

Hemorrhagic Septicemia

Last Updated: August 2019



The Center for
Food Security
& Public Health



INSTITUTE FOR
INTERNATIONAL
COOPERATION IN
ANIMAL BIOLOGICS

IOWA STATE UNIVERSITY
College of Veterinary Medicine



OIE Collaborating Centre for
• Diagnosis of Animal Disease and
Vaccine Evaluation in the Americas
• Day-One Veterinary Competencies
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Importance

Hemorrhagic septicemia is a bacterial disease that mainly affects cattle and water buffalo, and is an important cause of livestock mortality in tropical regions of Asia, Africa and the Middle East. It also occurs occasionally in other animals and has caused severe outbreaks in endangered saiga antelope (*Saiga tatarica*) in Kazakhstan. One outbreak in 2015 killed more than half the saiga population. The clinical signs usually progress rapidly from fever and depression to death, within hours to a few days. Because the disease course is so short, few animals can be treated in time, and recovery is rare. Young animals are mainly affected in endemic regions, and outbreaks are particularly common during rainy weather, when the organism can spread readily. In areas where animals have no immunity, severe disease is expected to occur in all ages.

Etiology

Hemorrhagic septicemia is caused by certain members of *Pasteurella multocida* subsp. *multocida*, a Gram-negative coccobacillus in the family Pasteurellaceae. *P. multocida* isolates are traditionally identified by a letter designating the organism's serogroup (A, B, D, E or F), based on the capsular antigen, and a number for the somatic antigen. Classically, hemorrhagic septicemia was considered to be caused by just two serotypes of *P. multocida* ssp. *multocida*, which are called B:2 and E:2 in the Carter-Heddleston serotyping system, or 6:B and 6:E, respectively, in the alternative Namioka-Carter system. However, other serotypes (e.g., types A:1 and A:3 in cattle and water buffalo in India) have occasionally been isolated from animals with a syndrome clinically indistinguishable from hemorrhagic septicemia. Some authors have called these cases hemorrhagic septicemia; others term them septicemic pasteurellosis. Septicemic pasteurellosis has especially been used for disease outbreaks in cervids and other wild ungulates.

Recent studies suggest that genetic techniques, such as multi-locus sequence typing (MLST), may be a more accurate way to define the causative organisms. In these analyses, hemorrhagic septicemia appears to be caused by one particular clonal complex, which contains closely related isolates of *P. multocida* ssp. *multocida*. Although the majority of these organisms belong to serotypes B:2 and E:5, this clonal complex also contains other serotypes, including members of serogroups A and D. Most, though not all, of the MLST types in this complex are ST122.

Species Affected

Hemorrhagic septicemia is seen most often in cattle and water buffalo (*Bubalus bubalis*), which are important reservoir hosts. This disease has also been reported in other species including pigs, sheep, goats, American bison (*Bison bison*), African buffalo (*Syncerus caffer*), dromedary camels (*Camelus dromedarius*), elephants, saiga antelope, some cervids (e.g., fallow deer, *Dama dama*), horses, donkeys and yaks. Experimental infections are readily established in laboratory rabbits and mice. Hemorrhagic septicemia-associated strains of *P. multocida* were apparently isolated from gerbils in Kazakhstan during two outbreaks in ungulates.

Zoonotic potential

There are no published reports of infections with *P. multocida* serotypes B:2 or E:2 in people, and human illnesses have not been associated with outbreaks of hemorrhagic septicemia in animals. However, *P. multocida* is an opportunistic pathogen in humans, and precautions should be taken to avoid unnecessary exposure. While this organism most often causes soft tissue infections, it is occasionally involved in other conditions such as osteomyelitis, endocarditis, meningitis, respiratory infections or septicemia, especially in people who are immunocompromised or have other underlying diseases. Serogroups A and D have been reported from some human illnesses, but the serotype of the causative organism was not determined in many or most cases.

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Geographic Distribution

Hemorrhagic septicemia is an important disease of cattle and water buffalo in Asia, Africa and the Middle East. The highest incidence is in Southeast Asia. Cases have also been reported sporadically in Europe, where this disease is said to occur mainly in southern Europe but has also been seen occasionally in other countries, including those with cold climates (e.g., Estonia, Latvia, Georgia, Ukraine). Several outbreaks have been reported since 2010 in Central Europe (e.g., Germany, Hungary, Serbia), suggesting that the causative organisms may have been introduced to this region after apparently being absent for decades. Hemorrhagic septicemia-causing strains of *P. multocida* are not thought to circulate in North America, Australia or New Zealand. They were also thought to be absent from South and Central America; however, this disease was reported to the World Organization for Animal Health (OIE) from Colombia in 2007, Venezuela in 2015 and Ecuador in 2018. There seems to be little or no published information about these outbreaks.

Serotype B:2 is the major cause of hemorrhagic septicemia in Asia, although a few clinical cases are apparently caused by other serotypes, including members of serogroup E. B:2 is also prominent in Europe and the Middle East. At one time, most cases of hemorrhagic septicemia in Africa were thought to be caused by serotype E:2. However, B:2 organisms have increased in frequency there, and the relative contributions of these two serotypes are currently unclear.

Serotypes other than B:2 and E:2 have been found in ungulates in North America (e.g., pronghorn [*Antilocapra americana*] and elk [*Cervus canadensis*]), Australia (fallow deer and chital deer [*Axis axis*]) and some other countries where hemorrhagic septicemia is reported to be absent. These outbreaks were considered to be septicemic pasteurellosis, and were caused by various organisms including members of serogroups A and B.

Transmission

Hemorrhagic septicemia can be transmitted by ingestion or inhalation, either during direct contact or via fomites such as contaminated feed and water. The causative organisms are thought to spread mainly in respiratory secretions, but they can also be found in other secretions and excretions, including feces and urine. Some infected animals become carriers, maintaining *P. multocida* ssp. *multocida* in the lymphatic tissues (e.g., tonsils) associated with the upper respiratory tract, and periodically shedding it in nasal secretions. Shedding may be triggered by stress. One study also found nucleic acids in the lung, reticulum, ileum and ureter of experimentally infected buffalo calves, 6 weeks after inoculation, although the administration of corticosteroids did not induce shedding from these sites after 15-17 days. *P. multocida* carriage in cattle and water buffalo appears to be highest soon after an outbreak: up to 20% of the surviving animals may become carriers for a

time, but this is thought to decrease to 5% or less after 6 months. Information about carriage in other species is limited, but it is known to occur in at least some hosts.

P. multocida does not remain viable for long periods in the environment, but it can survive for hours and possibly days in damp soil or water. Rainy conditions and high humidity facilitate transmission. Biting arthropods do not seem to be important in the epidemiology of this disease.

Disinfection

P. multocida is susceptible to many common disinfectants, as well as to mild heat (55°C/131°F) or UV light. Specific agents reported to be effective against *Pasteurella* sp. include phenolic disinfectants, 70% ethanol, 1% sodium hypochlorite, iodophors, formaldehyde, glutaraldehyde and peracetic acid.

Incubation Period

The incubation period is thought to be 3-5 days in most cases, although it can be much shorter (e.g., a few hours) in experimentally infected cattle or water buffalo that are inoculated with lethal doses. Some animals carry the organism asymptotically for varying periods before becoming ill.

Clinical Signs

Hemorrhagic septicemia is an acute or peracute illness. Most clinical cases have been described in cattle and water buffalo. Although the disease is very similar in both species, buffalo tend to have more severe signs and a shorter course. Typically, a fever, depression and other nonspecific clinical signs (e.g., a drop in milk production) are quickly followed by excessive salivation and a profuse serous nasal discharge. The nasal discharge may become mucopurulent if the animal survives longer. Other characteristic signs include dyspnea, which may be accompanied by frothing at the mouth or nostrils, and edematous swellings in the submandibular region. These swellings may spread to the neck and brisket, and sometimes to the forelegs. Some animals may have diarrhea and abdominal pain, or hemorrhagic gastroenteritis. Although neurological signs do not seem to be evident in most cases, evidence of meningitis or hemorrhagic encephalitis was found in the brains of some cattle and water buffalo at necropsy. Animals with hemorrhagic septicemia usually collapse and die within a few hours to a few days after the onset of the illness. Sudden death with few or no clinical signs can also be seen. Symptomatic animals, especially buffalo, rarely recover.

The signs of hemorrhagic septicemia seem to be similar in other species; however, neurological signs (e.g., tetraparesis, opisthotonos) have been noted in some pigs, and pigs that survived occasionally had persistent discolored and necrotic skin lesions in the ventral neck, throat and/or abdomen. Typical subcutaneous edema was

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absent in some experimentally infected goats, although other signs were consistent with hemorrhagic septicemia.

Similar clinical signs have been seen in some wild ruminants with septicemic pasteurellosis.

Post Mortem Lesions [Click to view images](#)

The gross lesions are consistent with severe sepsis, and are usually characterized by widespread hemorrhages, edema and hyperemia. However, there may be few or no lesions other than a few scattered petechial hemorrhages in some peracute cases.

Subcutaneous edema (a gelatinous mass with straw-colored or bloodstained fluid) can usually be found in the submandibular region and neck, sometimes extending to the brisket or legs. Similar swellings may occur in the musculature, and petechiae may be detected in the subcutaneous connective tissues. The thoracic and abdominal cavities and pericardial sac often contain blood-tinged, serous to serofibrinous fluid, and petechiae are common throughout the internal organs, especially on the serosal surface. Ecchymotic hemorrhages may also be found, particularly on the heart. The lungs are diffusely congested and edematous and may contain hemorrhages. Foam is often found in the airways. Extensive pneumonia, though possible, is atypical. The digestive tract of some animals may be hyperemic and congested, and the abomasum and intestinal mucosa sometimes contain petechiae and ecchymoses. The brain is rarely examined, but meningitis was found in cattle in one outbreak, and a group of experimentally inoculated buffalo calves, which additionally received corticosteroids, developed hemorrhagic encephalitis. Neither group of animals was reported to have any obvious neurological signs before death.

Similar lesions have been seen in animals with septicemic pasteurellosis.

Diagnostic Tests

The *P. multocida* strains that cause hemorrhagic septicemia can be cultured from blood in the terminal stages of the disease, but may be absent from samples collected earlier. These organisms can also be found sometimes in nasal secretions or body fluids, though they are not consistently present. They are usually recovered on nonselective media such as blood agar; thus, culture is more likely to be successful if a fresh sample free from contaminating bacteria, including post-mortem invaders, can be collected. At necropsy, these organisms can often be cultured from a blood sample or swab collected from the heart within a few hours of death. Other visceral organs may also be sampled. The spleen and brain are among the last organs to remain free of contaminants after death. If an animal has been dead longer, it may be possible to find *P. multocida* in a long bone freed of tissue: the marrow is cultured after sterilization of the bone's surface.

In blood or tissue smears, *P. multocida* is a Gram-negative, short rod or ovoid form with bipolar staining.

Bipolar staining is more apparent with methylene blue, Leishman's stain or Giemsa. A definitive diagnosis is usually made by culturing hemorrhagic septicemia-associated *P. multocida* strains from affected animals. These organisms grow well on blood agar or chocolate agar, but some other media (e.g., casein/sucrose/yeast (CSY) agar with 5% blood, dextrose starch agar) can also be used. Biochemical and serological tests and/or polymerase chain reaction (PCR) techniques can be used for the identification of colonies. Some pleomorphism can be expected when examining bacterial morphology, especially in older cultures, and bipolar staining may be lost after serial passage. The B:2 and E:2 serotypes produce hyaluronidase, but other serotypes associated with hemorrhagic septicemia can be hyaluronidase-negative.

Serological tests used for serotyping include rapid slide agglutination or indirect hemagglutination assays for capsular typing, an agglutination test for somatic typing, agar gel immunodiffusion for both capsular and somatic typing, and counter-immunoelectrophoresis for the rapid identification of capsular types B and E. Some isolates can be difficult to type with these traditional methods. Serotyping systems based on genetic techniques, including PCR-based methods, are used in some laboratories. Genetic techniques such as pulsed-field gel electrophoresis (PFGE) or multi-locus sequence typing can characterize isolates further for epidemiological investigations, but are generally available only in research laboratories.

PCR tests may also be used to identify hemorrhagic septicemia-associated serotypes directly in clinical samples. Loop-mediated isothermal amplification (LAMP) assays have been published. Animal inoculation into a mouse can be used to isolate *P. multocida* when *in vitro* culture is unsuccessful, especially if the carcass was overgrown with contaminants. However, animal inoculation should be avoided whenever possible for welfare reasons.

Clinically affected animals usually die quickly, before developing antibodies, and serological assays are generally not useful for diagnosis. However, serology may be employed occasionally for retrospective diagnosis. High titers (1:160 or higher by indirect hemagglutination) in surviving or in-contact animals are suggestive. ELISAs to detect antibodies have also been developed for some species. Immunohistochemistry for antigen detection is mainly used in research.

Treatment

Antibiotics are effective only if they are started very soon after the onset of clinical signs. A common practice during outbreaks is to monitor animals for fever and treat febrile animals immediately. Some drugs used to treat hemorrhagic septicemia include oxytetracycline, trimethoprim/ sulfamethoxazole, a combination of penicillin and streptomycin, or sulphaquinoxaline. Antibiotic resistance has been reported in some endemic areas.

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Control

Disease reporting

Veterinarians who encounter or suspect hemorrhagic septicemia should follow their national and/or local guidelines for disease reporting. In the U.S., state or federal authorities should be informed immediately upon diagnosis or suspicion of this disease.

Prevention

In hemorrhagic septicemia-free countries, outbreaks are usually eradicated by stamping out. This generally includes quarantines, movement controls, tracing of contacts, euthanasia of infected and exposed animals, and cleaning and disinfection of the premises.

In endemic areas, this disease is mainly prevented by vaccination. Vaccines may be available for cattle, small ruminants and pigs. Annual vaccination of livestock is generally recommended, but where vaccination coverage tends to be poor, ring vaccination is frequently part of the response to an outbreak. A recent study suggests that the standard vaccines might not be effective for hemorrhagic septicemia in camels, as the causative organisms may not be B:2 or E:2. Other preventive measures can include the removal of persistent carriers from an infected herd, and management to keep animals in good condition, which is thought to reduce shedding from carriers and decrease the risk that asymptomatic carriers will develop clinical signs. Not crowding animals is also expected to decrease transmission and stress levels.

Morbidity and Mortality

The isolates of *P. multocida* that cause hemorrhagic septicemia can be carried subclinically or with only mild signs for long periods. Some of these animals never develop clinical signs; others abruptly become ill and die. What causes this is unclear, but stressors (e.g., poor nutrition, concurrent illnesses) are thought to play a role. Stressors can also stimulate subclinical carriers to shed *P. multocida*. Outbreaks can occur when either carriers or sick animals excrete large numbers of organisms near susceptible animals.

The morbidity rate depends on environmental conditions, herd management, the animals' immunity and other factors. Although hemorrhagic septicemia can be seen at any time of the year, close herding and wet conditions contribute to the spread of the disease; the worst epidemics tend to occur during the rainy season. In endemic regions, most adults have some immunity to the organism, and clinical cases mainly affect young animals between the ages of 6 months and 2 years. Outbreaks can occur when healthy carriers are introduced into a herd. Some areas experience periodic epidemics, in part because many farmers do not follow the recommendations for annual vaccination unless there have been recent outbreaks. All ages are affected

where hemorrhagic septicemia is not endemic, and the morbidity rate can be high.

The case fatality rate typically approaches 100% unless the animal is treated very early; few animals survive once they become visibly ill. Nevertheless, a few spontaneous recoveries are possible, especially late in an outbreak. Buffaloes seem to be more susceptible to hemorrhagic septicemia than cattle, with higher morbidity and mortality rates. Free-living saiga antelope have been severely impacted by this disease, with extensive outbreaks that killed large numbers of animals. Some of these outbreaks occurred around the time of calving. No other species appeared to be affected during at least one outbreak. Susceptibility to hemorrhagic septicemia/ septicemic pasteurellosis may vary among cervids. In a series of outbreaks at a deer park in Denmark, more than 300 clinical cases occurred in fallow deer, but only a single death was observed in a sika deer (*Cervus nippon*). Red deer (*Cervus elaphus*) in the park were unaffected.

Internet Resources

The Merck Veterinary Manual
<http://www.merckvetmanual.com>

United States Animal Health Association. Foreign Animal Diseases
http://www.aphis.usda.gov/emergency_response/downloads/nahems/fad.pdf

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

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
<http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/>

OIE Terrestrial Animal Health Code
<http://www.oie.int/international-standard-setting/terrestrial-code/access-online/>

Acknowledgements

This factsheet was written by Anna Rovid Spickler, DVM, PhD, Veterinary Specialist from the Center for Food Security and Public Health. The U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) provided funding for this factsheet through a series of cooperative agreements related to the development of resources for initial accreditation training.

The following format can be used to cite this factsheet. Spickler, Anna Rovid. 2019. *Hemorrhagic Septicemia*. Retrieved from <http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php>.

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