



Bacterial Pathogenesis

Case 3 | Path 417 | Abigail Ngan

Case Summary

Tom and his family went on a cruise to celebrate his retirement. Tom enjoyed the various hot tubs aboard the massive ship in the first few days, relishing the relaxation after a busy final year at work. On the fifth day, Tom wakes up in a sweat with a cough that continues throughout the day. This was followed by headache, muscle aches, and nausea. A doctor examines Tom and notes his high temperature, nonproductive cough, and recent history of asthma and corticosteroid therapy resulting in a pneumonia diagnosis. She starts Tom on azithromycin. By the time the ship returns to port two days later, 5 more people have been diagnosed with a similar pneumonia, several of whom have a slightly compromised immune system, as Tom does. One of the others is admitted to hospital, where sputum and urine samples are tested and reveal a diagnosis of **Legionellosis**.

Presentation

Encounter

Entry

Multiplication and Spread

Bacterial Damage

Encounter

Geographic distribution, Location in host, Bacterial characteristics

Geographic distribution of *Legionella* spp.

Legionella spp. contains 58 species and 3 subspecies. These bacteria inhabit natural and anthropogenic aquatic environments [1,2].

Natural

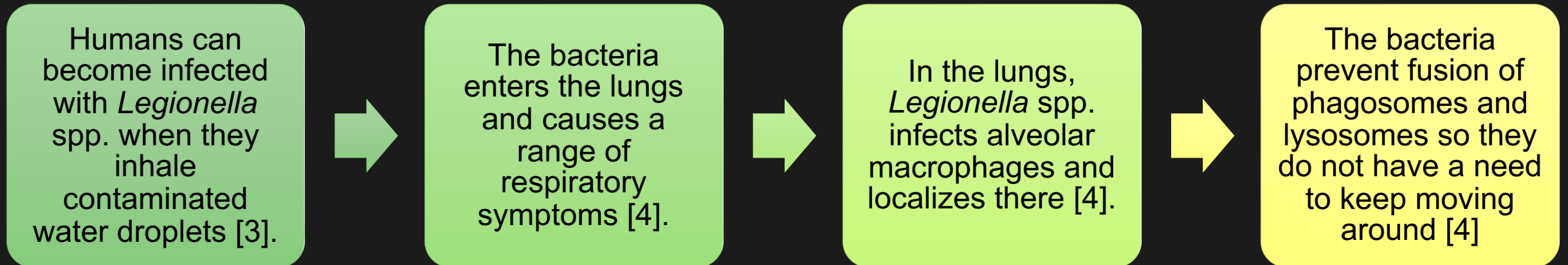
Ex: Lakes, rivers, groundwater, compost, and soil [2]

Anthropogenic

Ex: Water fountains, plumbing systems, bathtubs, air humidifiers, and hot tubs [2]

Location in the human host

Legionella spp. reside in the lungs of humans. [2]



Bacterial characteristics

Legionella spp. exhibit strong pleomorphism and may become rod-shaped, coccoid, or filamentous in response to different environmental factors [2].

survive in temperatures between 0 and 68°C with the optimum growth temperature being around 35°C [2]; (hot tub temperatures don't exceed 40°C) [5]

produce multispecies biofilms, complex interspecies microbiome structures that adhere to the surface, which enable high resistance to environmental factors [2,6]

infect freshwater protozoa, phagocytic monocytes, and alveolar macrophages via their hydrophobic cell surface and their less toxic lipopolysaccharide (LPS) which enables environmental resistance and provides a protected environment for multiplication [2,7,8,9]

exist extracellularly through physiological, morphogenic, and metabolic changes that facilitate intra/extracellular transitions allowing them to become motile, stress-resistant, and transmissible [7]

Entry

Host contact, Mechanisms of entry and adherence from the bacterium and host

Host contact

Human exposure to *Legionella* most frequently occurs during **aquatic recreational activity** [2].

- Tom likely encountered the bacteria in the hot tub, most likely through inhalation of contaminated bioaerosols, by consumption, or direct exposure to contaminated water [2].
- Tom's weakened immune system may have made him more susceptible to infection.

The hydrophobic side chains of *Legionella* contribute to its ability to distribute in aerosols [9]. When inhaled as an aerosol, they are engulfed by human alveolar macrophages and replicates in them [7].

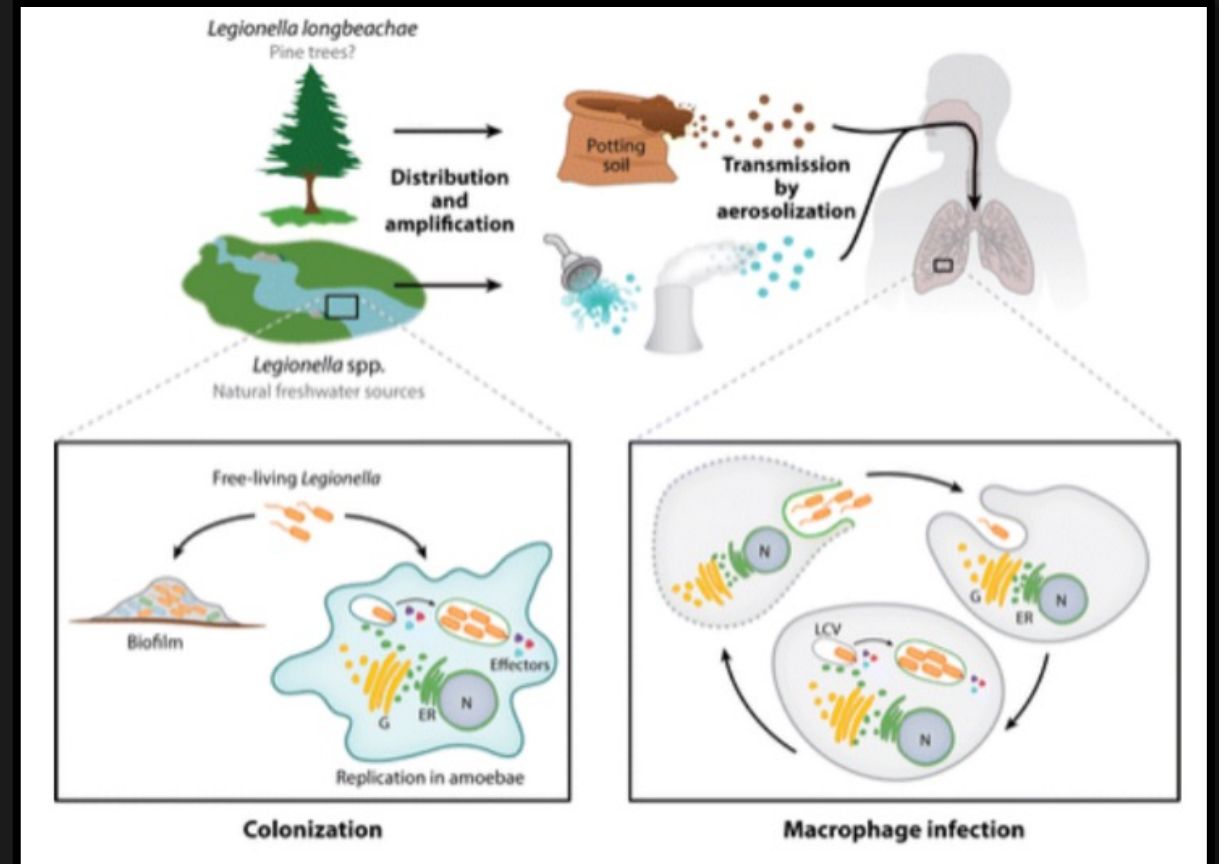
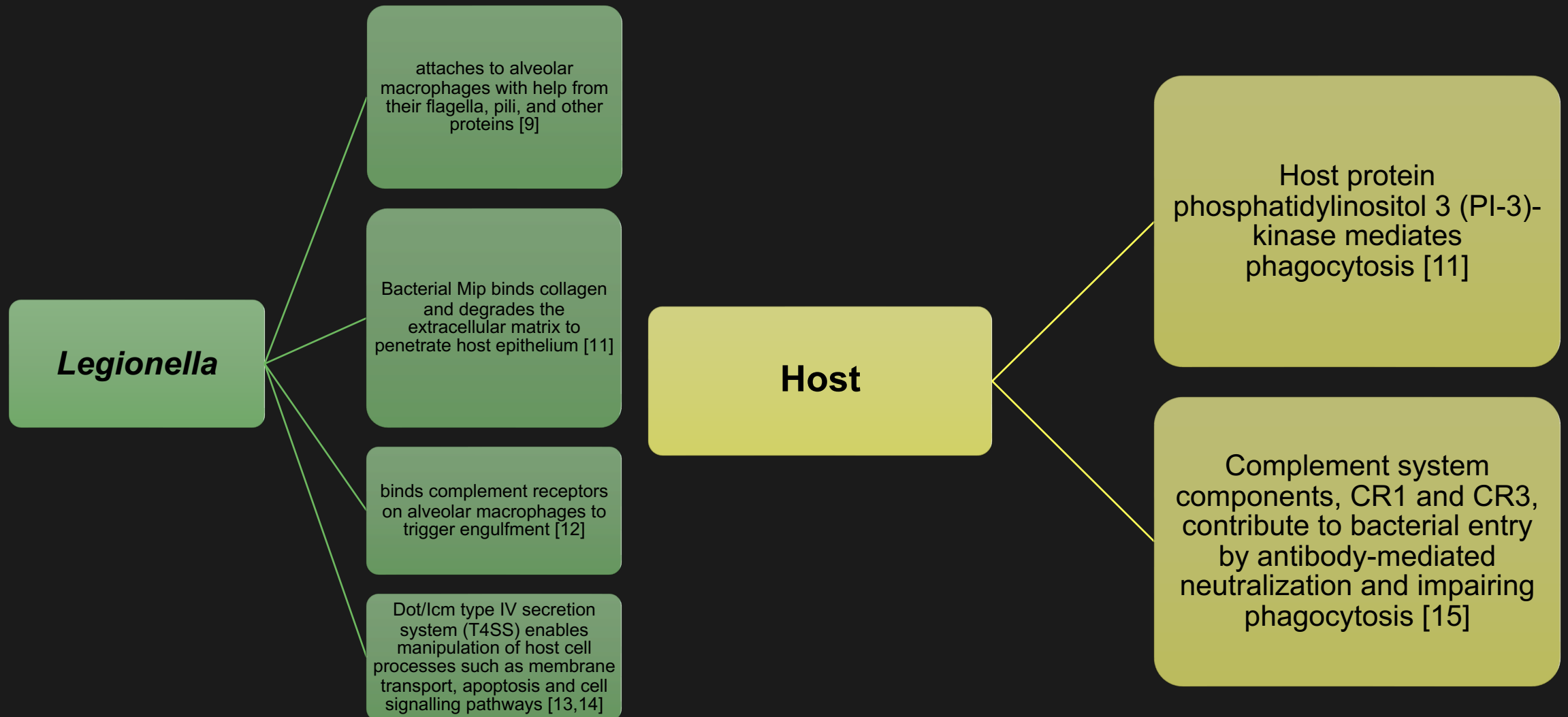


Figure 1. *Legionella* sp. transmission and life cycle [10]

Mechanisms of entry and adherence from the bacterium and host

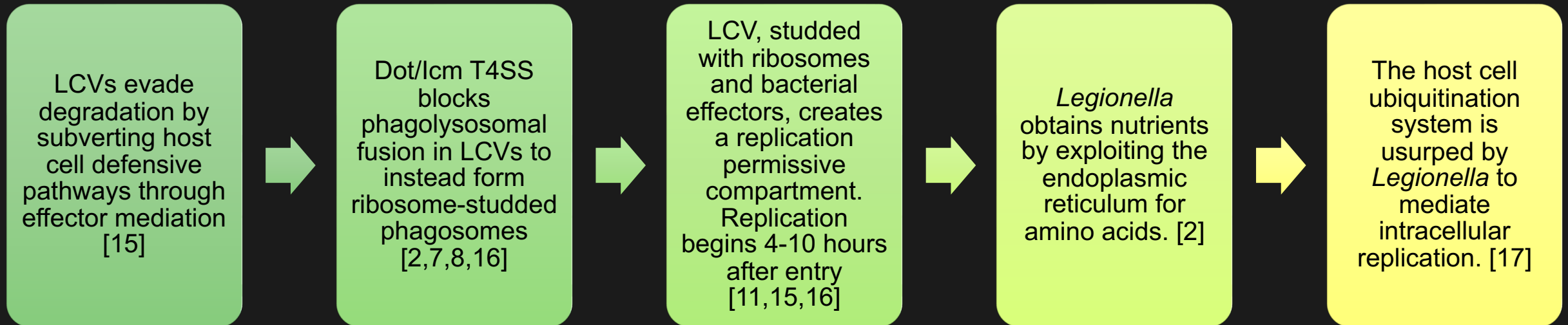


Multiplication and Spread

Bacterial location after infection, Secondary infection sites

Bacterial location after infection

Legionella spp. enter human alveolar macrophages and replicates in them [11]. They exist inside vacuoles of these cells and are called *Legionella*-containing vacuoles (LCVs). [15]



Bacterial location after infection

After intracellular replication in LCVs, *Legionella* induces cytotoxicity and host cell lysis in response to nutrient depletion. [8]

Morphologic and metabolic changes switch the bacteria from a replicative to a transmissive form. [7]



Host cell lysis is mediated by the *Legionella* protein intracellular multiplication T (lcm-T). [11]



To escape the host cell, *Legionella* induces pore-formation in membranes and triggers cell lysis. [11]



Legionella secretion pathway (LSP) secretes other factors important for motility and cell membrane breakdown. [11]



Mip enables dissemination by degrading extracellular matrices to promote epithelial barrier penetration. [11]

Secondary infection sites

Secondary infection might be due to:

- direct invasion into the muscle
- release of endotoxin into circulation that causes muscle injury
- due to its ability to invade host immune cells, cells that usually travels extensively throughout the body. [18,19,20]

Secondary infection sites include the following: [12,21,22]

spleen

kidney

liver

skeletal
muscle

heart

Skin

soft
tissues

brain

Bacterial Damage

Damage to the human host

Damage to the human host

Bacterial damage to the human host primarily occurs in the lungs.

Alveolar and tissue destruction

due to neutrophil and monocyte-mediated damage and bacterial enzymes [12]

Inflammation

leading to symptoms such as cough, fever, and chest pain. [12]

Compromised gas exchange and respiratory function

induces reactive oxygen species (ROS), type I interferon (IFN), NFκB activation of pro-inflammatory cytokines, and the mitogen-activated protein kinase (MAPK) pathway [12,23]

Protease-mediated tissue-destruction

Via zinc metalloprotease, ProA, that directly damages the lung tissue [15,24].

Secondary lung abscesses

necrosis and cavitation of the lung tissue in immunocompromised individuals [15,25].

Acute respiratory distress syndrome (ARDS)

severe case of *Legionella* spp. infection that requires mechanical ventilation [26]

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