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Review Article

Etiopathogenesis and Pharmacological Management of Legionnaires Disease

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Abstract

Legionnaires' disease is a severe form of atypical pneumonia caused primarily by Legionella pneumophila. The disease was first identified following a 1976 outbreak at an American Legion convention in Philadelphia. It is transmitted through inhalation of contaminated aerosols from water sources such as cooling towers, air-conditioning systems, hot water systems, and decorative fountains. The incubation period typically ranges from 2 to 10 days. Clinical manifestations include fever, cough, dyspnea, headache, gastrointestinal symptoms, and confusion, with severe cases leading to respiratory failure, septic shock, or multiorgan dysfunction. Diagnosis is primarily based on urinary antigen testing, culture, and polymerase chain reaction (PCR). Prompt treatment with macrolides or fluoroquinolones significantly reduces morbidity and mortality. Preventive strategies focus on proper maintenance and disinfection of water systems to control bacterial growth. Early diagnosis, appropriate antibiotic therapy, and effective public health measures are essential for reducing disease burden and preventing outbreaks.

Keywords: Legionnaires' disease, Clinical manifestations, Multiorgan dysfunction, Morbidity, Mortality.

INTRODUCTION

History [1]:

Legionella was discovered after an outbreak in 1976 among people who went to a Philadelphia convention of the American Legion. Those who were affected suffered from a type of pneumonia that eventually became known as Legionnaires' disease.

The deadly effects of legionella bacteria of course, the Legionella bacterium existed long before 1976. However, it was the outbreak in Philadelphia that led the illness associated with it to be called Legionnaires' disease after the American Legionnaires' it affected. Furthermore, the same bacterium was confirmed to be the cause of the illness, and of an earlier outbreak of Pontiac fever that had developed in 1968. That fever was so-called because it broke out in Pontiac. Legionnaires' disease was first discovered about in 1967.when a group of people in Philadelphia, attending an American Legion convention meeting were exposed to this disease. Those affected suffered from a type of pneumonia, now referred to as Legionnaires' disease.

The first identified cases of Pontiac fever occurred in 1968 in Pontiac, Michigan, among people who worked at and visited the city's health department. It wasn't until Legionella was discovered after the 1976.Legionnaires' disease outbreak in Philadelphia that public health officials were able to show that Legionella causes both diseases.

Obtaining a comprehensive medical and exposure history from any patient with a respiratory complaint is paramount. Inquiries into circumstances that increase the risk of exposure to Legionella pneumophila provide crucial epidemiological information; this includes foreign and domestic travel, hobbies, or contact with potentially contaminated water sources, such as air conditioning systems, cooling

towers, hot tubs, or decorative fountains. Certain occupations, such as construction, healthcare, or those in buildings with complex water systems, may confer an elevated risk. The medical history can also reveal risk factors for legionellosis, such as tobacco use, chronic lung disease, immunosuppression, exposure to sick contacts, or information about exposure during an outbreak.

The incubation period for L pneumophila is 2 to 10 days. Symptoms typical of legionellosis include fatigue, fever, cough, myalgias, headache, chest pain, and dyspnea; fatigue and fever may appear before the onset of cough. Although most clinical symptoms are similar to those in other types of pneumonia, particular symptoms, such as nausea, vomiting, and confusion, elevate the suspicion of legionellosis.

A comprehensive physical examination is required to identify the signs of pneumonia, such as fever, tachypnea, dry or productive cough, dyspnea, and rales. Hypotension, tachycardia, cyanosis, altered mental status, meningism's, and stigmata of endocarditis may be seen in patients with more severe respiratory cases or extrapulmonary infections. Legionnaires' disease is a serious type of pneumonia caused by Legionella bacteria. Certain people are at increased risk for this infection. Legionnaires' disease is treatable with antibiotics.

Name Origin:

The disease was named Legionnaires' disease after the Legion convention where it was first identified. The 1976 Philadelphia epidemic Legionnaires' disease was first recognized as a distinct entity during an epidemic of pneumonia that occurred in Philadelphia, in the July1976. About 4,000 members of the Pennsylvania State American Legion, an organization of former military veterans, met in July for American Bicentennial celebration, which lasted from 21 - 24 July.on 27th July, one of the legionnaires died of a pneumonia like illness.On 30th July a physician in Bloomsburg, realized that the 3 patients he was treating from similar condition had all attended the convention on the same day, a nurse in Chambersburg Hospital noted a similar condition in 3 patients who had gone to the convention. By Aug 2nd it was realized that there was some undeniable connection. By August18 legionnaires had already died, it attracted huge media coverage.

Out of the 221 cases 72 were people who were not involved in the American Legion convention people who had either been inside the Bellevue Stratford Hotel, or had walked past it.

On January 18, 1977 CDC (Centers for Disease Control and Prevention) announced that the cause of Legionnaire's disease was isolated.

The source of the breeding site of the organism traced to the cooling towers that were connected to the air conditioners of the hotel.

Class: Legionnaires Disease.

Definition: [**2,3]**

Legionnaires' disease and Pontiac Fever are collectively known as Legionellosis, a disease caused by Legionella bacteria. Legionnaires' disease is a serious, potentially deadly, lung infection (i.e., pneumonia); and Pontiac Fever is a less serious infection with milder symptoms similar to the flu (i.e., seasonal influenza). Although Legionella are usually harmless and found naturally in water and soil, it becomes a potentially deadly human health hazard when it grows in places such as poorly maintained domestic and industrial water systems; cooling towers; or heating, ventilation, and air condition (HVAC) systems. Legionnaires' Disease is a severe form of pneumonia (lung infection) caused by a bacterium, known as Legionella. It can occur through inhalation of contaminated aerosols such as humidifiers, hot and cold-water systems, air conditioning cooling towers and whirlpool spas. Infection can also occur by exposure of babies during water births or aspiration of contaminated ice or water, particularly in susceptible hospital patients. It can be a cause of community acquired pneumonia or hospital acquired pneumonia. This disease is often screened for whenever a person is diagnosed with pneumonia because of the close resemblance Legionnaires has to pneumonia.

A pneumonia outbreak occurred during the 58th Annual Convention of the American Legion held in Philadelphia in 1976 and in 1977, Legionella pneumophila was identified as the cause, and Legionella pneumophila pneumonia was coined Legionnaires disease. The aquatic L pneumophila was aerosolized from the water in the air conditioning system and inhaled by the convention goers. Affected patients developed syndromes ranging from a flu-like illness to multisystem organ failure; 29 of the affected 182 patients died.

Legionnaires disease is an atypical pneumonia frequently clinically different from other bacterial pneumonia. The predominant symptoms of Legionnaires disease include fever, cough, dyspnoea, headache, and fatigue. The incubation period of L pneumophila ranges from 2 to 10 days following exposure to contaminated water. Radiographic findings of L pneumophila pneumonia will vary but are frequently described as patchy, fluffy, and unilobar infiltrates with a propensity to consolidate. Purulent sputum, pleuritic chest pain, and pleural effusion are less frequently encountered with L pneumophila pneumonia than other causes of bacterial pneumonia. Although Legionnaires disease may not differ from other types of community-acquired pneumonia, certain symptoms such as diarrhoea and confusion increase the index of suspicion for legionellosis. Laboratory abnormalities such as

hyponatremia, evidence of acute kidney injury, and elevations of transaminases, erythrocyte sedimentation rate, or C-reactive protein (CRP) may be indicative of legionellosis. The diagnosis of legionellosis is based on clinical features, laboratory tests, and imaging studies. Treatment of Legionnaires disease comprises antibiotics effective against intracellular bacteria such as fluoroquinolones, macrolides, or tetracyclines.

Legionnaires disease remains a critical public health concern due to its potential for outbreaks, high mortality rates in untreated cases, and the challenges associated with diagnosis and control. A comprehensive analysis of the genomic architecture and virulence determinants of L pneumophila illuminates the intricate mechanisms underlying its ability to establish intracellular infections within alveolar macrophages. Ongoing research seeks to elucidate the complex interactions between legionellae, their environmental niches, and human susceptibility factors, aiming to develop more effective preventive strategies and therapeutics. The prevention of Legionnaires disease requires proper maintenance and disinfection of water systems to reduce the risk of bacterial growth and exposure

Classification: **[4,5]**

Legionella most commonly causes one of two diseases:

1) Legionnaires' disease
2) Pontiac fever

1. Legionnaires Disease:

- Incubation period is usually 2-10 days (average 6-7 days)
- During a prodromal period of 1-2 days, patients may experience mild headache and myalgia, followed by high fever, chills, rigors, and a cough.
- About 90% of patients affected present with a dry cough at first that may progress to being productive, green, or bloodstained sputum.
- About one-third of patients have dyspnea, pleuritic chest pain, and haemoptysis.
- About one-third of patients experience nausea, vomiting, diarrhoea, and anorexia.
- Altered mental status, seizures, confusion, impaired cognition and ataxia
- Bradycardia.

2. Pontiac fever:

- Incubation period is 1-2 days
- Influenza-like illness with myalgia, fever, and headache
- About 50% of patients have a cough
- Pyrexia and tachypnea
- Patients look "sickly"
- Pericarditis, hepatomegaly, and impaired mental state are rare

Structure: **[6,7]**

Legionella pneumophila is a Gram-negative bacterium with a unique outer membrane containing lipoproteins, phospholipids, and other proteins. It is characterized by a single polar flagellum, which allows for motility. The bacterium is typically rod-shaped but can adopt filamentous or cocci-like forms under different conditions. It also possesses pili (fimbriae).

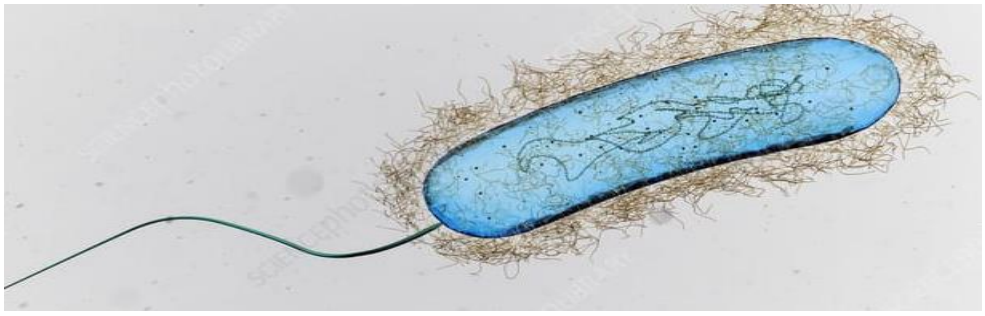

Figure 1: Legionella Bacterium

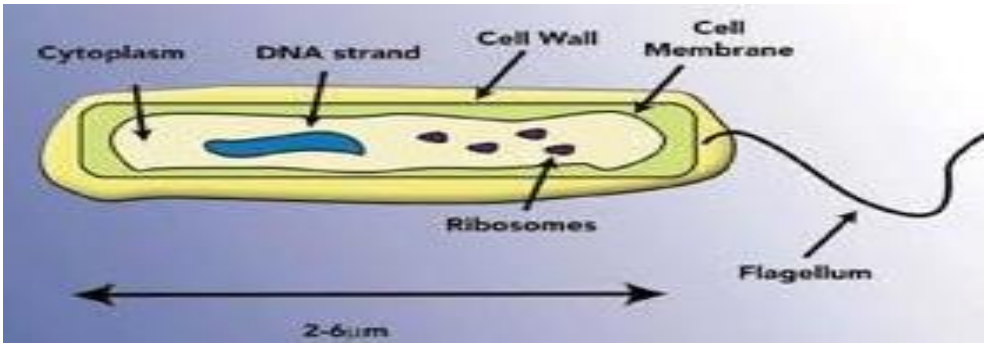

Figure 2: Diagram of bacterium

The Detailed Structure will includes:

- **Gram-Negative Cell Envelope:** Like all Gram-negative bacteria, L. pneumophila has an inner and outer membrane, separated by the periplasmic space.
- **Outer Membrane:** The outer membrane is a distinguishing feature, containing unique lipopolysaccharides (LPS) that play a role in pathogenicity and adhesion to host cells.
- **Flagellum:** The flagellum is crucial for motility and is composed of a basal body (flagellar motor) and an extracellular axial structure.
- **Pili (Fimbriae):** These surface appendages are involved in attachment and adhesion to host cells or surfaces.
- **Pleomorphic:** L. pneumophila can exhibit a range of shapes, including rod-like, filamentous, and cocci-like forms, depending on environmental conditions.

Key Features will include:

- **Lipopolysaccharides (LPS):** LPS on the outer membrane are a major surface antigen and play a role in virulence and host cell interaction.
- **Type II Secretion System (T2SS):** L. pneumophila utilizes the T2SS to secrete various proteins, including those involved in pathogenesis.
- **Dot Type IV Secretion System:** This system delivers effector proteins into host cells, subverting host cellular processes.
- **Biofilms:** Pneumophila can form biofilms, which are microbial communities that can protect the bacteria and facilitate the transfer of genetic material.

Taxonomial Classification of Legionella Bacteria: [8]
Kingdom: Bacteria
Phylum: Pseudomonad Ota (formerly Proteobacteria)
Class: Gammaproteobacteria
Order: Legionellales
Family: Legionellaceae
Genus: Legionella

Mode of Transmission: [9,10,11]

Legionella bacteria are found in various environmental settings and grow well in warm water (20 to 45°C). They can be found in aqueous environments such as water tanks, hot and cold-water systems, cooling towers, whirlpool spas, water fountains, humidifiers and home apparatus that support breathing.

People may get infected when they breathe in contaminated droplets (aerosols) and mist generated by artificial water systems. They may also get the infection when handling garden soil, compost and potting mixes. In general, the disease is not transmitted by person-to-person contact, eating or drinking.

Incubation period-About 2 to 10 days.
Inhaling Aerosols: The most common way to get Legionnaires' disease is by breathing in tiny, contaminated water droplets or mist from sources like:

- Air conditioning cooling towers
- Hot and cold-water systems
- Humidifiers
- Whirlpool spas
- Showers
- Fountains
- Decorative water features
- Misting systems, especially in grocery stores
- Ice-making machines

Aspiration:

In rare cases, Legionnaires' disease can be acquired by inhaling (aspirating) contaminated water or fluids into the lungs, which can occur with:

Babies during water births

Susceptible hospital patients, particularly when aspirating contaminated ice or water During medical procedures involving water.

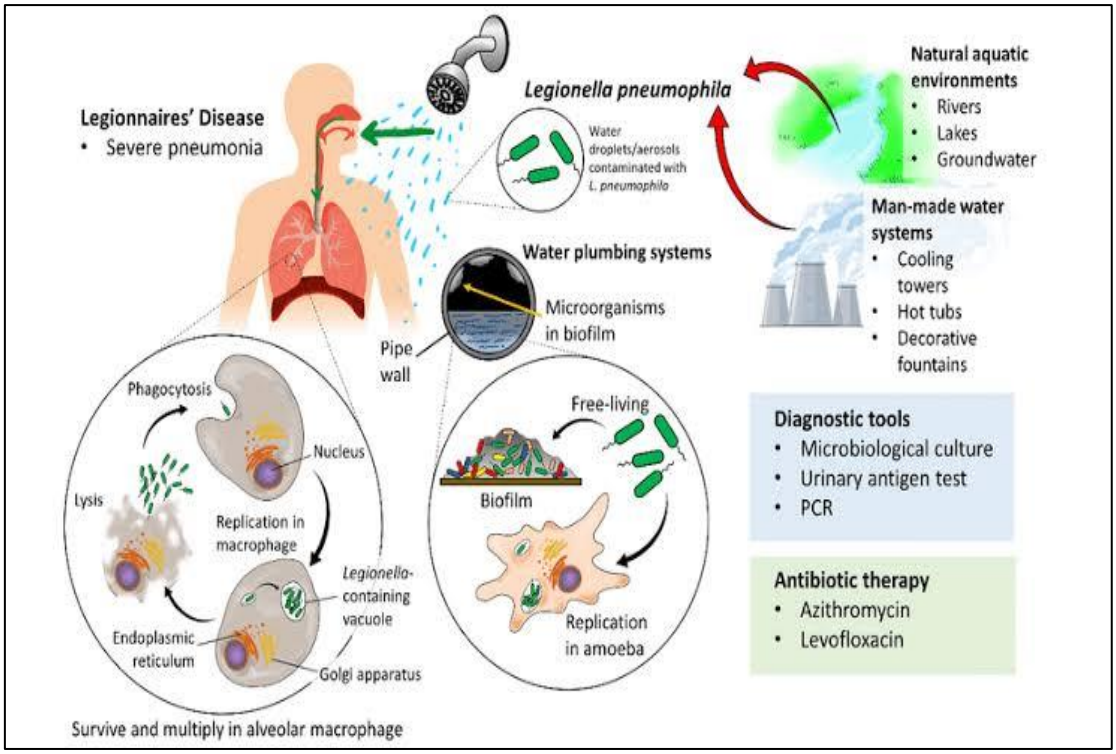

Figure 3: The transmission sources, life cycle within water systems and human macrophage, the diagnostic tools and antibiotic treatment for Legionella pneumonia.

An infected source (e.g. a fountain) can disseminate sprays or droplets of water containing legionellae, commonly referred to as aerosols. When this occurs, most or all of the water in the droplet evaporates quickly, leaving airborne particulate matter that is small enough to be inhaled. Particles of less than 5 µm in diameter can be deeply inhaled, and enter the respiratory airways to cause legionellosis.

Legionella infections have frequently been associated with sources at distances of up to 3.2 kilometres recent evidence suggests that infection may be possible at even longer Distances. There is evidence that virulence is an important factor in the survival of Legionella in aerosols, with the most virulent strains surviving longer than their less virulent counterparts.

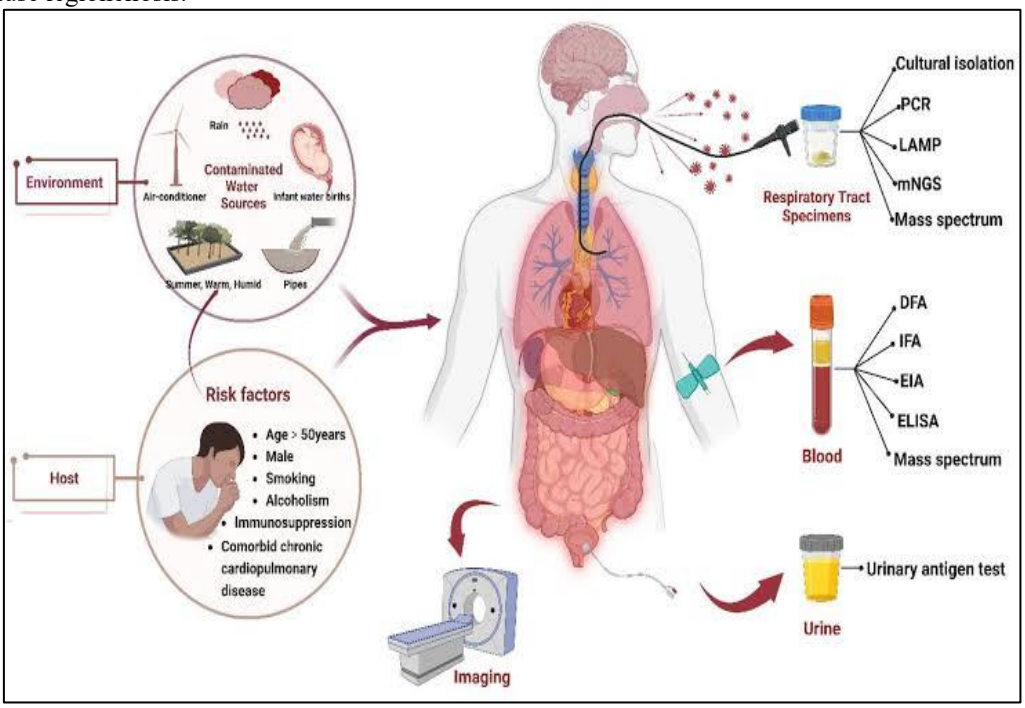

Figure 4: The various pathogenetic detection methods available for Legionella pneumonia

Etiology:[19]

The pathogen causing Legionnaires' Disease came from the Legionellaceae family of bacteria. Although the family Legionellaceae now contains more than 40 species. Legionella pneumophila causes over 90% of human infections. L micdadei, the second most frequently isolated species in human infection, evidently has lower virulence for humans than Legionella pneumophila as it appears to infect only immunocompromised hosts. Water is the major natural reservoir for Legionella, and the pathogen is found in many different natural and artificial aquatic environments such as cooling towers or water systems in buildings, including hospitals.

Common places that allow Legionella transmission:

1. Potable (drinking) water systems
2. Whirlpool spas
3. Cooling towers

Conditions for Legionella transmission:

1. Heat
2. Stasis
3. Aerosolization

Legionellae are diverse, gram-negative, facultatively intracellular bacilli; more than 60 species have been identified. However, the etiological agent of most clinical cases is Legionella pneumophila, serogroup 1. While more than 15 serogroups of legionellae have been identified, serogroups 1, 4, and 6 are the cause of human disease; serogroup 1 appears to be the etiologic agent of at least 80% of reported cases of L pneumophila pneumonia. Legionellae are found naturally in freshwater environments like lakes and streams but can survive in various environmental conditions and host organisms such as protozoa and amoebae. This intracellular bacterium is acquired from infected environmental sources, soil, or water. Legionellae prefer warm water, between 20 °C and 42 °C; this temperature range facilitates their growth and transmission. Legionellae can adapt to human-made water systems in buildings, including healthcare institutions, by forming biofilms and resisting disinfectants. Biofilm communities and a parasitic relationship with protozoa are critical to maintaining ecological reservoirs. These contaminated reservoirs are a source of human infection via inhalation of aerosolized contaminated water droplets.

Risk Factors: [12,13,14]

1. Most healthy people exposed to Legionella don't get sick.
2. People at increased risk of getting sick include:
   - Current or former smokers
   - People 50 years or older
   - People with specific health issues or conditions
3. Not everyone who comes in contact with legionella bacteria gets sick.
4. Smoke: Smoking damages the lungs. This makes the risk of getting all types of lung infections higher.
5. Have a weakened immune system:

This can be a result of HIV/AIDS or certain medicines. This includes steroids and medicines taken after a transplant to keep the body from rejecting the organ.

Have ongoing disease like:

- Chronic lung disease or other serious conditions.
- This includes emphysema,
- Diabetes.
- Kidney disease or cancer.
- Are 50 years of age or older.

A detailed standardized questionnaire was developed to evaluate risk factors possibly associated with colonization.

1. The first part collected information on family characteristics (number of components, age and sex, length of stay in residence) and on pneumonia events during their stay in the home.
2. The second part was devoted to home data: Type (flat, single house, villa), flats in the building, home floor, home rooms and bathrooms, building age, type of water supply, and disinfection systems used.
3. The third part collected information on the heating system (central or independent, electric or gas heater), distance of the sample site from the water distribution point, existence of a tank and its volume, age of the system, service frequency, and existence and characteristics of a softening and water recycling systems. Water operating temperature (temperature at the distribution site) was also recorded.

Legionnaires' disease can be a problem in hospitals and nursing homes. Those are places where germs spread easily, and people there are at high risk of infection.

Not everybody who comes into contact with the legionella bacteria gets sick. You have a higher chance of getting the infection if you:

Smoke: Smoking affects the lungs, increasing your risk for developing any kind of lung infection.

Compromised Immune System: Have a compromised immune system - HIV/AIDS, as well as several medications, particularly corticosteroids and those used to prevent organ rejection following a transplant can reduce your immunity and thus increase the chances of infection.

Major illness: Have a major illness, such as chronic lung disease. Emphysema, diabetes, kidney illness, and cancer are examples.

Are at least 50 years old: In hospitals and nursing homes, where germs can spread quickly and residents are more prone to illness, legionnaires' disease can be a problem. Risk factors for hospital-acquired pneumonia are recent surgery, intubation (the process of placing a tube in the trachea), mechanical ventilation, aspiration, presence of nasogastric tubes, and the use of respiratory therapy equipment. The most susceptible hosts are immuno-compromised patients, including organ transplant recipients and cancer patients and those receiving corticosteroid treatment.

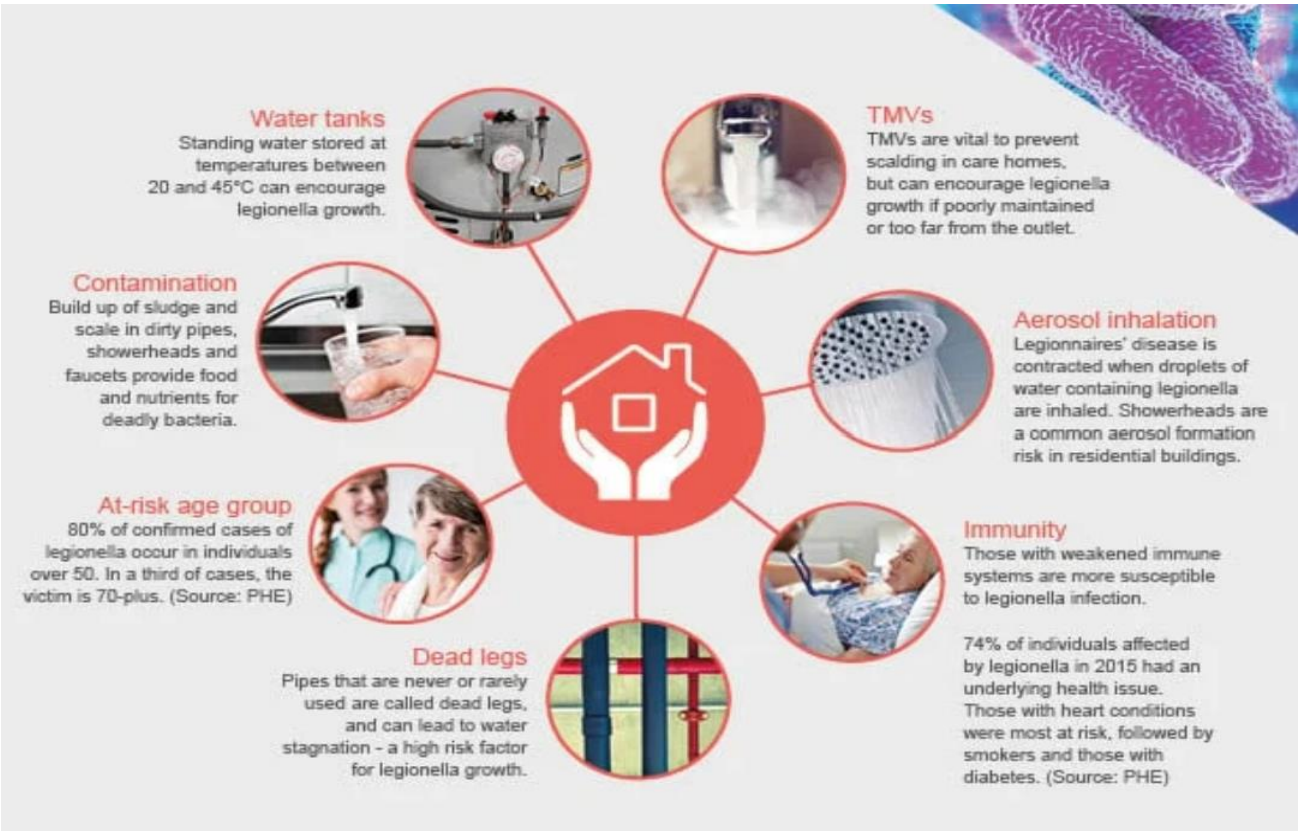

Figure 5: Seven risk factors for legionella in care home

Figure 6: Associated risks in legionnaires disease

Pathophysiology: [15]

Legionella species are obligate or facultative intracellular parasites. Water is the major environmental reservoir for Legionella; the bacteria can infect and replicate with in protozoa

such as Acanthamoeba and Hartmannella, which are free-living amoebae found in natural and manufactured water systems.

Within the amoebic cells, Legionella species can avoid the endosomal-lysosomal pathway and can replicate within the phagosome. Surviving and growing in amoebic cells allows Legionella to persist in nature. This electron micrograph depicts an amoeba, Hartmannella vermiform is (orange), as it entraps a Legionella pneumophila bacterium (green) with an extended pseudopod. After it is ingested, the bacterium

can survive as a symbiont within what then becomes its protozoan host. The amoeba then becomes a so-called "Trojan horse," since, by harbouring the pathogenic bacterium, the amoeba can afford it protection. In fact, in times of adverse environmental conditions, the amoeba can metamorphose into a cystic stage, enabling it, and its symbiotic resident, to withstand the environmental stress. Image courtesy of the Centers for Disease Control and Prevention and Dr. Barry S Fields.

Legionella species infect human macrophages and monocytes; intracellular replication of the bacterium is observed within these cells in the alveoli. The intracellular infections of protozoa and macrophages have many similarities.

Activated T cells produce lymphokines that stimulate increased antimicrobial activity of macrophages. This cell-mediated activation is key to halting the intracellular growth of legionellae. The significant role of cellular immunity explains why legionellae are observed more frequently in immunocompromised patients. Humoral immunity is thought to play a secondary role in the host response to Legionella infection.

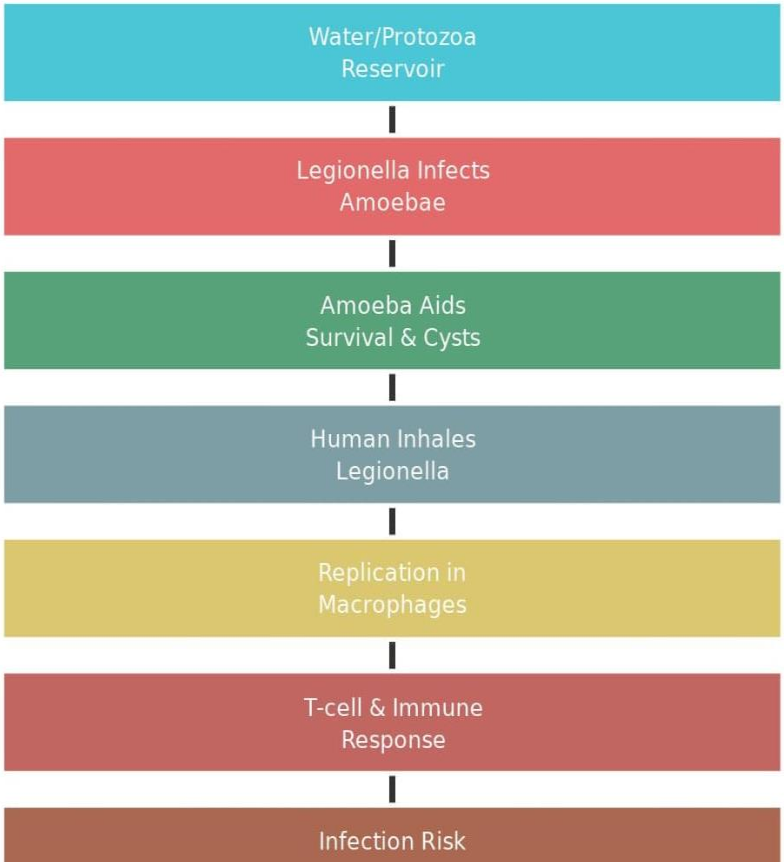

Figure 7: Pathophysiological flow chart of Legionella

Epidemiology: [16]

Legionella species (spp) are Gram-negative bacteria with strict growth requirements, given that between three and 5 days of incubation are required for its colonies to be detectable. Historically, this pathogen has presented a major diagnostic challenge. In humans it has the ability to cause a severe pneumonia, a non-pneumonic disease (generally benign) called Pontiac fever, and extrapulmonary legionellosis. The clinical and radiological presentation of LD is non-specific and can mimic other types of pneumonia. This review focuses on severe LD, although severe extrapulmonary forms of Legionella infection may also occur, particularly in immunocompromised patients.

Legionella species are located in aquatic habitats, soil, and water distribution systems. They have the ability to survive intracellularly in various protozoans and to proliferate within biofilms which provide additional protection from the environment. More than 65 species of Legionella have been recorded, but not all of them are equally responsible for infectious disease. Legionella pneumophila (Lp) is the most frequent cause of disease, which account for 80–90% of cases in Europe and in the US. In Australia and New Zealand, the predominant species is L. longbeachae which accounts for up to 51% of causative agents for LD, while Lp represents 31%. This heterogeneous distribution may be attributed to several factors: for example, in New Zealand there is a more systematic use of Legionella

screening by Polymerase Chain Reaction (PCR), and clusters of L.longbeachae infections are seen in early spring–summer and might be linked to increased outdoor activity, such as gardening in the warmer months. However, the exact reason for its predominance remains unknown as L. longbeachae strains display a high genetic diversity, probably indicating the presence of multiple sources of infection.

Human infection occurs due to the inhalation or aspiration of aerosols containing the pathogen. After inhalation, Legionella invades lung alveolar macrophages, inhibiting their bactericidal activity and turning them into a niche for its replication, in a similar way to the mechanisms that it uses to survive with in its protozoan hosts. With the exception of a single documented case, human-to-human transmission does not occur.

The main sources of contamination are water network systems, spas and cooling towers. Interestingly, L. longbeachae disease has been associated with gardening and the use of potting soil, commercial bagged soil, and compost materials containing this bacterium, and L. Anisa with dental practices. Risk factor analysis reveals that temperatures > 20 ℃ are a significant risk factor for Legionella colonisation in dental chair equipment. Water-bearing instruments and therapy in dental chair units requiring water-lines generate aerosols which may lead to an infection risk among dental staff and patients. Biofilms in contaminated pipes may generate infection in dialysis units or in hospitalised patients. Regular monitoring of the water quality to identify the presence of significant Legionella loads and the application of routine disinfection procedures are recommended to minimise the risk of infection. Furthermore, the maintenance of a minimum temperature for hot water (storage water > 60 ℃, distribution water > 50 ℃) and a maximum temperature for cold water < 20 ℃ is necessary to prevent the multiplication of Legionella inside a water network. Episodes of LD must be notified to the public health authorities to identify the source of contamination.

The proportion of Legionella pneumophila among the causative agents of community-acquired pneumonia (CAP) was estimated to be 4.6% in a recent meta-analysis, and nearly twice this figure in patients admitted to the Intensive Care Unit (ICU). Historically, it has been reported to be one of the three most common causes of severe CAP requiring ICU admission, although advances in prevention, early detection and early appropriate therapy have reduced its incidence as a cause of ICU admission over the last decade. LD may be a cause of severe hospital-acquired pneumonia but there is no evidence to suggest a role in aspiration pneumonia. In temperate climates, most LD cases occur from late spring to early autumn, but in tropical regions they may be recorded throughout the year. A general increase in incidence has been observed in Europe, the US, Canada and Australia in recent years. The reasons for this worldwide increase are not totally elucidated, but it is most pronounced in older age groups (> 60 years) and with a general accentuation of seasonal trends, without any systematic changes in the methods used for its diagnosis in Europe. Many studies have found that increased precipitation, temperature, and relative humidity are positively associated with the occurrence of LD, particularly a sequence of elevated temperatures followed by a period of increased precipitation, high relative humidity, and low wind. The intensification of extreme meteorological events due to climate change (for instance, high temperature variations and heavy rainfall), may create conditions for the development of Legionella and increase the incidence of LD.

Clinical Signs and Symptoms: [12]

Legionnaires' disease symptoms usually develop 2 to 14 days after exposure to Legionella bacteria, but it can take longer. The symptoms of Legionnaires' disease are similar to other types of pneumonia.

Symptoms include:

- Cough
- Fever
- Headaches
- Chest pain
- Muscle aches
- Shortness of breath
- Confusion or other mental charges
- Stomach (abdominal) pain
- Other symptoms, such as diarrhoea, or nausea can also occur
- The initial symptoms of Legionnaires' disease are similar to those of flu: high temperature, feverishness and chills
- It can also lead on to more serious symptoms such as:
- Pneumonia, diarrhoea

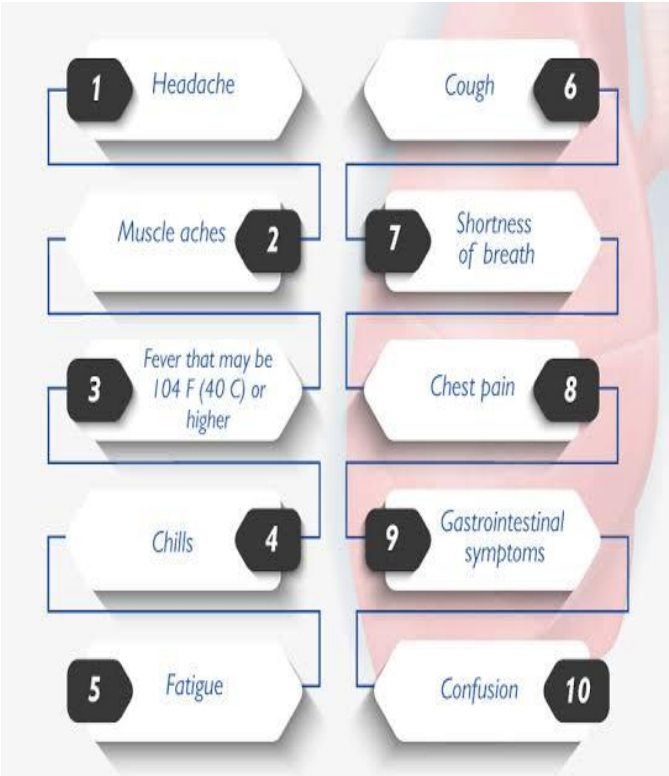

Figure 8: Ten Signs and Symptoms

Figure 9: Signs and symptoms

Clinical Complications: [12,18,19]

The complications of Legionnaires disease are diverse and negatively impact patient outcomes. Recognizing and managing these complications early and appropriately are essential to optimal patient care. Complications from Legionnaires disease include

- Acute respiratory failure frequently requiring mechanical ventilation and supportive care.
- Septic shock.
- Multiorgan failure.
- Acute kidney injury.
- Neurological defects.
- Endocarditis.
- Death.

Lung failure: This occurs when the lungs can't provide the body with enough oxygen or can't remove enough carbon dioxide from the blood.

Septic shock: This occurs when a severe, sudden drop in blood pressure reduces blood flow to vital organs, most often the kidneys and brain. As a result, the heart tries to pump harder. But the extra work weakens the heart and reduces blood flow even more.

Acute kidney failure: This is the kidneys not being able to filter waste from the blood. Acute kidney failure occurs all of a sudden. When kidneys fail, unsafe levels of fluid and waste build up in the body.

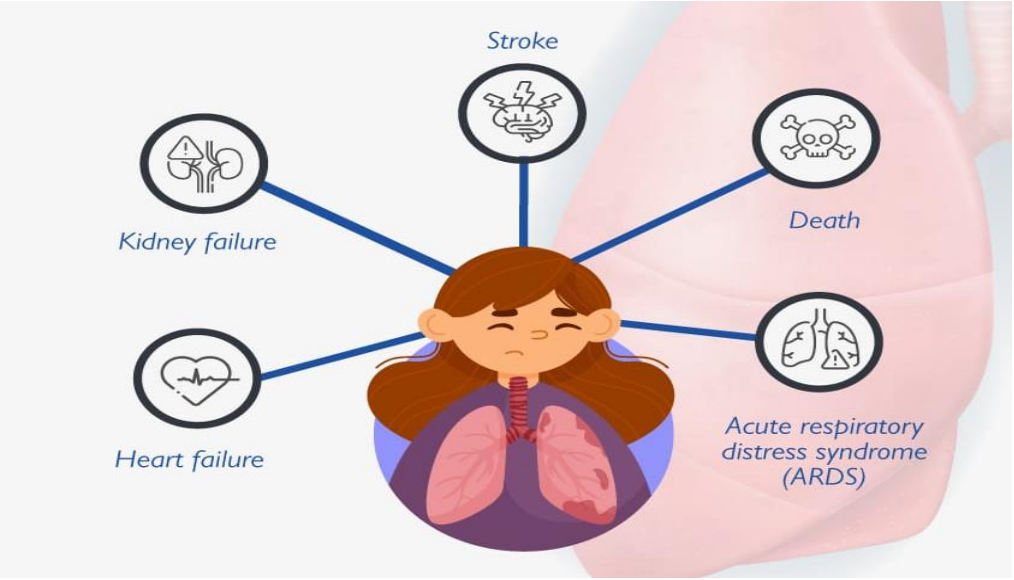

Figure 10: Clinical complication

Diagnosis: [20,21]

The diagnosis of legionellosis is based on a combination of the presence of clinical and/or radiological symptoms and laboratory tests. These tests are not routinely performed by the clinical microbiology laboratory and therefore must be specifically requested. According to a 2019 European Centre for Disease Prevention and Control (ECDC) report, most cases in Europe (90%) are diagnosed using the urine antigen test (UAT) method. This has been a consistent finding over the past decade. Polymerase chain reaction (PCR) detects 9% of the total number of reported cases, and the proportion of cases diagnosed or confirmed by culture is 10%. The species L. pneumophila alone is responsible for more than 90% of cases of Legionnaires' disease diagnosed worldwide. In Europe, most human cases (80%) are caused solely by L. pneumophila serogroup 1 , with other serogroups and species accounting for 16% and 3% of infections, respectively. In Australia and New Zealand, L. longbeachae is the predominant species and in 2019 accounted for up to 60% of the reported cases.

Test	Characteristics
Culture	Gold standard, detects most species, can be used for antibiotic sensitivity testing and for epidemiological analyses; variable sensitivity. Demanding test requiring expertise and growth for several days on complex media; depends on the availability of respiratory samples.
Urinary antigen test	The first-line diagnostic test, point-of-care format. Low cost, quick and uncomplicated procedure; urine samples are easily obtained. Only detects antigens of *L. pneumophila*, sensitivity nearly 75% but high positive predictive value.
Nucleic acid-based detection	Detects all known species; good specificity and sensitivity (nearly 90%), microbial identification and epidemiological studies.

Sputum culture (induced specimen preferred)	Often difficult to collect as cough frequently non-productive
PCR (broncho alveolar lavage (BAL) or induced sputum specimens	PCR may still be positive after sputum culture becomes negative

TREATMENT:

❖ **Preventive Measures: [22]**

Hospitals across the country frequently test water supplies. Proper decontamination of the water supply is recommended. This is by heating water to 70 C to 80 C, with flushing of distal sites. As well as using UV light to kill legionellae. Copper-silver ionization units are effective at preventing legionellae, providing protection. Hyperchlorination of water is not effective because legionellae are chlorine resistant, and chlorine decomposes at the higher temperatures. To prevent Legionella growth in water systems is ideal to prevent infection. In order to do this, timely identification and reporting of cases allow public health officials to act accordingly. This allows source of infection to be identified and this prevents outbreaks, by linking it to the cause.

Surgery:

1. General Principle:

Legionnaires' disease is an infectious pneumonia caused by Legionella pneumophila.
Standard treatment = antibiotics + supportive care.
Surgery is NOT a routine therapy for Legionnaires' disease.

2. When Surgery Might Be Considered: (rare, complications only)

Surgical intervention is not for the infection itself, but for complications of severe pneumonia such as:

- ✓ Lung abscess → may require surgical drainage or resection if it does not respond to antibiotics.
- ✓ Empyema (pus in pleural cavity) → may need chest tube drainage, VATS (Video-assisted thoracoscopic surgery), or open decortication.
- ✓ Massive necrotizing pneumonia → in very rare cases, lobectomy or segmental resection may be needed.
- ✓ Respiratory failure complications → tracheostomy (airway surgery) may be done for prolonged ventilatory support.

❖ **Pharmacological: [23]**

1. Background:

Legionnaires' disease is a severe pneumonia caused mainly by Legionella pneumophila.

It requires prompt antibiotic therapy because untreated cases can have high mortality.

2. First-line Therapy:

- ➢ Macrolides (preferred in many cases)
- ➢ Azithromycin (IV or oral) → widely used, especially in children and pregnant women
- ➢ Clarithromycin (less common)
- ➢ Fluoroquinolones, Levofloxacin (IV or oral) → highly effective, often first choice in adults, Moxifloxacin, Ciprofloxacin (alternatives)

3. Alternative / Adjunct Therapy:

- ➢ Doxycycline (a tetracycline) → alternative if macrolides or fluoroquinolones cannot be used.
- ➢ Rifampicin (Rifampin) → occasionally combined with fluoroquinolones or macrolides in severe/complicated cases (not routine).

4. General Pharmacological Notes:

Duration: Usually 7–10 days for mild disease; 10–14 days (sometimes longer) in immunocompromised or severe cases.
Route: IV for hospitalized/severe cases, then switch to oral.

Supportive pharmacological therapy:

- ➢ Antipyretics (paracetamol for fever)
- ➢ Oxygen therapy and IV fluids (not pharmacological but supportive)

❖ **Non-Pharmacological Therapy: [22]**

- ➢ Oxygen Therapy
- ➢ To treat hypoxemia caused by pneumonia and lung inflammation
- ➢ Maintains adequate oxygen levels; reduces respiratory distress
- ➢ Mechanical Ventilation
- ➢ For patients with respiratory failure acute respiratory distress syndrome (ARDS) Supports gas exchange and allows lung rest; used in ICU Mandell *et al.,* Principles and Practice of Infectious Diseases
- ➢ Hydration Therapy (IV/Oral) Prevent/treat dehydration due to fever and poor intake
- ➢ Maintains fluid balance, helps kidney function and supports recovery

❖ **Management Strategies: [12,24]**

Stage 1: Incubation Period (2–10 days)
Symptoms: None (asymptomatic)
Management: No treatment required.
Prevention is key: Monitor at-risk environments (cooling towers, hot tubs).
Ensure water systems are chlorinated and maintained.

Stage 2: Early Illness (Days 1–3 of symptoms)
Symptoms: Fever, fatigue, muscle aches, headache, dry cough, Mild Respiratory Issues.
Management: Begin empiric antibiotic therapy: Macrolides (e.g., azithromycin) or fluoroquinolones (e.g., levofloxacin) Supportive care (hydration, rest, fever management)

Diagnostic testing: Urinary antigen test, sputum culture, chest X-ray.

Stage 3: Progressive Illness (Days 4–7)
Symptoms: Worsening cough, shortness of breath**,** High fever, confusion, gastrointestinal symptoms (diarrhea, nausea), Hypoxia or abnormal chest X-ray.

Management:
Hospitalization often required
IV antibiotics (e.g., levofloxacin IV or azithromycin IV)
Oxygen therapy or mechanical ventilation if respiratory failure occurs
IV fluids and electrolyte correction
Monitor renal function (due to risk of acute kidney injury).
Stage 4: Recovery Phase (2–4 weeks or longer)
Symptoms:
Gradual resolution of fever, cough, and fatigue
Persistent weakness and breathlessness
Management:
Complete full 10–14 days of antibiotics (longer if immunocompromised)
Pulmonary rehabilitation for severe lung involvement
Chest physiotherapy, good nutrition, hydration
Follow-up chest X-ray at 6–8 weeks to ensure resolution.

Stage 5: Complicated/Severe Disease (ICU patients)
Possible complications:
Septic shock, respiratory failure, renal failure, myocarditis
Multi-organ dysfunction
Management:
ICU admission
Broad-spectrum antibiotics until Legionella confirmed
Mechanical ventilation, vasopressors, dialysis if needed
Infection control team to trace source and prevent outbreaks.

❖ **Alternative Treatments:[25]**
1. Pharmacological Alternatives :(when first-line cannot be used)
First-line = Fluoroquinolones (Levofloxacin) or Macrolides (Azithromycin).

- Alternatives if patient cannot tolerate or has contraindications:
  - Doxycycline (Tetracycline class) – effective against Legionella.
  - Rifampicin – sometimes used in combination for severe or refractory cases (not monotherapy).
  - Moxifloxacin / Ciprofloxacin – other fluoroquinolones if levofloxacin not suitable.

2. Non-Pharmacological / Supportive Alternatives:

- Oxygen therapy – for hypoxemia.
- Mechanical ventilation or ECMO (extracorporeal membrane oxygenation) – for respiratory failure.
- IV fluids & electrolyte balance – Legionnaires' often causes hyponatremia.
- Corticosteroids (under research, not routine) – some studies suggest benefit in severe pneumonia, but not yet standard.

3. Investigational / Adjunct Therapies Immunotherapy:

- No approved immunotherapy yet, but monoclonal antibodies and immune-modulating therapies are being studied.
- Probiotics / microbiome modulation: Still experimental, not standard of care Vaccines
- No licensed vaccine exists for Legionella, though several are in pre-clinical development.

4. Lifestyle / Preventive Alternatives:
No herbal or home remedies cure Legionnaires' disease.

❖ **Alternative approaches are mostly preventive:**

1. Regular cleaning of cooling towers, hot water systems, and hospital water systems.
2. Avoiding stagnant water and contaminated aerosols.

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