86. Huggins JW, Hsiang CM, Cosgriff TM, Guang MY, Smith JI, Wu ZO, et al. Prospective, double-blind, concurrent, placebo-controlled clinical trial of intravenous ribavirin therapy of hemorrhagic fever with renal syndrome. J Infect Dis. 1991;164(6):1119-27.

87. Maes P, Clement J, Gavrilovskaya I, Van Ranst M. Hantaviruses: immunology, treatment, and prevention. Viral Immunol. 2004;17(4):481-97.

88. Jonsson CB, Hooper J, Mertz G.Treatment of hantavirus pulmonary syndrome. Antiviral Res. 2008;78(1):162-169.

89. Attoui H, Mertens PPC, Becnel J, Belaganahalli S, Bergoin M, Brussaard CP, et al. Orthoreovirus, Reoviridae. *In*: Virus taxonomy. Classification and nomenclature of viruses: ninth report of the International Committee on the Taxonomy of Viruses. London: Elsevier Academic Press; 2011. 546-54.

90. Estes M, Greenberg HB. Rotaviruses. *In*: Knipe DM, Howley PM, Cohen JI, Griffin DE, Lamb RA, Martin MA, Roizman B, Racaniello VR, Fields virology. 6th ed. Pennsylvania: Lippincott Williams; 2013.1347-401.

91. Parra GI, Bok K, Martínez M, Gomez JA. Evidence of rotavirus intragenic recombination between two sublineages of the same genotype. J Gen Virol. 2004;85(6):1713-6.

92. Holmes EC, Worobey M, Rambaut A. Phylogenetic evidence for recombination din dengue virus. Mol Biol Evol.1999;16(3):405-9.

93. Matthijnssens J, Otto P, Ciarlet M, Desselberger U, Van Ranst M, Johne R. VP6 sequence-based cut-off values as a criterion for rotavirus species demarcation. Arch Virol. 2011;157(6):1177-82.

94. Mihalov-Kovács E, Gellért A, Marton S, Farkas SL, Fehér E, Oldal M, et al. Candidate new rotavirus species in sheltered dogs, Hungary. Emerg Infect Dis. 2015, 21(4):660-3.

95. BányaI K, Kemenesi G, Budinski I, Földes F, Zana B, Marton S, et al. Candidate new rotavirus species in Schreiber's bats, Serbia. Infect Genet Evol. 2017;48:19-26.

96. Matthijnssens J, Ciarlet M, Heiman E, Arijs I, Delbeke T, McDonalD SM, et al. Classification of Rotaviruses Reveals a Common Origin between Human Wa-Like and Porcine Rotavirus Strains and Human DS-1-Like and Bovine Rotavirus Strains. J Virol. 2008;82(7):3204-19.

97. Guo D, Liu J, Lu Y, Sun Y, Yuan D, Jiang Q, et al. Full genomic analysis of rabbit rotavirus G3P[14] strain N5 in China: identification of a novel VP6 genotype. Infect Genet Evol. 2012;12(7):1567-76.

98. Trojnar E, Sachsenroder J, Twardziok S, Jochen R, Otto PH, Johne R. Identification of an avian group A rotavirus containing a novel VP4 gene with a close relationship to those of mammalian rotaviruses. J Gen Virol. 2013;94(1):136-42.

99. Joshi MS, Deore SG, Walimbe AM, Ranshing SS, Chitambar SD. Evaluation of different genomic regions of Rotavirus A for development of real time PCR. J Virol Meth. 2019;266:65-71.

100. Yodmeeklin A, Khamrin P, Chuchaona W, Kumthip K, Kongkaew A, Vachirachewin R, et al. Analysis of complete genome sequences of G9P[19] rotavirus strains from human and piglet with diarrhea provides evidence for whole-genome interspecies transmission of nonreassorted porcine rotavirus. Infect Genet Evol. 2017;47:99-108.

101. Li K, Lin X-D, Huang K-Y, Zhang B, Shi M, Guo W-P, et al. Identification of novel and diverse rotaviruses in rodents and insectivores, and evidence of cross-species transmission into humans. Virol. 2016;494:168-77.

102. Ianiro G, DI Bartolo I, De Sabato L, Pampiglione G, Ruggeri FM, et al. Detection of uncommon G3P[3] rotavirus A (RVA) strain in rat possessing a human RVA-like VP6 and a novel NSP2 genotype. Infect Genet Evolut. 2017; 53: 206-11.

103. Vlasova AN, Amimo JO, Saif LJ. Porcine Rotaviruses: Epidemiology, Immune Responses and Control Strategies. Viruses. 2017;9(3):48.

104. Rigo-Adrover MDM, Knipping K, Garssen J, van Limpt K, Knol J, Franch À, et al. Prevention of Rotavirus Diarrhea in Suckling Rats by a Specific Fermented Milk Concentrate with Prebiotic Mixture. Nutrients. 2019;11(1). pii:E189.

105. Rocha TG, Silva FDF, Gregori F, Alfieri AA, Buzinaro MG, Fagliari JJ. Longitudinal study of bovine rotavirus group A in newborn calves from vaccinated and unvaccinated dairy herds. Trop Anim Health Prod. 2017;49(4):783-90.

106. Beserra LAR, Gregori F. Description of Rotavirus F in Broilers from Brazilian Poultry Farms. Avian Dis. 2014;58(3):458-61.

107. Molinari BLD, Possattia F, Lorenzetti E, Alfieri AF, Alfieri AA. Unusual outbreak of post-weaning porcine diarrhea caused by single and mixed infections of rotavirus groups A, B, C, and H. Vet Microbiol. 2016;193:125-32.

108. Silva FDF, Gregori F, McDonald SM. Distinguishing the genotype 1 genes and proteins of human Wa-like rotaviruses vs. porcine rotaviruses. Infect Genet Evolut. 2016;43:6-14.

109. Tonietti PO, Dahora AS, Silva FDF, Ferrari KL, Brandão PE, Richtzenhain LJ, et al. Simultaneous Detection of Group A Rotavirus in Swine and Rat on a Pig Farmin Brazil. Scientific World Journal. 2013;2013:648406.

110. Sachsenröder J, Braun A, Machnowska P, Ng TF, Deng X, Guenther S, et al. Metagenomic identification of novel enteric viruses in urban wild rats and genome characterization of a group A rotavirus. J Gen Virol 2014;95(12):2734-47.

111. Memon AM, Bhuyan AA, Chen F, Guo X, Menghwar H, Zhu Y, et al. Development and Validation of Monoclonal Antibody-Based Antigen Capture ELISA for Detection of Group A Porcine Rotavirus. Viral Immunol. 2017;30(4):264-70.

112. Holmes KV, Lai MMC. *Coronaviridae*: the viroses and their replication. *In*: Fields BN, Knipe DM, Howley PM., Virology. 3 ed. Philadelphia: Lippincott-Raven Publisher; 1996.1075-93.

113. Lai MM, Cavanagh D. The molecular biology of coronaviruses. Adv Virus Res. 1997;48:1-100.

114. Wan Z, Zhang Y, He Z, Liu J, Lan K, Hu Y, et al. A Melting Curve-Based Multiplex RT-qPCR Assay for Simultaneous Detection of Four Human Coronaviruses. Int J Mol Sci. 2016;17(11):1880.

115. Bukhari K, Mulley G, Gulyaeva AA, Zhao L, Shu G, Jiang J, et al. Description and initial characterization of metatranscriptomic nidovirus-like genomes from the proposed new family *Abyssoviridae*, and from a sister group to the *Coronavirinae*, the proposed genus Alphaletovirus. Virol. 2018;524:160-71.

116. Gorbalenya AE, Enjuanes L, Ziebuhr J, Snijder EJ. *Nidovirales*: evolving the largest RNA virus genome. Virus Res. 2006;117:17-37.

117. Woo PC, Lau SK, Lam CS, Lau CC, Tsang AK, Lau JH, et al. Discovery of seven novel Mammalian and avian coronaviruses in the genus *deltacoronavirus* supports bat coronaviruses as the gene source of *alphacoronavirus* and *betacoronavirus* and avian coronaviruses as the gene source of *gammacoronavirus* and *deltacoronavirus*. J Virol. 2012;86(7):3995-4008.

118. Yaoa Q, Mastersb PS, Yea R. Negatively charged residues in the endodomain are critical for specific assembly of spike protein into murine coronavirus. Virol. 2013;442(1):74-81.

119. Wang W, Lin XD, Guo WP, Zhou RH, Wang MR, Wang CQ, et al. Discovery, diversity and evolution of novel coronaviruses sampled from rodents in China. Virol. 2015;474:19-27.

120. Ge XY, Yang WH, Zhou JH, Li B, Zhang W, Shi ZL, et al. Detection of *alpha*- and *betacoronaviruses* in rodents from Yunnan, China. Virol J. 2017;14:98.

121. Monchatre-Leroy E, Boué F, Boucher JM, Renault C, Moutou F, Gouilh MA, et al. Identification of Alpha and Beta Coronavirus in Wildlife Species in France: Bats, Rodents, Rabbits, and Hedgehogs. Viruses. 2017;9(12):364.

122. Pana Y, Tianb X, Qin P, Wang B, Zhao P, Yang YL, et al. Discovery of a novel swine enteric *alphacoronavirus* (SeACoV) in southern China. Vet. Microbiol. 2017;211:15-21.

123. Bourgarel M, Pfukenyi DM, Boué V, Talignani L, Chiweshe N, Diop F, et al. Circulation of *Alphacoronavirus*, *Betacoronavirus* and *Paramyxovirus* in *Hipposideros* bat species in Zimbabwe. Infect Genet Evol. 2018;58:253-57.

124. Marandino A, Tomás G, Panzera Y, Greif G, Parodi-Talice A, Hernández M, et al. Whole-genome characterization of Uruguayan strains of avian infectious bronchitis virus reveals extensive recombination between the two major South American lineages. Infect Genet Evol. 2017;54:245-50.

125. Hu H, Jung K, Vlasova AN, Chepngeno J, Lu Z, Wang Q, et al. Isolation and characterization of porcine *deltacoronavirus* from pigs with diarrhea in the United States. J Clin Microbiol. 2015;53(5):1537-48.

126. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;14(8):523-34.

127. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirol. 2018;23(2):130-7.

128. Guan Y, Zheng BJ, He YQ, Liu XL, Zhuang ZX, Cheung CL, et al. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. Science. 2003;302(5643):276-8.

129. Hemida MG, Perera RA, Wang P, Alhammadi MA, Siu LY, Li M, et al. Middle East Respiratory Syndrome (MERS) coronavirus seroprevalence in domestic livestock in Saudi Arabia, 2010 to 2013. Euro Surveill. 2013;18(50):20659.

130. Alagaili AN, Briese T, Mishra N, Kapoor V, Sameroff SC, Burbelo PD, et al. Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. MBio. 2014;5(2):e00884-14.

131. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol. 2019;17(3):181-92.

132. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, Thrusting Coronaviruses into the Spotlight. Viruses. 2019;11(1):59.

133. Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. Nat Rev Microbiol. 2009;7(6):439-50.

134. Belouzard S, Millet JK, Licitra BN, Whittaker GR. Mechanisms of coronavirus cell entry mediated by the viral spike protein. Viruses. 2012;4(6):1011-33.

135. Gélinas AM, Boutin M, Sassevile AM, Dea S. Bovine coronaviruses associated with enteric and respiratory diseases in Canadian dairy cattle display diferente reactivities to anti-HE monoclonal antibodies and distinct amino acid changes in theis HE, S and ns4.9 protein. Virus Res. 2001;76(1):43-57.

136. Navas-Martin S, Weiss SR. SARS: Lessons learned from other Coronaviruses. Viral Immunol. 2003;16(4):461-74.

137. Cheever FS, Daniels JB, Pappenheimer AM, Bailey OT. A murine virus (JHM) causing disseminated encephalomyelitis with extensive destruction of myelin. J Exp Med. 1949;90(3):181-210.

138. Lane TE, Hosking MP. The pathogenesis of murine coronavirus infection of the central nervous system. Crit Rev Immunol 2010,30(2):119-30.

139. Funk CJ, Manzer R, Miura TA, Groshong SD, Ito Y, et al. Rat respiratory coronavirus infection: replication in airway and alveolar epithelial cells and the innate immune response. J Gen Virol 2009;90(12):2956-64.

140. Lau SK, Woo PC, Li KS, Tsang AK, Fan RY, Luk HK, et al. Discovery of a novel coronavirus, China *Rattus* coronavirus HKU24, from Norway rats supports the murine origin of *Betacoronavirus* 1 and has implications for the ancestor of *Betacoronavirus* lineage A. J Virol. 2015;89(6):3076-92.

141. Tsoleridis T, Onianwa, Horncastle E, Dayman E, Zhu M, Danjittrong T, et al. Discovery of Novel *Alphacoronaviruses* in European Rodents and Shrews. Viruses. 2016;8(3):84.

142. Phan MVT, Tri TN, Anh PH, Baker S, Kellam P, Cotton M. Identification and characterization of *Coronaviridae* genomes from Vietnamese bats and rats based on conserved protein domains. Virus Evol. 2018;4(2):vey035.

143. Okba N MA, Raj VS, Haagans BL. Middle East respiratory syndrome coronavirus vaccines: current status and novel approaches. Curr Opin Chem Biol. 2017;23:49-58.

144. Gonzalez JP, Emonet S, de Lamballerie X, Charrel R. *Arenaviruses*. Curr Top Microbiol Immunol. 2007;315:253-88.

145. Li K, Lin XD, Wang W, Shi M, Guo WP, Zhang XH, et al. Isolation and characterization of a novel Arenavirus harbored by Rodents and Shrews in Zhejiang province, China. Virology. 2015;476:37-42.

146. Hallam SJ, Koma T, Maruyama J, Paessler S. Review of *Mammarenavirus* Biology and Replication. Front Microbiol. 2018;9:1751.

147. Radoshitzky SR, Buchmeier MJ, Charrel RN, Clegg JCS, Gonzalez JPJ, Günther S, et al, and the ICTV Report Consortium. ICTV Virus Taxonomy Profile: *Arenaviridae*. J Gen Virol. 2019;100:1200-1.

148. Garry CE, Garry RF. Proteomics Computational Analyses Suggest that the *Antennavirus* Glycoprotein Complex Includes a Class I Viral Fusion Protein (α-Penetrene) with an Internal Zinc-Binding Domain and a Stable Signal Peptide. Viruses. 2019 14;11(8):e750.

149. Iannetta M, Di Caro A, Nicastri E, Vairo F, Masanja H, Kobinger G, et al. Viral Hemorrhagic Fevers Other than Ebola and Lassa. Infect Dis Clin North Am. 2019;33(4):977-1002.

150. Ly H. Differential Immune Responses to New World and Old World Mammalian *Arenaviruses.* Int J Mol Sci. 2017;18(5):1040.

151. Sarute N, Ross SR. New World *Arenavirus* Biology. Annu Rev Virol. 2017;4(1):141-58.

152. Vanella JM, Gonzalez LE, PaglinI S, Marquez A. Laboratory evidence of the activity of *Junin* virus in the southeast of Cordoba: hypothesis on its epidemiology. Dia Med. 1964;36:290-1.

153. Johnson KM, Mackenzie RB, Webb PA, Kuns ML. Chronic infection of rodents by *Machupo* virus. Science. 1965;150(3703):1618-9.

154. Coimbra TLM, Nassar ES, Burattini MN, Souza LTM, Ferreira IB, Rocco IM, et al. New arenavirus isolated in Brazil. Lancet. 1994;343(8894):391-2.

155. Fulhorst CF, Bowen MD, Salas RA, Duno G, Utrera A, Ksiazek TG, et al. Natural rodent host associations of *Guanarito* and *Pirital* viruses (Family *Arenaviridae*) in central Venezuela. Am J Trop Med Hyg. 1999;61(2):325-30.

156. Gerrard DL, Hawkinson A, Sherman T, Modahl CM, Hume G, Campbell CL, et al. Transcriptomic Signatures of *Tacaribe* virus-Infected Jamaican Fruit Bats. mSphere. 2017;2(5):e00245-17

157. Sayler KA, Barbet AF, Chamberlain C, Clapp WL, Alleman R, Loeb JC, et al. Isolation of *Tacaribe* virus, a Caribbean arenavirus, from host-seeking *Amblyomma americanum* ticks in Florida. PLoS One. 2014;9:e115769.

158. Charrel RN, de Lamballerie X. Zoonotic aspects of arenavirus infections. Vet Microbiol. 2010;140(3-4):213-20.

159. US Dep. Health Hum. Serv. (HHS). HHS public health emergency medical countermeasure enterprise implementation plan for chemical, biological, radiological, and nuclear threats. US Dep. HHS, Off. Public Health Emerg. Med. Countermeas., Off. Assist. Secr. Prep. Response, Washington, DC.[cited 2019 Dez 18]. Available from: https://www.medicalcountermeasures.gov/barda/documents/phemce_implplan_041607final.pdf

160. Castellar A, Guevara M, Rodas JD, Londoño AF, Arroyave E, Díaz FJ, et al. Primera evidencia de infección por el virus de la coriomeningitis linfocítica (arenavirus) en roedores *Mus musculus* capturados en la zona urbana del municipio de Sincelejo, Sucre, Colombia. Biomédica 2017;37(1):75-85.

161. Lavergne A, de Thoisy B, Tirera S, Donato D, Bouchier C, Catzeflis F, et al. Identification of *lymphocytic choriomeningitis* mammarenavirus in house mouse (*Mus musculus*, Rodentia) in French Guiana. Infect Genet Evol. 2016; 37:225-30.

162. Riera L, Castillo E, Del Carmen Saavedra M, Priotto J, Sottosanti J, Polop J, et al. Serological study of the *lymphochoriomeningitis* virus (LCMV) in an inner city of Argentina. J Med Virol. 2005;76(2):285-9.

163. Childs JE, Glass GE, Korch GW, Ksiazek TG, Leduc JW. *Lymphocytic choriomeningitis* virus infection and house mouse (*Mus musculus*) distribution in urban Baltimore. Am J Trop Med Hyg. 1992;47(1):27-34.

164. Childs JE, Glass GE, Ksiazek TG, Rossi CA, Oro JG, Leduc JW. Human-rodent contact and infection with *lymphocytic choriomeningitis* and *Seoul* viruses in an inner-city population. Am J Trop Med Hyg. 1991;44(2):117-21.

165. Center for Disease Control and Prevention (CDC). *Lassa* virus (CDC) [Internet]. 2019 [cited 2019 Dez 18]. Available from: https://www.cdc.gov/vhf/lassa/index.html.

166. Richmond JK, Baglole DJ. Lassa fever: epidemiology, clinical features, and social consequences. BMJ. 2003;327(7426):1271-5.

167. Olayemi A, Cadar D, Magassouba N, Obadare A, Kourouma F, Oyeyiola A, et al. New hosts of The *Lassa* virus. SciRep. 2016,6:25280.

168. Olayemi A, Oyeyiola A, Obadare A, Igbokwe J, Adesina AS, Onwe F, et al. Widespread arenavirus occurrence and seroprevalence in small mammals, Nigeria. Parasit Vectors. 2018;11(1):416.

169. Agbonlahor DE, Erah A, Agba IM, Oviasogie FE, Ehiaghe AF, Wankasi M, et al. Prevalence of *Lassa* virus among rodents trapped in three South-South States of Nigeria. J Vector Borne Dis. 2017;54(2):146-150.

170. Mills JN, Ellis BA, Childs JE, McKee KT Jr, Maiztegui JI, Peters CJ, et al. Prevalence of infection with Junin virus in rodent populations in the epidemic area of Argentine hemorrhagic fever. Am J Trop Med Hygiene. 1994. 51(5):554-62.

171. Enria DA, Briggiler AM, Sanchez Z. Treatment of Argentine hemorrhagic fever. Antivir Res. 2008; 78(1):132-9.

172. Salami K, Gouglas D, Schmaljohn C, Saville M, Tornieporth N. A review of Lassa fever vaccine candidates. Curr Opin Virol. 2019, 37:105-11.

173. Cashman KA, Wilkinson ER, Shaia CI, Facemire PR, Bell TM, Bearss JJ, et al. A DNA vaccine delivered by dermal electroporation fully protects cynomolgus macaques against Lassa fever. Hum Vaccin Immunother. 2017;13(12):2902-2911.

174. Gonzalez JP, Bowen MD, Nichol ST, Rico-Hesse R. Genetic characterization and phylogeny of *Sabiá* virus, an emergent pathogen in Brazil. Virology. 1996;221(2):318-24.

175. Vasconcelos PFC, Travassos da Rosa APA, Rodrigues SG, Tesh RB, Travassos da Rosa JFS, Travassos da Rosa ES. Infecção humana adquirida em laboratório causada pelo vírus SP H 114202 (Arenavirus: família *Arenaviridae*) - Aspectos clínicos e laboratoriais. Rev Inst Med Trop São Paulo. 1993;35(6):521-5.

176. Centers for Disease Control and Prevention (CDC). Arenavirus infection - Connecticut. MMWR Morb Mortal Wkly Rep. 1994;43(34):635-6.

177. Ellwanger JH, Chies JAB. Keeping track of hidden dangers - The short history of the *Sabiá* virus. Rev Soc Bras Med Trop. 2017;50(1):3-8.

178. Ministério da Saúde. Boletim epidemiológico - Secretaria de Vigilância em Saúde. Identificação de um caso de febre hemorrágica brasileira no estado de São Paulo, janeiro de 2020.[Internet] 2020; 51(3) [update 2020 Jan 20; cited 2020 Jan 21]. Available from: http://portalarquivos2.saude.gov.br/images/pdf/2020/janeiro/20/Boletim-epidemiologico-SVS-03.pdf

179. Bisordi I, Levis S, Maeda AY, Suzuki A, Nagasse-Sugahara TK, de Souza RP, et al. *Pinhal* Virus, a New Arenavirus Isolated from *Calomys tener* in Brazil. Vector Borne Zoonotic Dis. 2015;15(11):694-700.

180. Fernandes J, Guterres A, de Oliveira RC, Jardim R, Dávila AMR, Hewson R, et al. *Aporé* virus, a novel *mammarenavirus* (Bunyavirales: *Arenaviridae*) related to highly pathogenic virus from South America. Mem Inst Oswaldo Cruz. 2019;114:e180586.

181. Barry M, Russi M, Armstrong L, Geller DL, Tesh R, Dembry L, et al. Treatment of laboratory-acquired *Sabiá* vírus infection. N Engl J Med. 1995;333(5):294-6.

182. Kochhar DM, Penner JD, Knudsen TB. Embryotoxic, teratogenic, and metabolic effects of ribavirin in mice. Toxicol Appl Pharmacol. 1980;52(1):99-112.

183. Westover JB, Sefing EJ, Bailey KW, Wettere AJ, Jung K-H, Dagley A, et al. Low-dose ribavirin potentiates the antiviral activity of favipiravir against hemorrhagic fever viroses. Antiviral Res. 2016;126:62-68.

184. Torriani G, Trofimenko E, Mayor J, Fedeli C, Moreno H, Michel S, et al. Identification of Clotrimazole Derivatives as Specific Inhibitors of Arenavirus Fusion. J Virol. 2019; 93(6): e01744-18.

185. Lee AM, Rojek JM, Spiropoulou CF, Gundersen AT, Jin W, Shaginian A, et al. Unique small molecule entry inhibitors of hemorrhagic fever arenaviruses. J Biol Chem. 2008; 283(27):18734-42.

Erratum

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Here is the form in which the information is found: "According to the International Committee on Taxonomy of Viruses, two subfamilies belong to the *Coronaviridae* family; *Letovirinae*, which has one subgenus, *Milecovirus*, found only in frogs and a sea hare thus far[115], and *Orthocoronavirinae*, which is found in birds and mammals, and is divided into four genera due to the antigenic and genetic characteristics of the viruses[53,116]."

It should be read: "According to the International Committee on Taxonomy of Viruses, two subfamilies belong to the *Coronaviridae* family; *Letovirinae*, which has one subgenus, *Milecovirus*, found only in frogs (Microhyla fissipes) thus far[115], and *Orthocoronavirinae*, which is found in birds and mammals, and is divided into four genera due to the antigenic and genetic characteristics of the viruses[53,116]"