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YERSINIA PESTIS AND FRANCISELLA TULARENSIS: PATHOGENESIS, LABORATORY DIAGNOSIS, SPECIFIC PREVENTION, AND THERAPY

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Introduction

Yersinia pestis and Francisella tularensis are highly pathogenic Gram-negative bacteria responsible for severe zoonotic diseases in humans. Both organisms are considered important public health threats due to their high virulence, low infectious dose, and ability to spread through animal reservoirs and arthropod vectors. Yersinia pestis, the causative agent of plague, is mainly transmitted through infected fleas from rodents. After entering the human body, it rapidly spreads to lymph nodes and blood, leading to bubonic, septicemic, or pneumonic forms of the disease. Pneumonic plague is particularly dangerous due to its ability for human-to-human transmission via respiratory droplets. Francisella tularensis, the agent of tularemia, is transmitted through direct contact with infected animals, tick bites, contaminated food or water, or inhalation of aerosols. It is an intracellular pathogen that survives within macrophages, allowing systemic spread and immune evasion. Both pathogens are characterized by high infectivity and significant mortality if untreated, making them important targets for laboratory surveillance, early diagnosis, and effective therapeutic intervention.

Key Words

Plague, Tularemia, Yersinia pestis, Francisella tularensis, pathogenesis, zoonotic infections, intracellular bacteria, laboratory diagnosis, PCR, bacteriological culture, antibiotic therapy, streptomycin, gentamicin, biosafety, epidemiology, vector-borne diseases, public health.

Main Part

Plague is a severe acute zoonotic disease caused by Yersinia pestis. The pathogenesis begins after transmission through the bite of infected fleas, mainly associated with rodents. Once inside the human body, the bacteria migrate to regional lymph nodes, where they multiply and induce intense inflammatory responses, resulting in the formation of painful buboes. The pathogen possesses key virulence factors, including a capsule (F1 antigen) and a type III secretion system, which allows it to inhibit phagocytosis and suppress host immune responses. This enables rapid dissemination into the bloodstream, leading to septicemia, and in severe cases, secondary pneumonic involvement, which is highly contagious and often fatal without early treatment. Tularemia is a highly infectious disease caused by Francisella tularensis, a facultative intracellular bacterium. Infection occurs through multiple routes, including skin contact with infected animals, tick or deer fly bites, ingestion of contaminated food or water, or inhalation of infectious aerosols. After entering the host, the organism is rapidly taken up by macrophages but is able to escape the phagosome and replicate within the cytoplasm. This intracellular survival mechanism allows the bacterium to evade immune defenses and spread to lymphatic tissues and other organs. Clinically, tularemia may present in several forms, with ulceroglandular and pneumonic types being the most common and severe. Laboratory diagnosis of plague includes microscopic examination of clinical samples, where bipolar staining (“safety-pin” appearance) can be observed using special stains such as Wayson or Giemsa. Culture methods are also used, although they require caution due to the high virulence of the organism. Molecular techniques such as PCR are considered highly sensitive and specific, targeting genes responsible for

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virulence factors. Blood cultures may be positive in septicemic cases. In tularemia, laboratory diagnosis is more challenging because the organism is fastidious and slow-growing. PCR is the preferred diagnostic method due to its high sensitivity and rapid results. Culture requires cysteine-enriched media such as chocolate agar and must be performed under Biosafety Level 3 conditions because of the high infectivity of the pathogen. Serological tests, including agglutination assays, are also commonly used for retrospective diagnosis. Specific prevention of plague focuses on controlling rodent populations and reducing exposure to fleas in endemic areas. Personal protective measures are essential for individuals at risk. Post-exposure prophylaxis with antibiotics such as doxycycline or ciprofloxacin may be recommended in certain cases. A vaccine exists but is not widely used in routine practice due to limited availability and variable effectiveness. Prevention of tularemia includes avoiding contact with wild animals, especially rabbits and rodents, using insect repellent to prevent tick and fly bites, and following strict laboratory biosafety protocols. Although experimental vaccines exist, there is currently no widely available routine vaccine for general population use. Treatment of plague requires immediate antibiotic therapy. Streptomycin is considered the traditional drug of choice, while gentamicin is widely used as an effective alternative. Other options include doxycycline and ciprofloxacin. Early initiation of therapy is critical, especially in pneumonic plague, due to its high mortality rate and risk of rapid spread. Treatment of tularemia also relies on antibiotics, with streptomycin and gentamicin being the most effective first-line agents. Doxycycline and ciprofloxacin may be used in milder cases or as alternative therapy. Treatment duration is often longer compared to plague to ensure complete eradication of the pathogen and to prevent relapse.

Materials and Methods

This study was conducted using a systematic literature review approach focused on two highly pathogenic zoonotic bacteria: Plague and Tularemia. The purpose of the study was to analyze and summarize existing scientific knowledge regarding their pathogenesis, laboratory diagnosis, specific prevention, and therapeutic approaches.The materials used in this work included internationally recognized microbiology and infectious disease textbooks, peer-reviewed scientific articles, epidemiological reports, and clinical guidelines issued by global health organizations. Priority was given to recent publications describing the microbiological characteristics, virulence factors, and clinical behavior of Yersinia pestis and Francisella tularensis, as well as standardized diagnostic and treatment protocols. The methodological design was based on comparative and descriptive analysis. Comparative analysis was used to evaluate similarities and differences between the two pathogens in terms of transmission routes, host interaction, intracellular survival mechanisms, immune evasion strategies, and clinical manifestations. Descriptive synthesis was applied to integrate data from multiple sources into a unified scientific overview. Special attention was given to laboratory diagnostic methods, including microscopy, culture techniques, serological assays, and molecular methods such as polymerase chain reaction (PCR). The sensitivity, specificity, and biosafety requirements of each method were analyzed based on published data. In addition, therapeutic strategies were evaluated by reviewing antibiotic susceptibility patterns and clinical treatment recommendations. First-line and alternative antibiotics were compared, including streptomycin, gentamicin, doxycycline, and ciprofloxacin, depending on disease severity and clinical form. Ethical approval was not required, as the study did not involve human participants, animal experiments, or direct clinical sampling. All information was obtained from previously published and publicly available scientific sources.

Results

The analysis of scientific literature on Plague and Tularemia demonstrated that both diseases are highly dangerous zoonotic infections with significant epidemiological importance. It was found that both pathogens share common characteristics such as low infectious dose, high virulence, and the ability to cause severe systemic disease in humans. The results showed that Yersinia pestis primarily causes disease through rapid lymphatic spread following flea transmission. The most common clinical form is bubonic plague, characterized by painful lymph

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node enlargement (buboes). In more severe cases, the infection progresses to septicemic or pneumonic forms, with pneumonic plague showing the highest risk of human-to-human transmission. In contrast, Francisella tularensis demonstrates a strong ability to survive and replicate inside macrophages, which is a key factor in its pathogenesis. The most frequently observed clinical form is ulceroglandular tularemia, while pneumonic tularemia represents the most severe manifestation, often associated with inhalation of infectious aerosols. Laboratory diagnostic analysis revealed that PCR-based methods provide the highest sensitivity and specificity for both infections. For plague, microscopic identification of bipolar staining organisms remains an important rapid diagnostic tool, while culture methods are supportive. For tularemia, culture is technically difficult and requires cysteine-enriched media, making molecular methods the primary diagnostic approach. The study also showed that both diseases can be effectively treated if antibiotic therapy is initiated early. Streptomycin and gentamicin remain the most effective first-line drugs, while doxycycline and ciprofloxacin are widely used as alternative treatment options. Delayed treatment was consistently associated with increased mortality, especially in pneumonic forms. Preventive analysis indicated that vector control (flea and tick management), reduction of contact with wild animals, and strict laboratory biosafety measures are essential strategies in controlling disease spread. However, vaccine availability remains limited, particularly for tularemia, where no widely used vaccine exists. Overall, the results highlight that early diagnosis, rapid antibiotic therapy, and effective preventive measures are the key factors in reducing morbidity and mortality associated with both infections.

Conclusion

The present study on Plague and Tularemia highlights that both infections remain highly significant zoonotic diseases with serious public health implications. Their high virulence, low infectious dose, and ability to spread rapidly make them important targets for continuous epidemiological surveillance and medical preparedness. It was concluded that Yersinia pestis causes disease primarily through lymphatic spread following flea transmission, leading to bubonic, septicemic, and pneumonic forms, while Francisella tularensis is characterized by intracellular survival within macrophages and multiple clinical manifestations depending on the route of infection. Laboratory diagnosis plays a crucial role in early detection, with PCR-based methods identified as the most reliable and rapid tools for both infections. Traditional methods such as microscopy and culture remain supportive but are limited by biosafety requirements and slow growth characteristics, especially in tularemia. The study also confirms that early antibiotic therapy is the most effective approach to reduce mortality. Streptomycin and gentamicin remain the primary treatment options, while doxycycline and ciprofloxacin serve as important alternatives. Delayed treatment significantly increases the risk of severe outcomes, particularly in pneumonic forms of both diseases. In conclusion, effective control of these infections requires a combination of early diagnosis, timely treatment, strict preventive measures, and continuous epidemiological monitoring. Strengthening laboratory capacity and public health awareness is essential for reducing the impact of these potentially life-threatening diseases.

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