Vesicular Stomatitis

Sore Mouth of Cattle and Horses, Indiana Fever

Last Updated: January 30, 2008

the Center for Food Security & Public Health
IOWA STATE UNIVERSITY®
College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: 515.294.7189
Fax: 515.294.8259
cfsph@iastate.edu
www.cfsph.iastate.edu

INSTITUTE FOR INTERNATIONAL COOPERATION IN ANIMAL BIOLOGICS
an OIE Collaborating Center
Iowa State University
College of Veterinary Medicine
www.cfsph.iastate.edu/IICAB/

Importance

Vesicular stomatitis is an important livestock disease endemic in the Americas. This zoonotic viral disease is characterized by vesicles, erosions and ulcers on the mouth, feet and udder. Pain, anorexia and secondary mastitis can cause decreased productivity in all species, and swine infected with some viruses may die. Although vesicular stomatitis is endemic in limited areas of the southeastern United States, these viruses have not caused outbreaks in livestock since the 1970s. Epidemics in the Southwest are typically caused by newly introduced viruses, which usually disappear after 1 to 2 years. Affected herds are quarantined until the disease has run its course. Vesicular stomatitis closely resembles three vesicular diseases exotic to the U.S.: foot-and-mouth disease (FMD), swine vesicular disease, and vesicular exanthema of swine. Differentiation of these diseases is important, as a wrong diagnosis could mask the spread of an exotic disease. Prompt diagnosis is also important in containing outbreaks of vesicular stomatitis, which can restrict international trade.

Etiology

Vesicular stomatitis virus (VSV) is a member of the genus *Vesiculovirus* in the family Rhabdoviridae. The two major serotypes are New Jersey and Indiana. Currently, four viruses are known to cause vesicular stomatitis: vesicular stomatitis Indiana virus (VSV-IN; formerly known as the Indiana 1 subtype of VSV), vesicular stomatitis New Jersey virus (VSV-NJ), vesicular stomatitis Alagoas virus (VSV-AV; formerly Indiana 3) and Cocal virus (formerly Indiana 2). The genus *Vesiculovirus* also contains related viruses (such as Piry virus) which have been isolated from animals, humans and/or arthropods and may cause vesicles after experimental inoculation.

Species Affected

Vesicular stomatitis mainly affects horses, donkeys, mules, cattle and swine. South American camelids, sheep and goats occasionally have clinical signs. Serological evidence of infection has been found in many other animals including deer, pronghorn antelope, bighorn sheep, bats, raccoons, opossums, lynx, bobcats, bears, coyotes, foxes, dogs, non-human primates, rabbits, rodents, turkeys and ducks. In addition to livestock, guinea pigs, hamsters, mice, ferrets and chickens have been infected experimentally. Humans are also susceptible. The reservoir or amplifying hosts for VSV are unknown:

Geographic Distribution

Vesicular stomatitis is endemic in Mexico, Central America, northern South America and eastern Brazil, as well as in limited areas of the southeastern U.S. Occasional outbreaks are seen in other parts of the Western Hemisphere, both north and south of the endemic area.

The geographic distribution varies with the virus. VSV-NJ and VSV-IN outbreaks occur in North, Central and South America. In the U.S., VSV-NJ was once endemic in a large part of the Southeast, but it may now exist only in limited areas such as Ossabaw Island, Georgia. VSV-IN is not thought to be endemic in the U.S., but newly introduced viruses occasionally cause outbreaks. VSV-AV (Indiana-3) and Cocal virus (Indiana-2) have been seen only in parts of South America.

Transmission

The transmission of vesicular stomatitis, and the relative importance of the different transmission routes for each virus, is not completely understood. Insect vectors seem to introduce VSV into populations of domesticated animals. Important biological vectors include sand flies (*Lutzomyia* sp.) and blackflies (family Simuliidae). *Culicoides* midges may also be biological vectors. Blackflies can transmit VSV-NJ to uninfected blackflies feeding at the same time on an uninfected host. Transovarial transmission has been demonstrated in sandflies and blackflies, and it may be possible in *Culicoides*. VSV has also been isolated from *Aedes* mosquitoes, Chloropidae (eye gnats), and flies in the genus *Musca* or family Anthomyiidae; these insects may act as mechanical vectors. In addition, grasshoppers (*Melanoplus sanguinipes*) can be infected experimentally, and cattle the ingest experimentally infected grasshoppers can develop

clinical signs. There is also some speculation that VSV could be a plant virus found in pastures, with animals at the end of an epidemiological chain.

Once it has been introduced into a herd, vesicular stomatitis can spread from animal to animal by direct contact. Broken skin or mucous membranes may facilitate entry of the virus. Infected animals shed VSV in vesicle material, saliva and to a lesser extent, in nasal secretions. In experimentally infected horses, VSV has been found in the saliva of animals with or without oral lesions. Fecal shedding has been reported occasionally in experimentally infected swine, but it has not been seen in horses. VSV does not appear to be shed in milk. Animals can also be infected by exposure to contaminated fomites including food, water and milking machines. VSV in saliva can survive for 3-4 days on fomites; however, this virus is inactivated by sunlight, and does not remain viable for long periods in the environment except in cool, dark places. Experimental infection of livestock by aerosols has been demonstrated, but this route did not result in skin lesions in most species. VSV does not appear to cross the placenta or cause fetal seroconversion.

The reservoir and amplifying hosts for VSV are unknown. Viremia sufficient to infect insect vectors has not been reported in any domesticated or wild animal; however, insects could become infected by feeding on lesion material or contaminated secretions. Overwintering has been reported in some but not all outbreaks in the U.S.

Humans may be infected by contact with the lesions or secretions from infected animals, particularly vesicular fluid and saliva. Aerosol transmission occurs in laboratories. In addition, some people are probably infected through insect bites.

Incubation Period

The incubation period is usually two to eight days; however, longer or shorter incubation periods have also been reported. During one outbreak in California, the average incubation period was 8.9 days. In contrast, lesions or fever develop in 1 to 3 days in some experimentally infected horses and swine.

Clinical Signs

Vesicular stomatitis is characterized by vesicles, papules, erosions and ulcers; these lesions are found particularly around the mouth but may also be present on the feet, udder and prepuce. Excessive salivation is often the first symptom. Closer examination may reveal the characteristic raised vesicles (blisters). Vesicles vary widely in size; while some are as small as a pea, others can cover the entire surface of the tongue. They rupture to become erosions or ulcers; this may happen before any vesicles are seen. A transient fever usually develops when the lesions appear. In horses, vesicles occur most often on the upper surface of the tongue, the gums and lips, and around the nostrils and corners of the mouth. In some horses, the vesicles may go unnoticed and the disease may appear as crusting scabs on the muzzle and lips. In cattle, the vesicles are usually found on the hard palate, tongue, lips and gums, sometimes extending to the nostrils and muzzle. Some papules in cattle do not become vesiculated. In addition to the oral ulcers, cattle and horses may develop lesions on the teats or prepuce, and on the coronary band and interdigital spaces of the hooves. In pigs, vesicles usually appear first on the feet, and the first symptom may be lameness. The muzzle and lips are also frequently affected in swine. The predominant sites of lesions can vary in different outbreaks.

Vesicular stomatitis lesions are painful and can cause anorexia, refusal to drink, and lameness. In some cases, the epithelium of the tongue or muzzle may slough, and the nostrils and muzzle may swell. Some animals can have a catarrhal nasal discharge, bleeding from ulcers, or a fetid mouth odor. Dairy cattle with lesions on the teats can develop mastitis from secondary infections. Weight loss may be severe, and milk production can drop in dairy cows. Some cattle may appear to be normal, but eat approximately half of their feed. Unless secondary bacterial infections or other complications develop, animals recover in approximately two to three weeks. However, if recovering animals are transported, the stress may cause new lesions to develop. Subclinical infections are also seen.

Post Mortem Lesions

Click to view images

The necropsy lesions are similar to those in live animals, and may include vesicles, ulcers, erosions and crusting on the lips, nostrils, hooves, teats or prepuce, and in the mouth. Heart and rumen lesions, which may be seen in foot and mouth disease, do not occur in cases of vesicular stomatitis.

Morbidity and Mortality

From Mexico to northern South America, outbreaks of vesicular stomatitis caused by VSV-NJ or VSV-IN usually occur each year. This disease is seasonal: although cases may occur throughout the year, they are particularly common at the end of the rainy season or early in the dry season. VSV-AV outbreaks occur in parts of Brazil every 1 to 2 years, and Cocal virus is seen sporadically in Argentina and Southern Brazil. Both explosive epidemics and slowly spreading outbreaks with relatively few cases (an endemic pattern) can be seen in endemic areas.

Outside these regions, vesicular stomatitis occurs in epidemics that spread south in South America or north in North America. These outbreaks can sometimes involve hundreds or thousands of farms, as well as wildlife. In the U.S., they may be caused by either VSV-NJ or VSV-IN, but VSV-NJ is seen more often. Epidemics occur approximately every 10 years in the Southwest, the upper Mississippi, and the Rocky and Appalachian mountains. These outbreaks appear to be caused by new introductions

of viruses, possibly from Mexico. They tend to begin in the spring in states bordering Mexico, then spread north, often along riverways and in valleys. Some epidemics may extend as far as Canada. They usually end with the first frosts; however, overwintering has been reported a few times. Until the early 1970s, VSV-NJ also affected animals in an endemic pattern in the Southeast. This virus is no longer seen in domesticated animals, but it remains endemic in limited areas such as Ossabaw Island, Georgia, where feral pigs are infected.

The morbidity rate for vesicular stomatitis is highly variable, and ranges from 5% to more than 90%. Typically, 5-20% of the animals in a herd are symptomatic, but up to 100% seroconvert. Most cases occur in adults; young cattle and horses under a year of age are uncommonly affected. Deaths are very rare in cattle and horses, but higher mortality rates have been seen in some pigs infected with VSV-NJ.

Diagnosis

Clinical

Laboratory diagnosis is essential, as vesicular stomatitis cannot be reliably distinguished from other vesicular diseases including foot-and-mouth disease, vesicular exanthema and swine vesicular disease. However, the presence of symptoms in horses suggests vesicular stomatitis.

Differential diagnosis

In cattle, the differential diagnoses include foot and mouth disease, foot rot, and chemical or thermal burns. The oral lesions can also be similar to those of rinderpest, infectious bovine rhinopneumonitis, bovine viral diarrhea, malignant catarrhal fever and epizootic hemorrhagic disease. In pigs, FMD, swine vesicular disease, vesicular exanthema of swine, foot rot, and chemical and thermal burns should be considered. Bluetongue, contagious ecthyma, lip and leg ulceration, and foot rot are among the differentials in sheep. Toxic and mechanical causes of ulcers and erosions should be considered in horses.

Laboratory tests

Detection of the virus or viral antigens is preferred for a definitive diagnosis. VSV can be isolated in tissue culture, embryonated chicken eggs or mice. Many cell lines are susceptible to this virus; however, VSV, foot-and-mouth disease virus and swine vesicular disease virus cause different cytopathic effects in African green monkey kidney (Vero), baby hamster kidney (BHK-21) and IB-RS-2 cells. For this reason, inoculating all three cell lines with the sample aids diagnosis. Electron microscopy can also be helpful in differentiating these three viruses. The identity of the virus is confirmed in cultures by immunofluorescence, complement fixation, enzyme-linked immunosorbent assays (ELISAs) and other tests.

In tissue samples, viral antigens can be detected with ELISA, complement fixation or virus neutralization tests. Reverse transcriptase-polymerase chain reaction (RT-PCR) tests may also be used. A one-step multiplex RT-PCR assay for the simultaneous diagnosis of FMD, swine vesicular disease and vesicular stomatitis was published recently.

Animals develop serotype-specific antibodies within 5 to 8 days of infection. The most commonly used serological tests are ELISAs and virus neutralization. Complement fixation, agar gel immunodiffusion and counter immunoelectrophoresis techniques may also be used.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted.

Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Vesicular stomatitis is zoonotic; samples should be collected and handled with all appropriate precautions.

Samples should be handled and submitted as if they may contain either VSV, foot-and-mouth disease virus or swine vesicular disease virus. Vesicle fluids, the epithelium covering unruptured vesicles, epithelial flaps from freshly ruptured vesicles, or swabs of the ruptured vesicles are the preferred diagnostic samples. APHIS recommends collecting swabs from vesicles. Samples may be collected from any site including the mouth or feet. Sedation is often recommended before sample collection, as the lesions are highly painful. If epithelial tissue is not available, samples of esophageal/pharyngeal fluid can be collected with a probang cup from cattle, or throat swabs may be taken from pigs. Samples should be sent refrigerated unless shipping will take longer than 2 days; in this case, they may be sent frozen with dry ice.

Serum samples, or paired serum samples taken 1 to 2 weeks apart, may also be collected. In the U.S., paired serum samples are used only for the index case of the nation and index case for each state. Once an outbreak of vesicular stomatitis has been diagnosed in a state, an animal can be declared positive after a single positive test.

Treatment

Treatment is symptomatic. Cleansing the lesions with a mild antiseptic solution may aid healing and reduce secondary bacterial infections. Animals with mouth lesions should be provided with softened feed.

Recommended actions if vesicular stomatitis is suspected

Notification of authorities

State and federal veterinarians should be informed immediately of any suspected vesicular disease.

Federal: Area Veterinarians in Charge (AVIC):
http://www.aphis.usda.gov/animal_health/area_offices.htm
State Veterinarians:
http://www.aphis.usda.gov/vs/sregs/official.html

Control

VSV can spread between animals by direct contact; during outbreaks, uninfected livestock should kept away from any animals that could be infected. In the U.S., animal movements are restricted during epidemics. Movement testing requirements may vary with the state. Infected facilities are quarantined: there should be no movement of animals from an infected property for at least 21 days after all lesions are healed, unless the animals are going directly to slaughter. Isolating symptomatic animals helps control the spread of vesicular stomatitis within a herd. Horses appear to be most contagious for the first six days after infection.

Good sanitation and disinfection can reduce the spread of the virus on fomites. VSV is inactivated in sunlight and it does not survive for long periods in the environment except in cool, dark places. However, it can remain infectious for 3 to 4 days on fomites including pails, mangers and hay. Lower attack rates have been reported on dairies where feed and water troughs were cleaned regularly. Milking equipment should also be disinfected between uses, and cows with lesions should be milked last. VSV is susceptible to numerous disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, 2% sodium carbonate, 4% sodium hydroxide, iodophore disinfectants, formaldehyde and chlorine dioxide. It is also inactivated by UV light, lipid solvents, or heat.

Stabling animals appears to decrease the risk of disease; pastured livestock are more likely to become infected. Other insect control measures may also be helpful. Insect breeding areas should be eliminated or reduced, and insecticide sprays or treated eartags can be used on animals. In addition, the avoidance of hard or abrasive feeds may prevent oral abrasions that could facilitate infections. Commercial vaccines are used in some endemic regions of Central and South America, but are not available in the U.S.

Public Health

In people, vesicular stomatitis is an acute illness that resembles influenza. The incubation period is usually three to four days, but it can be as short as 24 hours or as long as six days. The symptoms may include fever, muscle aches, headache and malaise. Vesicles are rare, but can occasionally be found on the mouth, lips or hands. Deaths have not been reported, and most people recover without complications in four to seven days.

Humans can become infected when handling affected animals, contaminated fomites, tissues, blood or virus cultures. Aerosol transmission also occurs, particularly in laboratories. Before the advent of modern biological safety procedures and equipment, nearly all laboratory workers and animal handlers who had been exposed either seroconverted or became ill. Human infections remain common in endemic areas. In Central America, 48-100% of the population has been exposed. However, during the 1982-1983 VSV-NJ epidemic in the U.S., one study found that the infectivity of the virus for veterinarians, laboratory workers and other risk groups was low, and relatively close contact was required for infection. The percentage of infections that become symptomatic is unknown. Although some sources suggest this disease is rare, others point out that human infections may be underreported as they can easily be misdiagnosed as influenza. To prevent infection, protective clothing and gloves should be used when handling infected animals, and biological safety precautions should be taken in the laboratory.

Internet Resources

United States Animal Health Association. Foreign Animal Diseases
http://www.vet.uga.edu/vpp/gray_book02/fad/index.php

USDA APHIS Vesicular Stomatitis
http://www.aphis.usda.gov/vs/nahss/equine/vsv/

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Terrestrial Animal Health Code
http://www.oie.int/eng/normes/mcode/A_summry.htm

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/eng/normes/mmanual/a_summry.htm

References

Acha PN, Szyfres B [Pan American Health Organization (PAHO)]. Zoonoses and communicable diseases common to man and animals. Volume 2. Chlamydioses, rickettsioses, and viroses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Vesicular stomatitis; p. 347-353.

Drolet BS, Campbell CL, Stuart MA, Wilson WC. Vector competence of *Culicoides sonorensis* (Diptera: Ceratopogonidae) for vesicular stomatitis virus. J Med Entomol. 2005;42:409-18.

Fernández J, Agüero M, Romero L, Sánchez C, Belák S, Arias M, Sánchez-Vizcaíno JM. Rapid and differential diagnosis of foot-and-mouth disease, swine vesicular disease, and vesicular stomatitis by a new multiplex RT-PCR assay. J Virol Methods. 2008;147:301-11.

House JA, House C, Dubourget P, Lombard M. Protective immunity in cattle vaccinated with a commercial scale, inactivated, bivalent vesicular stomatitis vaccine. Vaccine. 2003;21:1932-1937.

Howerth EW, Mead DG, Mueller PO, Duncan L, Murphy MD, Stallknecht DE. Experimental vesicular stomatitis virus infection in horses: effect of route of inoculation and virus serotype. Vet Pathol. 2006;43:943-55.

International Committee on Taxonomy of Viruses Universal Virus Database [ICTVdB] Management. 01.062.0.01. Vesiculovirus. In: Büchen-Osmond C, editor. ICTVdB - The universal virus database, version 4 [online]. New York: Columbia University; 2006. Available at: http://www.ncbi.nlm.nih.gov/ICTVdb/ICTVdB. Accessed 21 Jan 2008.

Kahn CM, Line S, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2006. Vesicular stomatitis. Available at: http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/52500.htm. Accessed 21 Jan 2008.

Letchworth GJ, Rodriguez LL, Del C Barrera J. Vesicular stomatitis. Vet J. 1999;157:239-60.

Mead DG, Gray EW, Noblet R, Murphy MD, Howerth EW, Stallknecht DE. Biological transmission of vesicular stomatitis virus (New Jersey serotype) by *Simulium vittatum* (Diptera: Simuliidae) to domestic swine (*Sus scrofa*). J Med Entomol. 2004;41:78-82.

Mead DG, Howerth EW, Murphy MD, Gray EW, Noblet R, Stallknecht DE. Black fly involvement in the epidemic transmission of vesicular stomatitis New Jersey virus (Rhabdoviridae: Vesiculovirus). Vector Borne Zoonotic Dis. 2004;4:351-359.

Mebus CA. Vesicular stomatitis. In: Foreign animal diseases [online]. Richmond, VA: United States Animal Health Association; 1998. Available at: http://www.vet.uga.edu/VPP/gray_book02/fad/vst.php. Accessed 21 Jan 2008.

Nunamaker RA, Lockwood JA, Stith CE, Campbell CL, Schell SP, Drolet BS, Wilson WC, White DM, Letchworth GJ. Grasshoppers (Orthoptera: Acrididae) could serve as reservoirs and vectors of vesicular stomatitis virus. J Med Entomol. 2003;40:957-963.

Perez de Leon AA, Tabachnick WJ. Transmission of vesicular stomatitis New Jersey virus to cattle by the biting midge *Culicoides sonorensis* (Diptera: Ceratopogonidae). J Med Entomol. 2006;43:323-9.

Personal communication, Sabrina L. Swenson, DVM, PhD. Bovine and Porcine Viruses Section, Diagnostic Virology Laboratory. National Veterinary Services Laboratories, Ames, Iowa.

Public Health Agency of Canada, Office of Laboratory Security. Material Safety Data Sheet: Vesicular stomatitis virus [online]. Office of Laboratory Security; 2001 Feb. Available at: http://www.phac-aspc.gc.ca/msds-ftss/msds163e.html. Accessed 21 Jan 2008.

Rainwater-Lovett K, Pauszek SJ, Kelley WN, Rodriguez LL. Molecular epidemiology of vesicular stomatitis New Jersey virus from the 2004-2005 US outbreak indicates a common origin with Mexican strains. J Gen Virol. 2007;88:2042-51.

Reif JS, Webb PA, Monath TP, Emerson JK, Poland JD, Kemp GE, Cholas G. Epizootic vesicular stomatitis in Colorado, 1982: infection in occupational risk groups. Am J Trop Med Hyg. 1987;36:177-82.

Rodríguez LL. Emergence and re-emergence of vesicular stomatitis in the United States. Virus Res. 2002;85:211-9.

Stallknecht DE, Greer JB, Murphy MD, Mead DG, Howerth EW. Effect of strain and serotype of vesicular stomatitis virus on viral shedding, vesicular lesion development, and contact transmission in pigs. Am J Vet Res. 2004;65:1233-9.

U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services [USDA APHIS, VS]. Vesicular stomatitis [online]. Available at: http://www.aphis.usda.gov/lpa/pubs/fsheet_faq_notice/fs_ahvs.html. Accessed 26 Jan 2006.

U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services [USDA APHIS, VS]. Vesicular stomatitis: Questions and answers [online]. USDA APHIS, VS; 2005 June. Available at: http://www.aphis.usda.gov/lpa/pubs/fsheet_faq_notice/faq_ahvs.html. Accessed 26 Jan 2006.

World Organization for Animal Health [OIE]. Manual of diagnostic tests and vaccines for terrestrial animals [online]. Paris: OIE; 2004. Vesicular stomatitis. Available at: http://www.oie.int/eng/normes/mmanual/A_00025.htm. Accessed 26 Jan 2006.