

HAEMORRHAGIC SEPTICAEMIA

AETIOLOGY

Classification of the causative agent

Pasteurella multocida. Order: Pasteurellales. Family: Pasteurellaceae

- Haemorrhagic septicaemia (HS) is caused by certain serotypes of *Pasteurella multocida*, a Gram-negative coccobacillus residing mostly as a commensal in the nasopharynx of animals.
- The Asian serotype B:2 and the African serotype E:2 (Carter and Heddleston system), corresponding to the newer 6:B and 6:E classification (Namioka-Carter system), are mainly responsible for the disease
- Other serotypes, namely A:1, A:3, A:4, A:1,3, have been associated with a HS-like condition in cattle and buffaloes in India with mainly pneumonia leading to death
- The letter denotes the capsular antigen and the number stands for the somatic antigen

Resistance to physical and chemical action

Temperature: *Pasteurella multocida* is susceptible to mild heat (55°C).

Disinfectants: *Pasteurella multocida* is susceptible to most hospital disinfectants.

Survival: *Pasteurella 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.

EPIDEMIOLOGY

- HS is a major disease of cattle and buffaloes characterised by an acute, highly fatal septicaemia with high morbidity and mortality
- In many Asian countries HS disease outbreaks mostly occur during the climatic conditions typical of monsoon (high humidity and high temperatures); however, with climate change, incidences of disease may occur any month of the year
- Spatial and temporal variation in HS outbreaks are being reported

Hosts

- Cattle and water buffaloes (*Bubalus bubalis*) are the principal hosts of hemorrhagic septicaemia, and it is widely considered that buffaloes are the most susceptible. These species, as well as bison, appear to be the reservoirs of infection
- Although outbreaks of HS have been reported in sheep, goats and swine, it is not a frequent or significant disease. Infrequent cases have been reported in deer, camels, elephants, horses, donkeys and yaks
- Systemic pasteurellosis has been reported in various species of deer
- North American range bison may also be infected.
- Laboratory rabbits and mice are highly susceptible to experimental infection
- There are no reported cases of human infection

Transmission

- *Pasteurella multocida* is transmitted by direct contact with infected animals and on fomites
- Cattle and buffalo become infected when they ingest or inhale the causative organism, which probably originates in the nasopharynx of infected animals. In endemic areas, up to 5% of cattle and water buffalo may normally be carriers.
- The worst epidemics occur during the rainy season, in animals in poor physical condition
- Stresses such as a poor food supply are thought to increase susceptibility to infection, and close herding and wet conditions seem to contribute to the spread of the disease
- *Pasteurella multocida* can survive for hours and possibly days in damp soil or water; viable organisms are not found in the soil or pastures after 2–3 weeks
- Biting arthropods do not seem to be significant vectors

Sources of the agent

- Blood: septicaemia in HS occurs at the terminal stage of the disease, therefore, blood samples taken from sick animals before death may not always contain *P. multocida* organisms. Additionally, animals under chemotherapeutics may not show presence of *P. multocida* organisms in blood smears
- Nasal secretions: however, organisms are also not consistently present in sick animals

Occurrence

Hemorrhagic septicaemia is an important disease in Asia, Africa, and the Middle East. It has never been confirmed in Mexico, Central or South America

- The B:2 serotype has been seen in Southern Europe, the Middle East, Southeast Asia, Egypt, and the Sudan
- The E:2 serotype has been reported in Egypt, the Sudan, the Republic of South Africa, and several other African countries
- Three confirmed outbreaks have been reported in one bison herd in the United States; however, there is no evidence that the disease spread to neighbouring cattle

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information Database (WAHID) Interface
[<http://www.oie.int/wahis/public.php?page=home>]

DIAGNOSIS

- The incubation period varies from 3–5 days.
- Some characteristic epidemiologic and clinical features (sudden death) aid in the recognition of HS. Of particular significance is a history of earlier outbreaks and a recent failure to vaccinate
- Sporadic cases are more difficult to diagnose clinically
- The season of the year, rapid course, and high herd incidence, with fever and oedematous swellings and terminal death indicate typical HS
- Characteristic necropsy lesions (oedema, wide spread congestion/ haemorrhages on vital organs) support the clinical diagnosis; confirmation requires the isolation and characterisation of the pathogen using conventional and molecular techniques
- In experimental infections with lethal doses, cattle or buffalo develop clinical signs within a few hours and die within 18–30 hours
- Morbidity depends on immunity and environmental conditions, including both weather and husbandry practices; morbidity is higher when animals are herded closely, in poor rearing condition, or exposed to wet conditions
- Mortality is nearly 100% unless the animal is treated very early in the disease; few animals survive once they develop clinical signs

Clinical diagnosis

- Most cases in cattle and buffalo are acute or peracute
- Buffaloes are generally more susceptible to HS than cattle and show more severe forms of disease with profound clinical signs
- A fever, dullness, and reluctance to move are the first signs
- Salivation and a serous nasal discharge develop, and oedematous swellings become apparent in the pharyngeal region; these swellings spread to the ventral cervical region and brisket.
- Mucous membranes are congested
- Respiratory distress occurs, and the animal usually collapses and dies 6–24 hours after the first signs are seen
- Either sudden death or a protracted course up to 5 days is also possible
- Animals with clinical signs, particularly buffalo, rarely recover
- Chronic cases do not seem to occur in cattle and buffalo
- In endemic areas most deaths are confined to older calves and young adults
- Massive epizootics may occur in endemic as well as non-endemic areas
- In the recent past, HS has been identified as a secondary complication in cattle and buffaloes following outbreaks of foot and mouth disease or any immune-compromised/ stress conditions.
- Case fatality approaches 100% if treatment is not followed at the initial stage of infection

Lesions

- Widespread haemorrhages, oedema, and hyperaemia, consistent with severe sepsis
- Oedema consists of a coagulated serofibrinous mass with straw-coloured or blood stained fluid
- Swelling of the head, neck, and brisket occurs in nearly all cases
- Similar swellings can also be found in the musculature
- Subserosal petechial haemorrhages may occur throughout the body, and the thoracic and abdominal cavities often contain blood-tinged fluid
- Scattered petechiae may be visible in the tissues and lymph nodes, particularly the pharyngeal and cervical nodes; these nodes are often swollen and haemorrhagic
- Pneumonia or gastroenteritis occasionally occurs, but usually is not extensive
- Atypical cases, with no throat swelling and extensive pneumonia, are sometimes seen
- There are no microscopic features that are specific for hemorrhagic septicaemia – all lesions are consistent with severe endotoxic shock and massive capillary damage

Differential diagnosis

- Shipping fever is often mistakenly confused for HS, but has a multifactorial aetiology (often *Mannheimia haemolytica*), is not septicaemic, and does not cause multisystemic petechial haemorrhages
- The peracute nature of the disease and the extensive oedema and haemorrhage make it difficult to differentiate from blackleg and anthrax
- Acute salmonellosis, mycoplasmosis, lightning, snake bites, poisoning and pneumonic pasteurellosis should also be considered

Laboratory diagnosis

Samples

- *Pasteurella multocida* is not always found in blood samples before the terminal stage of the disease, and is not consistently present in nasal secretions or body fluids of sick animals
- Recently dead animals
 - a heparinised blood sample or swab should be collected from the heart within a few hours of death, and a nasal swab
 - other visceral organs may also be sampled. If a necropsy is not feasible, blood samples can be taken from the jugular vein by aspiration or incision; blood samples should be placed in a standard transport medium and transported on ice packs
 - Spleen and bone marrow provide excellent samples for the laboratory, as these are contaminated relatively late in the post-mortem process by other bacteria
- Animals that have been dead for a long time
 - A long bone (femur/humerus) should be taken from its carcass
- Live animals
 - Nasal swab or blood

Procedures

Identification of the agent

Culture and biochemical methods

- The diagnosis of HS depends on the isolation of the causative organism, *P. multocida*, from the blood or bone marrow of a dead animal by cultural and biological methods, and the identification of the organism by biochemical, serological and molecular methods
- Blood smears from affected animals can be stained with Gram, Leishman's or methylene blue stains. The organisms appear as Gram-negative, bipolar-staining short bacilli
- No conclusive diagnosis can be made on direct microscopic examinations alone
- Samples may be cultured on casein/sucrose/yeast agar containing 5% blood. Conventional blood agar may also be used. Details, including biochemical methods for identification of the organisms, can be found in the OIE *Terrestrial Manual*

Serotyping methods

- Serotyping methods include the rapid slide agglutination test, indirect haemagglutination test, somatic antigen agglutination tests, agar gel immunodiffusion and counter immunoelectrophoresis. The following techniques can be used to reach a diagnosis. Please find the details in the OIE *Terrestrial Manual*.
 - Rapid slide agglutination (capsular typing)
 - Indirect hemagglutination test (capsular typing)
 - Agar gel immunodiffusion tests
 - Counter immunoelectrophoresis
 - Agglutination tests (somatic antigen)

Nucleic acid recognition methods

- PCR technology can be applied for rapid, sensitive and specific detection of *P. multocida*; the rapidity and high specificity of two of the *P. multocida*-specific assays provide optimal efficiency without the need for additional hybridisation
- The *P. multocida*-specific PCRs identify all subspecies of *P. multocida*
- For capsular and somatic typing of isolates, Multiplex capsular PCR typing and LPS-mPCR assays may be used as alternative to serological typing
- Once presumptive (or definitive) identification has been made, further differentiation of isolates can be achieved by genotypic fingerprinting methods (restriction endonuclease analysis, RAPD-PCR [random amplified polymorphic DNA-polymerase chain reaction], enterobacterial repetitive intragenic consensus [ERIC]-PCR, repetitive extragenic palindromic [REP]-PCR, amplified fragment length polymorphism analysis, etc.). PCR fingerprinting is feasible for any laboratory with PCR capability

Serological tests

- Serological tests are not normally used for diagnosis; however, high titres (1:160 or higher by indirect haemagglutination) in surviving in-contact animals are suggestive of the disease

For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 3.4.10 Haemorrhagic Septicaemia, in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading “Diagnostic Techniques”

PREVENTION AND CONTROL

Sanitary prophylaxis

Vaccination is routinely practiced in endemic areas. Avoiding crowding, especially during wet conditions, will also reduce the incidence of disease.

Medical prophylaxis

- Antibiotic treatment is effective if it is started very early, during the pyretic stage.
- Various HS vaccines can provide protection for 6–12 months
- Antimicrobial susceptibility testing (AST) is particularly necessary for *P. multocida* for which resistance to commonly used antimicrobial agents has occurred
- Strains of *P. multocida* vary in susceptibility to chemotherapeutic agents. The following agents have proven their clinical efficacy: penicillin, amoxicillin (or ampicillin), cephalothin, ceftiofur, cefquinome, streptomycin, gentamicin, spectinomycin, florfenicol, tetracycline, sulfonamides, trimethoprim/sulfamethoxazole, erythromycin, tilimicosin, enrofloxacin (or other fluoroquinolones), Amikacin and norfloxacin
- However, there is gradual development of resistance for commonly used agents such as carbenicillin, amikacin, erythromycin and penicillin
- Animals that are exposed to *Pasteurella multocida* serotypes 6:B and 6:E and that survive are considered solidly immune

Inactivated vaccines

- Vaccination is routinely practiced in endemic areas
- Three preparations are used – dense bacterins combined with either alum adjuvant or oil adjuvant, and formalin-inactivated bacterins; the oil adjuvant bacterin is thought to provide protection for up to one year and the alum bacterin for 4–6 months
- Maternal antibody interferes with vaccine efficacy in calves

Live attenuated vaccines

- A live HS vaccine prepared using an avirulent *P. multocida* strain B:3,4 (Fallow deer strain) has been used for control of the disease in cattle and buffaloes over 6 months of age in Myanmar since 1989; it is administered by intranasal aerosol application
- The vaccine has been recommended by the Food and Agriculture Organization of the United Nations (FAO) as a safe and potent vaccine for use in Asian countries; however, there is no report of its use in other countries and killed vaccines are the only preparations in use by the countries affected with HS; a trial of the vaccine has been completed in Indonesia

For more detailed information regarding vaccines, please refer to Chapter 3.4.10 *Haemorrhagic Septicaemia*, in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading “Requirements for Vaccines”.

PUBLIC HEALTH

- There are no confirmed reports of human infections with *P. multocida* serotypes B:2 and E:2; however, other serotypes do cause human infections and precautions should be taken to avoid exposure

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the OIE *Terrestrial Animal Health Code*.

REFERENCES AND OTHER INFORMATION

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated January 2021.