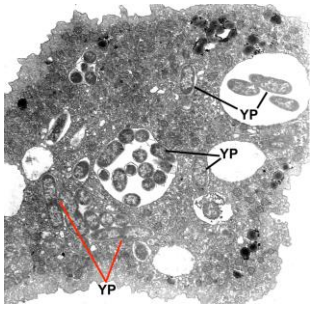
The Plague

General Facts

- Responsible for 3 major, deadly pandemics in the last 1000 years
- Causative agent was only recently discovered in 1894 by Alexandre Yersin
- Caused by bacteria *Yersinia pestis*
- Gram negative, bacillus, nonmotile, **facultative intracellular pathogen**
  - Can survive and reproduce intracellularly and extracellularly
- There are three major presentations of plague:
  - 1. Bubonic plague, 2. Pneumonic plague, 3. Septicemic plague



Transmission electron microscope image of plague bacteria inside an amoeba. YP indicates Yersinia pestis (plague bacteria). The red lines indicate bacteria that appear to be replicating. Credit: David Markman

Bubonic plague is an infection of the lymph nodes.

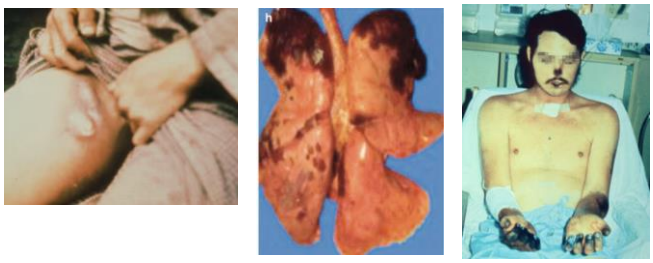
- Symptoms include high fever, chills headaches, formation of **buboes**:
  - swollen, tender lymph nodes often of the groin, armpits or neck
- The incubation period is between 2-7 days.

Pneumonic plague is an infection of the lungs.

- Symptoms include cough, chest pain, difficulty breathing, purulent sputum, hemoptysis
- The incubation period: 2-3 days, and can rapidly progress to death without treatment

Septicemic plague is an infection of the blood.

- Symptoms include abdominal pain, vomiting, diarrhea, organ failure, **gangrene**:
  - Widespread clotting in small vessels preventing the perfusion of the tissue resulting in cell death, often occurring in upper and lower extremities and nose
- Septicemic plague is often secondary to other types of plague after the infection spreads from the primary tissue to the blood.


Left to right: buboes on inner thigh from **bubonic plague**, lung of an african green monkey infected with **pneumonic plague**, gangrene on lips, nose, and fingers caused by **septicemic plague**

Reservoirs

- *Y pestis* can survive within **soil living amoebas**, even during the protozoan's cyst form
  - Some amoebas that *Y pestis* can survive in can lie dormant for 20 years
- Some species of mammals are be asymptomatic carriers of *Y. pestis*

Transmission

- Bubonic & septicemic is primarily transmitted via the flea vector *Xenopsylla cheopis*
  - Can also be spread through direct contact with infected bodily fluids/tissue
- Pneumonic plague is only spread through respiratory droplets from person to person.
  - Can also be domestic cat to person ≽^•ω•^≼

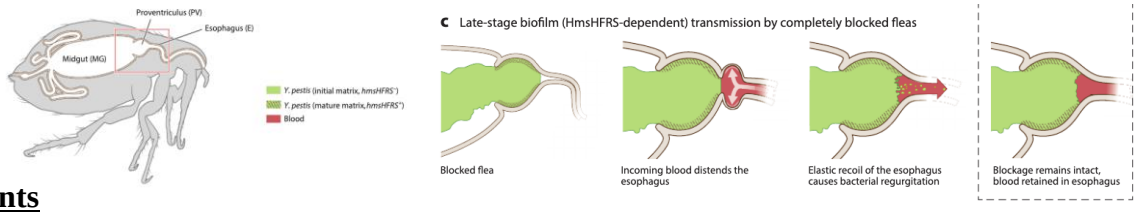
Pathogenesis

Human cycle

- 1. An infected flea vomits *Y. pestis* cells into a bite wound.
- 2. Macrophages attack and engulf the bacteria.
  - *Y. pestis* neutralizes enzymes, preventing digestion within the phagolysosome.
  - *Y. pestis* begins to reproduce within the macrophage.
- 3. Infected macrophage travels to the lymph nodes, increasing bacteria temp. to 37°C.
  - Initiates formation of antiphagocytic capsule and T3SS nano syringe that injects cells with **exotoxins** called *Yersinia* outer proteins (Yops).
- 4. Yops are injected into human immune cells, causing apoptosis of macrophage and releasing *Y. pestis* into extracellular space around lymph nodes.
  - Yops also inhibit our secondary immune response by blocking mechanisms of phagocytosis and preventing inflammatory response.
- 5. *Y. pestis* multiplies explosively at lymph nodes causing buboes.
  - Bacteria may spread to the bloodstream. Lysis of *Y. pestis* releases its lipopolysaccharide **endotoxin** causing septicemic plague.

Flea Cycle

- 6. A flea bites an infected host.
- 7. *Y. pestis* then begins to multiply in the flea's stomach.
- 8. A biofilm forms and creates a barrier blocking the stomach from the mouth.
- 9. The flea attempts to take a blood meal. The biofilm blocks blood entering the stomach and infects the blood which is regurgitated into the bite wound.
  - Flea becomes ravenous and bites and infects more hosts.



Current Events

- 1000-2000 cases worldwide per year with outbreaks as recent as 2021 in Madagascar
- About 7 cases per year in the U.S., almost all originating in the rural SW
- In 2025, there were 2 cases originating from Lake Tahoe and 2 cases in New Mexico

Treatment

- Combination of **antibiotics** that target the prokaryotic 70s ribosome (aminoglycosides, tetracyclines, chloramphenicols) and DNA synthesis (fluoroquinolones) are first line treatments for bubonic, pneumonic, and septicemic plague.

- Vaccines exist, but are only given under certain conditions (ex. plague researcher).
  - Only effective against bubonic plague.
  - Research for a more ideal vaccine is ongoing.