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EFSA – Disease profiles

Cache Valley virus infection Fact Sheet

1. Disease overview

Cache Valley virus (CVV) causes Cache Valley virus infection, a mosquito-borne viral disease of domestic and wild ungulates, primarily sheep, goats, cattle, and white-tailed deer. The disease is characterized by reproductive losses resulting from transplacental infection during early gestation, leading to abortions, stillbirths, and congenital malformations in newborns, while adult animals typically remain asymptomatic (Boston University, 2025; Hughes et al., 2023; Waddell et al., 2019; WOAH, 2025b).

Cache Valley virus infection is not a WOAH-notifiable disease, and it is not listed in the European AHL.

2. Agent

CVV is an enveloped, single-stranded, negative-sense RNA virus that belongs to the Orthobunyavirus genus of the Peribunyaviridae family. The virion is roughly spherical, 80–120 nm in diameter, and contains a tripartite genome composed of large (L), medium (M), and small (S) RNA segments. These segments encode the RNA-dependent RNA polymerase, glycoproteins Gn and Gc and, the nucleocapsid protein N and non-structural protein NSm and NSs. The glycoproteins Gn and Gc are responsible for host cell attachment and elicit neutralizing antibodies (Hughes et al, 2023).

The virus is moderately stable under ambient conditions but is inactivated by lipid solvents, detergents, and standard disinfectants (Boston University, 2025).

3. Geographical Distribution

Since its first isolation in 1956 in Cache Valley, Utah (USA), CVV has been detected throughout much of the United States and Canada, and in parts of Mexico, the Caribbean, South America, Afrika and Australia

CVV infection is not reportable to WOAH. Evidence from published studies describing natural infections with this agent, as well as field epidemiological studies, are collected in the EFSA's systematic literature review (updated until 31/12/2025) and summarized in Figure 1. For more detailed information, dynamic maps, and references visit the online disease profile (accessible via the button in the top right corner).

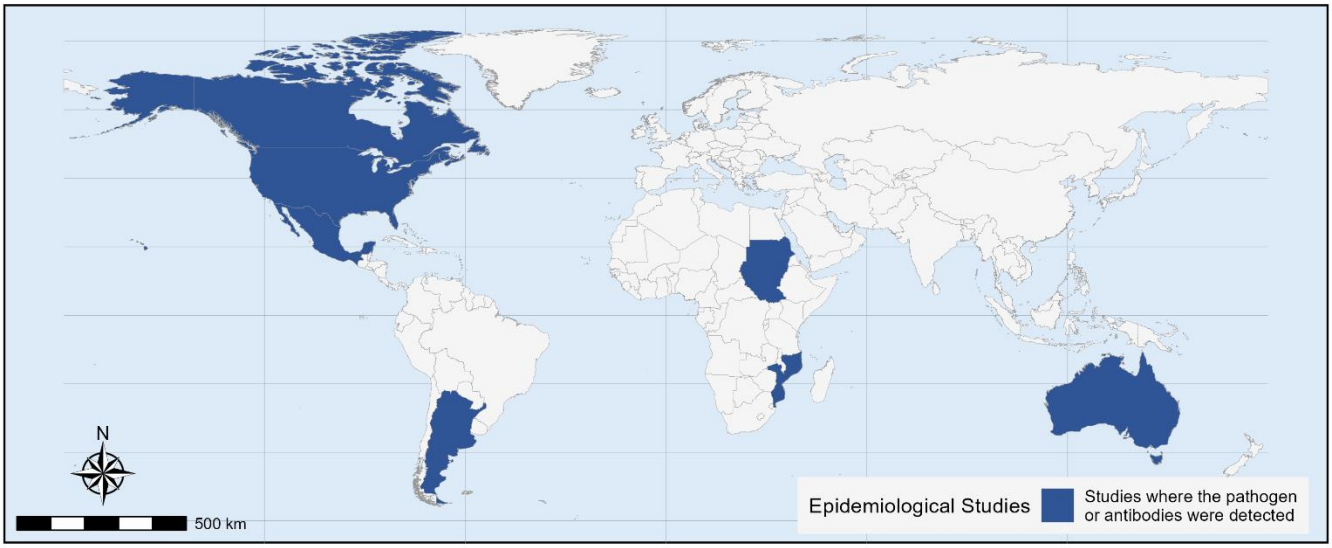

Figure 1. Geographical distribution of epidemiological studies addressing the occurrence of CVV, as identified by the EFSA's systematic literature review (covering years 1970-2025).

4. Animal hosts

4.1. Susceptible hosts

Based on epidemiological knowledge of host–pathogen–vector interactions and outbreak reports, the main hosts of CVV are deer, whereas domestic ruminants, horses and humans are considered as dead-end hosts. However, other susceptible species have been identified in the SLR. The SLR summary is given in Table 1.

Table 1. Susceptible host species of Cache Valley virus.

The systematic literature review reported in the CVV disease profile, identified the following susceptible species (updated until 31/12/2025, for references see online disease profile)
FIELD
Epidemiological studies carried out in the field **Pathogen was detected in the following animal species:** • Hominidae: *Homo sapiens* **Antibodies were detected in the following animal species:** • Bovidae: *Ovis aries* • Cervidae: *Odocoileus virginianus* • Hominidae: *Homo sapiens* • Leporidae: *Sylvilagus floridanus* **Outbreaks reported to WOAH included the following species:** • No species specified
EXPERIMENTS
Experimental studies demonstrated infection in: • Bovidae: *Bos taurus, Capra hircus* • Cervidae: *Odocoileus virginianus* • Leporidae: *Oryctolagus cuniculus* • Suidae: *Sus scrofa domesticus*

4.2. Clinical Signs

Clinical disease associated with CVV occurs almost exclusively in ruminant foetuses infected in utero, as adult animals typically remain asymptomatic. The severity and nature of foetal outcomes depend strongly on the stage of gestation at the time of maternal infection.

In sheep, infection of the ewe between approximately days 28 and 48 of gestation may result in abortions, stillbirths, mummified foetuses, or a spectrum of congenital malformations. Predominant lesions include arthrogryposis and hydranencephaly, along with other central nervous system and musculoskeletal abnormalities such as hydrocephalus, micromyelia, limb deformities, and severe muscle loss. Affected lambs may be born weak, unable to stand, or die shortly after birth.

Although infection can occur in other ruminants, including cattle and goats, clinical disease linked to CVV has been documented primarily in sheep. (Waddell et al, 2019).

4.2.1. Incubation Period

Since adult animals infected with CVV rarely show overt clinical signs, the incubation period in adults is not clearly defined. However, after exposure, vertebrate hosts (especially ungulates) may develop transient viraemia sufficient to infect feeding mosquitoes. The exact timing of viraemia onset and duration remains poorly characterized, owing to limited longitudinal data in naturally infected animals (Hughes et al, 2023).

4.2.2. Morbidity and case fatality

In adult ungulates and other vertebrates, morbidity is generally negligible; most seropositive animals are asymptomatic. Mild or transient illness in adults appears to be uncommon and is not well documented (Hughes et al, 2023). Fatal outcomes in adults are rare or undocumented under natural conditions (Waddell et al, 2019).

In contrast, the primary impact of CVV is on the foetus in infected pregnant animals. In small ruminants, especially sheep, infection during the susceptible gestational window has been repeatedly associated with high rates of foetal loss, stillbirths, or offspring born with severe congenital malformations. Because many malformed neonates are stillborn, die shortly after birth, or are non-viable, the case fatality rate among these affected offspring ca be very high (Waddell et al, 2019).

4.2.3. Zoonotic Potential

Cache valley virus infection is a zoonotic disease (WOAH, 2025).

5. Transmission

CVV is primarily transmitted by mosquitoes (Diptera; Culicidae). For more information on vector distribution, visit the Vector section in the online disease profile.

Seasonal patterns of CVV transmission and seroprevalence appear to correspond to periods of higher mosquito activity, though the data do not yet define a strictly regular "season" for outbreaks (Hughes et al, 2023).

For clinical disease to occur in offspring, transplacental transmission is key: infection of a pregnant dam results in virus crossing to the foetus producing the typical congenital malformations, stillbirths, or foetal death associated with CVV. There is no published evidence that non pregnant animals pass

the virus venereally, via vertical transmission other than transplacental infection, or by other non vector routes under natural conditions (Waddell et al, 2019; Hughes et al, 2023).

6. Diagnostic tests

WOAH-recommended tests (WOAH, 2025) for agent detection include virus isolation, Immunofluorescence Assay (IFA), immunohistochemistry (IHC), virus neutralisation (VNT) test, and RT-PCR.

CVV can be isolated from the blood of febrile or viraemic adult animals, although the window for successful detection is short. Isolation from newborn foetuses is usually unsuccessful, because viral clearance typically occurs before birth as the foetal immune response develops. Detection of viral antigen or infectious virus can be achieved using IFA, IHC or VNT tests. In addition, both group-specific and virus-specific RT-PCR assays are available and provide sensitive tools for identifying *Orthobunyaviruses*, including CVV (WOAH, 2025).

For immune response detection, the recommended tests are ELISA and VNT. The latter remains the reference method for confirming exposure and measuring functional neutralising antibodies. ELISA formats are also used for large-scale screening and surveillance. Because adult infections are usually subclinical, serology is the primary tool for identifying past infection at the herd level. Detection of antibodies in pre-colostrum foetal fluids or tissues from malformed or stillborn neonates provides strong evidence of in utero infection (WOAH, 2025).

To date, the systematic literature review has not found studies evaluating diagnostic tests meeting the eligibility criteria for inclusion.

7. Prevention and control

7.1. Vaccination

Experimental live-attenuated and inactivated vaccines against CVV have been developed, but none is yet commercially licensed for use in livestock (Hughes et al, 2023). A recent study compared a candidate live-attenuated CVV vaccine, which elicited a stronger and more durable neutralizing response than the inactivated vaccine (Ayers et al, 2023).

7.2. Treatment

There is currently no specific antiviral treatment for Cache valley virus infection. As adult ruminants typically develop subclinical or mild transient infections, clinical management is rarely required. In cases involving congenital infection, affected neonates often present with severe neurological or musculoskeletal malformations that are incompatible with life. Supportive care offers no meaningful benefit in these cases, and euthanasia is generally recommended on welfare grounds.

8. References

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Waddell L, Pachal N, Mascarenhas M, Greig J, Harding S, Young I, Wilhelm B (2019). Cache Valley virus: A scoping review of the global evidence. Zoonoses and Public Health. 2019 Nov;66(7):739-58. DOI: 10.1111/zph.12621

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