Journal of Zoonotic Diseases
https://jzd.tabrizu.ac.ir/
Published by the University of Tabriz
Online ISSN: 2717-2910

A review of pasteurellosis in humans and animals

Sayyed Jafar Hasani[1], Ahmad Enferadi[1], Saeedeh Sarani[2], Katayoon Nofouzi[3*]

[1] Department of Microbiology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran
[2] Department of Pathobiology, Faculty of Veterinary Medicine, Zabol University, Zabol, Iran
[3] Department of Pathobiology, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran

Article type:
Review article

Keywords:
Lung
Public health
Pasteurellosis
Pathogenesis

Article history:
Received:
February 21, 2024
Revised:
April 27, 2024
Accepted:
April 29, 2024
Available online:
June 18, 2024

Abstract

As humans increasingly interact with both domestic and wild animals, the risk of Zoonotic diseases is rising. This is a significant concern because most emerging and reemerging infectious diseases are zoonotic. *Pasteurellosis*, an important zoonotic disease, is a significant cause of bacterial infections in animals such as cattle, sheep, goats, pigs, rabbits, cats, dogs, birds, and others. This disease, caused by *Pasteurella spp.*, results in substantial economic losses in livestock and poultry production. Humans can contract *pasteurellosis* through bites or scratches from infected animals, or by coming into contact with the mucus or blood of these animals. Animal bites can lead to infections, with 3-18% of dog bites and 28-80% of cat bites resulting in infection. Studies indicate that *Pasteurella multocida* is present in 50% of dog bites and 75% of cat bites, part of the oral microbiota of various animals such as cats, dogs, pigs, and other wildlife. The symptoms of *pasteurellosis* in humans can vary and may include skin infections, as well as lung or central nervous system infections. In animals, *pasteurellosis* can manifest through symptoms like respiratory tract infections, fever, or skin infections, which can lead to bronchopneumonia and death if left untreated. Treatment of *pasteurellosis* usually involves antibiotics and other medical interventions. Various vaccines have been developed to prevent this disease. This article provides an overview of *pasteurellosis* in humans and different domestic animals.

Introduction

Pasteurella species are commonly present in the oral, nasal, and respiratory cavities of animals they are recognized as one of the most prevalent and opportunistic pathogens globally in both domestic and wild animals (1). *Pasteurella multocida (P. multocida)* is a microorganism that commonly resides in the nasopharynx of domestic and wild animals. Humans can acquire *P. multocida* infections through contact with animals or mucous secretions.

*Corresponding author: *nofouzi@tabrizu.ac.ir*
https://doi.org/10.22034/jzd.2024.18077
https://jzd.tabrizu.ac.ir/article_18077.html
Cite this article: Hasani SJ., Enferadi A., Sarani S., and Nofouzi K. A review of pasteurellosis in humans and animals. Journal of Zoonotic Diseases, 2025, 9 (3): 838-851.

Despite its infrequent occurrence in clinical settings, *P. multocida* is classified as a zoonotic pathogen (2). The World Organization for Animal Health (OIE) (www.oie.int), states that pasteurellosis, a symptomatic infection caused by Pasteurella, is a highly impactful disease in livestock. Both animals and humans can be affected by *Pasteurella* species, especially *P. multocida*, which can cause chronic and acute effects such as *pasteurellosis*, pneumonia, atrophic rhinitis, dermatosis, cellulitis, abscesses, meningitis, hemorrhagic septicemia (3), and even mortality in animals (4).

Pasteurella spp. are coccobacilli that are gram-negative, non-motile, and facultatively anaerobic. Alifragki et al. state that *Pasteurella* spp. are frequently present in the oral cavity and gastrointestinal tract of specific animals, potentially leading to infections (5). This species belongs to the *Pasteurellaceae* family, encompassing various other genera such as *Haemophilus, Actinobacillus, Mannheimia,* and *Aggregatibacter.* The length of *Pasteurella* spp. is 1 to 2 micrometers (6). Louis Pasteur was the first to confirm that *P. multocida* was responsible for fowl cholera in 1881 (1). To distinguish between various strains of *P. multocida,* five *serogroups* (A-F) based on capsular antigens and 16 serovars (1-16) based on somatic antigens are utilized, with certain strains being more frequently found in infected humans (7). There are over 30 species of *Pasteurella*, with *P. multocida* being the primary cause of human *pasteurellosis* due to its connection with the pharyngeal flora of domestic animals (8). *Pasteurella multocida* is very similar to Brucella in its biochemical and serological properties, but it causes different diseases from Brucella (8). *Pasteurella* does not have spores and has a bipolar state in isolation from a fresh. *Pasteurella multocida* is known to cause rabbit septicemia, swine plague (with severe mortality), and bovine pneumonia. *Pasteurella multocida* and *Mannheimia hemolytica (M. haemolytica)* have several hosts. *Pasteurellosis* in livestock is mostly caused by *P. multocida* and sometimes *M. haemolytica* or *pastorellas* close to these two. The predominant species of *Pasteurella* that causes disease in dogs and particularly cats is *P. multocida*, although other species such as *P. canis, P. dagmatis,* and *P. stomatis* may also be involved. These *Pasteurella* species are often present with other bacteria, including *Streptococcus canis*, other gram-negative bacteria, or anaerobes (9).

Pathogenesis

Pasteurella. multocida is a variety of bacteria that can be spread to humans using bites or scratches from cats and dogs (Fig. 1), or by coming into contact with their bodily fluids. However, there have been rare cases where the bacteria has been transmitted vertically from an infected mother to her newborn (10, 11). It is not always necessary for the bacteria to penetrate the skin for transmission, as there have been cases of infection after being licked by an infected animal (12). *Pasteurella. multocida* is a frequently occurring microbe that inhabits the oropharynx and upper respiratory tract of rabbits. The microorganism that causes this infection can be transmitted to humans through scratches, bites, licks, or inhaling air particles. Individuals with weakened immune systems or respiratory problems are more susceptible to contracting the infection. Infected rabbits may carry the microorganism without clinical symptoms (13). Several genes that could affect the pathogenicity of *P. multocida* include those related to fimbriae, adhesion, and colonization (such as *ptfa*, *fimA*, *pfhA*, and *tadD*), as well as genes involved in iron regulation and protein acquisition (*exbB*, *exbD*, *tonB*, *hgbA*, *hgbB*, *tbpA*, and *fur*). Other factors include superoxide dismutase (sodA and sodC), dermonecrotic toxins (toxA), various outer membrane proteins (*OMPs*) acting as protective agents (*ompA*, *ompH*, *omp87*, and *plpB*), and neuraminidase (*nanB* and *nanH*) (14-18). Currently, researchers are investigating how these small organisms can enter the mucous membrane, evade natural immunity, and cause widespread sickness. Important factors contributing to their ability to

cause disease include the capsule and lipopolysaccharide. The bacterial capsule prevents phagocytosis and resists complement, while complete lipopolysaccharide is crucial for bacterial survival in the host. Other factors that contribute to virulence have been discovered through targeted and random mutagenesis, including *P. multocida* toxin (PMT), potential surface adhesins, and iron acquisition proteins. Probably, there are still numerous important factors that contribute to the virulence of *P. multocida*, including those necessary for attaching to and attacking host cells, as well as surviving in a harsh and nutrient-poor environment (1). This bacterium is responsible for bovine respiratory disease (BRD), which has a complex pathogenesis involving various infectious agents, environmental and stress factors, and the host's immune response (19). Although there has been significant investigation into the clinical, pathological, hematological, and biochemical characteristics of goats contaminated with *P. multocida*, the molecular mechanisms involved in such contamination remain largely unclear (20). *Pasteurella. multocida* is known to cause inflammation and cell death. When injected into mice, it triggers the production of proinflammatory cytokines such as TNF-α, IL-6, IL-1, IL-8, and IL-12, and increases the number of neutrophils (21). It is worth noting that Honnorat et al. found cases of septic arthritis caused by *P. multocida* that did not involve bite or scratch injuries (22). Respiratory disease resulting from *P. multocida* infection typically manifests with symptoms such as coughing, fever, shortness of breath, and chest pain. Although pneumonia is the most common type of *P. multocida* infection, tracheobronchitis, empyema, and lung abscesses are also possible outcomes (23). *Pasteurella* is part of the mucous flora of the respiratory system and the disease often follows stress such as the accumulation of livestock, cold, transportation, or simultaneous infections. *Pasteurella* can be pathogenic when it enters the body initially, and in these cases, transmission between animals is often through small droplets or contaminated water and food. While organisms such as ticks, lice, and flies have been found to harbor the bacterium *P. multocida*, they are not currently recognized as vectors for transmission to humans (23, 24). Unlike mammals, this bacterium is not the natural flora of birds and its presence in the bird is a sign of acute or chronic disease. Most respiratory diseases outbreaks in cattle and pigs are due to bacterial invasion from internal (endogenous) sources. Hemorrhagic septicemic diseases of cattle and sheep and fowl cholera are caused by highly invasive species (i.e. they are secondary infections) and bacteria cause disease in the first place. Studies have shown that particular OMPs present in *P. multocida* play a role in the onset of disease and possess characteristics that activate the immune system and eliminate bacteria (24-28).

Epidemiology, ways of transmission, and risk factors

Pasteurella multocida, initially discovered after a cat bite in 1930, is now regarded as the most significant microorganism of its kind in clinical settings. However, *Pasteurella* spp. was first isolated in 1878 from fowls with cholera (6). According to Iaria and Cascio, *P. multocida* infects around 20-50% of the 1-2 million individuals who suffer from dog and cat bites or scratches in the United States annually (29). *Pasteurella multocida* is widespread in cats and dogs but can also harm humans, primarily resulting in soft-tissue infections following animal bites or scratches. Immunocompromised individuals or those with chronic illnesses may experience invasive diseases from *P. multocida* infections (30). Pregnant women and immunocompromised individuals are at a higher risk of contracting pet-induced zoonoses (3, 30).

Clinical signs in human

The clinical symptoms of *Pasteurellosis* in humans typically occur when an animal bites and leads to a skin and soft tissue infection. Although infective endocarditis is rare, it can be difficult to diagnose

and treat due to its infrequency. According to a recent study by Alifragki et al., 28 patients with infective endocarditis caused by *Pasteurella* spp. exhibited common clinical symptoms such as fever, sepsis, septic shock, and heart failure (5). The aorta was frequently impacted within the heart, and approximately 21.4% of patients had a valve replacement. These microorganisms are often present in the oral and digestive tracts of specific animals and can lead to infections such as septicemia (6). *Pasteurella multocida* is commonly linked to skin and soft tissue infections but can cause several human diseases, such as meningitis, urinary tract infections, pneumonia, endocarditis, brain abscesses, conjunctivitis, and epiglottitis. However, the incidence of reported cases is restricted (30). Breen et al. found that *P. multocida* contamination was only diagnosed 23 times in a major teaching hospital laboratory in Australia over a decade (31). While *P. multocida* is not a common cause of prosthetic joint infections, other microorganisms like *Staphylococcus aureus*, coagulase-negative *staphylococci*, and *Streptococcus* species are often responsible (32). Christenson et al. reported a case of severe *P. multocida* sepsis in a renal transplant patient caused by cat-licking venous stasis ulcers on the patient's legs (33). In humans, *P. multocida* infections are linked to respiratory symptoms such as pneumonia, tracheobronchitis, lung abscesses, and pulmonary emphysema (34).

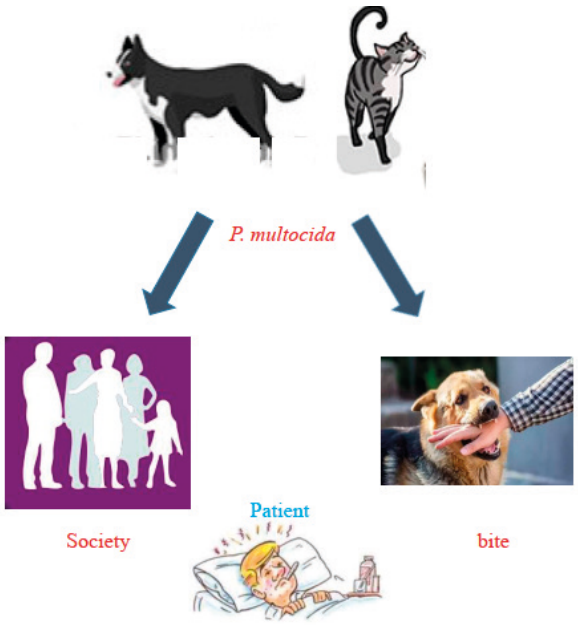

Fig. 1. The transmission process of *Pasteurella multocida* bacteria from dogs and cats to humans.

Clinical signs of *pasteurellosis* in animals

According to some studies, pasteurellosis is a common illness in both wild and domestic animals. It typically appears as upper respiratory symptoms such as nasal inflammation and discharge, as well as lower respiratory problems like pneumonia. The severity of symptoms can vary from mild to severe (34-37). Non-toxic capsular strains of *P. multocida* can cause Pneumonic Pasteurellosis without any signs of atrophic rhinitis.

Symptoms of *pasteurellosis* in ruminants

Respiratory illness is commonly caused by *P. multocida* in hoofed mammal animals such as cattle. This pathogen, along with other bacteria like *M. haemolytica*,

Histophilus somni (H. somni), Mycobacterium bovis (M. bovis), and *Trueperella pyogenes (T. pyogenes*), is frequently linked to Bovine respiratory disease (BRD) or "shipping fever," which is a complicated form of non-septic pneumonia (38, 39). Bovine respiratory disease is a complex condition that results in high mortality rates among young calves and significant financial losses for the global cattle industry (40). The most common cause of BRD cases is *M. haemolytica*, which leads to severe pleuropneumonia with hemorrhage or coagulative necrosis due to extreme inflammation caused by LPS and the production of a leukotoxin specific to ruminants (38). According to Wang et al., BRD results in negative impacts on animal health, carcass weight, welfare, and financial costs due to increased expenses for treatment and vaccination in affected herds (41). *Pasteurella multocida* species are known as secondary invaders of respiratory injuries in cattle, sheep, and goats, viral and mycoplasmic infections favor the occurrence of Pneumonic *Pasteurellosis* (32, 41). Cows can be infected at any age, but at 6 to 24 months (2 years), it has a higher sensitivity.

Clinical symptoms of hemorrhagic septicemia in cows and buffaloes

The disease occurs due to introduction of bacteria into the blood in an acute and sub-acute manner. Clinical signs are high fever (42 to 41 ˚C), lethargy, excessive salivation, bloody diarrhea, and subcutaneous edema. In advanced cases of cyanosis (bruising) of mucous membranes Rapid death is one of the important symptoms (such as enterotoxemia and heartburn). Sometimes, there is bleeding from the pores of the body (same as scalding, but it should not be confused with scalding) (42). Sadeghian et al. state that goats can suffer from two major illnesses caused by *pasteurellosis*, namely systemic *pasteurellosis* and pneumonic *pasteurellosis* (42). Pneumonic pasteurellosis is characterized by symptoms such as fever, lethargy, loss of appetite, swelling, excessive salivation, tearing, nasal discharge, coughing, and dullness. These symptoms quickly progress to respiratory distress, septic shock with severe bleeding, and ultimately death (42, 43).

Septicemia

Manhemia hemolytica is the cause of septicemia in sheep, which can be seen in two forms. One occurs in lambs less than three months old, characterized by swelling of the pleural membrane and pericarditis, and type A bacterium is responsible for it. The other occurs in lambs aged 5-12 months and is caused by type T. Young lambs acquire the bacteria from the mother, and the bacteria are replaced in the tonsils in the first few weeks of life. The spread of disease often follows a change in the diet from poor to rich. Bacteria multiply in the tonsils and then invade the adjacent tissues of the digestive system. A group of bacteria enters the bloodstream and causes embolism in the vessels of the lung, liver, and spleen, due to the release of endotoxin and the proliferation of bacteria in the lungs, liver, and spleen; the animal dies suddenly. According to Wilson et al. and Dabo et al., livestock, especially cattle, and buffalo, in tropical areas like Asia, India, Africa, southern Europe, and the Middle East can suffer from a serious and potentially deadly acute disease called hemorrhagic septicemia (3, 44, 45). The disease is primarily caused by *P. multocida* serotypes B: 2 and E: 2 and is commonly observed in the later stages of pasteurellosis disease. While Hemorrhagic septicemia (HS) is less frequently seen in pigs, sheep, goats, and deer, it is more commonly associated with serotype B:2 strain (46). Hemorrhagic septicemia can go unnoticed until the acute phase, which starts suddenly and progresses quickly within a few hours. Symptoms typically involve fever, fatigue, and swelling, along with excessive salivation, watery eyes, and nasal discharge. Soon after, the affected person experiences issues with breathing, septic shock accompanied by heavy bleeding, and passes away within 1-3 days. Even though there has been thorough research, there is limited understanding of the factors that lead to the disease or how it progresses from a mild chronic state

to a severe disseminated condition. The pasteurellosis agent in sheep and goats (*M. haemolytica*) causes two distinct syndromes: pneumonia and septicemia. In addition, a kind of gangrenous mastitis also occurs near the end of the lactation period in ewes. One of its characteristics is one-sidedness and necrotic inflammation of the mammary gland (5, 46).

Pasteurella pneumonia in sheep

Endemic and sporadic pneumonia in sheep is similar to transportation fever in calves. Although transportation is not a significant factor in the pathogenesis of sheep, since the sheep are constantly moving, other stressors are important in this context. Biotype A is the causative agent of sheep pneumonia (Fig. 2). The onset of the disease is rapid (such as enterotoxemia and hemorrhagic septicemia). In addition, it often causes the death of one or two lambs and respiratory diseases of different severity in the rest of the lambs. In acute disease, fever, cough, nasal and eye discharge, and diarrhea occur (15, 47).

Symptoms of mastitis caused by *Pasteurella* species

It is common in ewes and manifests as a super-acute, dangerous, and fatal gangrene. However, it occurs relatively rarely and in isolated cases in cattle and goats, where the cause is *M. hemolytica* and *P. multocida* (12, 18, 47). The infected teat becomes extremely swollen, and the milk becomes watery with blood. Calves can contract pasteurellosis through contaminated milk, but the disease is not fatal in cattle.

Clinical signs of *pasteurellosis* in rabbits

The wide range of microorganisms is evident in the different clinical presentations related to *pasteurellosis* in rabbits. These presentations majorly affect the respiratory system (Fig. 3), but may also involve otitis, pyometra, mastitis, orchitis, abortions, subcutaneous abscesses, and intense septicemic forms (47). Infected rabbits might not show any symptoms or may experience severe symptoms. The pathogenicity of *P. multocida* is impacted by different virulence factors, including capsule proteins and lipopolysaccharides. These factors are more widespread when there is immunosuppression, stress, or unfavorable environmental conditions (1, 17).

Clinical signs of *pasteurellosis* in dogs and cats

Pasteurella species have been linked to various disease manifestations, including pyothorax, upper respiratory tract infections (often resulting from viral infections or chronic rhinosinusitis), bronchopneu monia, urinary tract infections, ocular surface infections, wound infections, cutaneous abscesses, otitis externa, bacteremia, and, infrequently, infective endocarditis (9).

Clinical signs of bird *pasteurellosis* or fowl cholera

Poultry infected with *P. multocida* can develop fowl cholera, which is a significant economic concern in commercial production. It can manifest in various forms, including peracute, acute, and chronic infections (48). The histological features, clinical signs, and macroscopic lesions linked to *P. multocida* infections in poultry and pigs are not distinctive and can be mistaken for other respiratory system infections that are characterized by inflammation of the upper respiratory tract, pneumonia, airsacculitis, polyserositis, and septicemia. Therefore, it is crucial to accurately detect the causative organism to make a proper diagnosis (49, 50).

Laboratory diagnosis

The ailment agent is present in the lung and tracheal secretions, and the diagnosis is established by culture and isolation of the agent. *Pasteurella multocida* can grow on different culture media, such as sheep and chocolate agar, but generally not on MacConkey

agar. Furthermore, most strains give a positive outcome for indole, catalase, and oxidase tests (6). According to Townsend et al., *P. multocida* colonies typically display a smooth, blue, and iridescent appearance on standard growth media (Fig. 4, 5). However, encapsulated isolates may exhibit a mucoid appearance (7). Currently, molecular techniques such as *16SrRNA* are commonly used instead of serotyping to distinguish between various types of *Pasteurella* spp. (30, 51).

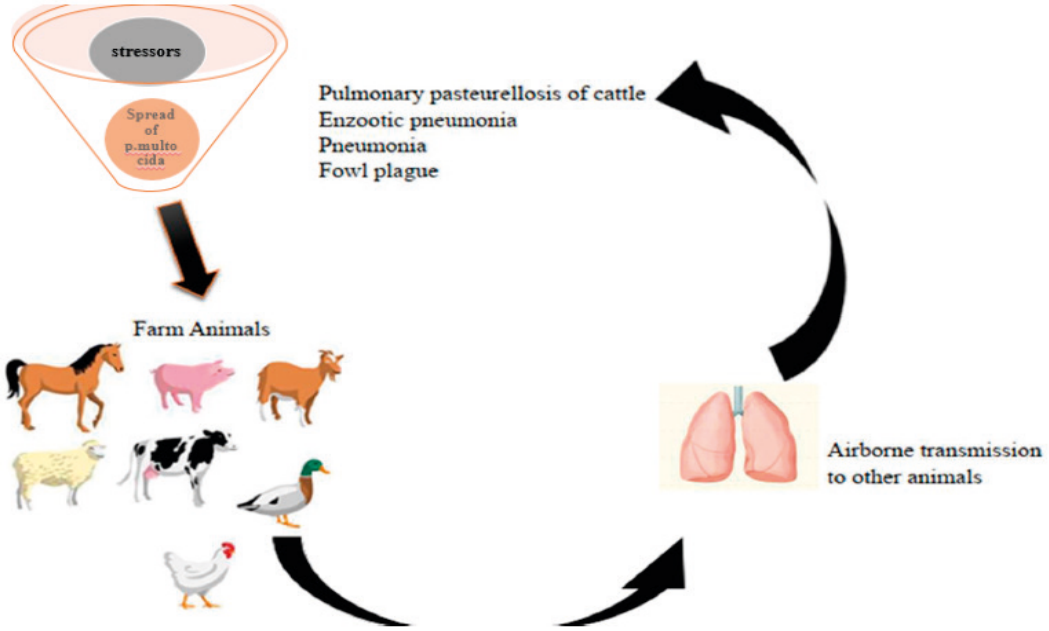

Fig. 2. Transmission of *Pasteurella* among domestic animals, causing respiratory disease in farm animals.

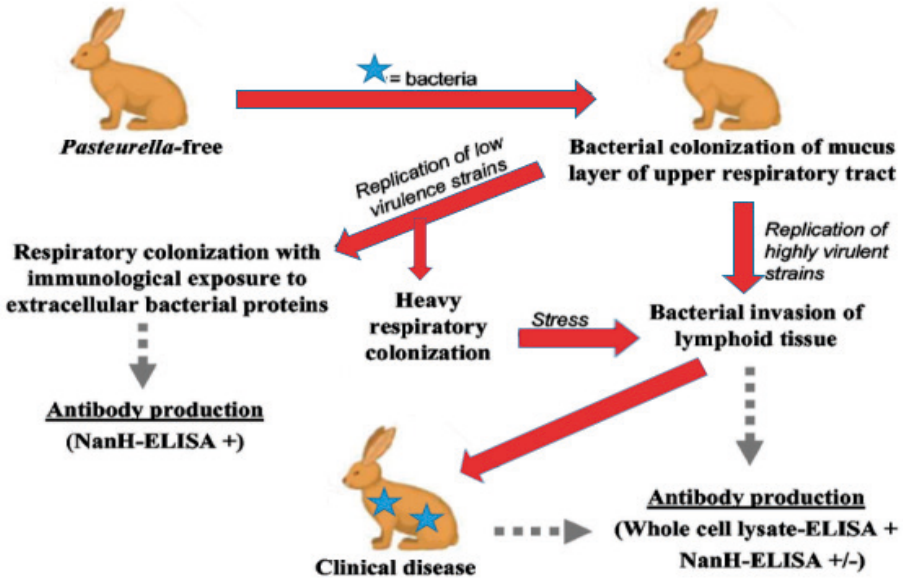

Fig. 3. Clinical lesions caused by *Pasteurellosis* and its detection methods in rabbits.

Autopsy findings

Pneumonic *Pasteurellosis* in ruminants

In sheep, Lesions in acute cases are hemorrhagic bronchopneumonia with pneumonia (pneumonia and pericarditis). Lung lesions are limited to anterior and abdominal regions. Autopsy and pathological signs of pasteurellosis hemorrhagic septicemia in cows and buffaloes are observed in all the organs of the body, from mucous membranes to different parts. Due to the rapid progress of the disease and the rapid loss of animals, the lesions are limited to bleeding points in the serous areas, accumulation of blood in the chest and abdomen, swelling of the intestine, and swelling of subcutaneous tissues (in subacute forms) (16, 51).

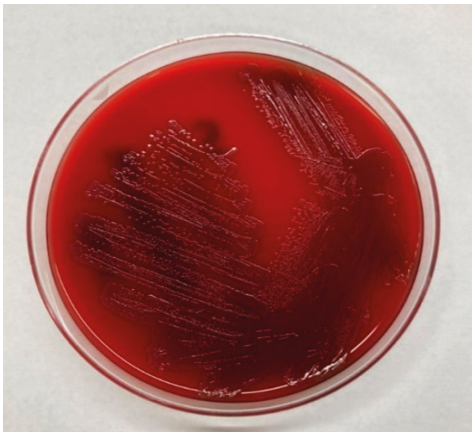

Fig. 4. *Pasteurella multocida* identified on sheep blood agar as grayish and non-hemolytic colonies (2).

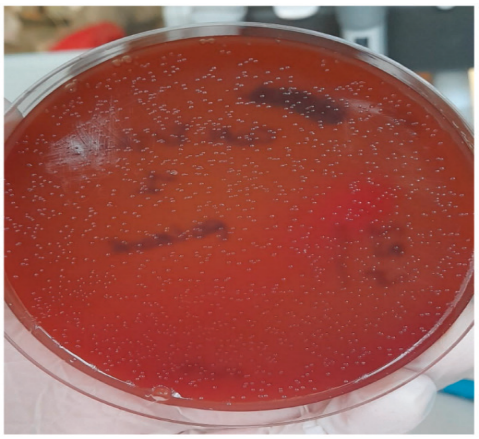

Fig. 5. This displays the microbiological results of a conjunctival specimen. Colonies were grown on blood agar and identified as *Pasteurella multocida* (13).

Pathological signs of pulmonary *pasteurellosis* or transportation fever in cows and buffaloes

Pulmonary *pasteurellosis* manifests with hepatization of the lung. The stages of pneumonia are different in different parts of the lung, starting with hyperemia and goes through different stages of liver development and is associated with the accumulation of mucous and fibrinous secretions in the space between the lobes of the lung. In chronic cases, pleural membrane adhesion is present, which causes severe shortness of breath and prevents inhalation and exhalation. It also becomes a place of infection (51).

Differential diagnosis

It is crucial to take into account other pathogens besides *P. multocida*, which is the most commonly detected pathogen when diagnosing animal bites or scratches. These additional pathogens comprise *Bartonella henselae, Clostridium tetani, Staphylococcus aureus*, and Rabies lyssavirus (52).

Treatment

Penicillin is the preferred treatment for *P. multocida* infections as they are usually responsive. However, in uncommon instances of penicillin resistance, alternative antibiotics like cephalosporins, fluoroquinolones, or tetracyclines may be utilized (52). For prophylaxis or local infections, amoxicillin-clavulanate is the first-line antibiotic. Other treatment options may involve using a blend of antibiotics that have anti-*Pasteurella* properties, like doxycycline, trimethoprim-sulfamethoxazole, penicillin V, cefu-

roxime, ciprofloxacin, or levofloxacin, along with an anti-anaerobic agent such as metronidazole or clindamycin to address other bacteria in the mouth. During the initial stages of treatment, antibiotics can be given through injection and may consist of ampicillin-sulbactam, piperacillin-tazobactam, or a carbapenem such as imipenem-cilastatin, meropenem, or ertapenem. Another option is to use ceftriaxone or fluoroquinolone in conjunction with an anti-anaerobic medication like metronidazole or clindamycin. It is crucial to modify antibiotic therapy based on culture and sensitivity test results when appropriate. Antibiotics that are ineffective against *Pasteurella*, such as cephalexin, dicloxacillin, and erythromycin, should be avoided (53). Enrofloxacin was selected as a treatment option due to its effectiveness in controlling *P. multocida* in rabbits and authorization for use in pets. In a recent study, enrofloxacin was administered through drinking water at a concentration of 200 mg/L for 15 days. This resulted in a reduction of rhinitis and conjunctivitis symptoms in rabbits and an improvement of symptoms in adults (13). Non-steroidal anti-inflammatory drugs are used as auxiliary drugs in severe cases of the disease.

Prognosis

Soft-tissue infections caused by *P. multocida,* usually have a simple course and can be cured with proper treatment. In severe cases like bacteremia, meningitis, and endocarditis, the outlook is significantly poorer. Mortality rates range from 25% to 30% in such situations (30).

Prevention and control

Creating vaccines based on *Pasteurella* is crucial for reducing major economic and domestic wildlife losses caused by pasteurellosis. Different vaccines have been developed for Pneumonic *Pasteurellosis*, and their efficiencies are different from each other (54). New vaccines are required to combat *P. multocida*, the primary cause of infections in farm animals, as commercial vaccines only offer temporary immunity. Studies have revealed that both the DNA vaccine and inactivated vaccines lead to a substantial rise in serum antibody levels in rats with infections. DNA vaccine provides better protection than the live attenuated vaccine, although it only offers partial protection. Yassein et al. have reported that the recombinant vaccine shows high immunogenicity and has the potential for use as a vaccine in the future (55). DNA vaccine designed for *P. multocida* toxin (PMT) can protect animals from infections caused by *P. multocida*. The vaccineeffectively protects against avian pasteurellosis using two different outer membrane proteins (OMPs), OmpH and OmpA, resulting in the highest level of protection (56, 57). There is another DNA vaccine called pVAX1-ABA392 that has demonstrated potential for use as a vaccine by producing significant levels of anti-HS antibodies against *P. multocida* (58). This vaccine has a good chance of being selected to serve as a strong candidate for vaccination. Over 30 vaccines have been created for *P. multocida*. Vaccines for *pasteurellosis* should be investigated for short-term or long-term serious side effects (Table 1)**.**

Conclusion

Pasteurella multocida can cause illness in various species of animals and birds. It is a significant cause of respiratory infections in animals and is also an important zoonotic disease. If an elderly patient with a chronic lung condition has a history of exposure to cats or dogs, the clinician should be aware that *Pasteurella* could potentially be a cause of their pulmonary illness.

Acknowledgments

Not applicable.

Ethical approval

Not applicable.

Conflict of interest

There is no conflict of interest in conducting this research.

Table 1. *P. multocida* vaccines and vaccine candidates (3).

Vaccine type	Animal	Vaccine/Vaccine candidate	Challenge strain/ serotype	Protection %
Killed	Turkeys	A:1, A:2, A:3	X-73	80/88
Killed	Rabbits	B:2	B:2 serotype	100
Killed	Mice	*P. multocida* loaded alginate MPs	B:2 serotype	6 logs less than control group
Avirulent	Broiler chickens	CU2 strain	P-1059	50
Avirulent	Turkeys	P-1059	X-73	90
Avirulent	Holstein-Friesian calves	A:3	A:3	NA
Avirulent	Ducks	0818 strain fur mutant	0818 strain	62
Subunit	Piglet	Truncated PMT	Type D	Significantly decreased clinical symptoms
Recombinant	Goats	Fimbrial protein	B: 2	Significantly increased
DNA Vaccine	Chicken	pOMPHA	CVCC474	75
DNA Vaccine	Chicken	ptfA g	CVCC474	100
Subunit	Rabbits	PTE	D:3	Significantly increased

References

1. Harper M, Boyce JD, Adler B. Pasteurella multocida pathogenesis: 125 years after Pasteur. Fems Microbial Lett. 2006;265(1):1-10. https://doi.org/10. 1111/j.15 74-6968.2006.00442.x

2. Malhotra S, Phan T. Pasteurella multocida bacteremia in a patient with septic arthritis. Infect Med. 2022;1(3):221-3.https://doi.org/10.1016/j.imj.2022. 08.0 01

3. Mostaan S, Ghasemzadeh A, Sardari S, Shokrgozar MA, Brujeni GN, Abolhassani M, et al. Pasteurella multocida vaccine candidates: A systematic review. AJMB. 2020;12(3):140. PMID: 3269 5276

4. Souza MJ. Bacterial and parasitic zoonoses of exotic pets. *Vet Clin North Am Exot Anim Pract*. 2009;12(3):401-15. https://doi.org/ 1094-9194(09) 00036-X

5. Alifragki A, Kontogianni A, Protopapa I, Baliou S, Ioannou P. Infective endocarditis by Pasteurella species: A systematic review. J Clin Med. 2022; 1(17):5037. https://doi.org/10.3390/jcm11175037

6. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-Book: 2-Volume Set: Elsevier health sciences; 2019.https://doi.org/10.1159/000007313

7. Townsend KM, Boyce JD, Chung JY, Frost AJ, Adler B. Genetic organization of Pasteurella multocida cap loci and development of a multiplex capsular PCR typing system. J Clin Microbiol. 2001; 39(3): 924-9.https://doi.org/10.1128/jcm.39.3.924-92 9.2001

8. Hurtado R, Maturrano L, Azevedo V, Aburjaile F. Pathogenomics insights for understanding Pasteurella mult ocida adaptation. Med Microbiol. 2020;310(4): 151417.https://doi.org/10.1016/j.ijmm.2020.151 417

9. Sykes JE. Greene's Infectious Diseases of the Dog and Cat-E-Book: Elsevier Health Sciences;

2022. https://doi.org/10.1016/j.ijmm.2022.151857

10. Kristinsson G, Adam H. Pasteurella multocida infections. Pediatr Rev. 2007;28(472473):2. https://doi: 10.1542/pir.28-12-472

11. Nakwan N, Atta T, Chokephaibulkit K. Neonatal pasteurellosis: a review of reported cases. Archives of Disease in Childhood-Fetal and Neonatal Edition Adc Fetal & Neonatal Edition. 2009; 94(5):F373-F6. https://doi.org/10.1136/adc.2008. 143982

12. Perrin I, Blanc P, Karam T, Carbajal R. Meningitis and osteitis caused by Pasteurella multocida in a three-month-old infant. Archives de Pediatrie: Organe Officiel de la Societe Francaise de Pediatrie sfpediatrie. 2003;10(5):439-41. https:// doi.org/10. 1016/s0929-693x(03)00093-9

13. D'Amico F, Casalino G, Bozzo G, Camarda A, Lombardi R, Dimuccio MM, et al. Spreading of Pasteurella multocida infection in a pet rabbit breeding and possible implications on healed bunnies. Vet Sci. 2022;9(6):301. https://doi.org/10. 3390/vetsci 9060301

14. Ewers C, Lübke-Becker A, Bethe A, Kießling S, Filter M, Wieler LH. Virulence genotype of Pasteurella multocida strains isolated from different hosts with various disease status. Vet Microbiol. 2006; 114(3-4):304-17. https://doi.org/10.1016/ j.vetmic. 2005.12.012

15. Hatfaludi T, Al-Hasani K, Boyce JD, Adler B. Outer membrane proteins of Pasteurella multocida. Vet Microbiol. 2010;144(1-2):1-17 https://doi. org/10.1016/j.vetmic.2010.01.027.

16. Katoch S, Sharma M, Patil R, Kumar S, Verma S. In vitro and in vivo pathogenicity studies of Pasteurella multocida strains harbouring different ompA. Vet Res Commun. 2014;38:183-91. https://doi.org/10.1007/s11259-014-9601-6

17. Massacci FR, Magistrali CF, Cucco L, Curcio L, Bano L, Mangili P, et al. Characterization of Pasteurella multocida involved in rabbit infections. Vet Microbiol. 2018;213:66-72. https:// doi.org/10. 1016/j.vetmic.2017.11.023

18. Tang X, Zhao Z, Hu J, Wu B, Cai X, He Q, et al. Isolation, antimicrobial resistance, and virulence genes of Pasteurella multocida strains from swine in China. J Clin Microbiol. 2009;47(4) :951-8. https:// doi.org/10.1128/jcm.02029-08

19. Apley M. Bovine respiratory disease: pathogenesis, clinical signs, and treatment in lightweight calves. *Vet Clin N Am-Food*. 2006;22(2) :399-411. https://doi.org/10.1016/ S0749-0720 (06)00024-7

20. Zhang W, Jiao Z, Huang H, Wu Y, Wu H, Liu Z, et al. Effects of Pasteurella multocida on histopathology, miRNA and mRNA expression dynamics in lung of goats. Animals. 2022;12(12) :1529. https: //doi.org/10.3390/ani12121529

21. Praveena PE, Periasamy S, Kumar A, Singh N. Cytokine profiles, apoptosis and pathology of experimental Pasteurella multocida serotype A1 infection in mice. Res J Vet Sci. 2010;89(3):332-9. https://doi.org/10.1016/j.rvsc.2010.04.012

22. Honnorat E, Seng P, Savini H, Pinelli P-O, Simon F, Stein A. Prosthetic joint infection caused by Pasteurella multocida: a case series and review of literature. BMC Infect Dis. 2016;16(1):1-7. https://doi.org/10.1186/s12879-016-1763-0

23. Weber DJ, Wolfson JS, Swartz MN, Hooper DC. Pasteurella multocida infections: report of 34 cases and review of the literature. *Med*. 1984; 63(3):133-54. https://pubmed.ncbi.nlm.nih.gov /6371440

24. Azama FM, Zamri-Saadc M, Rahima RA, Chumnanpoend P. Antigenic outer membrane proteins prediction of Pasteurella multocida serotype B: 2. AsPac J Mol Biol Biotechnol APJMBB. 2020;28(4): 102-16. https://doi.org/1 0.1016/6006699f299bf14088a62ec9

25. Basagoudanavar S, Singh D, Varshney B. Immunization with outer membrane proteins of

Pasteurella multocida (6: B) provides protection in mice. *J Vet Med A* . 2006;53(10):524-30. https://doi.org/10.1111/j.1439-0442.2006.00900.x

26. Haynes AM, Fernandez M, Romeis E, Mitjà O, Konda KA, Vargas SK, et al. Transcriptional and immunological analysis of the putative outer membrane protein and vaccine candidate TprL of Treponema pallidum. *Plos* Negl Trop Dis . 2021;15 (1):e0008812.https://doi.org/10.1371/journal.pntd.0008812

27. Lee J, Kim YB, Kwon M. Outer membrane protein H for protective immunity against Pasteurella multocida. J Microbiol. 2007;45(2): 179-84. https://doi.org/10.1016/S0378-1135(02)00300-0

28. Tan H, Nagoor N, Sekaran S. Cloning, expression and protective capacity of 37 kDa outer membrane protein gene (ompH) of Pasteurella multocida serotype B: 2. Trop Biomed. 2010;27 (3):430-41. https://pubmed.ncbi.nlm.nih.gov/21399583

29. Iaria C, Cascio A. Please, do not forget Pasteurella multocida. Clin Infect Dis. 2007;45(7):940-. https://doi.org/10.1086/521247

30. Wilson BA, Ho M. Pasteurella multocida: from zoonosis to cellular microbiology *Cell. Microbiol Clin Microbiol Rev*. 2013;26(3):631-55. https://doi. org/10.1128/cmr.00024-13

31. Breen MS, Tom Au, ELizabeth Reiss-Levy, Dorothy. Pasteurella multocida: a case report of bacteremic pneumonia and 10-year laboratory review. Pathol. 2000;32(2):152-3. Published online: 06 Jul 2009. https://doi.org/10.1080/00313020010444 8

32. Beam E, Osmon D. Prosthetic joint infection update. Clin Infect Dis. 2018;32(4):843-59. https ://doi.org/ 10.1016/j.idc.2018.06.005

33. Christenson ES, Ahmed HM, Durand CM. Pasteurella multocida infection in solid organ transplantation. *Lancet Infect Dis* . 2015;15(2):235-40. https://doi.org/10.1016/S1473-3099(14)70895-3

34. Klein NC, Cunha BA, editors. Pasteurella multocida pneumonia. *Semin Respir Infect;* 1997. PMID: 9097378. https://pubmed.ncbi.nlm.nih.gov/ 9097378

35. Ackermann MR, Register KB, Stabel JR, Gwaltney SM, Howe TS, Rimler RB. Effect of Pasteurella multocida toxin on physeal growth in young pigs. A Am J Vet Res. 1996;57(6):848-52. https://doi.org/10.2460/ajvr.1996.57.06.848

36. Deeb BJ, Digiacomo RF, Bernard B, Silbernagel S. Pasteurella multocida and Bordetella bronchiseptica infections in rabbits. J Clin Microbiol. 1990;28(1):70-5. https://doi.org/10.1128/jcm.28.1.70-75.1990

37. Thurston J, Rimler R, Ackermann MR, Cheville N. Use of rats to compare atrophic rhinitis vaccines for protection against effects of heat-labile protein toxin produced by Pasteurella multocida serogroup D. Vet Immunol Immunopathol. 1992;33(1-2):155-62. https://doi.org/10.1016/0165-2427(92)90042-O

38. Confer AW. Update on bacterial pathogenesis in BRD. Anim Health Res Rev. 2009;10(2):145-8. https://doi.org/10.1017/S1466252309990193

39. Welsh RD, Dye LB, Payton ME, Confer AW. Isolation and antimicrobial susceptibilities of bacterial pathogens from bovine pneumonia: 1994–2002. J Vet Diagn Invest. 2004;16(5):426-31. https://doi.org/10.1177/104063870401600510

40. Hashem YM, Mousa WS, Abdeen EE, Abdelkhalek HM, Nooruzzaman M, El-Askary A, et al. Prevalence and molecular characterization of Mycoplasma species, Pasteurella multocida, and Staphylococcus aureus isolated from calves with respiratory manifestations. Animals. 2022; 12(3):312. https://doi.org/ 10.3390/ani12030312

41. Wang M, Schneider LG, Hubbard KJ, Grotelueschen DM, Daly RF, Stokka GS, et al. Beef producer survey of the cost to prevent and treat

bovine respiratory disease in preweaned calves. Avma. 2018;253(5):617-23. https://doi.org/10.2460/javma. 253.5.617

42. Sadeghian S, Dezfouli MRM, Kojouri GA, Bazargani TT, Tavasoli A. Pasteurella multocida pneumonic infection in goat: Hematological, biochemical, clinical and pathological studies. Res. 2011;100(2-3):189-94. https://doi.org/10.1016/j.smallrumres. 2011.07. 006

43. Shafarin M, Zamri-Saad M, Khairani BS, Saharee A. Pathological changes in the respiratory tract of goats infected by Pasteurella multocida B: 2. J Comp Pathol. 2009;140(2-3):194-7. https://doi.org/ 10.1016/j.jcpa.2008.10.005

44. Dabo S, Taylor J, Confer A. Pasteurella multocida and bovine respiratory disease. Health Res Rev. 2007;8(2):129-50. https://doi.org/10.1017/S1466252307001399

45. Wilson MA, Rimler RB, Hoffman L. Comparison of DNA fingerprints and somatic serotypes of serogroup B and E Pasteurella multocida isolates. J Clin Microbiol. 1992;30(6):1518-24. https://doi.org/10.1128/jcm.30.6.1518-1524.1992

46. Dey S, Singh V, Kumar A, Sharma B, Srivastava S, Singh N. Comparative sequence analysis of 16S rRNA gene of Pasteurella multocida serogroup B isolates from different animal species. Res J Vet Sci. 2007;83(1:(1-4. https://doi.org/10.1016/j.rvsc.2006. 10.002

47. Deeb BJ. Respiratory disease and pasteurellosis. Ferrets, Rabbits, and Rodents. 2004:172. https: //doi.org/ 10.1016/B0-72-169377-/50019-8

48. Christensen J, Bisgaard M. Fowl cholera. Revue scientifique et technique (International Office of Epizootics) Rev Sci Tech Off Int Epizoot. 2000;19(2):626-37. https://doi.org/10.1002/9780470344668

49. Cameron R, O'BOYLE D, Frost A, Gordon A, Fegan N. An outbreak of haemorrhagic septicaemia associated with Pasteurella multocida subsp gallicida in a large pig herd. Aust Vet J. 1996;73(1):27-9. https://doi.org/ 10.1111/j.1751-0813. 1996.tb09949.x

50. Mackie J, Barton M, Kettlewell J. Pasteurella multocida septicaemia in pigs. Aust Vet J. 1992;69(9):227-8.https://doi.org/10.1111/j.1751-0813.1992.tb09931.x

51. Arumugam N, Ajam N, Blackall P, Asiah N, Ramlan M, Maria J, et al. Capsular serotyping of Pasteurella multocida from various animal hosts-a comparison of phenotypic and genotypic methods. Trop Biomed. 2011;28(1):55-63. http://eprints.um. edu.my/id/eprint/5455

52. Giordano A, Dincman T, Clyburn BE, Steed LL, Rockey DC. Clinical features and outcomes of Pasteurella multocida infection. Medicine. 2015;94(36). https://doi.org/10.1097/MD.0000000000001285

53. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(2):e10-e52. https://doi.org/10.1093/ cid/ciu296

54. Srinand S, Ames T, Maheswaran S, King V. Efficacy of various vaccines against pneumonic pasteurellosis in cattle: a meta-analysis. Prev Vet Med. 1995;25(1):7-17. https://doi.org/10.1016/0167-5877 (95)00493-9

55. Yassein AA, Teleb AA, Hassan GM, El Fiky ZA. The immune response and protective efficacy of a potential DNA vaccine against virulent Pasteurella multocida. JGEB. 2021;19(1):81. https: //doi.org/ 10.1186/s43141-021-00180-

56. Muenthaisong A, Nambooppha B, Rittipornlertrak A, Tankaew P, Varinrak T, Muangthai K, et al. An intranasal vaccination with a recombinant outer membrane protein H against haemorrhagic septicemia in swamp buffaloes. Vet Med Int.

2020;26:2020:3548973. https://doi.org/10.1155 /2020/3548 973

57. Qiang G, Ming C, Ming-fu N. Out membrane protein DNA vaccines for protective immunity against virulent avian Pasteurella multocida in chickens. Procedia Environ Sci. 2011;8:723-9. https://doi.org/10.1016/j.proenv.2011.10.110

58. Chelliah S, Velappan RD, Lim KT, Swee CWK, Nor Rashid N, Rothan HA, et al. Potential DNA vaccine for haemorrhagic septiceamia disease. Mol Biotechnol. 2020;62:289-96. https://doi. org/10. 1016/j.jcpa.2008.10.005