

## Hemorrhagic Septicaemia

Hemorrhagic Septicaemia is an acute, highly fatal form of pasteurellosis that affects buffalo and cattle. As per, World Organization for Animal Health (OIE) - Hemorrhagic Septicaemia is considered as the most economically important bacterial disease of buffalo and cattle in tropical areas of Asia, particularly in India where buffalo population is high. Disease is most devastating to small-holder farmers where husbandry and preventive practices are poor and free-range management is common. Natural occurrence of this disease is infrequently in pigs, sheep and goats and has been reported in camels, elephants, rhinoceros, horses, donkeys, yaks and various species of deer and other wild ruminants. In an outbreak in 2015, Hemorrhagic Septicaemia caused death of around 50% endangered Saiga antelope in Kazakhstan.

### Etiology

Hemorrhagic Septicaemia is caused by *Pasteurella multocida* (Gram negative coccobacillus) serotype B:2 (Asia). Serotype B:2 has also been identified in most areas where the disease is endemic, whereas serotype E:2 has been found only in Africa. Other serotypes, namely A:1, A:3, A:4, A:13 have been associated with a HS-like condition in cattle and buffaloes in India with mainly pneumonia leading to death. The alphabet denotes the capsular antigen and the number stands for the somatic antigen.

As per new classification, *Pasteurella multocida* strains causing pasteurellosis, including Hemorrhagic Septicaemia are called as *Pasteurella multocida* *sup sp multocida*. The organism does not survive outside the animal body, therefore mostly transmitted by close contact of infected and susceptible animals. However, moist conditions prolong the survival of organism and therefore disease tend to occur more commonly during wet/rainy season.

As per, estimates of economic losses due to Hemorrhagic Septicaemia in Cattle and Buffaloes in India

- Buffaloes are more susceptible to it than cattle and young animals are more prone than adult.
- As per NADRES (National Animal Diseases Referral Expert System), it is the second most reported disease in India during 1991 to 2010 and is the cause of maximum number of the reported deaths. Around 97% of the HS outbreaks reported by NADRES are in large ruminants.
- Morbidity losses account for 23% of the total losses and the rest 77% are due to mortality of animals.
- Of the total morbidity losses, about half have been due to its effect on growth and one-fifth due to loss in milk.
- As per report by the Department of Animal Husbandry, Dairying and Fisheries (DAHDF), an average annual loss of 287.81 lakh is recorded due to Hemorrhagic Septicaemia in cattle in India based on the number of cases and deaths reported during 1991-2005.
- As per latest survey, the total economic loss per infected animal due to Hemorrhagic Septicaemia has been estimated as 6,816 INR in case of cattle and 10,901 INR in buffalo.
- These losses when scaled-up at the national level have indicated a loss of 5255 crores.
- The direct losses contributed 80.3 percent and indirect losses contributed 19.7 percent to the total economic loss.
- The study has found that calves contribute 74.8 percent and adults contribute 25.2 percent to the total economic loss due to Hemorrhagic Septicaemia.

### Epidemiology

- Hemorrhagic Septicaemia is important disease in Asia, Africa, some countries in southern Europe and Middle East with the highest incidence in South Asia.
- Cattle, buffalo and bison appear to be the reservoirs of infection.
- Animals of all ages are susceptible but most commonly recorded between 6 months to 2 years of age.
- Outbreaks of disease are mainly associated with wet humid weather during rainy season.
- During intervening period, the organism persists on tonsillar and nasopharyngeal mucosa of carrier animals.

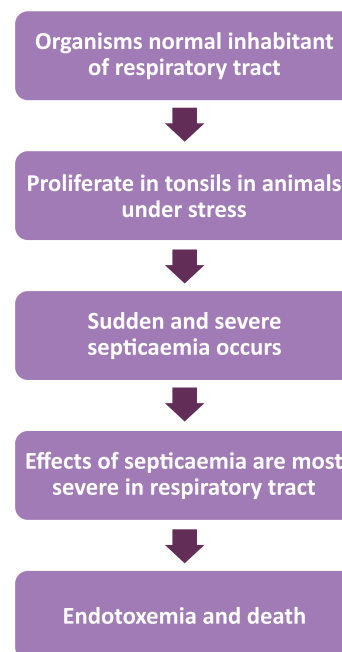
- Occasional sporadic outbreaks lead to heavy mortalities, whereas regular seasonal outbreaks in endemic areas lead to low mortalities confined to young animals.

## Transmission

- It has been estimated that up to 5% of healthy buffalo and cattle are colonized by small numbers of *Pasturella multocida* serotype B:2 or E:2, which are shed during stress.
- Common stressors associated with outbreaks of Hemorrhagic Septicaemia include high temperature and humidity, concurrent infection (blood parasites or foot and mouth disease), poor nutrition or work stress.
- Although outbreaks can occur at any time, disease is most prevalent during the rainy season. Increased outbreaks associated with high rainfall are most likely due to the multiple stressors present during this time and the moist conditions, which prolong the survival time of the organism in the environment.
- Infection occurs by inhalation or ingestion of contaminated food or water.
- The infection may originate from clinically normal carriers.
- The saliva of affected animals contains large number of organisms during early stages of the disease.
- Pasturella 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.
- Hemorrhagic Septicaemia is also known as Shipping fever as the condition is predisposed during transportation of animals.

## Pathogenesis

- Infection occurs by contact with infected oral or nasal secretions from either healthy carriers or animals with clinical disease or by ingestion of contaminated feed or water.
- Infection begins in the tonsils and adjacent nasopharyngeal tissues.
- Subsequently, bacteremia leads to dissemination and rapid growth of bacteria in various locations, tissue injury, host cytokine response and release of lipopolysaccharides that results in rapidly progressing endotoxemia.
- Clinical signs can appear 1–3 days after infection and death can occur within 8–24 hours after the appearance of first clinical sign.
- In endemic areas, HS affects older calves and young adults and morbidity and mortality are variable.
- In non-endemic areas, epizootics can occur with high morbidity and mortality that can reach 100%.
- Buffalo tend to have higher morbidity with more severe clinical disease than cattle.
- Recovery can stimulate acquired immunity to homologous and often heterologous strains of *Pasturella multocida* and some of these animals become healthy carriers that can be source of infection for future outbreak.



## Clinical Findings

In bovines, only per-acute and acute stages have been reported. Animal usually collapses and dies 6 to 48 hours after the severe initial clinical signs. Sub-acute and chronic cases have not been reported.

The clinical syndrome may broadly be divided into three phases

- Phase-1** dominated by increased temperature, loss of appetite, general apathy and depression. If closely monitored, rise in rectal temperature to 40–41°C (104–106°F) is recorded, which lasts throughout the course, dropping to sub-normal levels during the terminal phase, a few hours before death.
- Phase-2** is a respiratory syndrome. There will be an increased respiration rate (40–50/minute), laboured breathing, clear nasal discharge and salivation. Sub-mandibular oedema may also begin to show during this phase. As the disease progresses, the nasal discharge becomes opaque and mucopurulent, froth comes out from mouth (Fig. 1)



Fig. 1. Froth from mouth in HS affected cattle\*

- **Phase-3** dominated by recumbency. The respiratory distress becomes more acute, the animal lies down, terminal septicaemia sets in and death follows. Case fatality approaches 100% if treatment is not followed at the initial stage of infection.
- In many instances, there are varying degrees of overlap between the phases and shorter the course, less distinct are the phases. Acute disease can persist for up to 3 days and less often up to 5 days.
- **Sheep and goat:** In lambs and kids, pneumonic pasteurellosis can be acute, characterized by fever, lethargy, poor appetite and sudden death. Sheep and goats that survive the acute stage may recover or become chronically affected showing reduced lung capacity, reduced weight gain and sporadic deaths may occur. Symptoms associated with pneumonia include fever, fast or difficult breathing, nasal discharge and decreased activity.
- **In pig:** High temperature (104 to 107°F) with dullness, depression, anorexic and copious nasal discharge is seen in pig. Pasteurellosis in pig is usually seen in acute form. Neurological signs also have been reported in pigs.

### Lesions

- The characteristic lesion of Hemorrhagic Septicaemia is swelling of subcutaneous and muscle of the submandibular region, neck and brisket with clear to blood-tinged oedema fluid as well as congestion and froth in trachea (Fig. 2).
- Serous to serofibrinous fluid present in thorax, pericardium and abdominal cavity. There may be pericarditis with marked thickening of pericardial wall.
- In the abdominal cavity, petechial haemorrhages are widespread in all tissues. Massive ecchymotic or petechial haemorrhages may be seen on the abomasal wall and mesentery. Liver may be congested with focal to discrete necrotic areas (Fig. 3).
- There is typically widespread congestion with petechiae and ecchymoses in tissues and on serosal surfaces throughout the body, particularly in respiratory and urinary systems.
- Scattered petechiae may be visible in tissues and lymph nodes, particularly the pharyngeal and cervical nodes. The lymph nodes are usually enlarged.
- Pulmonary congestion and oedema, sometimes with interstitial pneumonia and gastroenteritis may occur in some cases. The lungs may be congested with varying degrees of consolidation and with a marked thickening of the interlobular septa (Fig. 4).



Fig.2. Congested trachea with froth\*

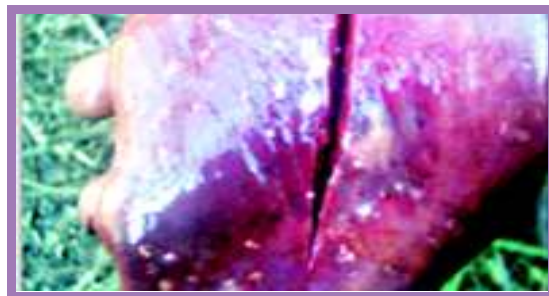


Fig.3. Multifocal hepatic necrosis\*

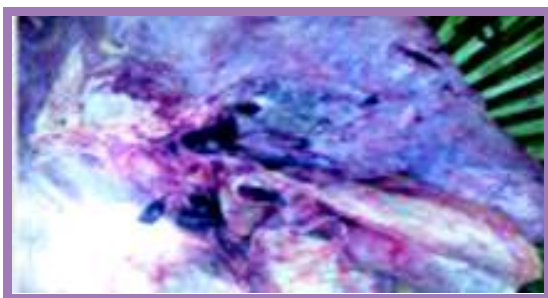


Fig.4. Congested and consolidated lungs\*



Fig.5. Extensive pulmonary abscess\*

- Fibrino-purulent necrotic lesions may be seen over pulmonary surface with pleural adhesions, pleurisy and pulmonary abscess (Fig. 5).
- Atypical cases, with no throat swelling and extensive pneumonia, are sometimes observed.
- There are no microscopic features that are specific for Hemorrhagic Septicaemia – all lesions are consistent with severe endotoxic shock and massive capillary damage.

### Diagnosis

- Clinical diagnosis of Hemorrhagic Septicaemia in endemic areas is based on history, clinical signs and characteristic lesions.



## Characteristic epidemiological and clinical features

- ▲ Season of year
  - ▲ Environmental conditions
  - ▲ Vaccination failure
  - ▲ Rapid course
  - ▲ High herd incidence with fever
  - ▲ Oedematous swelling
- Laboratory diagnosis based on culture and blood tests.
  - A definitive diagnosis of HS is based on isolation of *P multocida* serotype B:2 or E:2 from blood and tissues of a patient with typical clinical signs.
  - Other tests like indirect hemagglutination, coagglutination, counter-immunoelectrophoresis and immunodiffusion tests have also been used in some laboratories.
  - Diagnosis confirmed by methylene blue staining of blood smears (bipolar organisms), culture of blood agar plates, biological tests (mice inoculation test) and PCR.
  - Respiratory form differentiation is a major problem when outbreak is there and should be differentiated from nitrite toxicity i.e. no fever, dark colour blood and history of toxicity.
  - The organism is not always found in blood samples before terminal stages of disease and is consistently present in nasal secretions.

## Treatment

- The infected animal should be placed in a warm, well-ventilated stall and segregated from healthy animals.
- The body of infected animal should be maintained warm by blanketing.
- Consequently a careful lookout must be kept for a failing pulse-especially loss of volume and tendency to imperceptibility. If this occurs 2-5 ml of Adrenaline chloride solution (1:1000), should be administered subcutaneously and repeated if necessary.

## Specific Treatment

- Treatment of Hemorrhagic Septicaemia can be successful only if advocated at the initial stages of the disease.
- Intravenous antimicrobials should be administered as soon as possible to quickly obtain systemic bactericidal antimicrobial concentrations.
- Antimicrobial susceptibility testing (AST) is particularly necessary for *Pasteurella multocida* for which resistance to commonly used antimicrobial agents is reported.
- Strains of *P. multocida* vary in susceptibility to chemotherapeutic agents.
- The following agents have proven their clinical efficacy: Amoxicillin, Ampicillin, Ceftiofur, Cefquinome, Streptomycin, Gentamicin, Spectinomycin, Tetracycline, Sulfonamides, Trimethoprim/Sulfamethoxazole, Erythromycin, Tilimicosin, Enrofloxacin, Marbofloxacin, Ciprofloxacin, Amikacin and Norfloxacin.
- Earlier various combinations of sulpha drugs and antibiotics were considered to be more effective, while currently Cephalosporins and Fluoroquinolones are preferred choice of treatment.
- Plasmid and chromosomal-mediated multidrug resistance seems to be increasing for some strains of *P multocida* and resistance to Tetracyclines, Penicillin and Sulphonamides has been reported for serotype B:2.
- The use of higher generation antibiotics viz Cefquinome, Ceftiofur, Ceftriaxone, Enrofloxacin or Marbofloxacin is indicated for immediate management of the disease.
- Once the susceptibility results are known, the specific use of lower generation antibiotics like Sulphonamides or Enrofloxacin can be prioritized.
- As per reported studies, intramuscular administration of Ceftiofur HCl with Non-steroidal anti-inflammatory drug provides recovery rate of 80%. The administration was undertaken dosage of **XYROFUR**(Ceftiofur) inj. (Cattle- 1.1 to 2.2 mg / kg body weight, Buffalo- 2 - 2.4 mg / kg Body weight I/M).
- In an another study, it was concluded that the Ceftriaxone plus Tazobactam (**INTACEF Tazo**) reported good activity against *Pasteurella multocida* in both *in-vitro* and *in-vivo* trials with excellent results in treatment of Hemorrhagic Septicaemia. Ceftriaxone plus Tazobactam (**INTACEF Tazo**) @10mg / kg body weight I/M twice daily for 5 days was higher (72%) than group treated with Sulphadiazine-Trimethoprim @30 mg / kg body weight I/V twice daily for 5 days with recovery rate of 27%.



- Administration of Cefquime was done @ 1mg/kg of body weight *via* intravenous and intramuscular route. The drug levels remain above the MIC ( $T_{max} > MIC$ ) in serum was 14.10 hours after intravenous and 14.46 hours after intramuscular dosing, indicating likely high level of effectiveness in clinical infections caused by *Pasteurella multocida* of MIC 0.04 µg/mL or less.
- In a clinical study of Cefquinome against Hemorrhagic Septicaemia, Cefquinome exhibited a potent antibacterial effect against *P. multocida*. When  $T_{max} > MIC$  reached 73.44%, Cefquinome exhibited a bactericidal effect against *P. multocida* after three successive daily administrations.
- Marbofloxacin (**MARBOMET**), Enrofloxacin (**FLOBACSA/QUININTAS**) and Ciprofloxacin (**CFLOX POWER**) are also a preferred choice of Veterinarians because of their broad spectrum coverage, post antibiotic effect (PAE) and efficacy even in presence of pus, mucus and tissue debris.

### Supportive Treatment

- Intravenous fluid administration plays a vital role in the management of sepsis and septic shock.
- It corrects the body electrolytes and fluid balance.
- Maintain an adequate cardiac output and blood pressure through restoration of intravascular volume.
- Use of NSAIDs help in reducing body temperature and inflammatory conditions. The combination of Meloxicam with Paracetamol (**MELONEX PLUS**) is really effective.
- Combination of multivitamins are also recommended for carbohydrate and fat metabolism, as well as for protein synthesis. Animals under stress frequently have poor appetite, which is improved by water-soluble B complex vitamins (**TRIBIVET**, 5-10ml I/M or I/V.).

**Note:** Early recognition and treatment with antibiotics is essential for successful therapy. If one treatment fails, treatment should be continued with other drugs.

### Prevention by Vaccination

- Vaccination provides protection for 6-12 months only.
- Killed vaccines are most commonly used for prevention and include bacterins. Bacterins used against HS include formalized bacterin, aluminum hydroxide gel and oil adjuvant vaccines (OIE, 2017). Among these, aluminium hydroxide gel vaccine and oil adjuvant vaccines elicit a good immune response in the studies conducted in many Asian countries including India during the last few years, and are the vaccine of choice.
- In patients >3 years old, an initial two doses, 1–3 months apart are recommended, followed by booster vaccinations once or twice yearly.
- The oil-adjuvant vaccine provides protection for 9–12 months and is administered annually. It is most effective when administered 1 month before the onset of monsoon or rainy season.

### Preventive Measures

Following preventive measures should be taken in endemic areas:

- Vaccination on a routine prophylactic basis.
- Establishing a good reporting system.
- Creating awareness of the disease among farmers to recognise disease signs.
- Preventing mixing of animals from non-endemic areas.
- Quarantine animals after transport to the new location.

### Preventive measures during an outbreak

- Vaccination is recommended even during suspected outbreaks. In such situations broth bacterins or the alum precipitated (or aluminium hydroxide gel) vaccine is preferred. Broth bacterin and the oil adjuvant vaccine may be administered at different sites simultaneously.
- Early detection and isolation of new cases and their immediate treatment with a parenteral broad-spectrum antibiotic.
- Rectal temperature of all immediate incontact animals in the herd should be checked at least once every morning and animals showing increased temperatures should be treated as above.
- Confining herds as much as possible and preventing movement of animals in and out of diseased premises or villages.

- Specimens should be stored and transported to the nearest diagnostic laboratory under appropriate condition for confirming diagnosis.
- Deep burial or incineration for proper disposal of carcasses.
- Proper disposal of unconsumed fodder, bedding etc. from infected premises. Deep burial or drying and burning should be carried out within the premises. Effluent from cattle/buffalo sheds, dung etc. should be prevented from being washed away from the premises. Drains carrying such material should be led into a deep protected pit within the premises, or subjected to disinfectant treatment.

## Eradication

Eradication of Hemorrhagic Septicaemia is difficult to achieve because of the existence of latent carriers.

The existence of among free ranging ruminant also make eradication of HS disease difficult.

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## Did you Know

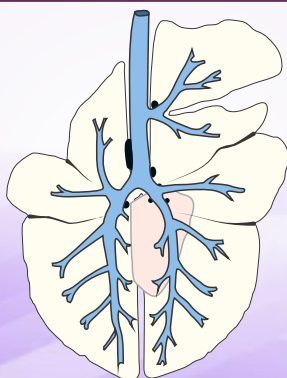
- As per recent practices, 2% Xylazine solution (0.05 to 0.12 mg/kg b.wt.) diluted to a volume of 5 to 12 ml with 0.9% sterile saline used for epidural injection in place of Lignocaine.
- The onset of perineal anaesthesia with Xylazine within 10 to 20 minutes and duration of epidural anaesthesia is 3 to 4 hours.
- Thus, Xylazine-induced analgesia lasts longer than 2% Lignocaine.
- Xylazine in combination with Lignocaine can be used for epidural anaesthesia in cattle.
- The recommended doses for 450 kg. cattle are 0.03 mg/kg of Xylazine added to 2 % Lignocaine hydrochloride to a total volume of 5 ml.
- The combination of Xylazine and Lignocaine provides a longer duration of analgesia (about 4 to 5 hours).

## Win Over Hemorrhagic Septicaemia (HS)



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**INTAS PHARMACEUTICALS LIMITED,**

Corporate House, Near Sola Bridge, Sarkhej-Gandhinagar Highway, Thaltej, Ahmedabad - 380054. Gujarat. INDIA

E-mail: [face2vet@intaspharma.com](mailto:face2vet@intaspharma.com) | Telephone: +91 (79) 61577000, 61577843

Website: [www.intasanimalhealth.com](http://www.intasanimalhealth.com) | Corporate website: [www.Intaspharma.com](http://www.Intaspharma.com)