

## A REVIEW ON BLACK DEATH DISEASE

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### ABSTRACT

The Black Death, caused by the bubonic plague bacterium *Yersinia pestis*, was one of the deadliest pandemics in human history, claiming an estimated 75 to 200 million lives in the 14th century. This review provides an overview of the disease's etiology, epidemiology, and impact on European society. We examine the pandemic's spread, symptoms, and mortality rates, as well as the social, economic, and cultural consequences of the disaster. We also discuss the scientific understanding of the plague at the time, the various theories about its origin, and the responses of medieval societies to the crisis. This review aims to provide a comprehensive understanding of the Black Death's significance in human history and its continued relevance to contemporary public health issues.

**KEYWORDS:** Black Death, bubonic plague, pandemic, medieval Europe, public health.

### INTRODUCTION

Killing more than 25 million people or at least one third of Europe's population during the fourteenth century, the Black Death or bubonic plague was one of mankind's worst pandemics, invoking direct comparisons to our current corona virus "modern plague".<sup>[1]</sup>

An ancient disease, its bacterial agent (*Yersinia pestis*) still causes periodic problems with strong outbreaks and remains endemic in some parts of the world.<sup>[2]</sup> It could be weaponized for world bioterrorism, understanding its clinical syndromes, epidemiology, and treatment options remains critical for medical practitioners.<sup>[3]</sup>

Bubonic Plague can be transmitted in three main ways: transmission via flea bites, transmission by ingestion of infected animals and transmission through contact with body fluids from infected animal.

The Health authorities had established importance of a 40 day quarantine period, which became the gold standard for continental Europe for the next 300 years. The 40 day quarantine was adopted until the 16th century and even then it was changed to 30 days only to find that this was completely ineffective, whereupon this regulation was speedily rescinded. The complete success of the quarantine period confirms that the plague was a directly infectious disease and it also shows that it had a long incubation period.

During the 14<sup>th</sup> century, people had limited understanding of disease transmission and treatment. Efforts to contain the disease often involved quarantine measures and isolation of infected individuals, though these were largely ineffective at the time. Medical treatments included herbal remedies and bloodletting, which did little to combat the plague.

**The risk factors for Bubonic Plague include:**

- Camping, hiking and hunting
- Contact with an infected person or contact with sick animals or rodents.
- Occupational exposure: researcher, veterinarian
- Presence of a food source for rodents
- Residing in areas exposed to plague.<sup>[4]</sup>

**HISTORY OF BUBONIC PLAGUE**

Bubonic plague has been responsible for at least **three great pandemics** and multiple epidemics in History.

The **First pandemic** occurred from the Middle East to the Mediterranean basin during the 5<sup>th</sup> and 6th centuries AD, killing approximately 50% of the population in these areas. It is also called as Justinian plague probably came from India and reached Constantinople in 541-542 CE. At least 18 waves of plague spread across the Mediterranean basin into distant areas like Persia and Ireland from 541 to 750 CE.<sup>[5]</sup>

The **Second pandemic** afflicted Europe between the 8th and 14th centuries, destroying nearly 40% of the population. One third of the European population (more than 25 million people) died between 1347 and 1352 from the Black Death. The plague spread to France and Spain in 1348 and then to Germany, Switzerland, and Austria. It decimated London in 1349 and reached Scandinavia and northern England by 1350. In 1656-1657, two thirds of the population in Naples and Genoa from the city of Italy died for the disease. In 1665-1666, London lost about one quarter of its citizens to plague, about 100,000, and the same number died in Vienna in 1679.

The **Third pandemic** started in approximately 1855 in China, and, although it has been mostly controlled, it is still ongoing. Where outbreaks had occurred since 1772, and spread to Taiwan. It hit Canton in 1894, where it caused 70,000 deaths, and then appeared in Hong Kong. Ships carried it to Japan, India, Australia, and North and South America between 1910 and 1920.<sup>[6]</sup>

It is estimated that more than **200 million people** have died from the plague throughout human History and still it continues.

## PLAGUE AS BIO TERRORISM

- The Imperial Japanese Unit 731 during World War II developed and deployed biological weapons in Manchuria and China. On October 27, 1940, Japanese warplanes dropped plague-contaminated rice and fleas into Cuisine, China, which led to an outbreak of pneumonic plague.
- The World Health Organization estimates that if only 50 kg of *Y. pestis* were released in aerosolized form over a major city, the deadly pneumonic plague subtype could cause widespread devastation and death. Because a main goal of bioterrorism would be to incite fear among its population, plague is an ideal biological tool because its victims die quickly in a horrific fashion with hemoptysis, respiratory failure, high fever.<sup>[7]</sup>

## ETIOLOGY

- Bubonic plague is caused by a bacterium known as *Yersinia pestis*. *Yersinia pestis* (formerly *Pasteurella pestis*) is a Gram-negative rod-shaped bacterium. It is a facultative anaerobe that can infect humans and other animals.
- The bacterium is named for the Pasteur Institute physician Alexander Yersin, who provided the first most accurate description of its causative agent in 1894 during the Hong Kong outbreak.

## Scientific classification

Domain: Bacteria

Kingdom: Eubacteria

Phylum: Proteobacteria

Class: Gamma proteo bacteria

Genus: *Yersinia*

Species: *Y. pestis*

Name: *Yersinia pestis* <sup>[8]</sup>

## TRANSMISSION

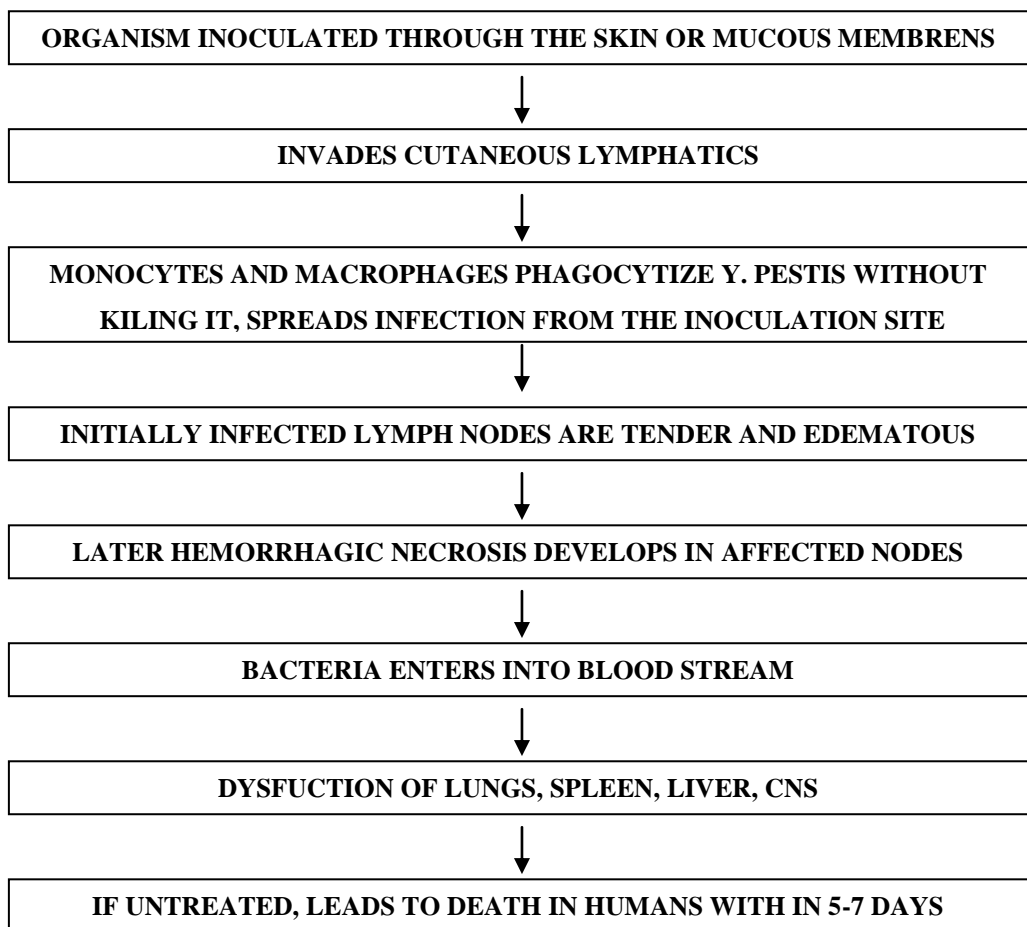
*Yersinia Pestis* is mainly transmitted into **Fleas, Rodents** and **Rats** easily. If an any infected wild rodent strays near human habitations and then shares its fleas with rats living around the settlement, *Yersinia* can spread from rodent to rat, and from rat to man. The rat is just an intermediary and is not a reservoir of bubonic plague: its role is to die and then pass on the infection. A number of dead rats will usually be found during an outbreak of bubonic plague in humans: in a small village perhaps just a few; in a large township perhaps many barrow loads.<sup>[9]</sup>

## SYMPTOMS

- **Acral gangrene:** Gangrene of the extremities such as toes, fingers, lips and tip of the nose.
- General ill feeling (malaise).
- High fever (39 °Celsius; 102 °Fahrenheit), Muscle Cramps and Seizures.
- Smooth, painful lymph gland swellings called **buboes** commonly found in the groin but may occur in the armpits or neck.
- Bleeding out of the cochlea will begin after 12 hours of infection.
- Chills, Myalgias, Sore throat, Headache and body weakness.
- **Abdominal pain:** May occur as an only presenting symptom, more commonly in a patient with septicemic plague (primary blood-borne) will occur.

- Nausea, vomiting (bloody at times)
- Constipation, diarrhea, and black or tarry stools
- Gastrointestinal complaints
- Cough, which may be productive of bloody sputum
- Gangrene from plague sepsis
- Bubonic plague leads to sepsis and acral amputation
- General symptoms of infectious disease, such as malaise, confusion, delirium,
- In severe cases, it leads to coma.<sup>[10]</sup>

#### **PATHOGENESIS<sup>[11]</sup>**



#### **CLINICAL MANIFESTATION**

Clinical plague infection manifest itself in three forms depending on the route of infection and the three forms are,

- **Septicemia plague**
- **Bubonic plague**
- **Pneumonic plague**

#### **SEPTICEMIC PLAGUE**

In another form of plague, called septicemia plague, bacteria enter the blood and cause infection throughout the body. This is a rapidly fatal form that usually results in death within two days if not immediately treated.<sup>[12]</sup>

## BUBONIC PLAGUE

Bubonic plague usually results from a flea bite and is characterized by swollen lymph glands called **buboes** that are extremely painful and that give this form its name. Other symptoms include fever, muscle aches, and weakness. **Hemorrhaging (heavy bleeding)** under the skin can result in patches of dead tissue that appear black (Hence, this disease is sometimes referred to as the Black Death). If not treated, bubonic plague has a death rate of about 60 percent, meaning three out of every five people who contract it will die.<sup>[13]</sup>

## PNEUMONIC PLAGUE

The most virulent and least common form of plague is pneumonic form is due to: Secondary spread from advanced infection of an initial bubonic form. Primary pneumonic plague results from inhalation of aerosolized infective droplets and can be transmitted from human to human without involvement of fleas or animals.

- The usual incubation period for pneumonic plague is 2 to 3 days. Patients usually present with: Tachypnea, Productive cough, Blood-tinged sputum, Cyanosis.
- Primary plague pneumonia is usually fatal and present as fulminate pneumonitis with bloody, frothy sputum and sepsis.<sup>[14]</sup>

## TREATMENT

- The bubonic plague involves **antibiotic treatment** and a myriad of supportive Medications including vasopressin agents, antiulcer and antipyretic agents.
- It also involves laboratory diagnosis, confirmation test, serology test, and modern treatment.<sup>[15]</sup>

## LABORATORY DIAGNOSIS

- TLC -->> elevated 15,000 - 25,000 cells/ $\mu$ l, with a shift to the left.
- Leukemoid reactions (> 50,000 cells/ $\mu$ l) can occur.
- Platelet count may be normal or mildly depressed or may be low if DIC is present.
- Fibrin split products is frequently elevated. Hepatic aminotransferases and bilirubin are often increased.<sup>[16]</sup>

## CONFIRMATION TEST

- Recovery and identification of *Y. pestis* culture from Bubo aspirates, Blood, Sputum.
- The organism can easily grow in Blood agar, MacConkey agar, Infusion broth.<sup>[17]</sup>

## SEROLOGY

- Serum taken during the early and late stages of infection can be examined to confirm infection.
- Direct immune fluorescence (**Rapid dipstick test**) quickly screens for *Y. pestis* antigen in patients.
- **Passive hem agglutination test.**<sup>[18]</sup>

## DIAGNOSIS (LABORATORY STUDIES)

- **Complete blood count:** WBC count may be markedly elevated to levels of 20,000 or greater. In late septic shock, the WBC count may be low.
- **Urinalysis:** Urinalysis may demonstrate gross hematuria, RBC casts, and proteinuria. Arterial blood gas level may reveal hypoxia and acidosis.
- ***Y. pestis*:** Coccobacillus identified in peripheral smear. In up to 20% of patients according to some studies.

- **Gram stain:** Gram stain may identify the gram negative pleomorphic or else coccobacillus. Gram stain can be performed on bubo aspirate, sputum, and blood.<sup>[19]</sup>

### PLAGUE DOCTOR

The origin of the Plague Doctor costume in the 17<sup>th</sup> century was France and Italy. The costume served to safeguard medical professionals from contracting the plague while treating patients.

In epidemics of the bubonic plague that occurred during the 14th to 18th centuries, doctors treating the patients were referred to as plague doctors. Their distinctive dressing included a waxed coat, boots, gloves, a broad-brimmed hat, and a mask that had a long beak and glass eye slits. In exchange for curing plague victims, plague doctors were employed by cities and towns.

**WILD HAT:** Those days, such a hat identified someone as a doctor.

**Scalpel:** For the opening of buboes.

**Leather Gloves:** Pomander: On the neck were a casket for aromatic herbs and substances that were supposed to scare off the plague.

**Garlic:** Doctor chews garlic as their prevention.

**Primitive Mask:** In the Form of a Bird's Beak. It was believed that a mask in the form of a bird would repel the plague from the sick person and bring it to the doctor's attire. At that time, the plague was spread, because of the spoiled air.

The beak of the mask was filled with fragrant medicinal herbs to protect from miasma and from stench, which also could carry the plague. By crane measure, the herbal dulled the smell of non-corpse, corpses, the murders of the bursting buboes of the victims of the plague.

**Cane:** For examining patients without touching them, as well as for self-defense against the jaded and patients.<sup>[20]</sup>

### MODERN TREATMENT

- Antibiotic treatment duration should be 10 days. In severe cases, a 2-drug regimen should be used. Antibiotic regimens for post exposure prophylaxis should be considered.
- **Streptomycin:** (30 mg/kg I.M. in divided doses every 12 hours) reduces mortality to approximately 5%. Alternative DOC in combination with consideration of use with a secondary agent. Drug often not commercially available.
- **Tetracycline or doxycycline:** (Doryx, Vibramycin, Bio-Tab) Inhibits the protein synthesis and thus bacterial growth by binding to 30S and possibly 50S ribosomal subunits of susceptible bacteria.
- **Ciprofloxacin (Cipro):** Fluor quinolones that inhibits bacterial DNA synthesis and consequently growth by inhibiting DNA gyrate and topoisomerases, which are required for replication, transcription, and translation of genetic material.
- **Chloramphenicol:** DOC to be used as a secondary agent in plague meningitis (better CNS penetration), profound hypotension and pleural or pericardial involvement.
- **Gentamicin:** (Garamycin) The main Amino glycoside antibiotic for the gram-negative coverage (more widely available than streptomycin) also appears to be effective.

- To prevent relapses antibiotic treatment should be continued for 10 days or for at least 3 days after effervescence and clinical recovery.
- Most patients improve rapidly and defervesce within 72 hours of initiation of antimicrobial therapy, although buboes can persist for weeks some authorities switching from streptomycin to different antibiotic for completion of therapy after 5 days of treatment in order to minimize the risk of **ototoxicity** and **nephrotoxicity**.<sup>[21]</sup>

### PREVENTION

- Inform people to be aware of the areas where zoonotic plague is active.
- Take precautions against flea bites.
- Handling carcass while in plague- endemic.
- Avoid direct contact with infective tissues.
- Avoid exposure to patients with pneumonic plague.<sup>[22]</sup>

### CONCLUSION

From pre history to the modern era *Y.pestis* has killed millions of people. Outbreaks of worldwide plague foci in both developed and underdeveloped countries continue to occur. Although modern medicine has greatly improved therapies and limited its spread, many clinical practitioners remain unfamiliar with its symptomatology, thus preventing timely recognition and treatment.

### REFERENCES

1. Benedictow OJ. The Black Death 1346-1353. The Complete History. Woodbridge, UK: Boydell Press, 2004; 3–67.
2. Kelly J. The Great Mortality. An Intimate History of the Black Death, the Most Devastating Plague of All Time. New York, NY: HarperCollins, 2006; 138–41.
3. Narayanan N, Lacy CR, Cruz JE, et al. Disaster preparedness: biological threats and Treatment options. *Pharmacotherapy*, 2018; 38(2): 217–34.
4. Kman NE, Nelson RN. Infectious agents of bioterrorism: a review for Emergency physicians. *Emerg Med Clin North Am*, May 2008; 26(2): 517-47.
5. Riedel S. Plague: from natural disease to bioterrorism. *BUMC Proc*, 2005; 18(2): 116–24.
6. Cohn SK, Alfani G. Households and plague in early modern Italy. *J Interdisc Hist*, 2007; 38: 177–205.
7. Kugeler KJ, Staples JE, Hinckley AF, et al. Epidemiology of human plague in the United States, 1900-2012. *Emerg Infect Dis*, 2015; 21(1): 16–22.
8. Ryan KJ, Ray CG (editors) (2004). *Sherries Medical Microbiology* (4th Ed.). McGraw Hill. pp.484–488. ISBN 0-8385852-9-9.
9. Perry RD, Fetherston JD. *Yersinia pestis*-etiologic agent of plague. *Clin Microbiology Rev.*, 1997; 10(1): 35–66.
10. Waterer GW, Robertson H. Bioterrorism for the respiratory physician, *Respirology*, Jan 2009; 14(1): 5-11.
11. Simonet, M, B. Riot, N. Fortineau, P. Berche, Invasin production by *Yersinia pestis* is abolished by insertion of an IS200-like element within the *inv* gene. *Infect Immun*, 1996; 64(1): 375-9.
12. World Health Organization (WHO). (2019). Plague
13. "Health. De-coding the Black Death"
14. "Plague: A History" by William C. Summers: Offers a detailed historical perspective on plague outbreaks.

15. Kummer LW, Szaba FM, Parent MA, Adamovicz JJ, Hill J, Johnson LL. Antibodies and cytokines independently protect against pneumonic plague, *Vaccine*, Dec 9-2008; 26(52): 6901-7.
16. WHO - Plague: Laboratory Diagnosis (2018).
17. Chanteau et al., Development of a rapid test for plague. *Journal of Clinical Microbiology*, 2003; 41(10): 4561-4564
18. Dennis et al. (1999) - *Plague Manual: Epidemiology, Distribution, Surveillance and Control*.
19. Inglesby, T. V., et al., Plague as a biological weapon: Medical and public health management. *JAMA*, 2000; 283(17): 2281-2290.
20. Waller, J., *The Dancing Plague: The Strange, True Story of an Extraordinary Illness*. Sourcebooks, Inc, 2008.
21. Mwengee W, Butler T, Mgema S, Mhina G, Almasi Y, Bradley C. Treatment of plague with gentamicin or doxycycline in a randomized clinical trial in Tanzania. *Clin Infect Dis*, Mar 1 2006; 42(5): 614-21.
22. *Plague: A Manual for Public Health Workers*, by the California Department of Public Health: A practical guide for public health workers, 2019.