International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1498-1503 www.ijprajournal.com ISSN: 2456-4494

"A Review on the Plague Disease"

Mr. Suryawanshi Swapnil, Mr. Sonawane Vaibhav, Mrs. Jambhale Kanchan
Bachelor Of Pharmacy, Savitribai Phule Pune University, Pune
Hon. Shri. Babanrao Pachpute Vichardhara Trust's, Group of Institutions's,
Faculty of Pharmacy, Kashti.Tal:-Shrigonda, Dist:-Ahmednagar.414701
2021-2022

Submitted: 10-04-2022 Accepted: 28-04-2022

ABSTRACT:
Plague is caused by yersinia pestis is not commonly encountered in clinics, although natural plague foci are widely distributed around the world y. pestis has been listed as a category. A bioterrorism agent A neglecated diagnosis will cause serve consequences. Therefore, this miniroview briefly introduces the current understanding on Y pestis and then focuses on the practical aspect of plague, including clinical manifestitations, diagnosis, treatment and prevention, to alert clinicians about this notorious disease. Our review concluded that the deliberate release of plague is feasible but unlikely to occur, and that a rebust public health reaponse and early treatment would rapidly half the transmission of plague in the population front line clinicians should be weary of the possibility of suicide attackers mindfull of the early escalation to public health organization.

Keywords: Plague; Y pestis; deliberate release; Bioweapon; antibiotic resistant plague; plague mimic.

INTRODUCTION:

Plague is a vector-borne illness transmitted by fleas to a variety of wildlife rodents, which represent natural reservoirs for the disease in a wide range of habitats around the world [1]. The etiological agent of plague is the Gramnegative bacterium Yersinia pestis [2], discovered by the Institut Pasteur, bacteriologist Alexandre Yersin during a plague outbreak in Hong Kong in 1894 [3]. Plague has impacted the history of humankind through several pandemics that have initially spread from Central Asia to Africa and Europe, and plague has reached every continent during the last 150 years[4] . In the 21st century, plague is present in Asia, Africa and America [6] , and recent outbreaks in Uganda [6] , China [7] , Democratic Republic of Congo, and Madagascar remind that plague is still a major public health concern. Y. pestis is highly similar on a genomic level to the enteric pathogen Y. pseudotuberculosis; however, a series of gene gain and gene loss events have led to the appearance of markedly different mechanisms of disease as well as niche preference and lifestyle Y. pestis displays a quite unique set of virulence factors that allow successful infection of fleas and subversion of immune responses in mammalian hosts, leading to rapid host death in the absence of adequate treatment. In this article, we review recent advances in plague research, particularly in the fields of evolution, virulence determinants, and subversion of mammalian immune responses, as well as an overview of the critical aspects of vaccination and pneumonic plague diagnosis. For other aspects of Y. pestis infection, such as Y. pestis adaptation to the flea.

Clinical manifestations of natural infection:

Plague is a severe clinical infectious disease that can rapidly progress to death if not diagnosed and treated early [8] .As plague is not commonly encountered in clinics, it can be difficult for clinicians who do not have experience diagnosing and treating plague to correctly diagnose the disease [9] .

1.Bubonic plague: Most cases of plague today are of the bubonic form, which has a distinctive clinical picture, recognizable to clinicians and patients – especially in endemic areas.[12] Bubonic plague results from the bite of a flea infected with Y. pestis that had previously fed on an infected organism, such as a rodent.[10] In the flea, Y. pestis forms a biofilm that blocks access to the flea's midgut and, as a result, the flea regurgitates the obstructive biofilm into the mammalian host while feeding[13] leading to the inoculation of thousands of organisms into a patient's skin.[11] Bubonic plague may also develop from exposure of open wounds to infected material.[14] The onset of bubonic plague is sudden

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1498-1503 www.ijprajournal.com ISSN: 2456-4494

and characterized by malaise, high temperature and a severe lymphadenitis.

Fig:1. Axillary and inguinal buboes in patients with bubonic plague.

The bacteria deposited from the flea bite migrate rapidly to a regional lymph node and multiply during an incubation period of 2–6 days.[25] Alongside the onset of sudden fever and chills, a recognizable and extremely painful bubo[3] appears from the significant bacterial proliferation and inflammation, in as early as up to one day.[11] Within the lymph node they are phagocytosed but evade destruction, and subsequently cause necrosis of the lymph node architecture.[11] The bubo most typically develops in the inguinal region but can also be distributed anywhere there is a lymph node in the body, commonly in the cervical and axillary regions[11] (Fig. 1). Often the buboes are so painful they completely restrict movement of the affected limb, and range between 1–10 cm in diameter.

2.septicemic plague:

Primary septicemic plague is the second most common form of plague,[8] beginning with no evidence of any palpable lymph nodes but with bacteremia. The disease can be rapidly fatal within a few days, with high fevers, rapidly developing sepsis and multiorgan failure from hypotension and shock.[15] Once the infection reaches the end stages it leads to disseminated intravascular coagulation and vasculitis, leading to gangrene particularly in the extremities resulting in the need for amputation.[1] This black discoloration of the gangrenous necrotic tissues is where "The Black Death" obtained its name from, as patients would turn black and then soon die.[15] (Fig. 2).

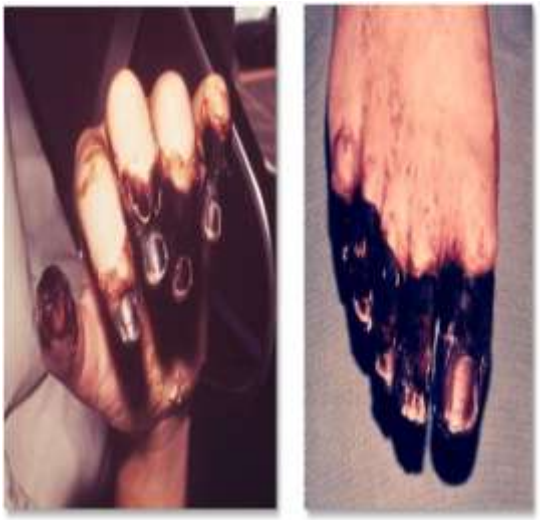


Fig. 2. Digital gangrene and gangrene of the right foot.

3. Pneumonic plague:

which is transmissible from human-to-human. In this review paper we will discuss clinically relevant aspects of pneumonic plague, including diagnosis, treatment and prophylaxis, history and current epidemiology of Y. pestis.

This disease progresses rapidly with an acute onset within 1–4 days of inoculation, beginning with non-specific symptoms and signs as seen in humans and non-human primates.[16] The initial disease is very similar to influenza with coryzal symptoms, fever, headache, chills and malaise.[16,17] Within one day this progresses to significant lower respiratory tract symptoms such as dyspnea, tachypnoea, cough and haemoptysis[18] with bilateral pulmonary infiltrates developing rapidly, as observed on chest x-ray (Fig. 3). The initial purulent sputum may become tinged with blood or be acutely haemorrhagic.[19] Over time the cough becomes increasingly productive and in the final stages patients produce vast volumes of bright red sputum containing "an enormous number of plague bacilli in almost pure culture".[20] In pneumonic plague, if antibiotics are not started within 24 h, the mortality rates can reach 100%.[2,25] Even with proper antibiotic treatment up to 50% of patients can still die due to the severity of the infection and many would require admission to an intensive care facility.[12]

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1498-1503 www.ijprajournal.com ISSN: 2456-4494

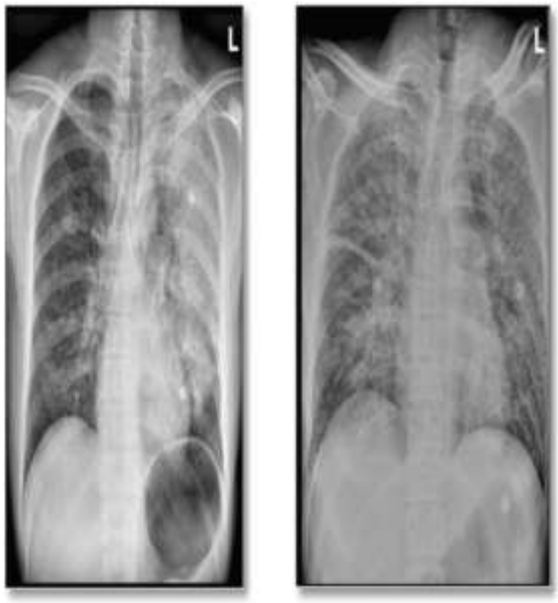


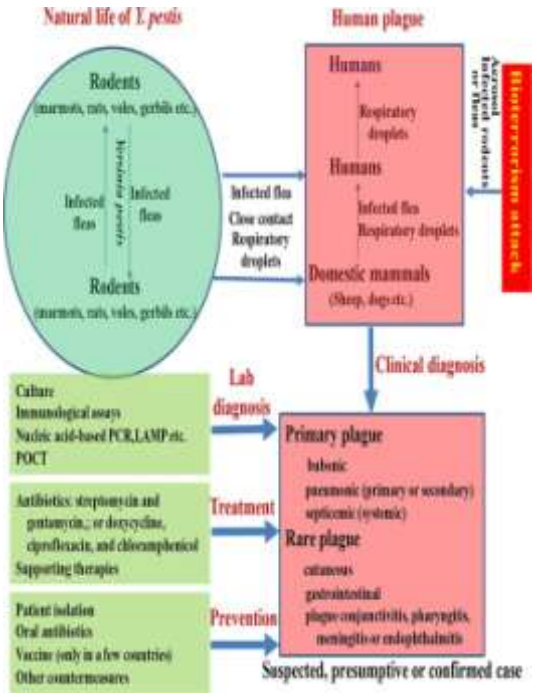
Fig. 3. Chest radiographs of two patients with pneumonic plague.

Epidemiology :

In ancient times, plague spread was associated with human activities, such as maritime trading and the Silk Road, etc., which could transport fleas associated with live rodents and/or products that led to the plague spread. Now, natural plague foci are widely distributed in Asia, Eurasia, Africa, and the greater American region. Since 2001, 14 major outbreaks have been reported to the World Health Organization (WHO) mainly from Africa and Asia.[21] This review intends to provide practical information for clinical staff to recognize plague early and provide effective treatment and prevention (Fig. 1).Plague is thought to be a disease of the past; however, in recent times outbreaks have occurred on every continent apart from Antarctica,[22] and it is endemic in parts of Africa, Asia and The Americas.

Plague is thought to be a disease of the past; however, in recent times outbreaks have occurred on every continent apart from Antarctica, [22]and it is endemic in parts of Africa, Asia and The

Americas. [21]Since the 1990s plague has been considered a reemerging disease by the World Health Organization (WHO).[24] In nature, plague is transmitted between rodents and other mammals through fleas and feeding, with natural foci of Y. pestis existing without the need of human hosts. [21]Typically, Y. pestis infection causes the death of large numbers of rodents. As a result, the fleas which were feeding on them lose their main food supply and start feeding on humans spreading the plague-causing bacteria through their bites.[24] The index case of this outbreak was one gentleman who had spread his infection to others travelling along-side him on public transport, eventually spreading the disease throughout the capital.19 Through epidemiological studies we can understand that plague is endemic in many areas of the world but is still very uncommon.[25]



History of plague:

The 1994 plague in India was a bubonic and pneumonic plague outbreak that lasted from August 26 to October 18, 1994 in south-central and western India.[17] The five afflicted Indian states, as well as the Union Territory of Delhi, have recorded 693 suspected cases and 56 deaths. Maharashtra (488 instances), Gujarat (77 cases), Karnataka (46 cases), Uttar Pradesh (10 cases), Madhya Pradesh (4 cases), and New Delhi (4 cases) were among the states involved (68 cases). No cases have been reported to have been exported to other Nations Plague is an ancient disease that was first recorded in North Africa and the Middle East around Classical times.[25] It's frequently assumed to be the sickness that caused various historic epidemics, such as the pestilence reported in 1 Samuel as afflicting the Philistines. The discovery of genomic traces of Y. pestis in the teeth of Neolithic farmers in Sweden dated to around 4,900 years ago, as well as analyses of ancient DNA in the teeth of Bronze

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1498-1503 www.ijprajournal.com ISSN: 2456-4494

Age humans, provide unequivocal evidence for its early existence. However, verifying the true nature of these outbreaks is impossible.[26]

What is plague?

The bacterium Yersinia pestis causes plague, an infectious disease. Fever, weakness, and headache are among the symptoms. This often occurs one to seven days following exposure. There are three types of plague, each of which affects a different bodily area and causes various symptoms. The lungs are infected with pneumonic plague, which causes shortness of breath, coughing, and chest pain; the lymph nodes are infected with bubonic plague, which causes them to swell; and the blood is infected with septicemic plague, which causes tissues to turn black and die.

Signs and symptoms of plague:

People infected with plague usually develop acute febrile disease with other non-specific systemic symptoms after an incubation period of one to seven days, such as sudden onset of fever, chills, head and body aches, and weakness, vomiting and nausea.There are two main forms of plague infection, depending on the route of infection: bubonic and pneumonic.Bubonic plague is the most common form of plague and is caused by the bite of an infected flea. Plague bacillus, Y. pestis, enters at the bite and travels through the lymphatic system to the nearest lymph node where it replicates itself. The lymph node then becomes inflamed, tense and painful, and is called a 'bubo'. There are several different clinical manifestations of plague. The most common form is bubonic plague, followed by septicemic and pneumonic pplague[28] Other clinical manifestations include plague meningitis, plague pharyngitis, and ocular plague.[28 ,29] General symptoms of plague include fever, chills, headaches, and nausea.[27] Many people experience swelling in their lymph nodes if they have bubonic plague.[27] For those with pneumonic plague, symptoms may (or may not) include a cough, pain in the chest, and haemoptysis.[27]

Treatment of plague

The various forms of plague are usually highly responsive to antibiotic therapy. [28] The antibiotics often used are streptomycin, chloramphenicol and tetracycline. Amongst the newer generation of antibiotics, gentamicin and doxycycline have proven effective in monotherapeutic treatment of plague.[28 ,29] Guidelines on treatment and prophylaxis of plague were published by the Centers for Disease Control and Prevention in 2021.[29] The plague bacterium could develop drug resistance and again become a major health threat. One case of a drug-resistant form of the bacterium was found in Madagascar in 1995. Further outbreaks in Madagascar were reported in November 2014 and October 2017.[31]

Prevention:

1. Vaccination:

Bacteriologist WaldemarHaffkine developed the first plague vaccine in 1897. [32,33]He conducted a massive inoculation program in British India, and it is estimated that 26 million doses of Haffkine's anti-plague vaccine were sent out from Bombay between 1897 and 1925, reducing the plague mortality by 50%-85%.[32,34] Since human plague is rare in most parts of the world as of 2021, routine vaccination is not needed other than for those at particularly high risk of exposure, nor for people living in areas with enzootic plague, meaning it occurs at regular, predictable rates in populations and specific areas, such as the western United States. It is not even indicated for most travelers to countries with known recent reported cases, particularly if their travel is limited to urban areas with modern hotels. The United States CDC thus only recommends vaccination for:

(a)all laboratory and field personnel who are working with Y. pestis organisms resistant to antimicrobials.

(b) people engaged in aerosol experiments with Y. pestis.

(c) people engaged in field operations in areas with enzootic plague where preventing exposure is not possible (such as some disaster areas). A systematic review by the Cochrane Collaboration found no studies of sufficient quality to make any statement on the efficacy of the vaccine.[35]

2. Early diagnosis:

Diagnosing plague early leads to a decrease in transmission or spread of the disease.

3. Prophylaxis:

Pre-exposure prophylaxis for first responders and health care providers who will care for patients with pneumonic plague is not considered necessary as long as standard and droplet precautions can be maintained.[29] In cases of surgical mask shortages, patient overcrowding, poor ventilation in hospital wards, or other crisis

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1498-1503 www.ijprajournal.com ISSN: 2456-4494

situations, pre-exposure prophylaxis might be warranted if sufficient supplies of antimicrobials are available. Postexposure prophylaxis should be considered for persons who had close (<6 feet), sustained contact with a patient with pneumonic plague and were not wearing adequate personal protective equipment. Antimicrobial postexposure prophylaxis also can be considered for laboratory workers accidentally exposed to infectious materials and persons who had close (<6 feet) or direct contact with infected animals, such as veterinary staff, pet owners, and hunters.Specific recommendations on pre- and post-exposure prophylaxis are available in the clinical guidelines on treatment and prophylaxis of plague published in 2021.[29]

REFERENCES:

[1]. Stenseth NC, Atshabar BB, Begon M, Belmain SR, Bertherat E, Carniel E, et al. Plague: past, present, and future. PLoS Med.2008;5:e3.
[2]. Perry RD, Fetherston JD. Yersinia pestis—etiologic agent of plague. Clin Microbiol Rev. 1997;10:35–66.
[3]. Yersin A. La peste bubonique a Hong-Kong. Ann Inst Pasteur (Paris). 1894;8:662–7.
[4]. Vogler AJ, Chan F, Nottingham R, Andersen G, Drees K, Beckstrom-Sternberg SM, et al. A decade of plague inmahajanga, madagascar: insights into the global maritime spread of pandemic plague. mBio. 2013;4:e00623–12–e00623–12.
[5]. Bertherat E. Plague around the world, 2010–2015. Wkly Epidemiol Rec. 2016;91:89–104.
[6]. Respicio-Kingry LB, Yockey BM, Acayo S, Kaggwa J, Apangu T, Kugeler KJ, et al. Two distinct Yersinia pestis populations causing plague among humans in the West Nile region of Uganda. PLoS Negl Trop Dis. 2016;10:e0004360.
[7]. Shi L, Yang G, Zhang Z, Xia L, Liang Y, Tan H, et al. Reemergence of human plague in Yunnan, China in 2016. PLoS ONE. 2018;13:e0198067.
[8]. Yang R. Plague: Recognition, Treatment, and Prevention. J Clin Microbiol. 2018;56(1).
[9]. Cosgrove SE, Perl TM, Song X, Sisson SD. Ability of physicians to diagnose and manage illness due to category A bioterrorism agents. Arch Intern Med. 2005;165(17):2002–2006.
[10]. R.D. Pechous, V. Sivaraman, N.M. Stasulli, W.E. Goldman Pneumonic Plague: The Darker Side of Yersinia pestis Trends Microbiol, 24 (3) (2016), pp. 190-197
[11]. Consultants GoW Health aspects of chemical and biological weapons WHO, WHO (1970)
[12]. Yang R. Plague: Recognition, Treatment, and Prevention. J Clin Microbiol.2018;56(1)
[13]. Pechous RD, Sivaraman V, Stasulli NM, Goldman WE. Pneumonic Plague: The Darker Side of Yersinia pestis. Trends Microbiol. 2016;24(3):190–197..
[14]. 14.Prentice MB, Rahalison L. Plague. The Lancet.. 2007;369(9568):1196–1207.
[15]. Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon:medical and public health management. Working Group on Civilian Andersson Biodefense. Jama. 2000;283(17):2281–2290.
[16]. Layton RC, Mega W, McDonald JD, et al. Levofloxacin cures experimental pneumonic plague in African green monkeys. PLoS Negl Trop Dis.. 2011;5(2) e959.
[17]. Andersson J. Combating Plague: Fighting a War on Two Fronts Through Vaccine Design and New Therapeutic Intervention. Doctoral Dissertation. UTMB Health: UTMB. Health. 2017.
[18]. Narayanan N, Lacy CR, Cruz JE, et al. Disaster preparedness: biological threats and treatment options. Pharmacotherapy.. 2018;38(2):217–234.
[19]. Kwon EH, Reisler RB, Cardile AP, Cieslak TJ, D"Onofrio MJ, Hewlett AL,, et al. Distinguishing Respiratory Features of Category A/B Potential Bioterrorism Agents from Community-Acquired Pneumonia. Health Secur. 2018;16 (4):224–238.
[20]. Li Y-F, Li D-B, Shao H-S, Li H-J, Han Y-D. Plague in China 2014-All sporadic case report of pneumonic plague. BMC Infectious Diseases. 2016;16:85-.
[21]. . Organisation WH. Plague around the world 2010-2015. WHO – weekly epidemiological review; 2016.
[22]. Organization WHO.WHO report on global surveillance of epidemic pioneinfectious desease plague WHO 2000
[23]. Organisation WH. Plague Fact Sheet. 2017.
[24]. Randremanana R, Andrianaivoarimanana V, Nikolay B, et al. Epidemiological characteristics of an urban plague epidemic

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1498-1503 www.ijprajournal.com ISSN: 2456-4494

in Madagascar, August– November, 2017: an outbreak report. Lancet Infect Dis. 2019;19(5):537–545.

[25]. Andam CP, Worby CJ, Chang Q, Campana MG. Microbial Genomics of Ancient Plagues and Outbreaks. Trends Microbiol. 2016;24(12):978–990.

[26]. Khan IA. Plague the dread fel visitation occupying the human mind for centuries. Trans soc trop hyg. 2004;98 (5):270-277.

[27]. "Symptoms Plague". CDC. September 2015. Retrieved 8 November 2017.

[28]. Nelson, Christina A; Fleck-Derderian, Shannon; Cooley, Katharine M; Meaney-Delman, Dana; Becksted, Heidi A; Russell, Zachary; Renaud, Bertrand; Bertherat, Eric; Mead, Paul S (2020-05-21). "Antimicrobial Treatment of Human Plague: A Systematic Review of the Literature on Individual Cases, 1937–2019". Clinical Infectious Diseases. **70** (Supplement_1): S3–S10. doi:10.1093/cid/ciz1226. ISSN 1058-4838. PMID 32435802.

[29]. Nelson, Christina A. (2021). "Antimicrobial Treatment and Prophylaxis of Plague: Recommendations for Naturally Acquired Infections and Bioterrorism Response". MMWR. Recommendations and Reports. **70** (3): 1–27. doi:10.15585/mmwr.rr7003a1. ISSN 1057-5987. PMC 8312557. PMID 34264565. Thisarticle incorporates text from this source, which is in the public domain.

[30]. Mwengee W; Butler, Thomas; Mgema, Samuel; Mhina, George; Almasi, Yusuf; Bradley, Charles; Formanik, James B.; Rochester, C. George (2006). "Treatment of Plague with Genamicin or Doxycycline in a Randomized Clinical Trial in Tanzania". Clin Infect Dis. **42** (5): 614–21. doi:10.1086/500137. PMID 16447105.

[31]. "WHO scales up response to plague in Madagascar". World Health Organization (WHO). 1 October 2017. Retrieved 5 October 2017.

[32]. "Waldemar Haffkine: The vaccine pioneer the world forgot". BBC News. 2020-12-11. Retrieved 2021-01-20.

[33]. ^ "WALDEMAR MORDECAI HAFFKINE". Haffkine Institute. Retrieved 2021-01-20.

[34]. ^ Hawgood, Barbara J. (February 2007). "Waldemar Mordecai Haffkine, CIE (1860-1930): prophylactic vaccination against cholera and bubonic plague in British India". Journal of Medical Biography. **15** (1): 9–19. doi:10.1258/j.jmb.2007.05-59. ISSN 0967-7720. PMID 17356724. S2CID 42075270.

[35]. Jefferson T, Demicheli V, Pratt M (2000). Jefferson T (ed.). "Vaccines for preventing plague". Cochrane Database Syst Rev (2): CD000976. doi:10.1002/14651858.CD000976. PMC 6532692. PMID 10796565.