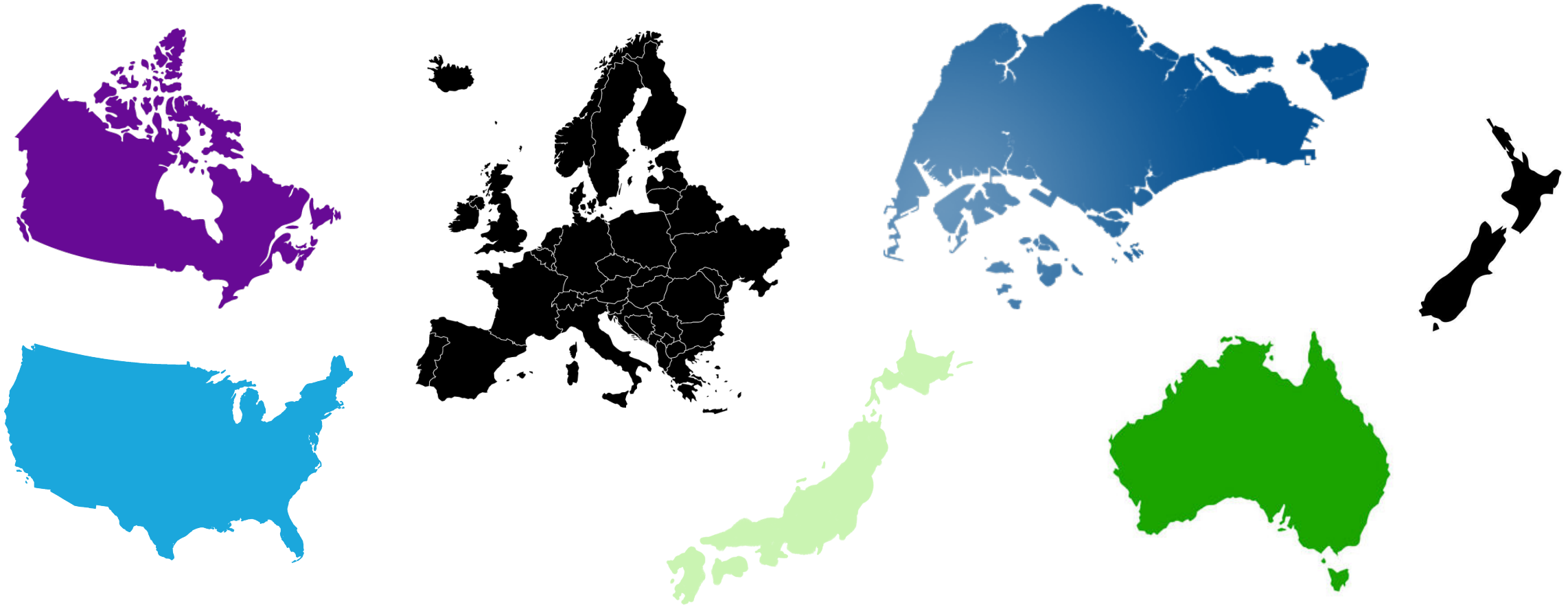
LEGIONELLA PNEUMOPHILA

BY: BRITTANEY LUU

L. Pneumophila has been found all around the world



Canada | USA | Europe | Japan | Singapore | Australia | New Zealand

L. pneumophila's preferred environments:

- *L. pneumophila* is commonly found in **freshwater environments** like rivers and lakes or in human-made water systems like cooling towers. They can also survive in warm and moist soil.

- They are capable of residing and growing within amoebae or ciliated protozoa to seek protection from the environment
  - Some common host species include Hartmanella, Acanthamoeba, and Naeglaria

- Within human hosts, they colonize alveolar macrophages and neutrophils

- They can grow within a temperature range of 20 °C to 50 °C

Legionella

Photo: Robert Koch Institute Berlin

Legionella in amoeba

Photo: Robert Koch Institute Berlin

BACTERIAL CHARACTERISTICS THAT ALLOW INTRACELLULAR SURVIVAL:

Through **residing within alveolar macrophages and neutrophils**, *L. pneumophila* can escape bacterial degradation

Use a **Type IV secretion system** to inject effectors that prevent endocytic maturation and recruit Endoplasmic reticulum (ER) -derived vacuoles. **Type II secretion system** that allows intracellular replication.

They transform the phagosome using the **ER-derived vacuoles** to produce a replicative phagosome

They contain 2 important genes that allow them to grow intracellularly. The **dot** gene allows defective organelle trafficking and the **icm** gene allow intracellular multiplication.

HOW TOM CAME IN CONTACT WITH THE BACTERIA

- Tom most likely contracted the pathogen through the hot tub.

THE HOT TUB

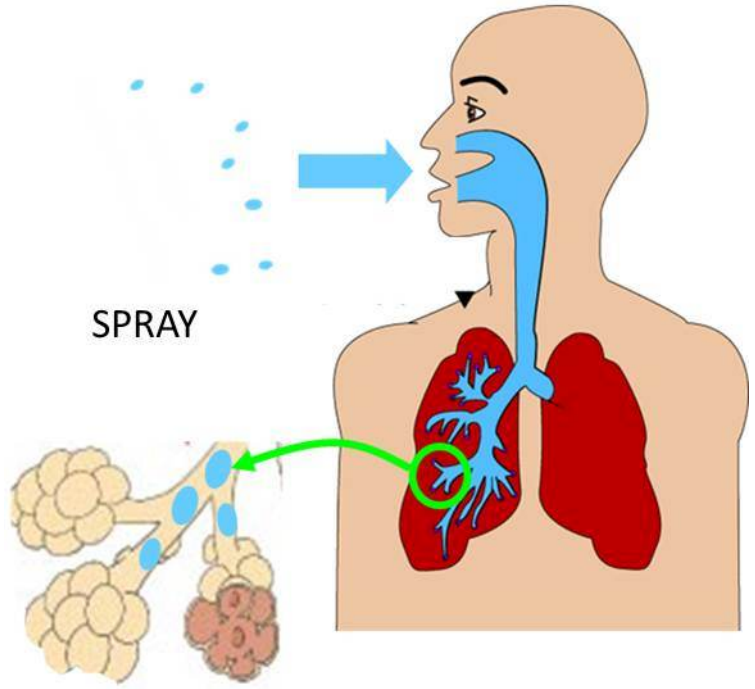
- Optimal environment and temperature for growth
- Large number of people using the facility may deplete the disinfectant levels
- Aerosolizes the bacteria

WHAT FACILITATES ENTRY INTO THE HOST:

Inhalation of the aerosolized pathogen facilitates entry into the respiratory system

Immunocompromised host

- Weakened immune system or compromised mucociliary clearance



Initial entry and adherence:

Pathogen's point of view

Factor	Role
Type IV pili	L. pneumophila use their Type IV pili to adhere to the surface of the host cell and promote biofilm formation. Biofilm formation enhances bacterial survival.
IbtA and IbtB	These genes code for iron siderophores which help recruit iron for the pathogen to grow.
EnhC	Helps evade recognition by Nod1 and contains many tetratripeptide repeats to aid in entry mediated by LpnE
LpnE	Mediates attachment to the host cell and was found it is required for full entry into the cell
C3 & C3bi	MOMPs (major outer-membrane protein) on the bacterial surface contain complement components, C3 and C3bi. These components bind to the CR1 and CR3 receptors on the host to mediate phagocytosis of the pathogen while limiting the hosts potential for oxidative burst.
Hsp60	A surface-associated chaperonin is important for bacterial entry through mediating phagocytosis and macrophage functions.
RtxA	Aids in entry and replication within the macrophage.
Type IV secretion system	Inject effector proteins into the host cell

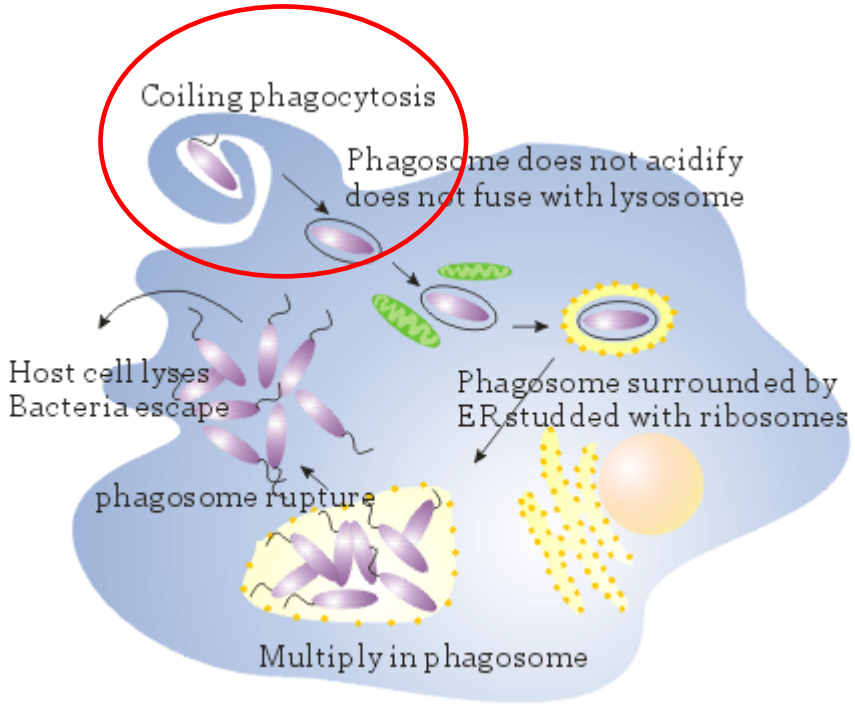
Initial entry and adherence:

Host's point of view

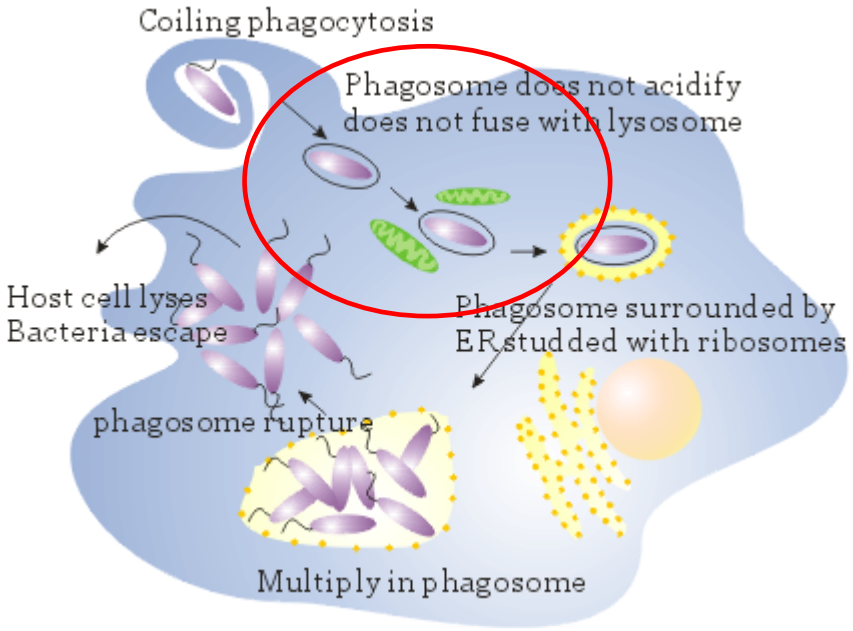
Factor	Role
Pyroptosis	Induces pro-inflammatory cell death when activated by caspase-1. Cell death warns neighboring cells of an invasion and results in enhancement of the immune system.
Birc1e	Detects bacterial invasion and activates the innate immune system. They also contains inhibitors for apoptosis repeat domains that regulate caspases.
Ipaf	A Nod-LRR protein that recruits caspase-1 into inflammasomes which is important for inhibition of bacterial replication.
Toll-like receptor 5	Senses flagellin and activates a signalling pathway that still requires further research. It was found that the MyD88 pathway is not required.
Interleukin-1 receptor	Used for detection of pathogens

Entry:

- *L. pneumophila* is an **intracellular pathogen**
- Phagocytosis must first be induced. Some strains make use of **coiling phagocytosis**. This involves activating the rearrangement of actin filaments in the host cell to form asymmetrical pseudopods that engulf the pathogen.
- Effectors, such as **VipA**, are injected into the host cell prior to phagocytosis. VipA is an actin nucleator and may play a role in the rearrangement of actin to help engulf the pathogen.



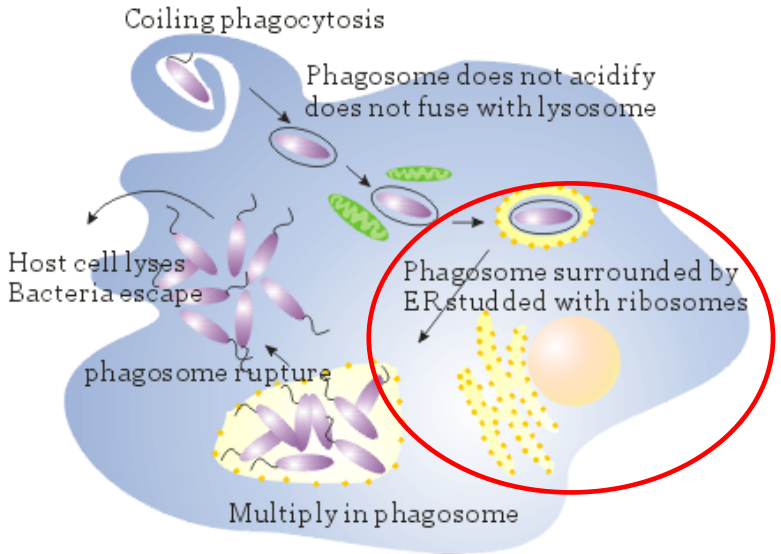
Survival in the phagosome:

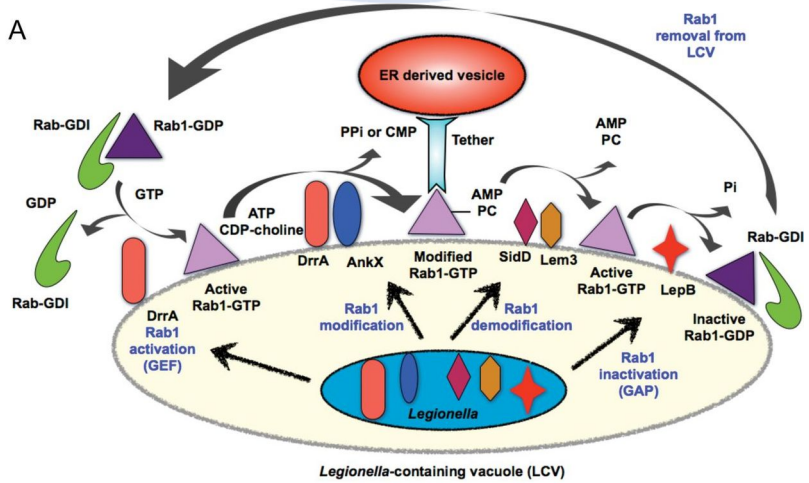


- Once inside the cell, the pathogen must **prevent maturation** of the phagosome
- It is hypothesized that **outer membrane vesicles** (OMVs) are shed from the pathogen and used to prevent phagosome-lysosome fusion and prevent phagosome maturation. It is also believed that v-ATPase is regulated in some way to prevent early-stage acidification.

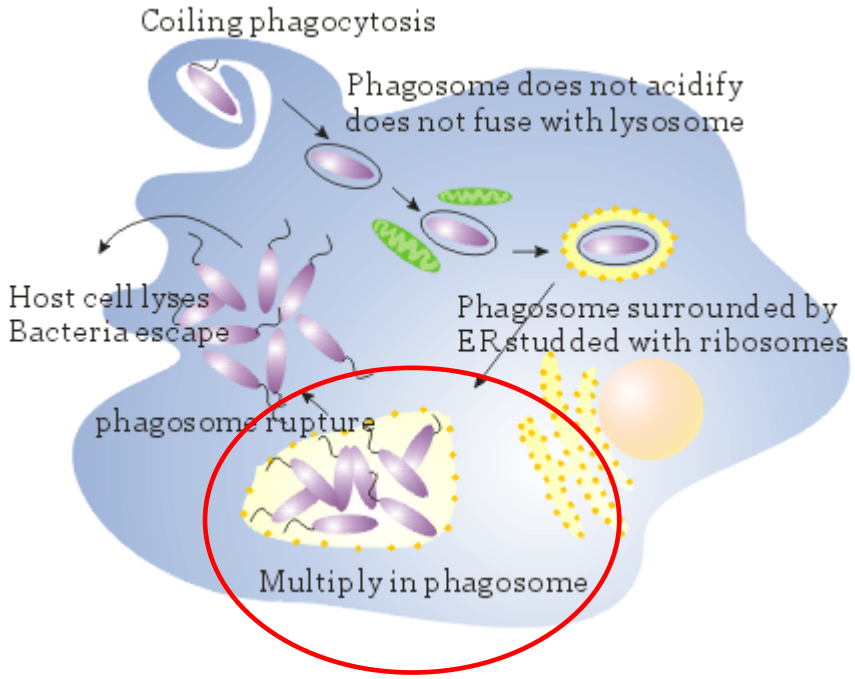
Transformation:

- Transformation of the endosomal membrane into an **rER-like organelle** to allow replication to occur
- **Dot/icm effectors** aid in trafficking the secretory vesicles leaving the ER to fuse with the LCV (Legionella containing vacuole)
- SidM/DrrA and RalF recruit **Rab1** and **Arf1** to aid in the tethering and fusion of ER-derived vesicles into the phagosome.
- The pathogen's SNARE, **Sec22b complex**, is also used for ER-derived vesicle fusion.
- Other effectors help in the recruitment of the ER-derived vesicles
- **Phosphoinositides** (PI) are used as an attachment site for effectors and to recruit more ER vesicles.
- ER vesicles become replaced with ribosomes





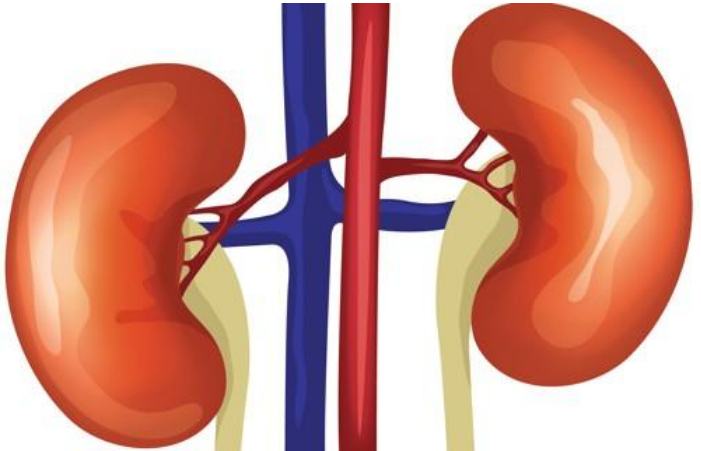
Multiplication:



- **Sufficient nutrient levels** are important for replication
- Use **AnkB** to recruit and degradate ubiquitinated proteins as an **amino acid supply** for replication
- Phagosomal transporters are also created to transport in amino acids
- **Siderophores** and transport proteins are used to retrieve **iron**
- **Autophagy,** the process of phagocytosing autophagosomes, degrading them, and using the **recycled macromolecules** is also used by some strains.
- Some effectors released by the dot/Icm system inhibit apoptosis of the host cell to allow for replication to occur

Spread:

- As amino acid starvation begins, **ppGpp** will begin to accumulate and induce the process of escaping the phagosome
- **Cytotoxins** are released to lyse the cell and genes are expressed to change the replicative state of the bacteria into a non-replicative motile state.
- Legionnaire's disease is usually found to be secondary to a pulmonary infection.
- The pathogen travels throughout the body in the alveolar macrophages through the **blood stream**
- Secondary infections are rare, however, Legionella have been found in other parts of the body such as the kidneys.



Bacterial Damage:

Direct

Deprivation of nutrients

Production of cytotoxins

Bacterial proteases may cause tissue damage

Uncontrolled lyses of host cell, through apoptosis or necrosis, when it enters the motile transmissive state can also affect neighboring cells

Bacterial Damage:

Indirect

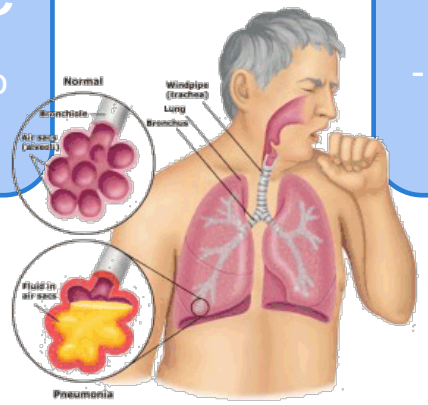
Accumulating toxic concentrations of O2

- Result from innate immune system

Accumulation of protein-rich fluid

Inflammatory Response

- Leaky capillaries result in serum and fibrin to accumulate and result in pneumonia



Pneumonia

- Damages alveoli and decreases oxygen-blood transport

Links to signs and symptoms:

Activation of the innate immune system
- Specifically the production of interleukin-1 may have caused his fever

Muscle aches may have been due to the inflammatory response and tissue damage

Tumor necrosis factor may have caused his headaches