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Zoonotic and emerging orbivirus infections

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Summary

Many novel emerging orbiviruses have been isolated in the past 15 years. Important viruses include *Peruvian horse sickness virus* (PHSV) and *Yunnan orbivirus* (YUOV), pathogens of equids which were originally isolated almost simultaneously from 1997 to 1999 in the People's Republic of China, Australia and Peru. YUOV has also been isolated from cattle, sheep and a dog. The isolation of YUOV from a dog is not the first case of an orbivirus being isolated from a carnivore. *Bluetongue virus* and *African horse sickness virus* were earlier detected in carnivores which fed on contaminated meat. PHSV and YUOV both offer an opportunity to study the emergence of a single pathogen in geographically distant locations, although the original point of emergence is still unidentified. PHSV has been isolated from horses with neurological disease both in Australia and in Peru (where it is now endemic). Serological and molecular diagnostic assays have been developed for these viruses to assist in their identification and diagnosis.

Other orbiviruses, such as *Palyam virus* and *Equine encephalosis virus*, have more recently been identified outside their geographical boundaries and may represent a threat to domesticated livestock and horses, respectively. The article also reviews four zoonotic orbivirus species (*Corripata virus*, *Changuinola virus*, *Kemerovo virus* and *Orungo virus*) which have been identified in livestock and/or wildlife.

Keywords

Changuinola virus – *Corripata virus* – *Equine encephalosis virus* – *Kemerovo virus* – *Orbivirus* – *Orungo virus* – *Peruvian horse sickness virus* – *Yunnan orbivirus* – Zoonotic orbivirus.

Introduction

The genus *Orbivirus* is one of 15 recognised genera within the family *Reoviridae*. Orbiviruses have genomes composed of ten linear molecules of double-stranded RNA. The genus currently contains 22 recognised species. Over the past two decades, several novel orbiviruses have been isolated from arthropod vectors and fully sequenced, which brings the total number of identified novel *Orbivirus* species to 33 (Tables I and II) (1, 2). Orbiviruses are transmitted between their vertebrate hosts by a variety of haematophagous arthropods, although some orbiviruses have no known vectors. *Bluetongue virus* (BTV), *African horse sickness virus* (AHSV) and *Epizootic haemorrhagic disease virus* (EHDV) are the three most economically important orbiviruses and these are all transmitted by adult females of certain *Culicoides* species (3).

From an evolutionary perspective, the cell attachment and serotype-determining outer-capsid protein of orbiviruses (OC1) falls into one of three size classes, which correlate with the relevant vectors (4). The OC1 of *Culicoides*-borne

orbiviruses is designated VP2; that of mosquito-borne orbiviruses is designated VP3; while that of the tick-borne orbiviruses is designated VP4. The VP4 of tick-borne orbiviruses is only 50% the length of the VP2 of *Culicoides*-borne orbiviruses, while the VP3 of mosquito-borne orbiviruses is ~10% shorter than the VP2 of *Culicoides*-borne orbiviruses (4). Evolutionary studies indicate that orbiviruses have co-evolved with their arthropod vectors.

In the past decade, several novel emerging orbiviruses have been isolated from arthropod vectors and/or vertebrate hosts showing clinical signs of disease. Continuing research is attempting to establish the worldwide geographic distribution of these viruses, including *Peruvian horse sickness virus* and *Yunnan orbivirus*. However, known zoonotic orbiviruses have been overlooked and their implication in diseases of wildlife, domesticated animals and/or humans has received little attention.

This article will review selected emerging/zoonotic orbiviruses other than the economically important BTV, AHSV and EHDV (Table I).

Table I
Established *Orbivirus* species

Virus species (virus abbreviation)	Number of serotypes/strains	Vector species	Host species
<i>African horse sickness virus</i>	9 numbered serotypes (AHSV-1 to AHSV-9)	<i>Culicoides</i> spp. (biting midges)	Equids, dogs, elephants, camels, cattle, sheep, goats, humans (in special circumstances), predatory carnivores (by eating infected meat)
<i>Andasibe virus</i>	1 named serotype	<i>Anopheles</i> (mosquitoes)	
<i>Bluetongue virus</i> (orbivirus-type species)	27 numbered serotypes (BTV-1 to BTV-27)	<i>Culicoides</i> spp. (biting midges)	All ruminants, camelids and predatory carnivores (by eating infected meat)
<i>Changuinola virus</i>	13 named serotypes (including Tracambe virus, previously classified as a tentative species)	Phlebotomines, culicine mosquitoes	Humans, rodents, sloths
<i>Chenuda virus</i>	7 named serotypes	Ticks	Seabirds
<i>Chobar Gorge virus</i>	2 named serotypes	Ticks	Bats
<i>Corripata virus</i>	6 named serotypes/strains	Culicine mosquitoes	Humans, rodents
<i>Epizootic haemorrhagic disease virus</i>	10 numbered or named serotypes/strains (EHDV-1 to EHDV-8, EHDV 318, Ibaraki virus [atypical EHDV-2])	<i>Culicoides</i> spp. (biting midges)	Cattle, sheep, deer, camels, llamas, wild ruminants, marsupials
<i>Equine encephalosis virus</i>	7 numbered serotypes (EEV-1 to EEV-7)	<i>Culicoides</i> spp. (biting midges)	Equids
<i>Eubenangee virus</i>	4 named serotypes	<i>Culicoides</i> spp., anopheline and culicine mosquitoes	Unknown hosts
<i>Great Island virus</i>	33 named serotypes/strains	<i>Argas</i> , <i>Ornithodoros</i> , <i>Ixodes</i> ticks	Seabirds, rodents, humans
<i>Heramatsu orbivirus</i>	1 named strain	Unknown	Bats
<i>Ieri virus</i>	3 named serotypes	Mosquitoes	Birds
<i>Japanaut virus</i>	1 named serotype	Mosquitoes	Bats
<i>Kemerovo virus</i>	3 named serotypes	Hard ticks	Birds, sheep, humans, horses
<i>Lebombo virus</i>	1 numbered serotype (LEBV-1) and named isolate Tembe virus (TEMV)	Culicine mosquitoes	Humans, rodents
<i>Matucare virus</i>	1 named serotype	Soft ticks	Humans, bats (based on serology)
<i>Okhotskiy virus</i>	2 named serotypes	<i>Ixodes</i> ticks	Unknown
<i>Orungo virus</i>	4 numbered serotypes (ORUV-1 to ORUV-4)	Culicine mosquitoes	Humans, camels, cattle, goats, sheep, monkeys
<i>Mitchell River virus</i>	1 named serotype	<i>Culicoides</i> spp.	Marsupials and cattle
<i>Mobuck virus</i>	1 named strain	Possibly mosquitoes	Deer
<i>Palyam virus</i>	14 named serotypes/strains	<i>Culicoides</i> spp., culicine mosquitoes	Cattle, sheep
<i>Pata virus</i>	1 named serotype	Mosquitoes	Unknown
<i>Peruvian horse sickness virus</i>	1 numbered serotype (PHSV-1)	Mosquitoes	Horses
<i>St. Croix River virus</i>	1 numbered serotype (SCRV-1)	Ticks	Unknown
<i>Sathuvachari virus</i>	1 named strain	Mosquitoes	Starlings
<i>Tibet orbivirus</i>	1 named strain	<i>Anopheles</i> mosquitoes	Unknown
<i>Umatilla virus</i>	4 named serotypes and Sterch Lagoon orbivirus	Culicine mosquitoes	Birds
<i>Wad Medani virus</i>	2 named serotypes	<i>Boophilus</i> , <i>Rhipicephalus</i> , <i>Hyalomma</i> , <i>Argas</i> ticks	Domesticated animals
<i>Wallal virus</i>	3 serotypes/strains	<i>Culicoides</i> spp.	Marsupials
<i>Warrego virus</i>	3 serotypes/strains	<i>Culicoides</i> spp., anopheline and culicine mosquitoes	Marsupials
<i>Wongorr virus</i>	8 serotypes/strains	<i>Culicoides</i> spp., mosquitoes	Cattle, macropods
<i>Yunnan orbivirus</i>	2 serotypes	Mosquitoes	Cattle, equids, sheep, humans, dogs

Table II
Tentative *Orbivirus* species

Tentative <i>Orbivirus</i> species	Vector species	Host species
Breu Branco virus	Mosquitoes	Unknown hosts
Codajas virus	Mosquitoes	Rodents
Ife virus	Mosquitoes	Rodents, birds, ruminants
Itupiranga virus	Mosquitoes	Unknown hosts
Kammavanpettai virus	Unknown vectors	Birds
Lake Clarendon virus	Ticks	Birds, possibly cattle
Minacu virus	Mosquitoes	Unknown hosts
Golok virus	Mosquitoes	Unknown hosts

Emerging orbiviruses

Peruvian horse sickness virus and Yunnan orbivirus

Peruvian horse sickness virus (PHSV) and Yunnan orbivirus (YUOV) are two emerging orbiviruses which have been identified during the past decade as being pathogens of equids. PHSV was initially isolated in Peru and YUOV was originally reported from the People's Republic of China (5, 6).

Peruvian horse sickness virus

Peruvian horse sickness virus was initially isolated from horses which had died unexpectedly during the rainy season in the Department of San Martin in Peru. Between January and July 1997, more than 100 horses died from an infection with a mortality rate of ~1.25% and a case-fatality rate of ~78%. The epizootic, which lasted seven months, affected eight provinces of San Martin, reaching its peak during periods of particularly heavy rain between March and April of 1997 (6).

During the 1997 outbreak, isolates were made from the spleens, blood and/or brains of sick horses. They were initially identified by electropherotyping as PHSV isolates and subsequently confirmed through sequencing. PHSV was isolated from serum samples taken from horses showing signs of neurological disease, five to ten days post-onset. Some of the isolates were obtained from the brains of horses that showed neurological signs, although anti-PHSV immunoglobulin M (IgM) was not detected, indicating a chronic infection (6).

During surveillance studies conducted in 2002 in San Martin, several isolates of PHSV were obtained from blood samples taken from apparently healthy horses (6). PHSV has also been identified in Australia. In April and May 1999, Elsey virus (ELSV) was isolated from the blood and spleens of horses showing neurological signs on Katherine and Elsey stations in the Northern Territory of Australia. Genome characterisation confirmed that ELSV and the Peruvian isolate of PHSV were

almost identical (97–100% amino acid identity), indicating that they both belonged to PHSV serotype 1 (PHSV-1). Serogroup-specific enzyme-linked immunosorbent assay (ELISA) showed no cross-reactions using antisera against known orbiviruses such as AHSV and BTV (6).

Blood collected since 1998 throughout the Northern Territory, from both sick and healthy horses, has shown a seroprevalence of antibodies against ELSV of approximately 11%, by IgG ELISA. Weak positive reactions (indirect IgG ELISA) were detected in 11% of sera collected from kangaroos. Sera collected from fruit bats in the Northern Territory between 1996 and 2003 were also tested for IgG antibodies to ELSV and ~35% of sera were shown to be positive, with titres higher than those observed in horses (titres in bats up to 160). Wild and domesticated animals in the Northern Territory were also surveyed. No detectable ELSV-specific antibodies were found in rat sera, although a low prevalence of antibody was found in cattle and pigs (6).

Yunnan orbivirus

The first isolate of YUOV was identified in 2005 from *Culex* mosquitoes collected in 1997 in Yunnan Province in southern China. However, YUOV has not been isolated from wild or domesticated animals (5). After the sequencing of its genome, the virus was identified as a member of a novel virus species. Subsequently, multiple isolates belonging to the same species were identified in wild-caught mosquitoes collected in 1999 from various provinces in China. At the time of isolation, the virus was not associated with a specific mammalian host but was shown to replicate in experimentally infected animals, particularly mice (5).

During the 1997 outbreak in San Martin, Peru, YUOV isolates were obtained from the blood and/or brains of sick donkeys, cows, one sheep, and one dog showing signs of neurological disease. The virus was also isolated from the mosquito *Ochlerotatus scapularis* (6). These isolates all had a similar electropherotype to members of the species YUOV (5) and were identified as Rioja virus (RIOV). Sequence analyses showed that RIOV and YUOV were almost identical (97% amino acid identity) in the serotype-determining protein and confirmed that RIOV belongs to Yunnan orbivirus serotype 1 (YUOV-1), originally identified in China. The isolation of YUOV from a dog with neurological signs in Peru (6) parallels findings about carnivores in Africa (7) and, more recently, in Belgium (8) infected with BTV. Similarly, in 1995, AHSV was isolated from dogs and this infection was attributed to the ingestion of meat and organs from virus-infected prey species (7).

Middle Point orbivirus (MPOV) was first isolated in Australia in 1998 (9) from a healthy cow in Middle Point (Northern Territory). Sequencing the genome segment which encodes the protein that correlates with this species in mosquito-

borne orbiviruses (VP2) demonstrated that MPOV was a member of the YUOV species (99% amino acid identity). However, the amino acid identity in the protein defining the serotype in the mosquito-borne orbivirus (VP3) was low (78%), indicating that MPOV belonged to a distinct serotype of YUOV, designated YUOV-2. A real-time reverse-transcription polymerase chain reaction (RT-PCR) assay was developed for MPOV, which showed that more than 150 virus isolates obtained from cattle between 1994 and 2006 were MPOV isolates (9). YUOV (isolate MPOV) infections have been shown to persist in cattle for up to five months with periods of quiescence, followed by recrudescence of the viral titre (10).

Both YUOV and PHSV have recently been re-isolated in Peru (H. Attoui and M.R. Mendez-Lopez, unpublished data).

Diagnostic assays for *Peruvian horse sickness virus* and *Yunnan orbivirus*

In addition to a real-time RT-PCR assay developed specifically for MPOV (9), sequence comparisons of prototype strains of PHSV from Peru and YUOV from China, Australia and Peru have made it possible to design RT-PCR primers that can be used to specifically amplify and distinguish between genome segments from YUOV and PHSV isolates (6). Primer sequences and the sizes of PCR products are shown in Table III. These primers were recently used to identify several novel isolates of PHSV from South America (H. Attoui and M.R. Mendez-Lopez, unpublished data). Serological assays were also developed for YUOV and PHSV, based on recombinant expressed VP7 (the immune-dominant orbivirus antigen) in bacteria. These assays successfully detected antibodies to PHSV and YUOV in equid sera collected in Peru (H. Attoui and F. Mohd Jaafar, unpublished data).

Equine encephalosis virus

Equine encephalosis virus (EEV) is associated with mild or subclinical disease in horses in southern Africa (11). The virus is transmitted by *Culicoides* biting midges. EEV was first identified in 1967, from horses that died from an unknown peracute illness. Clinical signs included pyrexia (lasting up to five days), lethargy, loss of appetite, fast breathing and tachycardia. Serological investigation revealed that widespread EEV infections had occurred in horses during the summer of 1967 but that *Bluetongue virus* had not occurred in South Africa to any appreciable extent in the preceding ten years. In some of the years following 1967, EEV took on epidemic proportions. Seasonal outbreaks of the disease have been linked to the presence of the *Culicoides* vector (12). Outbreaks of EEV have also been associated with equine abortion during the first five to six months of gestation. Serological studies showed that 50–60% of South African donkeys and zebras

have antibodies against EEV. Six different EEV serotypes have been identified in southern Africa, of which Kyalami, Bryanston and Cascara are the best known. In recent years, evidence of the virus circulating in East and West Africa was obtained when EEV was identified in Ethiopia, Ghana and the Gambia. In 2009 the virus was identified in Israel, in animals displaying unrest, anorexia, fast breathing and clinical signs such as pyrexia, congestion of the mucosae, and oedema of the neck, legs, eyelids and lips. However, there were no reports of increased mortality during this outbreak (13). Horses in North African countries do not have antibodies to EEV (13).

Diagnostic assays for *Equine encephalosis virus*

A group-specific, competitive ELISA has been developed for EEV, based on a guinea pig polyclonal serum. This ELISA detects antibodies against all seven serotypes of EEV with a sensitivity and specificity of 100% (14). This test provides the means for a differential diagnosis between EEV and AHSV. A real-time PCR assay targeting genome segment 7 of EEV was also recently developed (15). The assay uses group-specific EEV primers (EEVVP7_F0028_0048: 5'-GATAGCGGCTAGAGCCCTTTC-3' and EEVVP7_R0085_0106: 5'-AACTTGAGGAGCCATRGTAGCT-3') and a TaqMan® MGB™ hydrolysis probe (EEVVP7_P0054_0072_MGBTM probe: 5'-TAAGAGCATGTGTTACTGC-3') to allow the detection of a median tissue culture infective dose (TCID₅₀) as small as 10^{2.9} TCID₅₀/ml of blood (with 95% confidence).

A recombinant VP7-based indirect ELISA has also been developed for EEV (unpublished data).

Palyam virus

Palyam viruses have been isolated from *Culicoides* biting midges and culicine mosquitoes. Isolates of *Palyam virus* infect cattle, goats and sheep (with clinical signs in cattle and goats only), and have been repeatedly isolated from aborted bovine fetuses. Chuzan virus (CHUV) is an isolate of *Palyam virus* which causes epizootics of congenital abnormalities, particularly hydranencephaly cerebellar hypoplasia syndrome, which occurred in Japan in 1985 and 1986 (16, 17). CHUV was isolated in Japan between 1987 and 1996 on several occasions, without any major outbreaks being recorded. It has also been isolated from *Culicoides oxystoma* in Japan (17). Serosurveillance of naive Korean goats between 2005 and 2006 identified specific antibodies against CHUV in 1% of the surveyed sera (18).

In regard to vaccines and diagnostic assays, a trivalent vaccine has been developed (19) to contain chemically inactivated Akabane, Aino and Chuzan viruses (Nisseiken Bovine Abnormal Parturition trivalent inactivated vaccine, Nisseiken Co. Ltd, Japan). A baculovirus-expressed VP7 of

Table III**Primers for polymerase chain reaction amplification of genomes of *Yunnan orbivirus* and *Peruvian horse sickness virus***

Primer name	Sequence (5' → 3')	Segment	Position (relative to YUOV or to PHSV)	Orientation	Amplicon size (bp)
YUOVSeg2S1	GATATTGCBATTTGGGTGAATTC	2	2109–2131	Forward	785
YUOVSeg2R1	TACACCACGTCCCGAAGGACTCGC	2	2870–2893	Reverse	
YUOVSeg2S2	GCAGTGTTTRGACACTCCAAATG	2	2180–2202	Forward	670
YUOVSeg2R2	CTATCCGTGRGACACTACGCCTCC	2	2825–2849	Reverse	
YUOVSeg3S1	TATTMRTAGRTTGCGMATRAARTAT	3	2205–2229	Forward	471
YUOVSeg3R1	TACAAACATCCGCGTTGATGTAGC	3	2675–2651	Reverse	
YUOVSeg3S2	RTAGRTTRCGMATAAAYTATGWWGAAAT	3	2210–2237	Forward	437
YUOVSeg3R2	AGCATACTACTCCGCGCCAGCAAT	3	2646–2623	Reverse	
PHSVSeg2s1	GTTTTAATCGATATTAGACAGGAACC	2	1125–1150	Forward	359
PHSVSeg2r1	CTTCTACTAACGTGTGAATAAGG	2	1483–1461	Reverse	
PHSVSeg2s2	GGAAAGATGATGTTTTCATATGG	2	1197–1219	Forward	258
PHSVSeg2r2	CCTTCTCCTTAACTATCAACTC	2	1554–1432	Reverse	
PHSVSeg3s1	GCAAAATTGAATTATGTTCAATGC	3	1244–1267	Forward	488
PHSVSeg3r1	CAATTCTACGATCTCGTAGGTGG	3	1731–1708	Reverse	
PHSVSeg3s2	TGGTAGAATGTCTGGCCTGAGAG	3	1308–1330	Forward	373
PHSVSeg3r2	GCTATATACTCTGATAAATATGG	3	1680–1657	Reverse	

bp : base pairs

YUOV : *Yunnan orbivirus*PHSV : *Peruvian horse sickness virus*

CHUV virus has been used to develop an indirect ELISA specific to CHUV and was able to differentiate antibodies against CHUV from those against BTV and EHDV (20).

Zoonotic orbiviruses

Several orbiviruses have been isolated from humans and wild or domesticated animals. In addition, antibodies indicative of orbivirus infection have also been detected in human and animal sera.

Corriparta virus

The species *Corriparta virus* (CORV) includes six named viruses:

- Corriparta virus MRM1 (CORV-MRM1)
- CS0109
- V654
- V370
- Acado virus
- Jacareacanga virus.

Isolates of CORV have been detected in Australia, Africa and South America (21). Corriparta MRM1 virus was initially isolated from *Culex* mosquitoes, and the mosquito *Aedeomyia catasticta* in Queensland, Australia, in 1960. Strains CS0109, V654 and V370 were subsequently isolated in Australia (3, 22, 23, 24). Acado virus was isolated from pools of *Culex* mosquitoes collected in Ethiopia in 1963 and

Jacareacanga virus from pools of *Culex* mosquitoes in Brazil in 1975 (21, 22). Isolates of CORV have been obtained from wild birds. Neutralising antibodies to CORV have been identified in humans, equids, cattle, marsupials and birds (25, 26, 27).

In terms of diagnostic assays for CORV, deoxycholate-treated cell lysates of CORV-infected baby hamster kidney-(BHK-) 21 cells have been used to develop an indirect ELISA (28). More recently, an indirect ELISA based on bacterially expressed recombinant VP7 of CORV has been developed, which showed no cross-reaction with other orbiviruses, including BTV, PHSV and YUOV (H. Attoui and F. Mohd Jaafar, unpublished data).

Changuinola virus

The species *Changuinola virus* (CGLV) contains 12 'named' serotypes that have been isolated from phlebotomine sandflies (3).

Changuinola virus was isolated from a human with a brief febrile illness in Panama (4, 22). The virus has also been isolated from phlebotomine sandflies, and antibodies were detected in rodents. Changuinola virus replicates in mosquito cell lines (in the same way as BTV replicates in C6/36 [*Aedes albopictus* cells]), *Culicoides sonorensis* KC cells and African green monkey kidney Vero cells. CGLV is pathogenic for newborn mice or hamsters by intracerebral inoculation (22, 29).

Historically, seven strains of CGLV were isolated from wild-caught sloths (*Bradypus variegatus* and *Choloepus hoffmanni*) in central Panama (30). Several strains were associated with prolonged or recrudescing viraemia in sloths (4). Antibodies against CGLV were widespread in both sloth species and especially prevalent in *Choloepus*, but virtually absent from all other wild vertebrate species tested (30). Antibodies to CGLV were detected in rodents (29).

Kemerovo virus

Kemerovo, Lipovnik and Tribec are three serotypes of tick-borne viruses belonging to the *Kemerovo virus* species (1, 2, 3, 31). These viruses have been implicated as the cause of non-specific fever or neurological infection in the Kemerovo region of Russia (Kemerovo virus [KEMV]) and central Europe (Lipovnik virus [LIPV], and Tribec virus [TRBV]). In 1962, more than 20 strains of KEMV were isolated in the Kemerovo region of Russia from *Ixodes persulcatus* ticks and from human patients with meningoencephalitis. The virus, which was also isolated from birds, can infect Vero or BHK-21 cells. Lipovnik and Tribec viruses have been isolated from *I. ricinus* ticks and implicated in central European encephalitis (CEE). Libíková *et al.* found that more than 50% of CEE patients had antibodies against LIPV (32). Isolates of TRBV were obtained from sentinel goats in the Tribec region (Slovakia). Antibodies against TRBV have been identified in cattle (4–31%) and goats (2.5–5%) in the Tribec region (22).

Kemerovo virus is also suspected in the aetiology of some chronic neurological diseases, including polyradiculoneuritis and multiple sclerosis. Antibodies against a Kemerovo-related virus have been detected in Oklahoma and Texas, in patients with Oklahoma tick fever (33).

A SYBR Green-based real-time PCR assay to diagnose viruses of the Kemerovo group has been developed (orbitickForsybr: 5'-GAGCAGCGGATTACYTCAGCAA-3' and orbitickRevsybr: 5'-ACGTCTCGRGGSCGCGTCTG-3') and validated, using cell culture isolates of KEMV, LIPV and TRBV, mixed with uninfected sheep blood (H. Attoui and F. Mohd Jaafar, unpublished data). As few as 12 genome copies can be detected using this assay.

A serological assay based on the bacterially expressed VP7 of KEMV is also available (H. Attoui and F. Mohd Jaafar, unpublished data).

Orungo virus

The species *Orungo virus* (ORUV) contains four distinct serotypes (ORUV-1 to ORUV-4), which are transmitted by *Anopheles*, *Aedes* and *Culex* mosquitoes (3, 4, 33). ORUV is widely distributed in tropical Africa, where it has been isolated from humans, camels, cattle, goats, sheep, monkeys

and mosquitoes. Antibodies against the virus have been identified in primates, sheep and cattle. ORUV was first isolated in Uganda during 1959 from the blood of human patients with fever and diarrhoea who developed weakness followed by flaccid paralysis of the legs and generalised convulsions. Despite a high prevalence of infection and three deaths in Uganda, only a few clinical cases of human disease (involving fever, headache, myalgia, nausea and vomiting) have been reported (33). ORUV infections cause lethal encephalitis in suckling mice and hamsters and the virus replicates in adult *Ae. aegypti* mosquitoes after intrathoracic inoculation (22). It also causes cytopathic effects and forms plaques in Vero and BHK-21 cells (22). High rates of co-infection with yellow fever and ORUV have been reported, reflecting their similar geographical distribution and transmission by *Aedes* mosquitoes, the principal vectors.

Conclusions

Multiple novel orbiviruses have emerged over the past 15 years. Particular attention should be drawn to PHSV and YUOV, which were isolated in China, Australia and Peru between 1997 and 2005. Initial isolations of PHSV were linked to neurological signs and mortality in horses, while later isolations were obtained from apparently healthy horses. YUOV has a wider host range and has been isolated from apparently healthy cattle and from donkeys showing neurological signs. The virus can also infect dogs, in a way similar to AHSV, which infected African dogs feeding on contaminated prey. If this mode of transmission is also demonstrated for YUOV, wild carnivores may represent an important reservoir of the virus. Studies are continuing in South America (Peru, Brazil) in wildlife, domesticated animals and human populations in an attempt to identify the extent of spread of PHSV and YUOV, and to clarify whether these viruses have any zoonotic potential.

Palyam virus and *Equine encephalosis virus* have been identified beyond their initial geographical borders (PALV in Korea and EEV in Israel and East Africa) and have been suggested as potential threats for livestock and cattle, respectively. Although EEV has reached Israel, it has not reached North African countries, possibly because the Saharan desert is acting as a barrier to virus spread.

Finally, many zoonotic orbiviruses have been overlooked and little is known about their active circulation and impact on human populations or on wildlife and domesticated animals in South America and Africa. The authors are currently trapping insects (particularly mosquitoes) in Africa and ticks in Europe to further assess the epidemiology of these viruses.

Several recombinant, protein-based serological assays have been developed for viruses such as KEMV, EEV, PHSV, YUOV

and CORV (H. Attoui and F. Mohd Jaafar, unpublished data), to conduct seroepidemiological surveys.

Infections à orbivirus zoonotiques et émergents

H. Attoui & F. Mohd Jaafar

Résumé

Un certain nombre d'orbivirus émergents d'apparition récente ont été isolés au cours des 15 dernières années. Parmi eux certains sont importants, notamment le *Virus de la maladie péruvienne du cheval* (PHSV) et l'*Orbivirus du Yunnan* (YUOV), qui affectent les équidés et ont été isolés de manière presque simultanée entre 1997 et 1999 en République populaire de Chine, en Australie et au Pérou. Le virus YUOV a également été isolé de bovins, d'ovins et d'un chien. L'isolement du virus YUOV à partir d'un chien n'est pas le premier cas d'orbivirus isolé d'un carnivore. Le *Virus de la fièvre catarrhale du mouton* et le *Virus de la peste équine* ont été détectés précédemment chez des carnivores qui avaient ingéré de la viande issue d'animaux infectés. Chacun des virus PHSV et YUOV permet d'étudier le phénomène d'émergence concomitante d'un même agent pathogène dans des régions géographiques distantes les unes des autres, bien que dans les deux cas le site d'origine de l'émergence reste à déterminer. Le virus PHSV a été isolé de chevaux présentant des troubles neurologiques aussi bien en Australie qu'au Pérou (où la maladie est désormais endémique). Des épreuves sérologiques et moléculaires ont été mises au point pour ces virus afin de contribuer à leur caractérisation et à leur diagnostic.

D'autres orbivirus tels que le *Virus Palyam* et le *Virus de l'encéphalose équine* ont été identifiés en dehors de leur aire de distribution géographique, ce qui représente une menace potentielle pour les populations d'animaux d'élevage et de chevaux, respectivement. Les auteurs font également le point sur quatre espèces d'orbivirus zoonotiques (*Virus Corripata*, *Virus Changuinola*, *Virus Kemerovo* et *Virus Orungo*) retrouvées chez des animaux d'élevage et/ou sauvages.

Mots-clés

Virus Changuinola – *Virus Corripata* – *Virus de l'encéphalose équine* – *Virus Kemerovo* – *Orbivirus* – *Virus Orungo* – *Virus de la maladie équine péruvienne* – *Virus Yunnan* – *Orbivirus zoonotique*.

Infecciones por orbivirus zoonóticos y emergentes

H. Attoui & F. Mohd Jaafar

Resumen

En los últimos quince años se han aislado muchos nuevos orbivirus emergentes. Entre los que revisten importancia están el *Virus de la peste equina peruana* y el *Orbivirus del Yunnan*, patógenos de los équidos aislados al principio casi simultáneamente, entre 1997 y 1999, en la República Popular China, Australia y el Perú. El *Orbivirus del Yunnan* también ha sido aislado en ganado bovino y ovino, así como en un perro. Este último no es el primer caso de orbivirus aislado en un carnívoro: anteriormente se habían detectado los *Virus de la lengua azul* y los *Virus de la peste equina* en carnívoros que habían ingerido carne contaminada. El *Virus de la peste equina peruana* y el *Orbivirus del Yunnan* ofrecen la oportunidad

de estudiar la aparición de un único patógeno en lugares geográficamente distantes, aunque todavía no se conoce el punto de partida inicial. El virus de la peste equina peruana ha sido aislado en caballos que presentaban síntomas neurológicos tanto en Australia como en el Perú (país en el que ahora es endémico). Para ayudar a identificar y diagnosticar estos virus se han elaborado pruebas serológicas y moleculares específicas.

En fechas más recientes se han detectado fuera de los límites de su área de distribución geográfica otros dos orbivirus, el *Virus Palyam* y el *Virus de la encefalosis equina*, que pueden constituir una amenaza para el ganado doméstico y los caballos, respectivamente. Los autores se detienen también en otras cuatro especies de orbivirus zoonóticos (*Virus Corripata*, *Virus Changuinola*, *Virus Kemerovo* y *Virus Orungo*) que han sido caracterizados en el ganado y/o en animales salvajes.

Palabras clave

Orbivirus – *Orbivirus del Yunnan* – Orbivirus zoonóticos – *Virus Changuinola* – *Virus Corripata* – *Virus de la encefalosis equina* – *Virus Kemerovo* – *Virus Orungo* – *Virus de la peste equina peruana*.



References

1. Attoui H., Nomikou K., Maan S., Belaganahalli S. & Mertens P.P.C. (2015). – Orbiviruses. In Reference module in biomedical sciences (B.W. Mahy, ed.). Elsevier (in press).
2. Mertens P.P.C. & Attoui H. (2015). – Orbiviruses and bluetongue virus. In Encyclopedia of life sciences. John Wiley & Sons (in press).
3. Mertens P.P.C., Maan S., Samuel A. & Attoui H. (2005). – Orbiviruses, Reoviridae. In Virus taxonomy: 8th Report of the International Committee on Taxonomy of Viruses (C.M. Fauquet, M.A. Mayo, J. Maniloff, U. Desselberger & L.A. Ball, eds). Elsevier/Academic Press, London, 466–483.
4. Mohd Jaafar F., Belhouchet M., Belaganahalli M., Tesh R.B., Mertens P.P.C. & Attoui H. (2014). – Full-genome characterisation of Orungo, Lebombo and Changuinola viruses provides evidence for co-evolution of orbiviruses with their arthropod vectors. *PLoS ONE*, **9** (1), e86392. doi:10.1371/journal.pone.0086392.
5. Attoui H., Mohd Jaafar F., Belhouchet M., Aldrovandi N., Tao S., Chen B., Liang G., Tesh R.B., de Micco P. & de Lamballerie X. (2005). – Yunnan orbivirus, a new orbivirus species isolated from *Culex tritaeniorhynchus* mosquitoes in China. *J. Gen. Virol.*, **86** (12), 3409–3417.
6. Attoui H., Mendez-Lopez M.R., Rao S., Hurtado-Alendes A., Lizaraso-Caparo F., Mohd Jaafar F., Samuel A.R., Belhouchet M., Pritchard L.I., Melville L., Weir R.P., Hyatt A.D., Davis S.S., Lunt R., Calisher C.H., Tesh R.B., Fujita R. & Mertens P.P.C. (2009). – Peruvian horse sickness virus and Yunnan orbivirus, isolated from vertebrates and mosquitoes in Peru and Australia. *Virology*, **394** (2), 298–310. doi:10.1016/j.virol.2009.08.032.
7. Alexander K.A., Maclachlan N.J., Kat P.W., House C., O'Brien S.J., Lerche N.W., Sawyer M., Frank L.G., Holekamp K., Smale L., McNutt J.W., Laurenson M.K., Mills M.O.L. & Osburn A.I. (1994). – Evidence of natural bluetongue virus infection among African carnivores. *Am. J. Trop. Med. Hyg.*, **51** (5), 568–576.
8. Jauniaux T.P., De Clercq K.E., Cassart D.E., Kennedy S., Vandebussche F.E., Vandemeulebroucke E.L., Vanbinst T.M., Verheyden B.I., Goris N.E. & Coignoul F.L. (2008). – Bluetongue in Eurasian lynx. *Emerg. Infect. Dis.*, **14** (9), 1496–1498. doi:10.3201/eid1409.080434.
9. Cowled C., Melville L., Weir R., Walsh S., Hyatt A., Van Driel R., Davis S., Gubala A. & Boyle D. (2007). – Genetic and epidemiological characterization of Middle Point orbivirus, a novel virus isolated from sentinel cattle in northern Australia. *J. Gen. Virol.*, **88** (12), 3413–3422.
10. Cowled C., Melville L., Weir R., Walsh S., Gubala A., Davis S. & Boyle D. (2012). – Persistent and recrudescence infection in cattle following natural infection with Middle Point orbivirus. *Arch. Virol.*, **157** (6), 1161–1165. doi:10.1007/s00705-012-1277-z.
11. Guthrie A.J., Pardini A.D. & Howell P.G. (2009). – Equine encephalosis. *Equine Vet. Edu. Manual*, **8**, 145–150.
12. Theodoridis A., Nevill E.M., Els H.J. & Boshoff S.T. (1979). – Viruses isolated from *Culicoides* midges in South Africa during unsuccessful attempts to isolate bovine ephemeral fever virus. *Onderstepoort J. Vet. Res.*, **46** (4), 191–198.
13. Oura C.A., Batten C.A., Ivens P.A., Balcha M., Alhassan A., Gizaw D., Elharrak M., Jallow D.B., Sahle M., Maan N., Mertens P.P.C. & Maan S. (2012). – Equine encephalosis virus: evidence for circulation beyond southern Africa. *Epidemiol. Infect.*, **40** (11), 1982–1986.

14. Crafford J.E., Guthrie A.J., Van Vuuren M., Mertens P.P.C., Burroughs J.N., Howell P.G., Batten C.A. & Hamblin C. (2011). – A competitive ELISA for the detection of group-specific antibody to equine encephalosis virus. *J. Virol. Meth.*, **174** (1–2), 60–64. doi:10.1016/j.jviromet.2011.03.024.
15. Rathogwa N.M., Quan M., Smit J.Q., Lourens C., Guthrie A.J. & van Vuuren M. (2014). – Development of a real time polymerase chain reaction assay for equine encephalosis virus. *J. Virol. Meth.*, **195**, 205–210. doi:10.1016/j.jviromet.2013.10.018.
16. Goto Y., Miura Y. & Kono Y. (1988). – Serologic evidence for the etiologic role of Chuzan virus in an epizootic of congenital abnormalities with hydranencephaly-cerebellar hypoplasia syndrome of calves in Japan. *Am. J. Vet. Res.*, **49** (12), 2026–2029.
17. Miura Y., Goto Y., Kubo M. & Kono Y. (1988). – Isolation of Chuzan virus, a new member of the Palyam subgroup of the genus *Orbivirus*, from cattle and *Culicoides oxystoma* in Japan. *Am. J. Vet. Res.*, **49** (12), 2022–2025.
18. Yang D.K., Hwang I.J., Kim B.H., Kweon C.H., Lee K.W., Kang M.I., Lee C.S. & Cho K.O. (2008). – Serosurveillance of viral diseases in Korean native goats (*Capra hircus*). *J. Vet. Med. Sci.*, **70** (9), 977–979.
19. Kim Y.H., Kweon C.H., Tark D.S., Lim S.I., Yang D.K., Hyun B.H., Song J.Y., Hur W. & Park S.C. (2011). – Development of inactivated trivalent vaccine for the teratogenic Aino, Akabane and Chuzan viruses. *Biologicals*, **39** (3), 152–157. doi:10.1016/j.biologicals.2011.02.004.
20. Yamakawa M. & Furuuchi S. (2001). – Expression and antigenic characterization of the major core protein VP7 of Chuzan virus, a member of the Palyam serogroup orbiviruses. *Vet. Microbiol.*, **83** (4), 333–341.
21. Gonzalez H.A. & Knudson D.L. (1987). – Genetic relatedness of corriparta serogroup viruses. *J. Gen. Virol.*, **68** (3), 661–672. doi:10.1099/0022-1317-68-3-661.
22. Karabatsos N. (ed.) (1985). – International catalogue of arboviruses including certain other viruses of vertebrates. American Society of Tropical Medicine and Hygiene, San Antonio, Texas.
23. Doherty R.L., Carley J.G., Mackerras M.J. & Marks E.N. (1963). – Studies of arthropod-borne virus infections in Queensland. III. Isolation and characterization of virus strains from wild-caught mosquitoes in North Queensland. *Aust. J. Experim. Biol. Med. Sci.*, **41**, 17–39. doi:10.1038/icb.1963.2.
24. Liehne P.F., Anderson S., Stanley N.F., Liehne C.G., Wright A.E., Chan K.H., Leivers S., Britten D.K. & Hamilton N.P. (1981). – Isolation of Murray Valley encephalitis virus and other arboviruses in the Ord River Valley 1972–1976. *Aust. J. Experim. Biol. Med. Sci.*, **59**, 347–356. doi:10.1038/icb.1981.29.
25. Boughton C.R., Hawkes R.A. & Naim H.M. (1990). – Arbovirus infection in humans in NSW: seroprevalence and pathogenicity of certain Australian bunyaviruses. *Aust. N.Z. J. Med.*, **20**, 51–55. doi:10.1111/j.1445-5994.1990.tb00371.x.
26. Whitehead R.H., Doderty R.L., Domrow R., Standfast H.A. & Wetters E.J. (1968). – Studies of the epidemiology of arthropod-borne virus infections at Mitchell River Mission, Cape York Peninsula, North Queensland. 3. Virus studies of wild birds, 1964–1967. *Trans. Roy. Soc. Trop. Med. Hyg.*, **62**, 439–445. doi:10.1016/0035-9203(68)90096-5.
27. Doherty R.L., Whitehead R.H., Wetters E.J., Gorman B.M. & Carley J.G. (1970). – A survey of antibody to 10 arboviruses (Koongol group, Mapputta group and ungrouped) isolated in Queensland. *Trans. Roy. Soc. Trop. Med. Hyg.*, **64**, 748–753. doi:10.1016/0035-9203(70)90017-9.
28. Blacksell S.D., Lunt R.A. & White J.R. (1994). – A rapid indirect ELISA for the serogrouping of Australian orbiviruses. *J. Virol. Meth.*, **49** (1), 67–78.
29. Travassos da Rosa A.P., Tesh R.B., Pinheiro F.P., Travassos da Rosa J.F., Peralta P.H. & Knudson D.L. (1984). – Characterization of the Changuinola serogroup viruses (*Reoviridae: Orbivirus*). *Intervirology*, **21**, 38–49. doi:10.1159/000149501.
30. Seymour C., Peralta P.H. & Montgomery G.G. (1983). – Viruses isolated from Panamanian sloths. *Am. J. Trop. Med. Hyg.*, **32**, 1435–1444.
31. Attoui H., Maan S., Anthony S.J. & Mertens P.P.C. (2009). – Bluetongue virus, other orbiviruses and other reoviruses: their relationships and taxonomy. In *Bluetongue* (P.S. Mellor, M. Baylis & P.P.C. Mertens, eds). Elsevier/Academic Press, London, 23–52.
32. Libíková H., Tesarová J. & Rajcáni J. (1970). – Experimental infection of monkeys with Kemerovo virus. *Acta Virol.*, **14** (1), 64–69.
33. Fields B.N., Knipe D.M. & Howley P.M. (eds) (1985). – *Fields' Virology*, 3rd Ed. Lippincott-Raven, Philadelphia.

