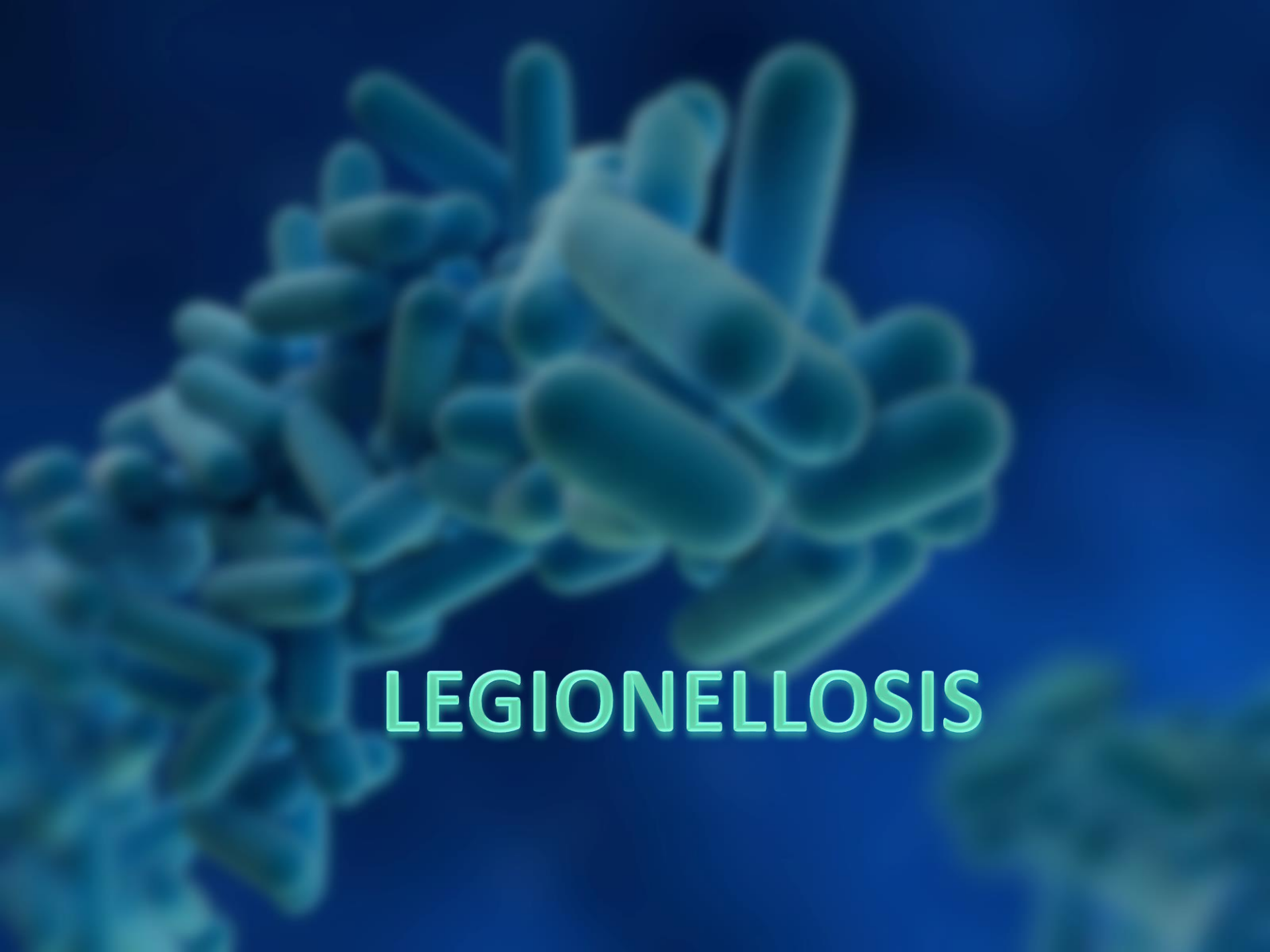

LEGIONELLOSIS


LEGIONELLOSIS
(LEGIONNAIRES DISEASE)

Disease definition

Legionellosis

"Legionnaires' disease";
other names - Pittsburgh pneumonia,
Pontiac fever,
Legionella infection,
Fort Bragg fever)

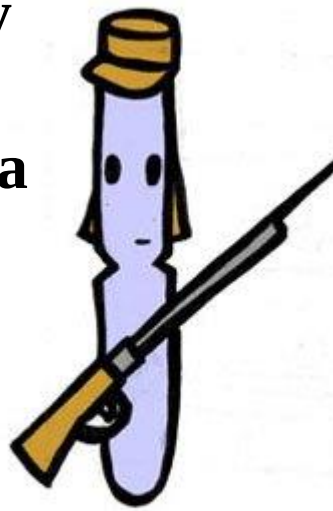
is an acute sapronous infectious disease caused by various types of microorganisms belonging to the genus Legionella.
The disease proceeds, as a rule, with severe fever, general intoxication, damage to the lungs, central nervous system, digestive organs, possibly the development of multiple organ failure syndrome.

Legionellosis or Legionnaires' disease (LD) is a bacterial lung infection characterized by a potentially fatal pneumonia.

The name of the disease is associated with the 1976 outbreak in Philadelphia of a severe respiratory illness, which proceeded as a pneumonia. In July 1976, over 4,000 members of the American Legion Convention gathered in Philadelphia, Pennsylvania, USA. It was the 49th annual convention of the organization. After the congress had ended safely, the participants, along with their families, went home. Three days after the end of the event, namely on July 27, 1976, one of the participants died suddenly from an illness similar to pneumonia.

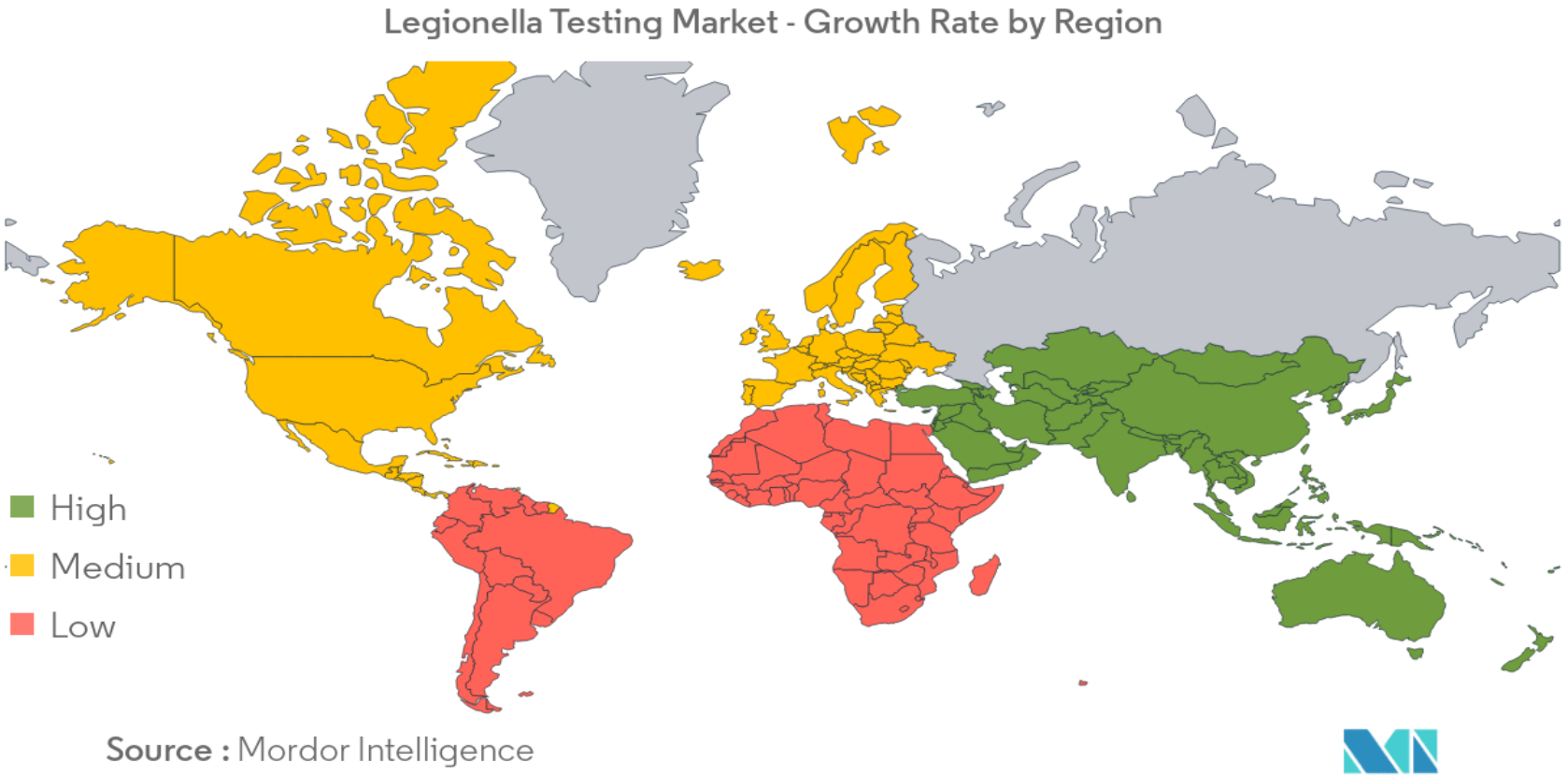
August 2, 1976. By this time, 18 legionnaires had already died. Proved that massive morbidity at the convention of the American Legion is not the first case of pneumonia caused by bacteria of the genus Legionella.

Despite this fact, the disease is called "Legionnaires' disease".



LEGIONELLA PNEUMOPHILIA

The number of cases that occur globally is not known. Legionnaires' disease is the cause of an estimated 2–9% of pneumonia cases that are acquired outside of a hospital. An estimated 8,000–18,000 cases a year in the United States require hospitalization. Outbreaks of disease account for a minority of cases. While it can occur any time of the year, it is more common in the summer and fall.



- **In November 2017, an outbreak was detected at Hospital de São Francisco Xavier, Lisbon, Portugal, with up to 53 people being diagnosed with the disease and five of them dying from it.**
- **In Quincy, Illinois, at the Illinois Veterans home, a 2015 outbreak of the disease killed 12 people and sickened more than 50 others. It was believed to be caused by infected water supply. Three more cases were identified by November 2017.**
- **In the autumn of 2017, 22 cases were reported in a Legionnaires' disease outbreak in Anaheim, CA's Disneyland theme park. It was believed to have been caused by a cooling tower that releases mist for the comfort of visitors. The contaminated droplets likely spread to the people in and beyond the park.**
- **In July 2019, eleven former guests of the Sheraton Atlanta hotel were diagnosed with the disease, with 55 additional probable cases.**
- **In September 2019, 141 visitors to the Western North Carolina Mountain State Fair were diagnosed with Legionnaires' disease, with four reported deaths, after a hot tub exhibit is suspected to have developed and spread the bacteria. At least one additional exposure apparently occurred during the Asheville Quilt Show that took place a couple weeks after the fair in the same building where the hot tub exhibit was held. The building had been sanitized after the outbreak.**
- **In December 2019, the Government of Western Australia's Department of Health was notified of 4 cases of Legionnaires' disease. Those exposed had recently visited near Bali's Ramayana Resort and Spa in central Kuta.**

Etiology

Initially designated as Legionnaires' disease bacterium.

DNA-DNA homology demonstrated that they were members of a distinct species .

The family Legionellaceae & the genus Legionella were subsequently defined.

50 species & subspecies and 71 serological types –isolated from human, environment or both.

Out of these 19 species associated with human infections.

L. pneumophila – most common (associated with 80-90% of human infections) consist of 15 serogroups

Majority of cases associated with serogroup 1 followed by 4 and 6

Etiology

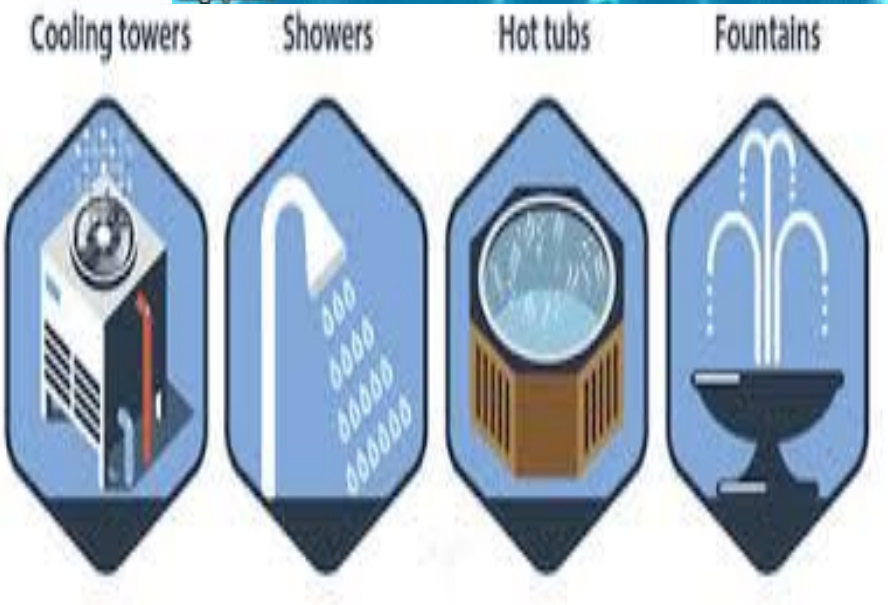
- Gram negative
- Facultative Aerobic coccobacilli
- Acid fact, non-sporulating, non capsulated
- Non-fermenting
- Urease-negative
- Oxidase- and catalase-positive
- Produce beta-lactamase
- Detected using indirect immunofluorescence test, ELISA.
- Poorly stains with gram stain, stains positive with silver
- Cultured on charcoal yeast extract with iron and cysteine.

Etiology

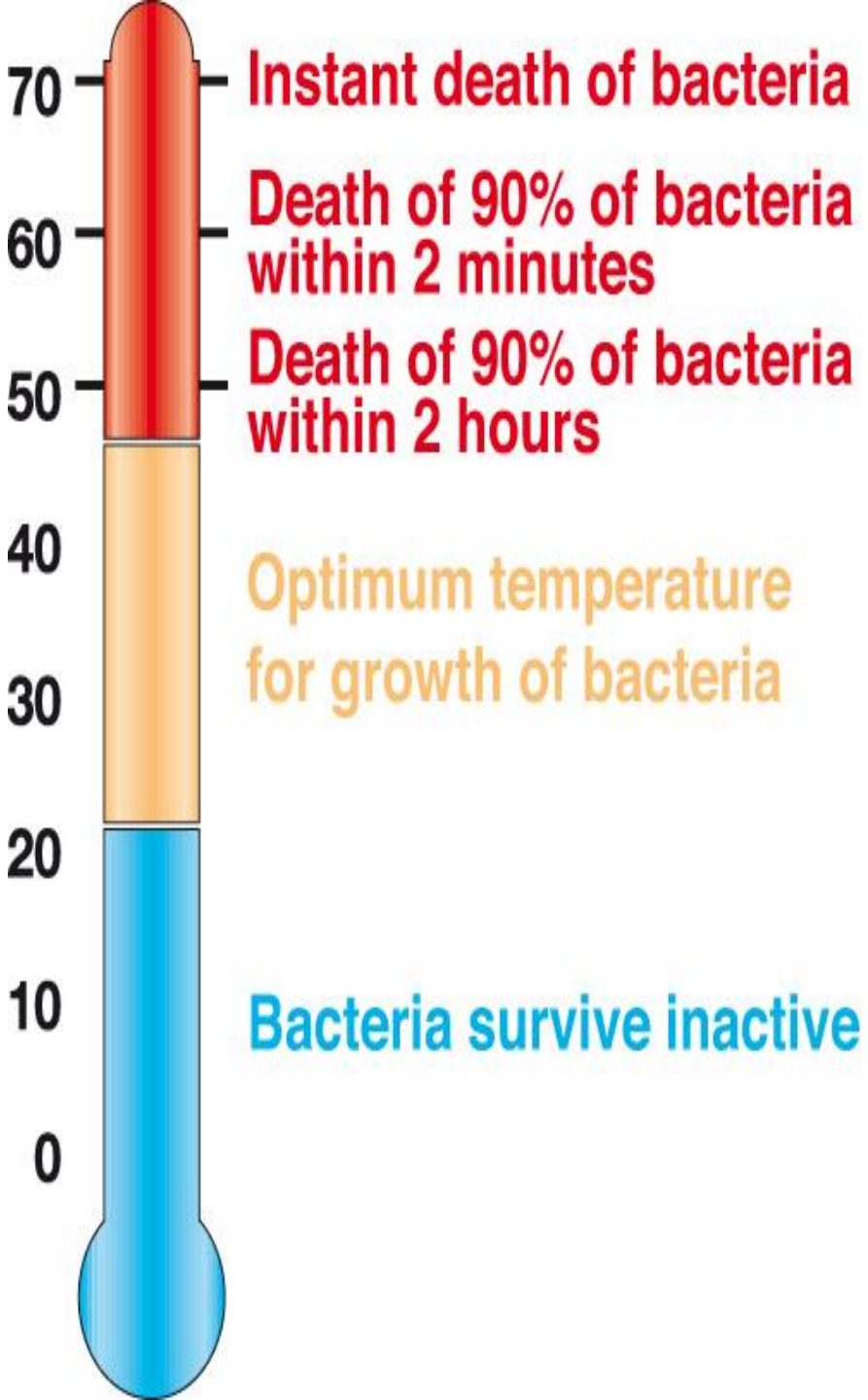
- Other species – rarely associated with human infection particularly in immuno-compromised state.

I. *L. micdadei* (Pittsburgh pneumonia)
II. *L. bozemanii*
III. *L. dumoffii*
IV. *L. longbeachae.*

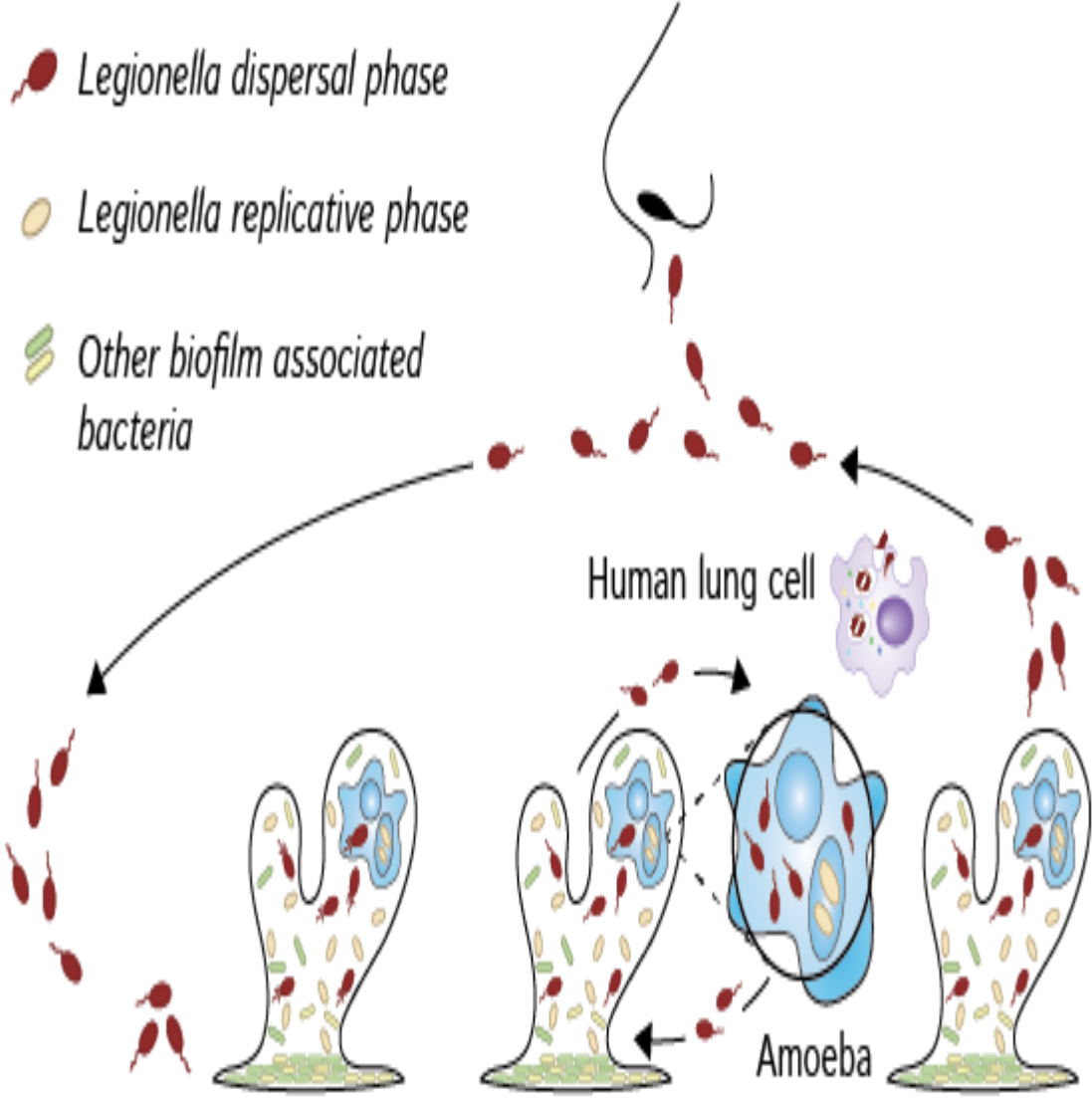
The causative agents are *Legionella* from water or potting mix. The most common cause of illness is the freshwater species *L. pneumophila* which is found in natural aquatic environments worldwide. However, artificial water systems which provide environments conducive to the growth and dissemination of *Legionella* represent the most likely sources of disease.



The bacteria live and grow in water systems at temperatures of 20 to 50 degrees Celsius (optimal 35 degrees Celsius).

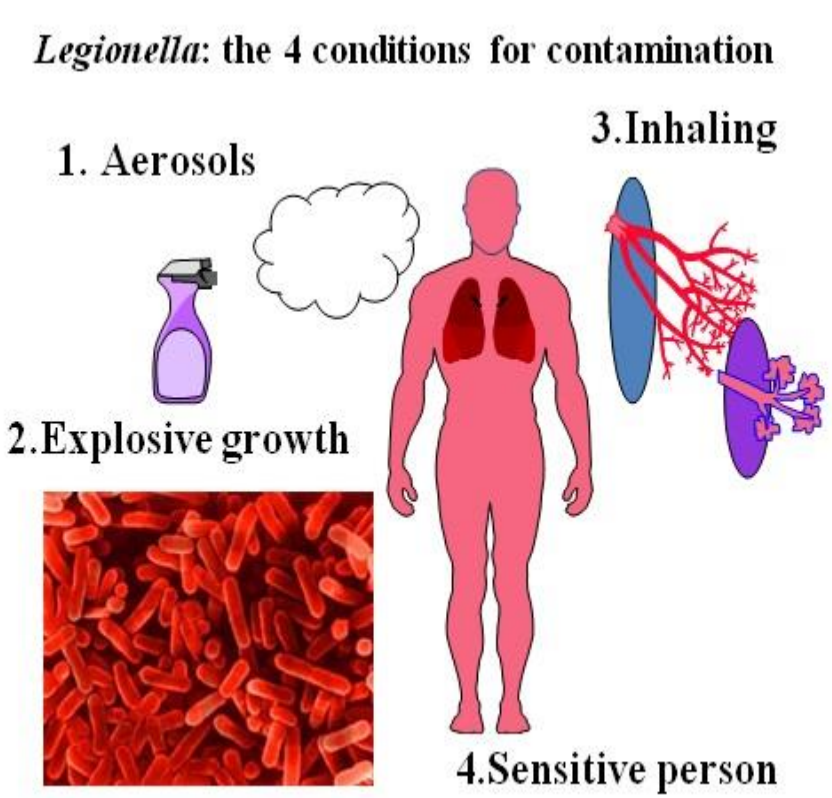


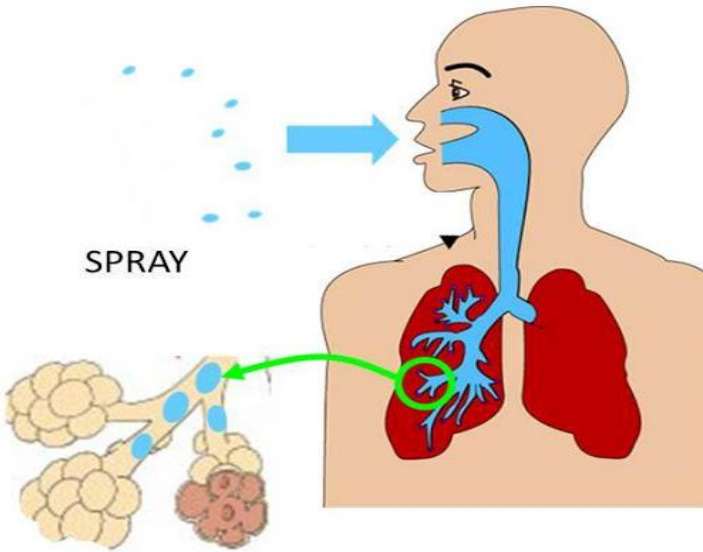
Legionella **can survive and grow as parasites within free-living protozoa and within biofilms which develop in water systems.**
They can cause infections by infecting human cells using a similar mechanism to that used to infect protozoa.



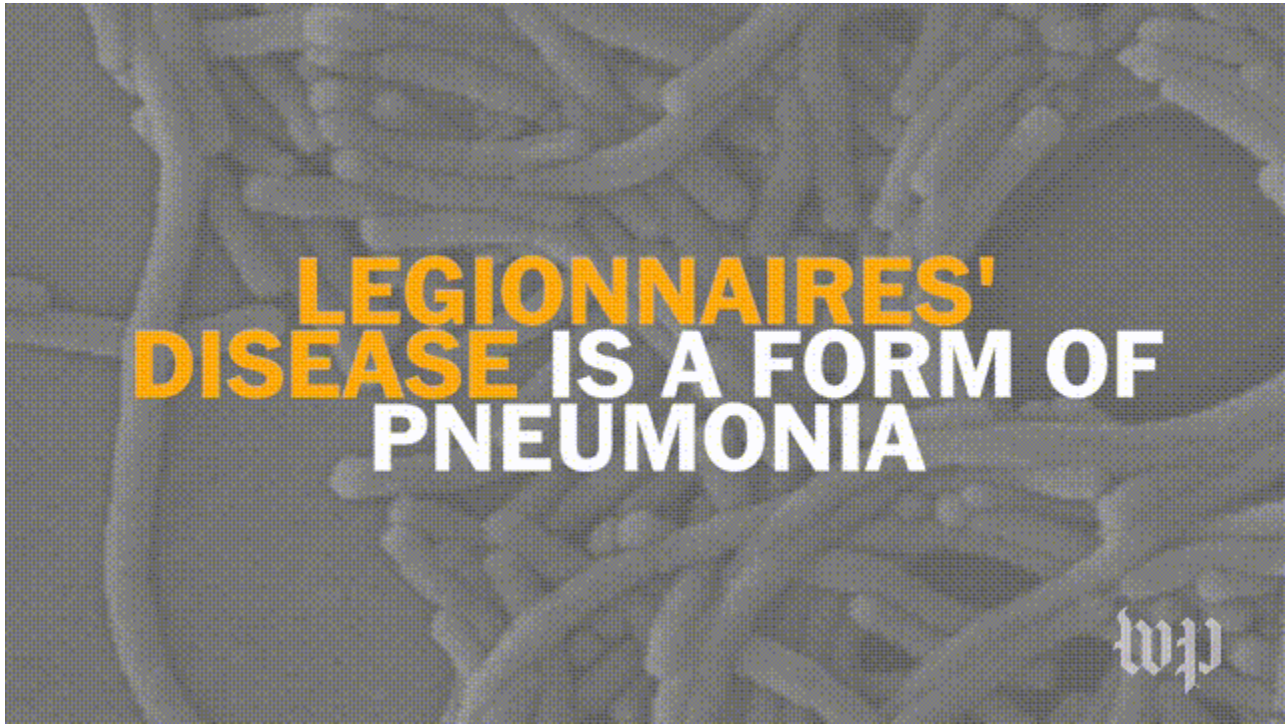
TRANSMISSION

The most common form of transmission of *Legionella* is inhalation of contaminated aerosols. Sources of aerosols that have been linked with transmission of *Legionella* include air conditioning cooling towers, hot and cold water systems, humidifiers and whirlpool spas. Infection can also occur by aspiration of contaminated water or ice, particularly in susceptible hospital patients, and by exposure of babies during water births.





There is no direct human-to-human transmission.



Pathogenesis

Legionella **spp. enter the lungs either by aspiration of contaminated water or inhalation of aerosolized contaminated water or soil. In the lung, the bacteria are consumed by macrophages, a type of white blood cell, inside of which the *Legionella* bacteria multiply, causing the death of the macrophage. Once the macrophage dies, the bacteria are released from the dead cell to infect other macrophages.**

Virulent strains of *Legionella* kill macrophages by blocking the fusion of phagosomes with lysosomes inside the host cell; normally, the bacteria are contained inside the phagosome, which merges with a lysosome, allowing enzymes and other chemicals to break down the invading bacteria

Classification

Legionellosis is a generic term describing the **pneumonic** and **non-pneumonic** forms of infection with *Legionella*.

Traditionally, all legionellosis is subdivided into Legionnaires' disease and Pontiac fever.

In addition to these forms of legionellosis, some researchers have identified Fort Bragg fever.

Legionnaires' disease occurs in the form of severe pneumonia, its course can be malignant.

Pontiac fever proceeds with symptoms of intoxication, hyperthermia, but without signs of pneumonia, the lesion of the respiratory tract is similar to that of the flu.

Fort Bragg fever is characterized by an increase in temperature and the development of exanthema

The non-pneumonic form (Pontiac disease) is an acute, self-limiting influenza-like illness usually lasting 2–5 days.

The incubation period is from a few and up to 48 hours.

The main symptoms are fever, chills, headache, malaise and muscle pain (myalgia).

No deaths are associated with this type of infection.

Legionnaires' disease, the pneumonic form, has an incubation period of 2 to 10 days (but up to 16 days has been recorded in some outbreaks).

Initially, symptoms are *fever, loss of appetite, headache, malaise and lethargy.* Some patients may also have *muscle pain, diarrhoea and confusion*. There is also usually an initial *mild cough*, but as many as 50% of patients can present *phlegm*. Blood-streaked phlegm or hemoptysis occurs in about one-third of the patients. The severity of disease ranges from a mild cough to a rapidly fatal pneumonia. Death occurs through progressive pneumonia with respiratory failure and/or shock and multi-organ failure.

Legionnaires' disease

Headache

Fever
Chills
Ataxia
Tiredness

Respiratory
Cough
Shortness
of breath

Gastric
Nausea
Diarrhea
Vomiting

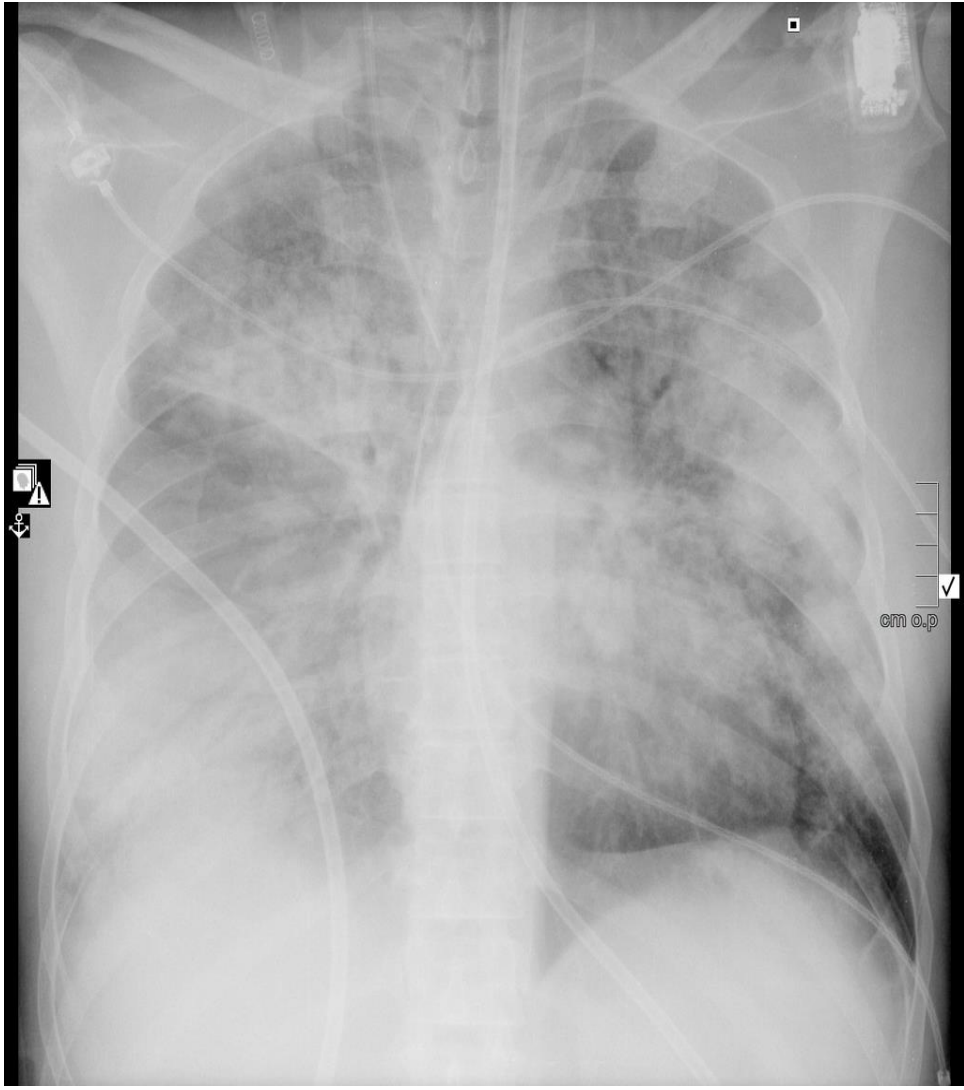
Muscle
Aches

Legionella pneumophila

The time between the patient's exposure to the bacterium and the onset of illness is 2 to 10 days.

The chest radiograph shows multiple bilateral airspace opacities.
There is also a basal right pleural effusion.
Normal cardiac profile.

Case Discussion
Blood culture was negative.
A urinary antigen test with Legionella-Ag was performed with rapid immunofluorescence technique.
The positive result permitted a rapid diagnosis.



Fort Bragg fever

In acute febrile illness with exanthema (Fort Bragg fever), incubation lasts from several hours to 10 days.
The main clinical symptoms:
fever up to 38-38.5 ° C,
chills,
headache,
polymorphic skin rash.
The exanthema can be
large-spotted, similar to measles,
petechial with different localization.
Peeling is not observed.
The duration of the disease is
3-7 days.
The current is favorable.

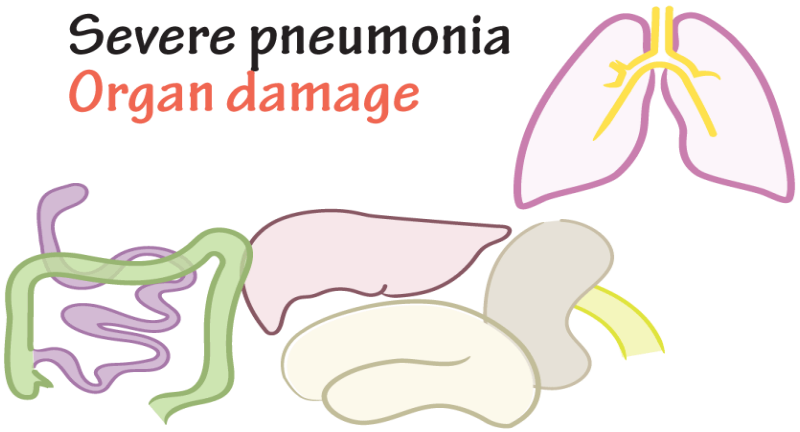
Legionella
L. pneumophila

WATER

Intracellular; Stimulates inflammatory response

✓ Legionnaires disease

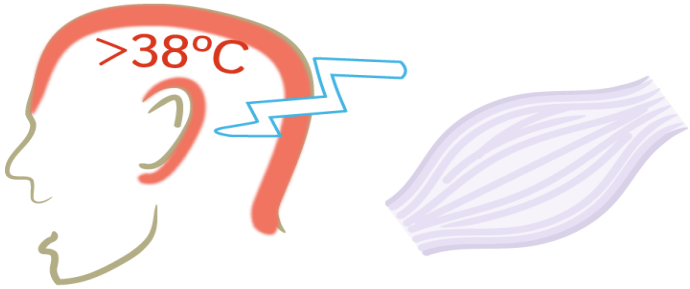
Severe pneumonia
Organ damage



Macrolides

✓ Pontiac fever

Flu-like: Fever, chills, myalgia, malaise, H/A



Self-limited.

Untreated Legionnaires' disease usually worsens during the first week.

In common with other risk factors causing severe pneumonia, the most frequent complications of legionellosis are respiratory failure, shock and acute kidney and multi-organ failure.

Recovery always requires antibiotic treatment, and is usually complete, after several weeks or months.

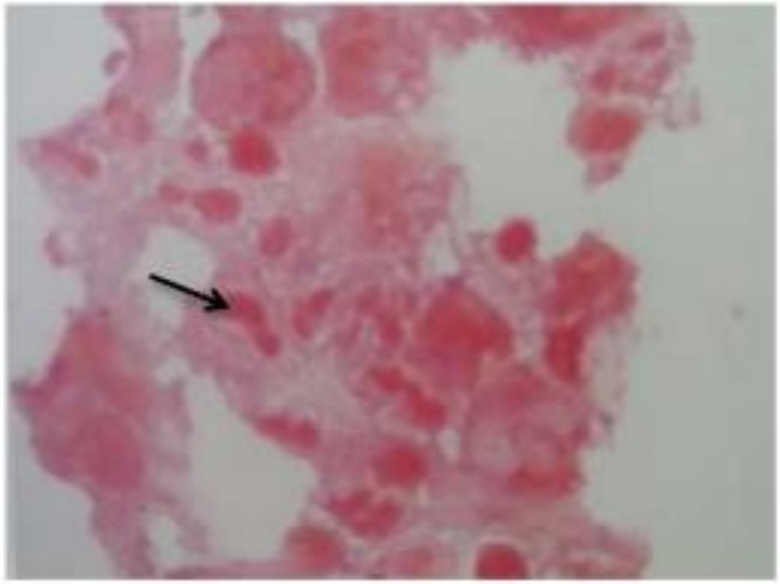
In rare occasions, severe progressive pneumonia or ineffective treatment for pneumonia can result in brain sequelae.

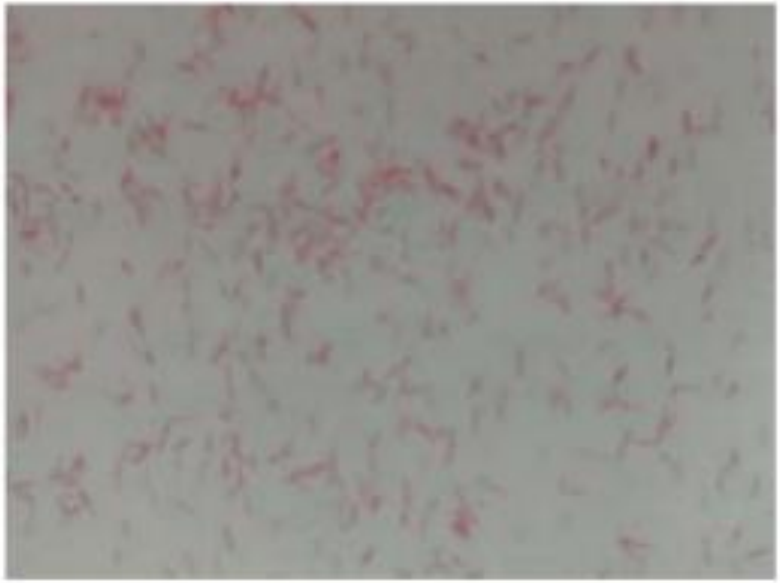
The death rate as a result of Legionnaires' disease depends on: the severity of the disease, the appropriateness of initial anti-microbial treatment, the setting where legionella was acquired, and host factors (for example, the disease is usually more serious in patients with immuno-suppression).
The death rate may be as high as 40–80%in untreated immuno-suppressed patients and can be reduced to 5–30% through appropriate case management and depending on the severity of the clinical signs and symptoms.
Overall the death rate is usually within the range of 5–10%.

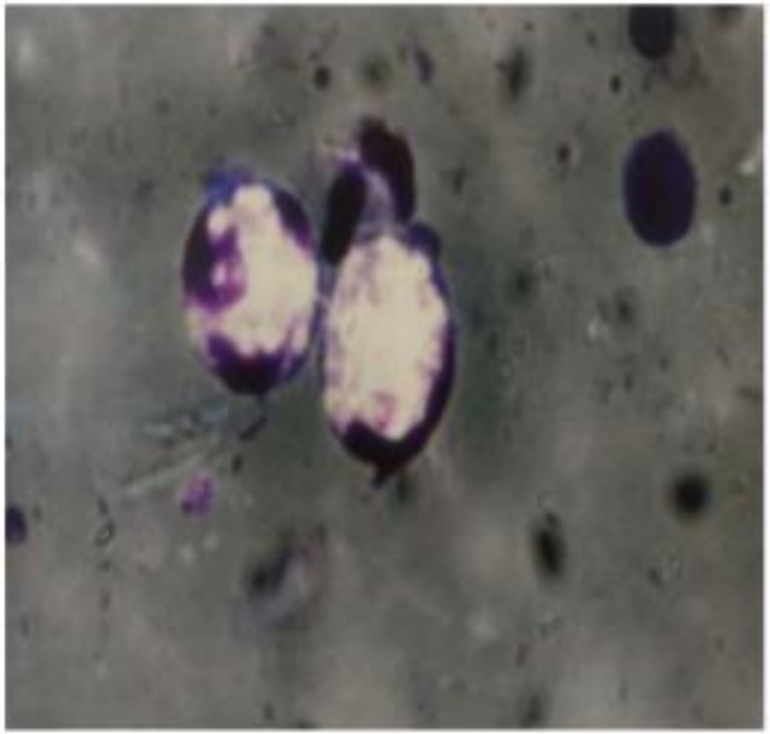
LABORATORY DIAGNOSIS

- Specimen:
  - Sputum
  - Bronchoalveolar lavage fluid
  - Bronchial wash
  - Pleural fluid
  - Blood
  - Urine

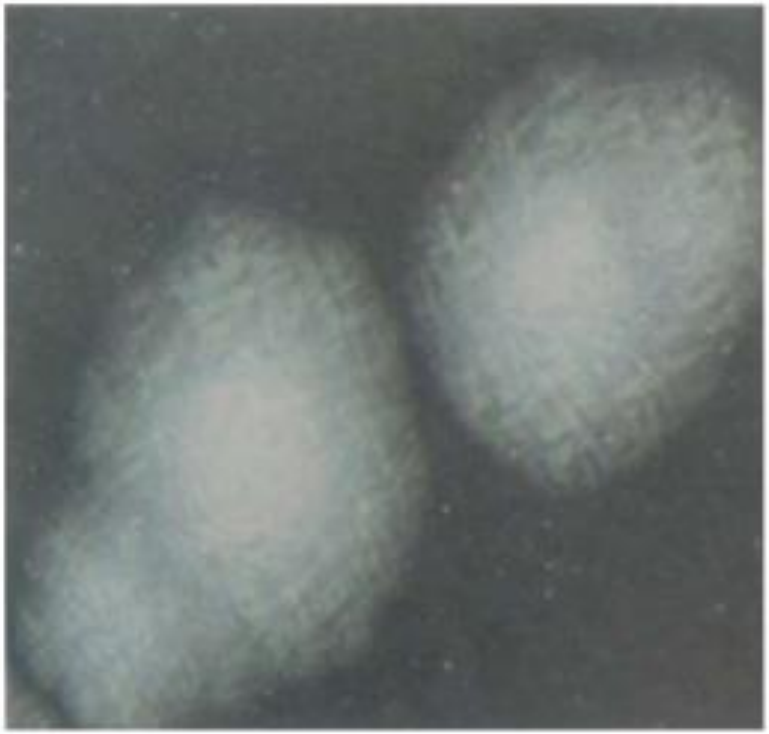
- **Microsopy:**
  - Gram stain reveals neutrophils but no organisms
  - legionellae are poorly stained, pleomorphic gram negative bacilli/coccobacilli.
  - Silver impregnation & Giemsa stains
  - *L. micdadei* is weakly acid fast.





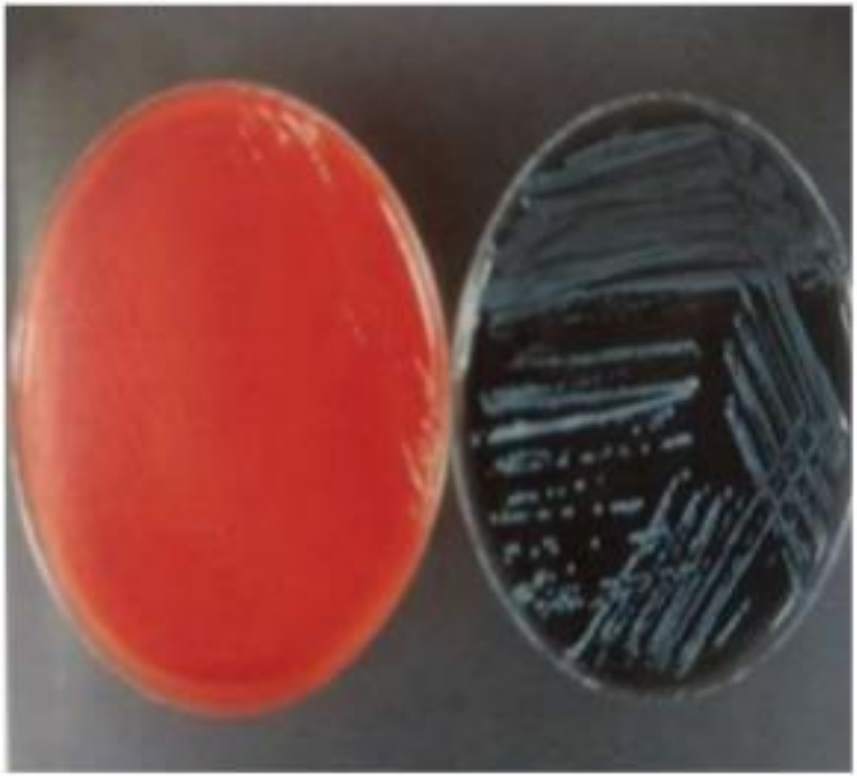


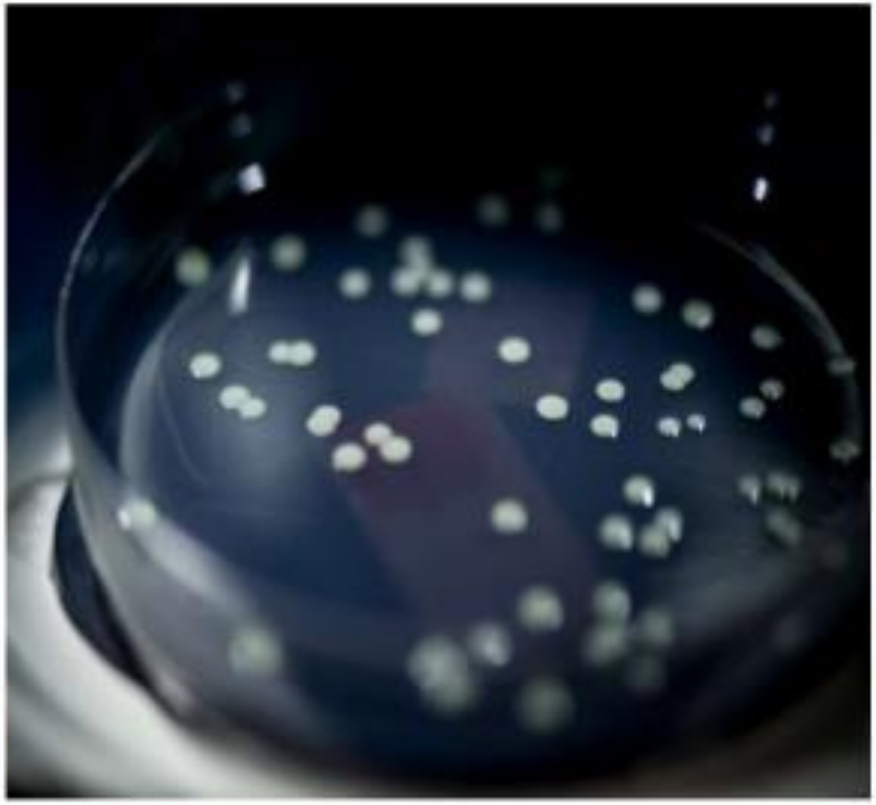
Gram-Weigert stain – lung biopsy specimen shows intracellular bacilli



Dissecting microscopic view of colonies on BCYE

- **Culture:**
  - Highly sensitive (80-90%) & specific (100%)
  - Legionella are fastidious & grow on complex media such as **BCYE**(buffered charcoal yeast extract) agar; pH 6.8-6.9
  - Incubated at 37°C in 5% CO_2 for 3-5 days.
  - Feeley Gorman agar

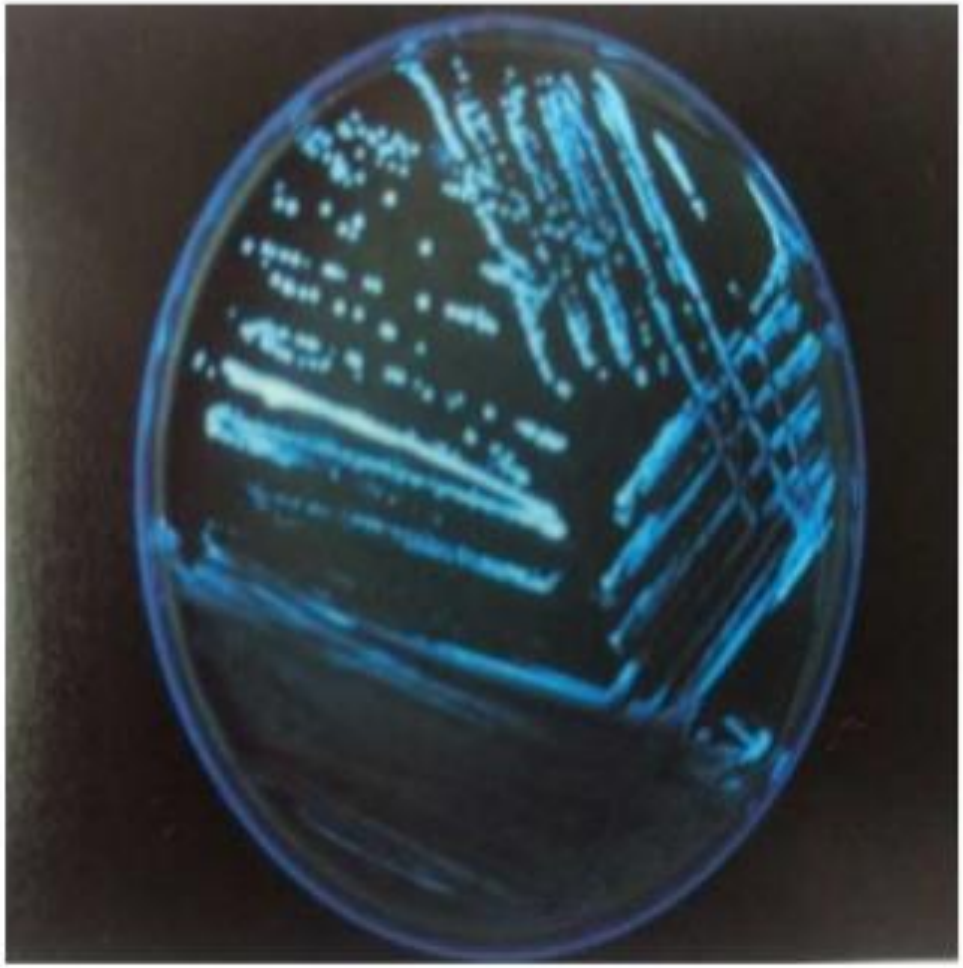




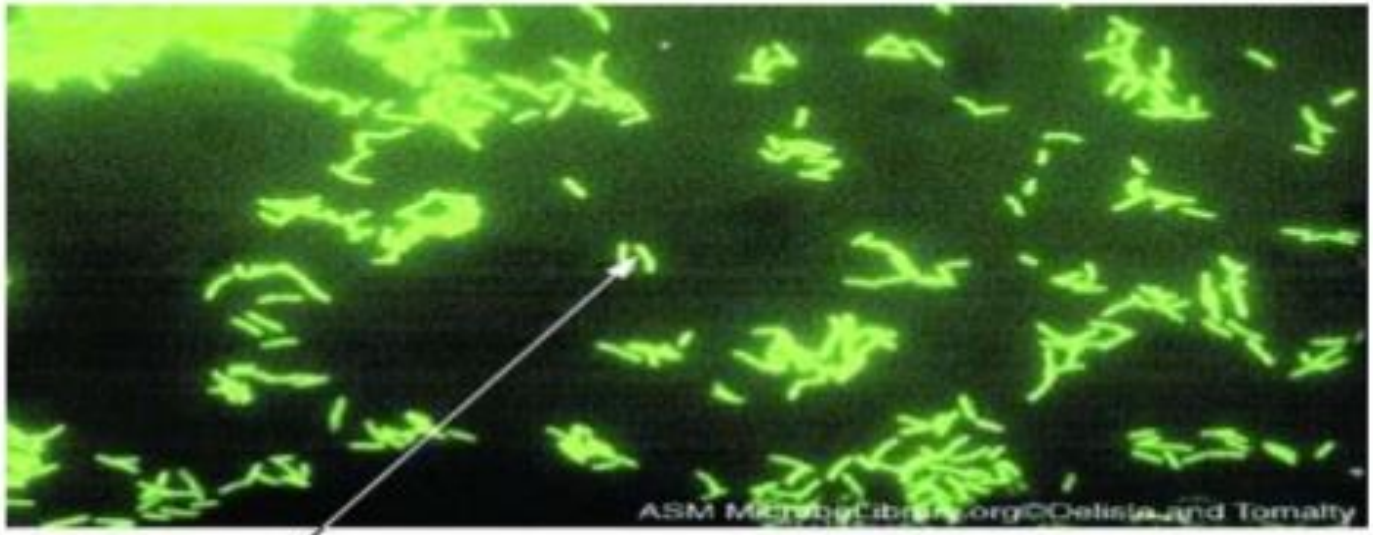
Round with entire edge, glistening, low convex, grey-blue & have granular opalescence resembling ground glass.

Blue-white autofluorescence of *L. bozemanii* on BCYE

Photographed under ultraviolet light,



- **Antibody detection**
  - Direct Fluorescent Antibody (DFA) & EIA
  - Single titre of >1:128 or four fold rise
  - Antibodies appear late after 12 weeks
  - Cross reactivity with other *Legionella spp*



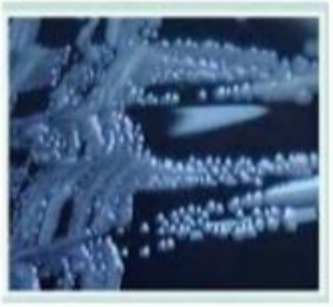
Fluorecein-labeled antibody attached to *Legionella* bacilli

- **Urinary antigen Detection**
  - Enzyme Immune Assay – *L. pneumophila* serogroup 1 specific soluble antigen in urine
  - Rapid, cheaper, easy to perform
  - Antigen is detectable 3 days after onset & disappears over 2 months

- **Molecular methods**
  - Polymerase chain reaction (PCR)

Legionella colonies on BCYE agar

- Small, white, colonies (become grey in a few days)
- Fluorescent under UV light
- Identification by latex agglutination from colonies



TREATMENT

Antimicrobial agent	Dosage
Macrolides	
Azithromycin	500mg PO/IV OD
Clarithromycin	500mg PO/IV BID
Quinolones	
Levofloxacin	750mg IV OD
	500mg PO OD
Ciprofloxacin	400mg IV QID
	750mg PO BID
Moxifloxacin	400mg PO OD
Ketolide	
Telithromycin	800mg PO OD

Harrison's Principles of Internal Medicine; 18th ed.(2010)

Antimicrobial agent	Dosage
Tetracyclines	
Doxycycline	100mg PO/IV BID
Minocycline	100mg PO/IV BID
Tetracycline	500mg PO/IV QID
Tigecycline	100mg IV load - 50mg IV BID
Others	
Trimethoprim-sulfamethoxazole	160/800mg IV QID 160/800mg PO QID
Rifampin	100-600 mg PO/IV BID

Pontiac fever – only symtom based treatment; not antimicrobial.

Harrison's Principles of Internal Medicine; 18th ed.(2010)

PREVENTION

There is no vaccine currently available for Legionnaires' disease.

PREVENTION

- Routine culture of hospital water supply
- Disinfection of the drinking water by

I. Superheat-and-flush method
II. Commercial copper & silver ionization system