Austin Journal of Infectious Diseases

Open Access

Austin Publishing Group

Review Article

Review on Bovine Pneumonic Pasteurellosis

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Received: October 18, 2023

Accepted: November 17, 2023

Published: November 24, 2023

Abstract

Bovine pneumonic pasteurellosis is an economically important disease of cattle mainly in feedlot industry; and is characterized clinically by acute bronchopneumonia with toxemia. The bacteria have many virulence factors like capsule, fimbriae, endotoxin and leukotoxin. The disease is mostly associated with stress factors as the bacteria are commensals in the upper respiratory tract. The most common predisposing factors that expose cattle to bovine pneumonic pasteurellosis are transportation, the presence of concurrent bacterial, viral and parasitic disease, overstocking, any mass veterinary and animal husbandry practices like mass vaccination, prophylactic treatment, castration, docking, dehorning etc. Suddenly change of macro and micro climatic conditions, starvation and water deprivation of cattle can also expose the cattle to pneumonic pasteurellosis. Because they are stress factors that reduce the immune status of animals; as the result the commensal organism becomes pathogenic to stressed cattle and cause bovine pneumonic pasteurellosis. Bovine pneumonic pasteurellosis can be diagnosed by considering the epidemiology, clinical signs and the necropsy findings. However, confirmatory diagnose of bovine pneumonic pasteurellosis is done by isolation and identification of the causative agent from clinical specimens. Bovine pneumonic pasteurellosis must be differentiated from CBPP; Infectious Bovine Rhinotrachitis (IBRT), lung worms that have almost similar clinical findings. Treatment of the disease is effective in the early stage of the disease by using different antimicrobial drugs. However, the bacteria have many antimicrobial resistance factors and resistant to many antimicrobial drugs. The disease can be prevented and controlled by reducing stress factors, by improving management, by using antimicrobial drugs in their prophylactic treatment and using effective vaccines. But the presence of many serotypes and antimicrobial resistance factors of the organism make the disease difficult to prevent and control. So that reducing stress factors, performing qualitative antibiogram and using efficient vaccine which contains the major serotypes of *Mannheimia haemolytica* are crucial to control the disease.

Keywords: Bovine pneumonic pasteurellosis; *Mannheimia haemolytica;* Serotype; Stress; Virulence

Introduction

Animal production has been considered as the main component of agricultural development in most parts of sub-Saharan Africa. Ethiopia is known for its high livestock population, being the first in Africa and tenth in the world. The countries most recent estimates of its livestock population about 44.3 million heads of cattle, 23.6 million sheep and 23.3 million goats [1]. Despite the large number of livestock in Ethiopia the sector is characterized by low productivity and, hence, income derived from this sector of agriculture's could not impart significant role in the development of the country's economy. The low productivity is attributed to the low genetic potential of indigenous cattle, poor nutrition and reproductive performance, inadequate management, high disease incidence and parasite burden. These illnesses have a variety of effects on the productivity and fertility of herds, including losses from mortality and morbidity, weight loss, slowed growth and a decline in physical strength.

Due to environmental factors such as high temperatures and humidity, topography that is sloppy and vulnerable to flooding, stress factors, and drought that are frequent in these areas, there are many livestock health issues in tropical areas. As a

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Citation: Woyessa MB, Umer AA. Review on Bovine Pneumonic Pasteurellosis. Austin J Infect Dis. 2023; 10(4): 1092.

result, there is a limited supply of feed and little vegetation coverage; additionally, there is a lack of knowledge about animal health services [2]. According to [3], organized research that can clarify major animal health problems is a key issue for further study of epidemiological study on the diseases of livestock. However, knowing the type and extent of the major health problems is very important for livestock owners, veterinarians, and researchers and can assist in the development of herd health strategies and the selections of potential interventions.

Infections of the respiratory system are frequently seen in a variety of domestic and farming animal species. The most prevalent instance, with a high incidence in ruminant animals, is pneumonic pasteurellosis, also referred to as respiratory mannheimiosis. Bovine Respiratory Disease (BRD) is the illness that causes the greatest morbidity and mortality in calf populations. It is known that two members of the Pasteurellaceae family, Mannheimia haemolytica and Pasteurella multocida, function as opportunistic pathogens in the BRD complex [4]. It is commonly known that pneumonic pasteurellosis is the leading cause of death in feedlot animals, with the illness being the reason for about 30% of all cattle deaths globally. More than one billion dollars are lost annually in the beef cattle business in North America alone as a result of the disease, which has a significant global economic impact [5]. Additionally, a considerable sum of money was lost virtually year for projects to improve farm management, animal husbandry, chemoprophylaxis, treatment, and vaccination. Therefore, the goals of this review are to understand the causes, epidemiology, and methods of preventing and controlling bovine pneumonic pasteurollosis.

Bovine Pneumonic Pasteurollosis

Pneumonic pasteurellosis (locally called “Fura” and “Gororsa” in Afan Oromo) and is one of the most important economical diseases in cattle. It is a multi - factorial respiratory disease of cattle that mainly affects calves. Bovine pneumonic pasteurellosis was first described in the United States in 1915 and in the United Kingdom in 1925. Bacteria belonging to the family *Pasteurellaceae* are involved. The bacteria are part of the normal microflora in the upper respiratory tract making the disease difficult to prevent [6].

Etiology

Mannheimia haemolytica biotype A, serotype 1 is considered to be the most common cause of the bovine pneumonic pasteurellosis. However, in some cases, other biotype strains have been isolated from cases of pneumonic pasteurellosis in cattle; that is why *Pasteurella multocida* is isolated in a few cases occasionally. Other pathogens like viruses or mycoplasmas may act synergistically with *Mannheimia haemolytica*. *Mannheimia haemolytica*, serotype 1 is the bacterium which is the most frequently isolated organism from the lungs of cattle with BRD; but *Haemophilus somni* is being increasingly recognized as an important pathogen in BRD; these bacteria are normal inhabitants of the nasopharynx of cattle. However, when pulmonary abscessation occurs, generally in association with chronic pneumonia, *Arcanobacterium pyogenes* is frequently isolated [3].

Under normal conditions, *M. haemolytica* remains confined to the upper respiratory tract, in particular the tonsillar crypts, and are difficult to culture from healthy cattle. After stress or viral infection, the replication rate of *M. haemolytica* in the upper respiratory tract increases rapidly. The increased bacterial growth rate in the upper respiratory tract, followed by inhalation and colonization of the lungs, may occur because of suppression of the host's defense mechanism related to environmental stressors or viral infections. It is during this log phase of growth of the organism in the lungs that virulence factors are elaborated by *M. haemolytica*, such as an exotoxin that has been referred to as leukotoxin. *Haemophilus somni* may invade the lung and cause pneumonia after damage to the respiratory defenses. This organism is capable of systemic spread from the lung to the brain, myocardium, synovial, and pleural and pericardial surfaces; often, death can occur later in the feeding period (40–60 days after arrival) from involvement of these additional organ systems [3].

Classification of *Mannheimia haemolytica* Based on its Biotypes and Serotypes

Organisms belonging to the bacterial family *Pasteurellaceae* are ubiquitously present in the respiratory, alimentary and reproductive tracts of different avian, mammalian, reptilian, and likely amphibian hosts.

Members of this family are small (0.2 - 2µm), Gram-negative, non-motile, facultatively anaerobic coccobacilli or rods. In addition they are, with few exceptions, fermentative and oxidase and catalase positive. Growth on artificial media is enhanced by the addition of serum or blood on which they appear after 24 hours of incubation as round, grayish colonies of moderate size [7].

During the last two decades, the combination of 16S r - RNA sequencing and other molecular techniques [8], has led to several new genera and over 58 formally recognized species and 25 unnamed taxa within the family *Pasteurellaceae* [9]. The most substantial reclassification in relation to bovine diseases was the redesignation of organisms formerly known as *Pasteurella haemolytica* into the new genus *Mannheimia,* with *Mannheimia haemolytica* as the type species besides. Organisms previously identified as *Pasteurella haemolytica* have earlier been categorized into 3 biotypes (sugar fermentation pattern of trehalose (T) and arabinose (A)), 12 biogroups (extended phenotyping including fermentation patterns of sugars and glycosides), and 17 serotypes (surface antigens) [10].

Despite this, strains formerly designated as *Pasteurella haemolytica* biotype T (fermenting trehalose) were redefined in 1990 and are currently still referred to us *Pasteurellatrehalosi* [11]. Remarkably confusing, two of the most detailed studied serotypes of *M. haemolytica* sensu latu (s.l.), i.e. A1 and A6, do not ferment arabinose although the original affiliation (“A”) was based on this characteristic and this typing is currently still used in vaccination leaflets. Species specific allocation of *M. haemolytica* [12] requires additional tests compared to the identification of *Pasteurella haemolytica* [13], but routine laboratory diagnosis and many peer reviewed manuscripts still regard these two as synonyms. *Mannheimia* (unless otherwise specified, e.g. *M. haemolytica* serotype A1), or where *M. haemolytica* was used as synonym for *Pasteurella haemolytica*. Although for several groups of *Pasteurellaceae*, host range and disease manifestations are not constant, the host animal species is indicative for routine bacterial identification [14]. In spite of the molecular advances, morphology and restricted phenotyping are routinely used for primary identification of *Pasteurellaceae*. Mostly, the primary identification of *M. haemolytica* is based on the isolation of round grayish colonies of moderate size with a small pronounced surrounding zone of haemolysis after 24 hrs of aerobic incubation on sheep blood agar. *M. haemolytica* does not pro-

duce indole and tolerates bile salts. *P. multocida* typically grows as mucoid confluent colonies, and in routine diagnostic bacteriology it is distinguished from *M. haemolytica* by production of indole from tryptophan, and by lack of haemolysis. A typical sweetish odour can be present ; whereas the habitat and the clinical relevance of *M. haemolytica* is predominantly restricted to ruminants, and more particularly cattle [7].

Historically, serotype A1 has been the predominant strain associated with pneumonic pasteurellosis but results of recent U.S survey reaffirmed that fact, including that serotype A1 accounted for approximately 60% of the total isolates recovered from pneumonic bovine lungs, where as serotype A 6 was isolated from 26% and serotype A 2 from 7%. The remaining 7% was composed of serotype A 9, A 11 or untypable strains bovine respiratory disease is multifactorial, involving environmental factors and concurrent infections with viruses (infectious bovine rhinotracheitis, bovine viral diarrhea [15]. The five current species in genus M*annheimia* are *Mannheimia haemolytica***,** *Mannheimia grannulomatis, Mannheimia glucosidal, Mannheimia gramulo* and *Mannheimia varigena* [16].

Geographical Distribution

Pneumonic pasteurellosis epidemiology is a common disease of cattle in all over the world including Europe, North America and Asia etc. In Canada and the United States the disease occurs most commonly in beef calves after weaning in the fall of the year and is the most important disease in cattle that has been recently introduced into feed lots. It also occurs in Africa including Ethiopia [17].

Occurrence

Pneumonic pasteurellosis is common in all farm animals including domestic and wild species of mammals and birds. *Pasteurella* and *Mannheimia* have an extremely broad spectrum of animal hosts. Many apparently healthy mammals and birds can harbor *Pasteurella* and *Mannheimia* organisms in upper respiratory tract and mouth; and according to the most accepted hypothesis, pasteurellosis is a disease of weakened animals that are subjected to stress and poor hygienic conditions. In animals with lowered resistance, *Pasteurella/ Mannheimia* harbored trachea and become pathogenic for their host [18].

Risk Factors

The disease occurs most commonly in young growing cattle from 6 months up to 2 years of age although all age groups are susceptible. While, the disease happens in young beef cattle soon after introduction to feedlot, it is uncommon in dairy herds, calves which originate from many different farms and mixed at the market are at high risk of infection. Beef calves may develop the disease before weaning if they are subjected to the stress of early snow storm in the late fall. The disease occurs commonly in outbreaks 7 - 10 days after cattle have arrived in the feedlot following stressful transportations of calves which are not immune to the disease [20].

The Bruce country beef cattle project in Canada identified some of the epidemiological factors associated with mortality in cattle shipped from Western Canada to small feedlots over a period of 3 successive years. Mixing of calves from different sources at auction markets was associated with increased risk of fatal fibrinous pneumonia in calves moved to feedlots in Canada. The role of stress as an epidemiological determinant in shipping fever pneumonia. Transportation and handling to mimic stress followed by an aerosol infection by *M .haemolytica* did not result in significant lesion of pneumonia but did mark the animals susceptible to bovine herpes virus. The transpiration and assembling of yearling in beef calves can result in an increase in the levels of plasma fibrinogen which is an induction of some stress. Deprivation of feed and water followed by confinement in unfamiliar surroundings also results in an increase in fibrinogen. The response of the animals was also dependent up on the previous environment and management applied to them before assembly and transportation. Experimentally, subjecting yearling bulls to a treated mill exercise makes them more susceptible to experimental pneumonia than bull which is not exercised [20].

The frequency of isolation of *Pasteurella* and *Mannheimia* spp. from the nasal passage of normal health unstressed calves is low but increases as the animals are moved to an auction market and then to a feedlot. The isolation rate of *M. haemolytica* biotype A serotype 1 in the nasal cavity and trachea can be low in beef calves from a closed herd that is maintained on range pastures, and serum antibody levels are also low, over time but there may be an increase in the frequency of isolation of the bacteria from healthy calves which were moved to pens held in low population densities and maintained under low stress conditions.

In some cases serotype 2 predominates while the calves are on the range pastures but serotype 1 predominates when the calves are in the feedlot and affected with pneumonia. There are relationships between the number of bacteria in the nasopharynx and the ambient temperature and humidity. In calves kept at a constant temperature of 16^0C (60^0F), the bacterial populations in the nasopharynx where at a minimum between 65 and 75% of relative humidity but tended to rest at humidity outside the range. The possibility might be infection with several different viruses and mycoplasmas that may predispose to pneumonic pasteurellosis [21].

Predisposing Factors

The multifactorial character of bovine pasteurellosis relates to predisposing factors of viral infections and the different bacterial and parasitic agents are involved. Predisposing factors are severe climate change and stress due to overcrowding and transport which are typically found in feedlots and veal calf industry. Following transport, the disease is also known as “shipping fever”. Generally speaking, both predisposing factors and concurrent viral, bacterial infections and parasitic diseases are capable of inducing impairment of pulmonary defenses which allow secondary infections mostly by opportunistic pathogenic of *Pasteurellaceae* [23].

Mode of Transmition

Transmission occurs by inhalation of infected droplets coughed up or exhaled by infected animals which may be clinical cases or recovered carriers in which the infection persists in the upper respiratory tract. *Mannheimia haemolytica* and *Pasteurella multocida* are highly susceptible to environmental influences and it is unlikely mediated contagion is an important factor in the spread of disease. When conditions are optimum, particularly when cattle are closely confined in inadequately ventilated barns over crowded in trucks or trains or held lots, disease spread very quickly and affects a high proportion within 48 hours [24].

Pathogenesis

The pathogenesis of pneumonic pasteurellosis remained a subject of considerable speculation and controversy due to the complex nature of the disease and lack of consistency. Pneumonic pasteurellosis is a secondary bacterial complication of a previous infection of the respiratory system [25]. However, the sequential development of the pulmonary lesions is highly mediated by complex interactions between the naturally existing causative organism in the upper respiratory tract, the immunological status of the animal and the role of predisposing factors in the initiation of infection. In either situation, the disease is essentially triggered by sudden exposure to a stressful condition or by initial infection with certain respiratory viruses, mycoplasmas or bacteria. Stress or viral infection would eventually impair the local pulmonary defense mechanisms by causing deleterious effects on the ciliating cells and mucous coating of the trachea, bronchi and bronchioles. The causative bacteria from the nasopharynx will then reach the ventral bronchi, bronchioles and alveoli by gravitational drainage along the tracheal floor and there become deeply introduced into the lung tissue. Endotoxin produced by rapid growth and multiplication of the bacteria in infected lobules will cause extensive intravascular thrombosis of pulmonary veins, capillaries and lymphatics. These vascular disturbances eventually result in focal ischaemic necrosis of the pulmonary parenchyma accompanied by severe inflammatory reaction dominated by fibrinous exudates [26].

Virulence Factors of Mannheimia haemolytica: The virulence factors of *Mannheimia haemolytica* include fimbriae, polysaccharide capsule, outer membrane proteins, endotoxin (lipopolysaccharide), and leukotoxin. The severity of lesions, depends on the rate and extent of bacterial proliferation and the amount of endotoxin released, which in turn depends on the virulence of the bacterial strain and the degree to which the defenses of the host are impaired. These factors are generally designated as virulence factors and constitute parts of the surface components of the bacterial cell and cellular products. Virulence factors are, in fact, capable of promoting adhesion, colonization and proliferation of the organism within the animal tissues. In other words, virulence factors are actively involved in conversion of the organism from commensals into pathogen. The roles of virulence factors in the pathogenicity of M. haemolytica have been extensively investigated [27].

Bacterial Capsule

The cell capsule constitutes an important virulence factor which plays vital roles in the pathogenicity of pathogenic bacteria and establishment of infection. The virulence mechanism of the cell capsule is mostly attributed to its ability to protect the invading organism against cellular and humoral defense mechanisms of the host. The capsular materials of *M. haemolytica* and other *Pasteurella* species were identified as polysaccharide and are basic structures produced during the logarithmic phase of growth of the bacteria. Each serotype of *M.haemolytica* produces a characteristic polysaccharide capsule in order to avoid phagocytosis by macrophages and polymorphonuclear leukocytes and to protect the organism against complement mediated destruction of the outer membrane in serum. The capsular material of *M. haemolytica* can also interact with the pulmonary surfactant and thereby facilitates the adhesion of the invading organism to the respiratory tract epithelium of susceptible animals [28].

Fimbriae

Fimbriae are smaller appendages present in the surface of many Gram negative bacteria. They are specific surface structures of the bacterial cell wall which permit or enhance adherence to and colonization of the target epithelium of the susceptible animals. Fimbriae are present in various strains of *Pasteurella* and *Mannheimia* species. Two types of fimbriae have been detected in serotype 1 of *M. haemolytica.* One of them is large and rigid; measuring 12 nm in width and the other is smaller, flexible and measures only 5 nm. The large rigid fimbriae are composed of 35 KDa subunits and proved to be highly immunogenic. The two types of fimbriae produced by *M. haemolytica* are both capable of enhancing mucosal attachment of the organism and colonization of the lower respiratory tract epithelium of cattle and sheep. Successful colonization will thus enable considerable increase in the number of bacteria seeded in the lung tissue beyond the level that normal lung capacity could efficiently resolve [29].

Endotoxin

Similarly to all other Gram negative bacteria, the cell wall of *M. haemolytica* contains a lipopolysaccharide (LPS) endotoxin. This endotoxin is one of the most important virulence factors involved in the pathogenesis of bovine pneumonic pasteurellosis. It has been shown that serotypes 2 and 8 of *M. haemolytica* possess a rough LPS while the other 14 serotypes have characteristic smooth LPS. Experimental evidence indicated that *M. haemolytica* endotoxin is directly toxic to endothelial cells and capable of altering leukocyte functions and causing lysis of blood platelets. Further subsequent investigations in calves also revealed a number of physiological effects of the purified LPS similar to those produced by chemical mediators such as thromboxane A2, prostaglandins, serotonin, cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP). All these previously mentioned mediators were known to be responsible for the clinical signs associated with endotoxic shock [30].

Leukotoxin

The leukotoxin is a102 KDa protein secreted at the logarithmic phase of growth of the bacteria and also considered as a main weapon or virulence factor for *M. haemolytica.* In fact, the leukotoxin is pore forming cytolysin which can produce several biological effects on leukocytes and blood platelets of ruminants. The most susceptible cells are bovine macrophages, neutrophils from most ruminant species. Lymphocytes and cultured lymphoma cells of ruminants are also susceptible to leukotoxin. At low concentration, leukotoxin impairs phagocytosis and lymphocyte proliferation while at higher concentration it has a cytotoxic effect resulting in cell death due to lysis. The lysis of cells is attributed to the formation of transmembrane pores in the target cell, and thereby allowing the movement of potassium, sodium and calcium ions through transmembrane gradients [31].

Leukotoxin also causes stimulation of polymorphonuclear leukocytes and activation of macrophages with consequent release of proinflammatory cytokines such as interleukin - 1 (IL - 1), interleukin - 8 (IL - 8), leukotrienes and tumour necrosis factor - α (TNF - α). Their action would further lead to the release of H_2O_2 which, in turn, is converted into hydroxyl radicals by alveolar endothelial cells. The free hydroxyl radicals cause considerable damage and necrosis of the pulmonary alveo-

lar epithelium resulting in accumulation of oedema fluid and fibrin inside alveoli and interstitial spaces. The leukotoxin and enzymes released following cytolysis are both chemotactic for various types of inflammatory cells causing more damage to the lung tissue due to increased cell recruitment into the area. Furthermore, *M. haemolytica* leukotoxin was found to induce "*in vitro*" morphological alterations in calves' neutrophils similar to those produced by the viable infective organism during the natural course of the disease in the living animal. The effect of leukotoxin and O-sialoglycoproteins produced by *M. haemolytica* A1 on bovine platelets activation was results in bovine blood platelets adhesion was considerably enhanced by both bacterial products. These two bacterial proteins could directly interact with bovine platelets to initiate platelet aggregation and fibrin formation in the alveolar tissue of the affected lungs [32].

Diagnosis

Clinical symptom

Clinical signs of pneumonic respiratory bacterial in cattle like depression and fever (104°F – 106°F (40°–41°C])), without any signs attributable to other body systems are the classic components of a case definition for early cases of BRD. Serous to mucopurulent nasal discharge; moist cough; and a rapid, shallow respiratory rate. Auscultation of the cranio ventral lung field reveals increased bronchial sounds, crackles, and wheezes. In severe cases, pleurisy may develop, characterized by an irregular breathing pattern and grunting on expiration. The animal will become unthrifty in appearance if the pneumonia becomes chronic, which is usually associated with formation of pulmonary abscesses [33]. Acute toxemic bronchopneumonia is characterized by moderate dyspnea, fever, and increased breathing sounds over ventral aspects of lungs. Moist crackles, coughing, pluritis, leucopenia and neutropenia are the main clinical signs and clinical pathology of bovine pneumonic pasteurellosis in severe cases. The disease usually develops in cattle within 10 to 14 days after they have been stressed. Sudden deaths without any previous warning signs may be seen in peracute form of the disease. Many calves are in the sign of an outbreak in which many claves are obviously affected and some are in the incubation stages of the disease. Viewed from a distance affected cattle are usually depressed and the respirations are shallow and rapid. There is a weak protective cough which may become more pronounced and frequent if they are urged to walk. Animals which have been ill for a few days will appear gaunt in the abdomen because of anorexia. A mucopurulent nasal discharge, crusty nose and an ocular discharge are common. Although affected cattle are anorexia they may continue to drink maintenance amount of water which may be useful in mass medication of the water supplies. Mucopurulent nasal discharge, crusty nose and ocular discharge are common and apparently health cattle may have temperature of 40°C - 41°C. In the early stages, loud breath sounds (bronchial tones) are audible over the anterior ventral parts of the lungs and as the disease progresses the breath sounds become launder and extend over a greater area and abnormal lung sounds like crackles and wheezes can be audible in few days; and rubs may be audible and in severe cases dyspnea is marked [34].

Table 1: Hosts and diseases caused by different species of *Mannheimia.*

Species	Host (s)	Significance
M. haemolytica	Cattle	Pneumonia
M. haemolytica	Sheep	Pneumonia and septicemia mastitis
M. grannulomatis	Cattle	Panniculitis(lechiquarna)
M. grannulomatis	Deer	Bronchopneumonia and conjunctivitis
M. grannulomatis	Hares	Bronchopneumonia and conjunctivitis
M. grannulomatis	Sheep	Normal respiratory flora
M. ruminalis	Cattle	Normal ruminal flora
M. ruminalis	Sheep	Normal ruminal flora
M. varigena	Pigs	Septicemia, enteritis pneumonia
M. varigena	Cattle	Septicemia, pneumonia, mastitis

Source: [16]

Table 2: Principal hosts and disease of the Pasteurella/ Mannheimia species in domestic animals.

*Pasteurella/ Mannheimia*spp	Bio-type	Host species	Disease
P. multocida	A	Cattle	Occasional but severe mastitis
P. multocida	A	Sheep	Pleuropneumonia mastitis
P. multocida	A	Pig	Pneumonia
P. multocida	A	Poultry	Fowl cholera
P. multocida	B	Cattle	Epizootic haemorrhagic septicemia
P. multocida	E	Cattle	Epizootic hemorrhagic septicemias
P. multocida	E	Buffalo	Epizootic hemorrhagic septicemias
M. haemolytica	A	Cattle	Pneumonia
M. haemolytica	A	Sheep	Enzootic pneumonia
M. haemolytica	A	Lamb	Septicemia in lambs under 3 months of age
M .haemolytica	T		Septicemia in lambs 5-12 months old
	Sheep		

Source: [19]

Table 3: Risk factors involved in bovine pneumonic pasteurellosis.

Types of risk factors	Factors involved
Environment	High temperature, cold stress, fluctuations in temperature and dust
Management	Weaning, shipping and crowding
Concurrent infectious	Viral infection(BHV-1, BRSV, PI-3 and BVDV) Many bacterial diseases that cause respiratory diseasedike Haemophilus somni Parasitic diseases like lung worms

Source: [22]

Clinical Pathology

Necropsy

In bovine pneumonic pasteurellosis, the post mortem on cranial ventral lobes of lungs that become ventral red; swollen and fibrinous pleural with epicardial effusions. There may be thickening of the interlobular septa and the lymph nodes that are found in the thoracic cavity are enlarged and hemorrhagic [35].

Field Diagnosis

Field diagnosis of bovine pneumonic pasteurellosis can be done based on the epidemiology, clinical signs and necropsy findings of the disease. In acute and toxemic form of the disease bronchopneumonia with a high fever and good response to treatment in bovine pneumonic pasteurellosis. Depression and anorexia are common in young beef calves recently stressed by weaning or mixed in markets and shipped to feed lot. In field diagnosis of bovine pneumonic pasteurellosis, there are many viral and bacterial diseases of cattle that have similar clinical symptom. Some are Infections Bovine Rhinotrachitis (IBRT) and Contagious Bovine Pleuropneumonia (CBPP). But in infections bovine rhinotrachitis, there is rhinitis usually with discrete lesions in the nares, and no toxemia unless secondary bacterial pneumonia is present; and recovery usually occurs gradually

over 4 - 7days. Clinically Contagious Bovine Pleuro Pneumonia (CBPP) also resembles bovine pneumonic pasteurellosis but occurs in plague form, and there is sever painful, toxemic pleuropneumonia and the case fatality rate is high in the case of Contagious Bovine Pleuro Pneumonia (CBPP) [36].

Laboratory Diagnosis

In acute cases, the standard laboratory methods such as culturing and phenotypic identification do not give rapid results. In recent years, genotypic methods especially nucleic acid based assay, allow the detection of microorganism and dramatically improving the sensitivity and decreasing the time required for bacterial identification [37]. A test of the drug - sensitivity of the bacteria should be carried out if possible as considerable variation in resistance to the standard. Drug resistance is emerging among field isolated of *M. haemolytica* and plasmid mediated drug resistance in a strain of the organism isolated from feedlot cattle is now known to occur differentiation between *P. multocida* and *M. haemolytica* may also be of value in prognosis as infection with the latter is thought to cause a more severe disease. Confirmatory diagnosis of bovine pneumonic pasteurellosis can be done by isolation and identification of the causative agent [38].

Isolation and identification of *Mannheimia haemolytica* can be made on the basis of colony morphology, haemolysis on blood agar, Gram staining and biochemical tests. Biochemical characteristics of the isolates are determined by using catalase, oxidase, nitrate reduction, ONPG, H_2S, ornithine decarboxylase, indole, urease, growth on MacConkey agar, VogesProskauer and fermentation of glucose, lactose, mannitol, raffinose, salicine, trehalose, xylose and arabinose. The primary identification of *M. haemolytica* is based on the isolation of round grayish colonies of moderate size with a small pronounced surrounding zone of haemolysis after 24 hrs of aerobic incubation on sheep blood agar. *M. haemolytica* does not produce indole and tolerates bile salts [39].

The isolates which are found positive for the catalase, oxidase, nitrate reduction, H_2S tests which grow on MacConkey agar and ferment mannitol, xylose and are found negative for the ornithine decarboxylase, indole, urease and VogesProskauer tests and don not ferment arabinose, glucose, lactose, raffinose, salicine, trehalose tests are identified as *Mannheimia haemolytica.* But *P. multocida* typically grows as mucoid confluent colonies on blood agar; and in routine diagnostic bacteriology it is distinguished from *M. haemolytica* by production of indole from tryptophan, and by lack of haemolysis on blood agar and does not grow on MacConkey agar and has typical sweetish colony odour on solid media [40].

Differential Diagnosis

Bovine pneumonic pasteurellosis must be differentiated from many bacterial, viral and parasitic respiratory diseases of cattle that have almost similar clinical sings. Some of them are Infectious Bovine Rhinotrachitis (IBRT) also called IBPV, CBPP and lung worm. Clinical findings of respiratory disease like IBRT are almost similar but abortion may be highly suggestive of IBRT (IBPV). The symptoms of IBPV in females are a thick white-brown colored vulvular discharge, swollen, reddened vulva with small pus - filled pimple in the lining of the vulva and vagina, loss of desire to mate, excessive tail switching and frequent urination. Pustules and discharge are observed on the bull's penis and prepuce. Since there is no definitive clinical diagnosis for IBRT (IBVV), laboratory confirmation of the virus is necessary in order to identify BHV-1 infection. Measurement of antibody in serum, plasma or milk helps us to know the past exposure of the cattle with BHV-1 [41].

Another parasitic disease of cattle that must be differentiated from bovine pneumonic pasteurellosis is pneumonia caused by lung worms. It can be differentiated as signs of pneumonia caused by lung worms are most frequently become apparent during the late summer and autumn. Infected calves start to cough, and usually have a rough hair coat and lower weaning weights. About 1 - 2% of infected calves may develop a hypersensitivity reaction to the lung worms that may cause an acute respiratory problem or sudden death .Contagious bovine pleuropneumonia is one of a mycoplasmal disease of cattle and which must be considered as differential diagnosis of bovine pneumonic pasteurellosis. In CBPP a typical respiratory disease develops with labored and painful breathing and the animal has abdominal type breathing with a respiratory rate of 50 to 55 breaths/minute; and the affected cattle may "grunt" when breathing out. Some animals develop a shallow, dry and painful cough, particularly noticeable on exercise. Application of pressure between the ribs is painful and resented by affected cattle [3].

Control and Prevention Measures

Antimicrobial Prophylaxis

The treatment of bovine pneumonic pasteurellosis are based on clinical examination. About 85 – 90% of affected cattle will recover within 24 hours if treated with almost any of the common antimicrobials such as oxytetracycline, trimethoprim, sulfadoxine and sulfonamides. One treatment is usually adequate in most cases but severely affected cattle or those which relapse require treatment daily or even two to three times daily dependent upon the drug used. To combat bovine pneumonic pasteurellosis, application of antibiotics may be performed for either therapeutic, prophylactic, or metaphylactic purposes. Whereas curative therapy indicates the treatment of the individual animal in which the diagnosis is made, prophylactic administration is frequently performed in many countries to prevent shipping fever prior to transport into feedlots [42].

Management

Satisfactory control of the disease will depend on successful integration of management and the use of biological and prophylactic antimicrobials. It is unrealistic to depend only on vaccine, an antibiotic or single management technique to control the disease and successful control begins with adoption of good management techniques when the calves are still in range; the use of efficacious vaccine and care in handling and transportation of cattle. Because of the common occurrence of the disease at the time of shipment from range feedlot, much attention has to be given to reduce the incidence of disease at this time. This led to the development of the concept of preconditioning in North America. The object of preconditioning was to prepare the weaned calves for the feedlot environment by vaccinating them for all commonly anticipated disease before weaning and distributing all stressful procedures such as castration ,dehorning , branding ,deworming, over a period of time rather than concentrating these at the weaning time [43].

Vaccination

Prevention of bovine pneumonic pasteurellosis is based on

minimizing the predisposing factors and vaccination. Vaccines have been worldwide developed for *M. haemolytica,P.multocida* and *H. somni.* Vaccination can reduce disease and improve production, but it should be stressed that protection against BRD is far from absolute. This is likely due to the complex multifactorial origin of the syndrome that include environmental factors like population density, housing conditions, climate changes, stress, and a wide variety of etiological microorganisms like viruses, *Pasteurellaceae* and *Mycoplasma* spp. Vaccines are mostly focused on one or only a small number of serotypes and cross-protection does not always occur [44].

In Belgium, three vaccines for the prevention of bovine pneumonic pasteurellosis are available, although none of these offer protection against *P. multocida* or *H. somni*. The currently registered Belgian products include vaccines against *M. haemolytica* serotype "A1" alone, or in combination with serotype "A6" or with BRSV (bovine respiratory syncytial virus) and BPI3 (bovine parainfluenza virus type 3). Despite the availability of vaccines against all three major bovine respiratory pathogens in the U.S.A., this practice remains far from routinely performed. As a consequence of this, and the ineffectiveness of vaccines because of the multifactorial nature of BRD, the current most effective control method for bovine pasteurellosis is antimicrobial therapy. Antimicrobial agents can be administered either alone or in combination with anti-inflammatory drugs, mucolytica, or pulmonary function sustaining drugs (e.g. atropine, diuretica). *Manneheima* and respiratory viral vaccines have been used extensively in attempt to control pneumonic pasteurellosis in cattle. High levels of naturally acquired antibody to *M. haemolytica* have been associated with protection against the disease. Calves which were naturally exposed to *M. haemolytica* or exposed by vaccination subcutaneously or intradermal to the like organisms developed same resistance to experimental challenge and developed antibodies to all surface antigens and cytotoxin [45].

Economic Importance

Manneheima haemolytica and *Pasteurella multocida* are known bacterial pathogens, which caused very severe respiratory diseases of cattle. The morbidity may reach 35%; the case fatality rate may range from 5 - 10% and the population mortality rate may vary from 0.75 - 1%. In United States, the annual loss due to this disease is estimated to be more than 25 million dollars. In addition to the death losses, the cost of treatment which includes the personnel involved in the detection and in actual treatment and the drugs used and the vaccine and loss of production following the illness which has been documented. Because of compensatory regrowth in animals which have recovered, there may be no correlation between overage daily gains, feed conversion [46].

Conclusion and Recommendations

Bovine pneumonic pasteurellosis is an economically important disease of cattle mainly in feedlot industry. It is characterized clinically by acute broncho pneumonia with toxemia. The peak incidence of the disease occurs very often within the first 3 weeks after the arrival of the calves in feedlots. Stress factors have the greatest epidemiological determinant in the occurrence of the disease. However, it must be emphasized that bovine pneumonic pasteurellosis can be reproduced experimentally without preceding infection with virus, and it is highly likely that naturally the disease can occur without concurrent viral infections. The disease can be diagnosed based on the epidemiology, clinical and necropsy of the disease which give the tentative diagnosis of the disease. Confirmatory diagnosis of the disease can be done by isolation and identification the agent from specimens. Bovine pneumonic pasteurellosis can be controlled and prevented by reducing the predisposing factors through improving management of animals, controlling many concurrent bacterial, viral and parasitic diseases of cattle. Bovine pneumonic pasteurellosis can be also controlled and prevented by administration of antimicrobial drugs at their prophylactic doses and by using efficient vaccine. However, the development of antimicrobial resistance factors and the presence of many serotypes make the disease difficult to prevent and control the disease in many countries of the world.

- In view of this conclusion the following recommendatiSince bovine pneumonic pasteurellosis shows a good response for antimicrobial treatment in the early stage of the disease, early diagnosis and treatment of the disease is crucial to control the disease.

- As the bacteria have many antimicrobial resistance factors, it is advisable to do qualitative antibiogram to select the efficient antimicrobial drugs.

- It is advisable to use efficient vaccine by incorporating the major serotypes of the causative agent that are circulating in the area.

Finally, since satisfactory and economical control of the disease depends on successful integration use of management, antimicrobials and vaccine, so that they must be used scientifically to reduce the occurrence of the disease.ons were forwarded.

References

1. CSA. Ethiopia agricultural sample enumeration. Addis Ababa: Central Statistical Agency of the Federal Democratic Republic of Ethiopia. 2004; 2: 48-50.
2. Assegid W. Constraints to livestock and its products in Ethiopia: policy implications [DVM thesis], FVM. Debre Zeit, Ethiopia: Arab Association of Urology. 2000.
3. Radostits C, OM, Blood DC, Gay. Vet Med. 8th ed, B. 1994; 747-77.
4. Quinn GR, PJ, Carter ME, Markey BK, Carter. Pasteurella species Clin. Vet Microbiol. 5th ed. 1994; 254-8.
5. Boudreaux CM. A novel strategy of controlling bovine pneumonic pasteurellosis: Trans infecting the upper respiratory tract of cattle with a gene coding for the antimicrobial peptide [BMSc thesis]. Louisiana State University USA. 2004.
6. Kehrenberg C, et al. Antimicrobial resistance in Pasteurella and Mannheimia: epidemiology and genetic basis to cite this version: HAL Id: hal-00902701 Review article antimicrobial resistance in Pasteurella and Mannheimia: epidemiology and genetic basis. 2001.
7. Shewen JA, Conlon R. Pasteurella pathogenesis of bacterial infections in animals. Ames: Iowa State University Press. 2000; 216-25.
8. Dewhirst FE, Paster BJ, Olsen I, Fraser GJ. Phylogeny of 54 representative strains of species in the family Pasteurellaceae as determined by comparison of 16S rRNA sequences. J Bacteriol. 1992; 174: 2002-13.
9. Christensen H, Faculty V, P Infectious, and D. Division. 26 the family Pasteurellaceae 2014.

10. Schwarz TR, S, Kehrenberg C, Walsh. Use of antimicrobial agents in veterinary medicine and food animal production. Int J Antimicrob Agents Trop Anim Heal Georg. 4th ed. 2001; 17: 431-7.

11. Stevens PK, Czuprynski CJ. Pasteurella haemolytica leukotoxin induces bovine leukocytes to undergo morphologic changes consistent with apoptosis in vitro. Infect Immun. 1996; 64: 2687-94.

12. Angen Ø, Ahrens P, Bisgaard M. Phenotypic and genotypic characterization of Mannheimia (Pasteurella) haemolytica -like strains isolated from diseased animals in Denmark. Vet Microbiol. 2002; 84: 103-14.

13. Majury PE, AL, Shewen. The effect of Pasteurella haemolytica "A1" leukotoxin culture supernatant on the "in vitro" proliferative response of bovine lymphocytes Vet. Immunol. immuno. Pathologe. 1991; 29: 41-56.

14. Bisgaard M. Ecology and significance of Pasteurellaceae in animals. J Cent Bacteriol. 2003; 279: 7-26.

15. Gleen W, J. Songer and Karen Post. 6th ed. 6th ed. Edinburgh, London, New York: Churchill Livingstone," Vet Microbiol. Text B. Syst. Bacteriol Mycol. 2005; 456-600.

16. Songer W, J. Gleen and Karen post, transtracheal swabs from cattle with clinical signs of bovine respiratory disease Vet. Microbiolo J. Clin Microbiol. 2005; 38: 327-32.

17. Kahsay YT. Review on the pneumonic pasteurellosis of cattle in. 2022; 9: 39-50.

18. Wilson BA, Ho M. Pasteurella multocida: from zoonosis to cellular microbiology. Clin Microbiol Rev. 2013; 26: 631-55.

19. Quinn FC, PJ, Markey BK, Carter ME, Donnelly WJ, Leonard. Microbial disease. Black well publishing company: Blackwell Science, London, UK Vet. Microbiol. 4th ed. 2002; 137-43.

20. Ribble CS. Epidemiology of total febriferous pneumonia in feedlot calves in Western Canada [PhD thesis]. Ontario, Canada: University of Glueloph, College of Veterinary Medicine. 1992; 200-6.

21. BW and GCC Hinchcliff KW, Clive, Veterinary medicine: A text book of disease of cattle, sheep, pig, goat and horse. London: Bailliere Tindall. Vet. Med. A text B. Dis. cattle, sheep, pig, goat horse. 9th ed. 2000; 841.

22. Abate FM, Fentie Kassa T. Isolation and identification of Mannheimia haemolytica and Pasteurella multocida from symptomatic and asymptomatic sheep and their antibiotic susceptibility patterns in three selected districts of north Gondar zone, Gondar Ethiopia. Vet Med Sci. 2023; 9: 1803-11.

23. Wikse JC, SE, Baker. 'The bronchopneumonia,' Large Anim. Intern. Med. 2nd ed. MO, London: Mosby Year Book. 1996; 632-55.

24. Deme DG. Pneumonic pasteurellosis (review). 2021; 10: 23-8.

25. RA Mohamed, EB Abdelsalam. A review on pneumonic pasteurellosis (respiratory Mannheimiosis) with emphasis on pathogenesis, virulence mechanisms and predisposing factors. Bulg J Vet Med. 2008; 11: 139-60.

26. Tadesse B, Alamirew K, Ketema A, Kiflie W, Endashaw M. Ruminant pneumonic pasteurellosis: review on epidemiology, pathogenesis and virulence mechanism. Acad J Anim Dis. 2017; 6: 30-9.

27. Laishevtsev AI. Mannheimiosis of cattle, sheep and goats. I.O.P. Conf Ser Earth Environ Sci. 2020; 548.

28. Boyce JD, Adler B. The capsule is a virulence determinant in the pathogenesis of Pasteurella multocida M1404 (B:2). Infect Immun. 2000; 68: 3463-8.

29. long MT. MECHANISMS OF Fungal Infections. 2020.

30. Leite F, O'Brien SO, Sylte MJ, Page T, Atapattu D, Czuprynski CJ. Inflammatory cytokines enhance the interaction of Mannheimia haemolytica leukotoxin with bovine peripheral blood neutrophils in vitro. Infect Immun. 2002; 70: 4336-43.

31. Jeyaseelan S, Kannan MS, Briggs RE, Thumbikat P, Maheswaran SK. Mannheimia haemolytica leukotoxin activates a nonreceptor tyrosine kinase signaling cascade in bovine leukocytes, which induces biological effects. Infect Immun. 2001; 69: 6131-9.

32. Nyarko KA, Coomber BL, Mellors A, Gentry PA. Bovine platelet adhesion is enhanced by leukotoxin and sialoglycoprotease isolated from Pasteurella haemolytica A1 cultures. Vet Microbiol. 1998; 61: 81-91.

33. Buczinski S, Pardon B. Bovine respiratory disease diagnosis: what progress has been made in clinical diagnosis? Vet Clin North Am Food Anim Pract. 2020; 36: 399-423.

34. OEE, DS Abaye GSJ. Antimicrob. Act. Ginger (Zingiber Off. Roscoe) Turmeric (Curcuma Louga) Extr. Against Propionibacterium Acnes Isol. from Hum. Pimples. Abuja, Niger. 2020; 8: 1137-43.

35. Kusiluka L, Kambarage D, VETAID K. Diseases of small ruminants: a handbook: common diseases of sheep and goats in sub-Saharan Africa. Cent. Trop Vet Med. 2016; 41-2.

36. Npoa-sharks P. J Am Chem Soc. 2009; 123: 2176-81.

37. JEC Iii. Impact of 16S rRNA gene sequence analysis for identification of bacteria on clinical microbiology and infectious diseases. 2004; 17: 840-62.

38. Younes JA, Ramsay D, Lacoste S, Deschner D, Hill JE, et al. Changes in the phenotypic susceptibility of *Mannheimia haemolytica* isolates to macrolide antimicrobials during the early feeding period following metaphylactic tulathromycin use in western Canadian feedlot calves. 2022; 63: 920-928.

39. Tabatabaei M, Abdollahi AF. Isolation and identification of Mannheimia haemolytica by culture and polymerase chain reaction from sheep's pulmonary samples in Shiraz, Iran. Vet World. 2018; 11: 636-41.

40. Public health investigation. Identification of Pasteurella species and morphologically similar organisms UK Stand. Microbiol Investig. 2015; 55: 1-21.

41. Dorso L, Rouault M, Barbotin C, Chartier C, Assié S. Infectious bovine respiratory diseases in adult cattle: an extensive necropsic and etiological study. Animals (Basel). 2021; 11: 2280.

42. Janzen ED, Stockdale PH, Acres SD, Babiuk LA. Therapeutic and prophylactic effects of some antibiotics on experimental pneumonic pasteurellosis. Can Vet J. 1984; 25: 78-81.

43. Taylor JD, Fulton RW, Lehenbauer TW, Step DL, Confer AW. The epidemiology of bovine respiratory disease: what is the evidence for preventive measures?. Can Vet J. 2010; 51: 1351-9.

44. McGill JL, Sacco RE. The immunology of bovine respiratory disease: recent advancements. Vet Clin North Am Food Anim Pract. 2020; 36: 333-48.

45. Capik SF, Moberly HK, Larson RL. Systematic review of vaccine efficacy against Mannheimia haemolytica, Pasteurella multocida, and Histophilus somni in North American cattle. Bov Pract. 2021; 55: 125-33.

46. Cengiz S. Detection of Pasteurella multocida, Mannhemia haemolytica, Histophilus somni and Mycoplasma bovis in cattle lung. 710-20.