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Systematic condensed outline: Legionnaires Disease Its Recognition and Management

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ABSTRACT
Pneumonia that is brought on by the legionella bacterium is known as legionnaires' illness. The disease Legionnaires' doesn't transfer between individuals. Rather, the bacterium disperses through mist, which comes from huge buildings' air conditioning units, among other sources. Many individuals exposed to the bacteria experience no symptoms at all. If symptoms manifest, they may include fever, chills, coughing, exhaustion, headaches, muscle aches, and diarrhoea.Antibiotics can be used to treat legionnaires' disease.According to information on the sickness, the American Legion, a veterans organization akin to the British Legion, held a convention in Philadelphia, Pennsylvania, in 1976, which is when the ailment first appeared.The pneumonic form of legionnaires' disease takes two to ten days to incubate, yet in extreme cases, outbreaks have taken up to sixteen days. The initial signs and symptoms include fever, tiredness, headache, nausea, and malaise. Additionally, some people may develop disorientation, diarrhoea, and muscle soreness.With 2.4 cases per 100,000 people, 2021 had the highest yearly notification rate of Legionnaires' illness in the EU/EEA to date. The EU/EEA region has heterogeneous rates, with age-standardized rates ranging from less than one to five cases per 100,000 people depending on the country.The aetiology, prevalence, potential therapies, and present state of legionnaires' disease are all included in this review study.

Keywords: *Legionnaires' Disease, Histopathology, Etiology, Pathophysiology, Management*

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I. INTRODUCTION

Legionella bacteria can cause two infections: Legionellosis, which is an infection that causes a non-pneumonic influenza-like condition, and Legionnaires' disease, which is a more serious illness that is characterized by pneumonia. Legionellosis is an underreported disease, but studies have repeatedly shown a high occurrence, making it a global public health concern of increasing importance. In addition, the disease's medical expenses are substantial. The primary method of diagnosing Legionnaires' illness is the identification of the serogroup 1 antigen of Legionella pneumophila in urine. On the other hand, diagnostic tests for legionellosis patients have advanced.Legionella pneumophila is the primary cause of human illnesses, while L. longbeachae has also been linked to disease in Australia and New Zealand. There are now about 65 species of Legionella that have been characterized, including several serogroups of L. pneumophila and other species(1). While looking into a significant pneumonia outbreak among American Legion members in Philadelphia for their annual convention in 1976, bacteria of the species Legionella were found. Legionella pneumophila was the name of the causative microorganism, an unidentified Bacteria. Legionellosis, namely the pneumonic variant, is called "legionnaires' disease" to describe the infection(2).Initially, it was thought that legionnaires' disease caused a typical clinical condition that fell under the category of illnesses known as "atypical pneumonia." A nonproductive cough, pulse-temperature dissociation, abnormal liver function test findings, diarrhoea, hyponatremia, hypophosphatemia, myalgia, disorientation, and repeated rigours are the hallmarks of this clinical condition. It's now clear that neither the usual nor the specific symptoms of nosocomial or community-acquired legionnaires' disease exist. Based on clinical findings, nonspecific laboratory findings, or chest radiography results, it is not possible to differentiate between legionnaires' disease and common causes of pneumonia, such as pneumococcal infection, at the time of initial presentation, according to several prospective comparative studies(3).The causative agent of Legionnaires disease is the gram-negative, aerobic, intracellular bacillus

known as Legionella pneumophila. Atypical pneumonia, such as legionnaires disease, is typically acquired in the community but can also occur in medical facilities. A major global public health concern is Legionnaires disease, which is caused by bacteria that are inhaled or aspirated through contaminated aerosolized water particles. Patients who are elderly or immunocompromised may be especially vulnerable to the severe symptoms of Legionnaires disease. The illness could be serious and potentially fatal, or it could be mild and self-limiting. Timely treatment action, made possible by an early and precise diagnosis, significantly lowers the morbidity and fatality rate of Legionnaires disease.Half of patients with Legionnaires disease will need intensive care, and the majority will need to be admitted to the hospital(4). Legionellosis may be indicated by laboratory abnormalities such as hyponatremia, signs of acute renal injury, and increases in transaminases, erythrocyte sedimentation rate, or C-reactive protein.Imaging scans, laboratory testing, and clinical characteristics are used to diagnose legionellosis. Antibiotics that are efficient against intracellular bacteria, such as tetracyclines, macrolides, or fluoroquinolones, are used to treat Legionnaires disease.A thorough examination of L pneumophila's genetic makeup and virulence factors reveals the complex processes that underlie its capacity to create intracellular infections in alveolar macrophages. To provide more potent prophylactics and treatments, ongoing research aims to clarify the intricate relationships between legionellae, their environmental habitats, and human susceptibility factors. Water systems must be properly maintained and disinfected to lower the danger of bacterial development and exposure and to prevent the disease known as Legionnaires disease(5–8).Bacterial colonization and growth are inhibited by using only sterile water to fill and rinse nebulization devices and by performing routine cooling tower maintenance. The majority of hospitals regularly test for legionellae in their water supply; adequate cleaning of the water supply is advised. Heating water to a temperature of between 70 and 80 degrees Celsius and flushing distant locations can effectively disinfect polluted water. Effectively eliminating legionellae, copper-silver ionization units offer long-term defence against bacterial development and colonization. Furthermore, legionellae are bactericidal by UV radiation. Water cannot be hyperchlorinated, though, as legionellae are very resistant to chlorine and chlorine breaks down at higher temperatures(9,10).

HISTOPATHOLOGY AND EPIDEMIOLOGY

Microscopic analysis of lung tissue from patients suffering from Legionnaires disease identifies interstitial inflammation as a characteristic. The visible infiltration of inflammatory cells within the alveolar septae, such as neutrophils, lymphocytes, and macrophages, is indicative of an effort to contain and eradicate the intracellular infection. Alveolar oedema, hyaline membranes, intra-alveolar exudates, and pneumocyte hyperplasia are indicative of diffuse alveolar injury. The buildup of fluid and protein in the alveolar gaps, known as alveolar oedema, hinders gas exchange and results in hypoxia. On the alveolar walls, hyaline membranes are eosinophilic membranes made of fibrin, plasma proteins, and cellular debris that worsen gas exchange and induce fibrosis. Mostly mononuclear, intra-alveolar exudates are a sign of the host immune response. When type I pneumocytes are injured, type II pneumocytes hyperproliferate.Depending on the infection's stage and severity, Legionnaire's disease may have a different histology. During the first week of infection, there is an exudative stage that is marked by erythroleukophagocytosis, intra-alveolar exudate, hyaline membranes, and alveolar oedema. Pneumocyte hyperplasia, fibroblast proliferation, and collagen deposition are the hallmarks of the proliferative stage, which lasts from the second to the third week of infection. Following the third week of infection, the fibrotic stage sets in, marked by severe fibrosis, a change in the honeycomb structure, and the production of cysts.By using immunohistochemical staining or molecular techniques to detect bacterial antigens or DNA in the lung tissue, Legionellae infection is verified. Prognostic information can be obtained via a histopathological examination; patients who have more extensive lung injury are at a higher risk of dying(11–13).Legionellae are quite common and can infect humans through contaminated water that has been aerosolized from the environment or from building water systems. The actual prevalence of Legionnaires disease is uncertain, as many nations lack the necessary tools for reporting, monitoring, or diagnosis. The most frequent cause of waterborne infections in the US is legionellae; between 60% and 65% of cases are estimated to be sporadic and environmental in origin. Most of the time, the bacteria's origin is still unknown.However, major structures and establishments like hotels, hospitals, and long-term care homes might experience illness epidemics due to contaminated water sources. According to reports, legionnaires disease is a travel-related sickness that is typically linked to lodgings that have hot tubs or water systems that are tainted. In the US, there is a 20% reported incidence of legionellosis linked to travel or medical care. Since 2000, the reported incidence of Legionnaires disease in the United States has quickly grown, according to data from the Centers for Disease Control. The CDC received reports of 9,933 cases of Legionnaires disease in 2018, with a 10% case fatality rate. However underreporting of infections is prevalent, and many infections remain untreated.Roughly ten per cent of the world's legionellosis infections are identified in the US, leading to eight to sixteen thousand hospital admissions every year. According to recent data, the number of cases of Legionnaires disease is estimated to be between 1.8 and 2.7 times greater than officially reported, with the disease becoming more commonplace worldwide. The epidemiology of Legionnaires disease differs according to population, season, and geographic area. In the US, Ohio, Pennsylvania, New York, and Illinois have higher rates of the illness. Notification rates in

the European Union/European Economic Area went from 1.2 to 1.4 per 100,000 persons in 2012 to 1.8 to 2.2 per 100,000 people in 2017 and 2019. Additionally, reports of the illness have come from Latin America, Africa, and Asia(14–17).

ETIOLOGY

The infection brought on by bacteria belonging to the genus Legionella is referred to as legionellosis. The clinical range includes Legionnaires' disease, a more severe presentation defined by pneumonia, and Pontiac fever, a non-pneumonic influenza-like condition. The first report of Legionella pneumophila linked to human illness was made in 1977 following a serious pneumonia outbreak at the American Legion Convention in Philadelphia, USA, 1976.More than 60 species of gram-negative, facultatively intracellular bacilli are known as legionellae. However, Legionella pneumophila, serogroup 1, is the etiological agent in the majority of clinical cases. Serogroups 1, 4, and 6 of legionellae are the ones that cause disease in humans, while there are more than 15 serogroups known to exist. Serogroup 1 is thought to be the causative agent of at least 80% of documented cases of L pneumophila pneumonia. Legionellae are normally found in freshwater habitats like lakes and streams, but they can also live in a variety of other environments and on host organisms including amoebae and protozoa.This intracellular bacterium enters the body through contaminated water, soil, or other environmental sources. Warm water, between 20 and 42 degrees Celsius, is what legionellae want since it promotes their growth and spread. Through the formation of biofilms and resistance to disinfectants, legionellae can adapt to artificially created water systems in buildings, including medical facilities. Ecological reservoir maintenance depends on parasitic relationships with protozoa and biofilm populations. By inhaling aerosolized polluted water droplets, humans can become infected from these contaminated reservoirs(18–23).

LEGIONNAIRES' DISEASE COMPLICATIONS

Awareness of increased vulnerability to Legionnaires disease is increased by education of risk factors for Legionella pneumophila pneumonia, such as underlying respiratory disorders, immunosuppression, and advanced age. Early detection and prompt medical intervention are made easier by educating the public and the medical team about the typical signs of Legionnaires disease, which include fever, coughing, and shortness of breath. Those exhibiting symptoms suggestive of pneumonia must get medical help as soon as possible, as this will lead to a rapid diagnosis and effective treatment. It is crucial to advise on safety measures to follow when utilizing public restrooms with water systems or lodging in motels, particularly for more vulnerable tourists.Numerous complications from Legionnaires disease might have a detrimental effect on the course of treatment. For patients to receive the best care possible, these problems must be identified and treated as soon as possible. Acute respiratory failure that frequently necessitates mechanical ventilation and supportive care, septic shock, multiorgan failure, acute renal injury, neurological abnormalities, endocarditis, and fatality are among the complications resulting from Legionnaires disease(24–27).

PATHOPHYSIOLOGY

By inhaling aerosolized contaminated soil or water or by aspirating contaminated water, legionellae can reach the lungs. The main way that humans are infected with this is by exposure to contaminated sources, and the risk of infection is determined by the length and intensity of exposure. Utilizing phagocytosis, legionellae infiltrate epithelial cells and alveolar macrophages. On the other hand, legionellae's Dot/Icm Type IV Secretion System (T4SS) introduces effector proteins into host cells, which prevent phagosome-lysosome fusion and promote bacterial growth. When the reproduction process runs out of nutrients, the host cells die, the bacterial flagellae release caspase-1, and the legionellae spread to infect additional cells.Innate and adaptive immunity play important roles in the complex immunological response to legionellae infection. The cellular damage caused by legionellae is further aggravated by the body's natural inflammatory reaction. Legionnaires disease susceptibility is influenced by the host's age, general health, and immune system. A particularly vulnerable subset consists of those over 50 and people of any age who smoke, have chronic lung illness, or are immunocompromised, including cancer patients and transplant recipients(28–31).

DIAGNOSIS

Clinically and radiographically, legionnaires disease may not be distinguished from other community-acquired pneumonia causes. Nonetheless, specific clinical indications, symptoms, and aberrant lab results raise the risk of legionellosis. These results include but are not limited to, high erythrocyte sedimentation rate or C-reactive protein, nausea, diarrhea, hyponatremia, and microscopic hematuria.Studies on Imaging: Unilateral or bilateral patchy or diffuse infiltrates are most frequently seen on chest radiography in patients with pneumophila pneumonia. To make the lung parenchyma easier to see if additional radiological investigations are needed, computed tomography of the chest is advised. Laboratory Studies: The use of immunochromatography for urine antigen testing is a common, fast diagnostic method that has a >85% sensitivity and >99% specificity for Legionella pneumophila. However, the assay that is now available only looks for L pneumophila serogroup 1.

The most reliable method for diagnosing legionellosis is sputum culture. It is possible to precisely identify a species, serogroup, and antibiotic susceptibility by sputum culture. Sputum collection can be difficult, though, and findings take a few days to become accessible. Patients receiving antibiotic medication already have a significant reduction in the sensitivity of their sputum culture. The exacting L pneumophila demands yeast extract agar with buffered charcoal for cultivation.DNA from legionellae can be extracted from a variety of materials using the polymerase chain reaction (PCR), including sputum, blood, urine, and tissue. In a matter of hours, PCR can yield highly specific and sensitive diagnostic results. Nevertheless, PCR is not broadly accessible, necessitates specialized knowledge and tools, and is unable to detect epidemiologic type or antibiotic susceptibility. Anti-legionellae antibodies, both acute and convalescent, are detected using serum serological testing. When testing convalescent-phase sera for acute infection, the microagglutination test is frequently used to confirm acute illness or offer a retrospective diagnosis.It can be difficult to diagnose Legionella pneumonia; therefore, attempts have been made to create clinical diagnostic criteria that are predictable and repeatable.Bilateral lung infiltrates with at least two of the following objective findings—respiratory rate > 30 breaths per minute, diastolic blood pressure < 60 mm Hg, and blood urea nitrogen ≥ 30 mg/dL—are indicative of severe L pneumophila pneumonia. In patients suspected of having legionellosis, Haubitz et al. used six diagnostic criteria: fever, cough, hyponatremia, raised lactate dehydrogenase, elevated C-reactive protein, and platelet count; the presence of less than two criteria had a 99% negative predictive value. Cunha et al. use six laboratory test results that are indicative of legionellosis, make the illness unlikely, and are typical and predictive of the illness. These include microscopic hematuria, hypophosphatemia, hyponatremia, high erythrocyte sedimentation rate of > 90 mm/h or C-reactive protein of >180 mg/L, serum ferritin twice the upper limit of normal, and creatinine phosphokinase twice the upper limit of normal(32–39).

LEGIONNAIRES' DISEASE IS MANAGED WITH MEDICINE.

Patients with legionnaires disease usually need to be hospitalized; the infection is often quite serious and has a high rate of complications and mortality. antibacterial therapy needs to target intracellular bacteria; macrolides and fluoroquinolones are the recommended antibacterial classes. Antimicrobial resistance, pharmaceutical availability, underlying medical disorders or allergies, and the severity of the infection all influence the course of antimicrobial therapy. Studies and certain recommendations point to the potential superiority of macrolides over fluoroquinolones. When a patient's condition improves, oral medications should be introduced to them; parenteral therapy is the recommended initial treatment option. Published treatment and clinical guidelines should be cited because they are regularly updated.When treating individuals with Legionnaires illness, supportive care is crucial. Patients who are experiencing hypoxemia or respiratory distress should pay special attention to oxygen therapy. For individuals with acute renal injury, hyponatremia, or severe sickness, fluid supplementation is essential. Corticosteroid therapy is a treatment option for patients with severe illness to enhance lung function and reduce inflammation in the lungs(40–46).

II. DISCUSSION AND CONCLUSION

An overview of legionnaires disease, including its different causes, epidemiology, and alternative therapies, is provided in the first section of our review articles. Our results show that antibacterial drugs are effective in treating. To treat Legionnaires disease, more randomized controlled trials are required. We plan to carry out an initial inquiry into Legionnaire's illness in the future. Future counseling-based research in our nation or state will evaluate patients' mental and physical well-being and generate more precise data on Legionnaires disease and its management, thanks to the help of our colleagues.

ETHICAL STATEMENT

A pharmacist should conduct themselves honestly and with integrity. A pharmacist refrains from actions that can jeopardize their dedication to acting in the best interests of their patients, such as biased acts or behaviours and unfavourable work circumstances that compromise their cognitive abilities. A pharmacist maintains their standing in the community.

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CONFLICT OF INTEREST

The authors attest that they are free of any known financial or personal conflicts of interest that would taint the findings of this study.

INFORMED CONSENT

Using websites, review articles, and other sources to produce research content.

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