World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

A Survey of the Literature on the Plague and Efficient Cure

Sampada V Bhagat [1], Samiksha S Bhambhurkar [1], Shivani P Gulhane [1], Gunjan P Malode [1,*], Chaitanya A Gulhane [1] and Prashant V Ajmere [2]

[1] *Department of Pharmaceutics, Faculty of Pharmaceutical Science, IBSS' s Dr. Rajendra Gode Institute of Pharmacy, Sant Gadge Baba Amravati University, Amravati.*
[2] *Department of Pharmacology, Faculty of Pharmaceutical Science, IBSS' s Dr. Rajendra Gode Institute of Pharmacy, Sant Gadge Baba Amravati University, Amravati.*

World Journal of Biology Pharmacy and Health Sciences, 2023, 14(01), 127–134

Publication history: Received on 02 March 2023; revised on 13 April 2023; accepted on 15 April 2023

Article DOI: https://doi.org/10.30574/wjbphs.2023.14.1.0167

Abstract

Yersinia pestis is causative agent of *plague* and is considered one of the most likely pathogens to be used as a bioweapon. In humans, plague is severe clinical infection that can rapidly progress with a high mortality despite antibiotic therapy. *Plague* is an acute infectious disease caused by gram-negative cocco-bacillus *Yersinia pestis*. This review provides an overview of its clinical manifestation, diagnosis, treatment, prophylaxis and protection requirements for the use of clinicians. I discuss the likelihood of a plagiarism of plague in an online world, and the feasibility of obtaining, isolating, culturing, transporting and dispersing plague in the context of an attack aimed at a westernized country. The lethality of plague with the resurgent in number of cases, development of antibiotic resistance, recent occurrence in urban areas and the lack of a vaccine make it a disease not to be missed in the mortuary. An extensive literature search on the Medline and Web of science database was conducted to collect papers relevant to plague. In autopsy, organ may be lymphadenopathy, fulminant pneumonia and diffuse interstitial pneumonitis. Conversely, any organ may be affected by myocarditis, meningitis, pharyngitis and hepatic and splenic necrosis. Front-line clinicians should be aware of the potential of deliberate release of plague and prepared to instigate early isolation of patient.

Keywords: Plague; Yersinia pestis; Bioweapon; Biowarfare; Bubonic; Pneumonic; Black Death

1. Introduction

Yersinia Pestis is the causing agent of plague and is considered one of the most likely pathogens to be used as a bioweapon. It is an major infection which occurs in humans and mammals other than rodents. In humans, plague is a severe clinical infection that cab progress rapidly despite antibiotic therapy and associated with a high mortility rate.[1,2] As with many primarily zoonotic disease, plague is a very severe disease in people with case fatality rates of 50-60% if left untreated. A deliberate or international release of plague is the act of using it as a weapon to infect a healthy population with the intention to cause harm. [3,4,2]

Plague in humans is a severe febrile illness caused by the Yersinia Pestis, a gram-negative bacillus member of the enterobacteria family. Human acquire infection most often by the bite of rodents fleas, occasionally by handling or ingesting infected animal tissues, or by inhaling contagious airborne particles. [5] It has a high epidemic impending pre-emptive step can be taken to reduce risks of exposure. Cases should be reported to health authorities immediately so that appropriate investigative and control measures can be implemented without delay and it should be mandated by national and international health regulation. [6]

* Corresponding author: Gunjan P Malode

2. History

In history, Plague is a well-known infectious disease with 3 foremost pandemics. The first great pandemic the 6th century Justinian plague, it is through that plague moved from upper Egypt to the Mediterranean and spread from there to Europe and Asia minor, resulted in the death of an estimated 100 million people. The second great pandemic is what as we refer to as "The Black Death" or in some place in Europe as "The Great Pestilence" and it is probably the most well-known of the three pandemics. The Black Death during 14th century causing an estimated 50 million deaths, approximately half of them in Asia and Africa and other half in Europe. The third and final great pandemic originated in China in the 1860s, but exploded across the globe after a major outbreak in Hong Kong 1894 by Alexandre Yersin, who isolated the organism from enlarged lymph nodes of plague victims and rapidly spread worldwide primarily through trade routes on steamships and railways, leading to the death of more than 10 million people. [7,8,9] A French scientist in 1898 Paul-Louis Simond send to investigate epidemic plague in Bombay and it was identified as the plague bacillus in the tissues of dead rats and subsequently proposed that the organism was transmitted from rat to rat, and from rats to humans by rat fleas. [7,9]

3. Clinical manifestations of natural infection (Human Plague)

Plague is a severe clinical infectious disease that can quickly progress to death if not diagnosed and treated early. It is readily treatable but a high index of suspicion is required to recognise the disease when transmission to humans is rare, when it appears after long periods of dormancy in endemic areas and when patient outside endemic areas. There are generally five forms of the plague infection such as:-

- Bubonic Plague
- Septicemic Plague
- Pneumonic Plague
- Meningitis Plague
- Pharyngeal Plague

3.1. Bubonic Plague

The bubonic plague marks from the bite of a flea infected with Y. pestis that had previously fed on an infected organism, such as a rodent. [10,1] The lymph node then becomes tense, inflamed and painful is called a bubo. The incubation period is between 2 and 8 days (rarely up to 15 days); it is characterised by sudden onset of fever of 380 C to 400 C, chills, headache and weakness followed shortly by intensely tender enlargement of regional lymph nodes usually in the groin, armpit or neck.[11]

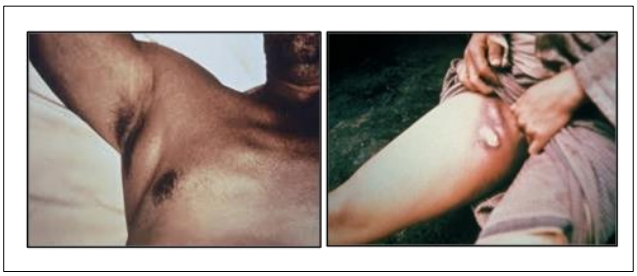

Figure 1 Axillary and inguinal buboes in patients with bubonic plague

Treated in the unsophisticated state with an fitting antibiotic then bubonic plague usually responds to quickly disappearance of fever and systemic symptoms over 2 to 5 days. As they had mentioned in above figure1. Septicemic and pneumonic plague can complicated bubonic plague. The mortality of untreated bubonic plague can be as high as 60%, but it is largely reduced to less than 5% if detected early and treated with effective antimicrobial therapy. [12,1]

3.2. Septicemic Plague

Primary septicemic plague occurs from a flea bite directly into the vasculature, or to catch to be bitten by a flea that had already bitten a black rat, when bacteria bypass the regional lymph node and multiply directly in the blood. [13,14,4] This form is the bloodstream infection with Y. pestis is characterised by lack of buboes. Bloodstream dissemination to diverse parts of the body including meninges may occurs. [15]

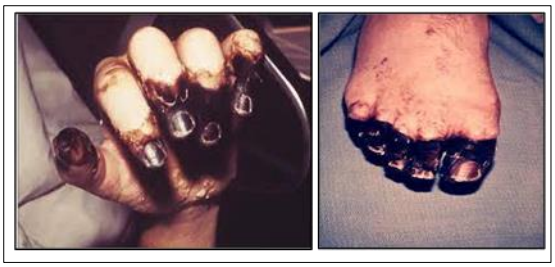

Figure 2 Digital gangrene and gangrene of the right foot

More on , patients with sepsis often present with gastrointestinal symptoms, such as nausea, vomiting, diarrhoea and abdominal pain. The resultant septicaemia may be overwhelming and very rapidly fatal. The black discoloration of the gangrenous necrotic tissue is where "The Black Death" obtained its name from as patients turn black and then soon die. [16] As they had shown in above figure 2.

3.3. Pneumonic Plague

Pneumonic plague is virulent form of plague, representing the most severe symptom of plague. It results from haematogenous spread of Y. pestis to the lungs by the respiratory droplet route and can initiate an epidemic of primary pneumonic plague incubation period is 1 to 7 days, but most cases arise 3 to 5 days after exposure. [17] As they had mentioned in above figure 3. Spread by respiratory droplets through an infected person's coughs or sneezes requires a distance of less than 2 meters and occurs from direct inhalation of aerosolized droplets of Y. pestis, originate from expelled respiratory droplets of mammals like cats and dogs and also it spreads from human-to-human. [18,19] Secondary pneumonic plague occurs from hemalogical spread of bacteria in bubonic or septicemic plague to the lungs. [20,21] Disease onset is characterised by chills, fever, headache, body pains, weakness, dizziness, chest discomfort, later followed by cough, bloodstained sputum production, increasing chest pain, difficulty in breathing, hypoxia and haemoptysis. During the 2017 Madagascar plague outbreak, 77%of the reported were pneumonic. [22,23]

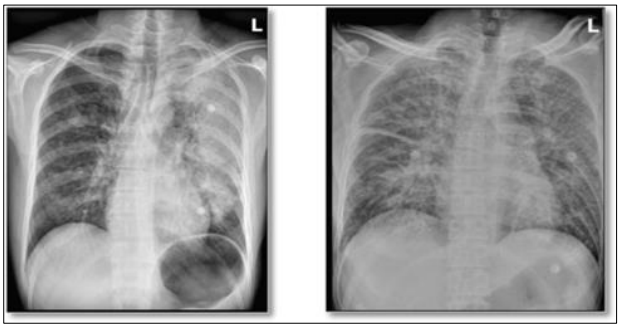

Figure 3 Chest radiographs of two patients with pneumonic plague

3.4. Meningitis Plague

Meningitis is a rare form of plague. From 1960 to 2004, there were 18 (4%) meningitis cases among the total 413 evaluable plague cases reported to the CDC in the United States. The majority of cases were secondary to bubonic plague, and 14 patients (78%) survived. Although meningitis may be present at the start of plague, its emergence is generally delayed and may be due to poor antibiotic therapy of the original infection. In the pre-antibiotic era, chronic, recurrent meningeal plague was recorded over weeks and even months. Plague meningitis is characterised by fever, headache, impaired mental status, meningismus, and polymorphonuclear leukocytic pleocytosis. [24,5]

3.5. Pharyngeal Plague

Plague pharyngitis is a rare illness characterised by fever, painful throat, and cervical lymphadenitis. It may be clinically indistinguishable from more prevalent causes of pharyngitis in its early stages. Cervical or submandibular buboes typically arise as a result of pharyngeal involvement. Instances occur as a result of respiratory droplet exposure or the consumption of raw meat. Secondary plague pneumonia can develop from pharyngeal plague. In the differential diagnosis of acute bacterial pharyngitis, healthcare workers working in plague-endemic areas should be aware of the risk of plague. Contacts with pneumonic plague may have pharyngeal colonisation with Y. pestis without symptoms. [18,22]

4. Treatment

Untreated plague kills more than half of bubonic plague cases and nearly all septicemic or pneumonic plague cases. For the last 50 years, the overall plague case-fatality ratio in the United States has been around 15%. [26] Delays in seeking care, misdiagnosis, and delayed or wrong treatment are virtually always the causes of fatalities. Early diagnosis and antibiotic therapy are critical. Patients with pneumonic plague who initiate treatment more than 18 to 24 hours after the beginning of pulmonary symptoms have a very high case-fatality ratio. [26]

4.1. Aminoglycosides(streptomycin and gentamicin)

Streptomycin is the most effective antibiotic against Y. pestis. However, no longer manufactured in the United States and can cause irreversible to toxicity in some patients. Streptomycin may be ototoxic and nephrotoxic to the foetus and therefore of its ready availability and ease of administration, it is replaced by gentamicin in the United States. When gentamicin when judiciously administered, is effective and safe for both mother and foetus, and in children. Because of its safety, intravenous or intramuscular administration, and the ability to have blood concentrations monitored, gentamicin is the preferred antibiotic for treating plague in pregnancy and children. Although not approved by the Food and Drug Administration (FDA) for treatment of plague, gentamicin is more readily available than streptomycin and has been used successfully.[27]

4.2. Chloramphenicol

Chloramphenicol is a suitable alternative to aminoglycosides in the treatment of bubonic or septicaemic plague and is the drug of choice for treatment of patients with Y. pestis. Chloramphenicol can be used separately used or in combination with an aminoglycoside. Chloramphenicol carries a risk of grey baby syndrome or bone-marrow suppression. [27,5]

4.3. Doxycycline (Tetracyclines)

This group of antibiotics is bacteriostatic but effective in the primary treatment of patients with uncomplicated plague, and as post-exposure prophylaxis. Tetracycline has an adverse effect on developing teeth and bones of the foetus.

4.4. Sulfonamides

Sulfonamides have been used extensively in plague treatment and prevention; and have shown higher mortality, increased complications, and longer duration of fever as compared with the use of streptomycin, chloramphenicol or tetracycline antibiotics..

4.5. Fluoroquinolones

Table 1 Treatment and prophylaxis of Y. pestis infection [28,7,25]

Treatment	Prophylaxis	Protection	Supportive Therapy
Adults	1st line; Streptomycin 1 g IM BD or Gentamicin 5 mg/kg IV/IM once daily and/or Doxycycline IV 200 mg once daily 2nd line; Ciprofloxacin, Levofloxacin, Moxifloxacin, Chloramphenicol	1st line; Doxycycline 100 mg oral BD or Ciprofloxacin 500 mg oral BD 2nd line; Chloramphenicol 25 mg/kg orally QDS For a minimum of 7 days Preventflea bites withinsect repellents suchas N,N-diethyl-meta-toluamide (DEET)	Tissue perfusion and oxygenation in septic patients should be maintained by fluid resuscitation and vasopressors if required. With the possibility of ECLS if needed.
Children	1st line; Streptomycin 15 mg/kg IM BD (2 g max) or Gentamicin 2.5 mg/kg IV/IM TD 2nd line; Doxycycline, Ciprofloxacin, Chloramphenicol - (maintain concentration between 5–20 mg/ml)	1st line; Doxycycline if > 45 kg give adult dose, if < 45 kg give 2.2 mg/kg orally BD or Ciprofloxacin 20 mg/kg orally BD 2nd line; Chloramphenicol 25 mg/kg orally QDS (maintain concentration between 5– 20 mg/ml) Preventflea bites withinsect,N-diethyl-meta-toluamide (DEET repellents suchas N)	Patients with pneumonic plague may require ventilatory support. Isolate patients with pneumonic plague (48 h minimum) and take precautions against droplet transmission in the form of surgical face masks. Report all cases of plague per local procedure.

Pregnant Women	1st line; Gentamicin 5 mg/kg IV/IM OD 2nd line; Doxycycline or Ciprofloxacin Avoid Streptomycin For breastfeeding women and their infants use Gentamicin	As for non-pregnant adults	Procedures that may aerosolize plague should be avoided, such as bone sawing in amputation.

Fluoroquinolones, such as ciprofloxacin, have been shown to have good effect against Y. pestis in both in vitro and in vivo. Ciprofloxacin is bacteriocidal and has broad-spectrum activity against Gram-negative and Gram-positive aerobic bacteria. Although it has been used successfully to treat humans with Francisella tularensis infection, no controlled studies have been published on its use in treating human plague. Fluoroquinolones are used empirically to treat seriously ill patients and have confirmed activity against Y.pestis but are not FDA approved for this indication.

5. Vaccination

Y. Pestis is one of the most virulent human pathogens and uptill now there are no licensed plague vaccines available. A plague vaccine is accessible for human use, but cannot be used normally and the vaccine should be consider for high-risk proffesionals only. Thus, the vaccine is indicated for persons whose work consistently brings them into close contact with Y. pestis. The WHO proposes two potential strategies for vaccination :- a reactive vaccine to plague during an outbreak and to interrupt the chains of transmission and a prophylactic vaccine used primarily in endemic areas.[29,3]

6. Prevention and Control of human plague transmission

The first concern in control of human plague is direct attack on report foci of infection. A multidisciplinary approach should be involved since one case constitutes an outbreak.This involves diagnosis and recognition of the disease, which is essential to establish firmly the existence of plague and isolation of the patient and of the immediate contacts as well as focal attack on the area invaded by plague through disinfestation of premises and persons.

6.1. Notification

All suspected and confirmed cases should be reported immediately to the local health authority, Port Health authority, provincial health authority and National DoH by telephone. International Health Regulations Department requires submission of case report of both suspected cases and confirmed cases straight away to the World Health Organization.

6.2. Sample

The local branch of the National Health Laboratory Service or the National Institute for Communicable Diseases (NICD) should be contacted immediately so that the necessary specimens can be safely collected for rapid confirmation of the diagnosis. Samples required are blood, sputum, bubo aspirate or tissue, but it is important to consult with the laboratory before collecting specimens.

6.3. Isolation

The patients' clothing and baggage should be cleared of fleas using an insecticide effective against local fleas and known to be safe for people; patients should be seen by a doctor, their condition evaluated and the patients hospitalised and barrier nursed. For patients with bubonic plague drainage/secretion precautions are indicated for 48 hours after start of effective therapy, if in casing there is no cough and the chest x-ray report is negative. In support of patients with pneumonic plague, strict isolation is required with safety measures against airborne spread which is necessary until 48 hours.

6.4. Concurrent disinfection

Disinfection of sputum and purulent discharges and articles soiled therewith, and terminal cleaning is required. Bodies of people and carcass of animals that had died due to plague should be handle with strict aseptic precautions.

6.5. Quarantine

Those who have been in household or face-to-face contact with patients with pneumonic plague should be provided with chemoprophylaxis and placed under surveillance for 7 days. [30,31]

7. Human surveillance

Surveillance, environmental management, and personal protective measures are the cornerstones of prevention and control. Plague is a notifiable condition in South Africa and is one of the infectious diseases the International Health Regulations (IHR) consider to be public health emergencies; IHR stipulate that all confirmed cases of human plague be investigated and reported through appropriate authorities to the World Health Organization.

7.1. Passive Surveillance

Whenever clinical symptoms or laboratory results suggest that a patient is infected with Y. pestis, the suspected case should be reported immediately.

This will allow public health authorities to:

- Advise on treatment and management of human plague cases;
- Initiate efforts to identify the source of infection;
- Determine the extent of any epizootic activity;
- Assess the potential for additional human cases;
- Disseminate information on plague to health care personnel; and
- Implement emergency prevention and control measures.

Prompt reporting is especially important for cases of pneumonic plague because this form of the disease can be transmitted directly from person to person via infectious aerosols. Emergency procedures as described below must be implemented immediately to prevent further human infections. Local doctors and other health care workers must be familiar with the symptoms of plague. If a patient's symptoms suggest human plague, samples should be collected for diagnostic confirmation at a laboratory.

7.2. Community surveillance

It should not be assumed that health care workers, laboratory personnel and other public health authorities in plague-endemic areas are familiar with plague diagnosis and treatment. It is important to ensure that members of the local health care community are aware of the possibility of cases of plague occurring. This can be accomplished through brief training courses, plague surveillance newsletters, brief notes in other health-related newsletters or periodic contact with other health personnel.

7.3. Active surveillance

A suspect case of human plague, surveillance personnel should immediately determine whether other cases exist or have occurred recently in the same vicinity. Hospital and clinical records from areas near where the case occurred should be reviewed and local health care providers should be interviewed to identify other potential cases. If possible, blood and other appropriate samples should be obtained from survivors who are considered to be potential cases to determine whether these persons are infected with or have antibody against Y. pestis. If possible, blood samples should be obtained from other family members or likely contacts. Record reviews and interviews with health care personnel should also be done when plague is identified for the first time in a region's animal or flea populations. In such situations, human cases might have occurred recently but may have been misdiagnosed or gone unreported. [32,33]

8. Conclusion

To utilise as a plague plagiarism in an internet word, one must be able to procure, isolate, culture, and transport plague, as well as use a variety of viable plague dispersal mechanisms to infect a significant number of humans. If an attacker's primary goal was to instill dread, plague would be a good choice of weapon, regardless of how many people were murdered. Our medical and public health response would be strong, limiting the spread of pneumonic plague transmission in the community as soon as the first case was recognised, but we would be stressed by the casualties—a considerable number of those originally infected may still die swiftly. A vaccination against Y. pestis would be ideal for reactive or chronic infections.

Compliance with ethical standards

Acknowledgments

Authors are thankful to Shri. Yogendraji Gode, President, Principal & Management of IBSS's Dr. Rajendra Gode Institute of Pharmacy, Amravati for providing necessary facility to undertake this work.

Disclosure of conflict of interest

The author declares no conflict of interest.

References

[1] Ansari I, Grier G, Byers M. Deliberate release: Plague – A review. Journal of Biosafety and Biosecurity. 2020 Mar; 2(1): 10-22. doi: 10.1016/j.jobb.2020.02.001.

[2] Christian MD. Biowarfare and bioterrorism. Critical Care Clinics. 2013; 29(3):717-756

[3] Organisation TWH. The WHO Plague Vaccine Target Product Profile (TPP) WHO 2018.

[4] Perry RD, Fetherston JD. Yersinia pestis- etiologic agent of plague. Clinical Microbial Review. 1997; 10(1):35-66.

[5] David T. Dennis and Paul S. Mead: Tropical Infectious Disease.2006:471-481. Published online 2009 May 15. doi 10.1016/B978-0-443-06668-9.50047-8.

[6] Centers for Disease Control and Prevention. Fatal human plague— Arizona and Colorado, 1996. Morbidity and Mortality Weekly Report (MMWR) 46:617, 1997.

[7] Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological Weapon: medical and public health management. Working Group on Civilian Biodefense. Journal of the American Medical Association (Jama). 2000; 283(17):2281-2290.

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

[9] Khan IA. Plague: the dreadful visitation occupying the human mind for centuries. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2004; 98(5):270-277.

[10] Prentice MB, Rahalison L. Plague. The Lancet.2007; 369(9568):1196-1207.

[11] Smego RA, Frean J, Koornhof HJ. Yersiniosis. I. Microbiological and clinico-epidemiological aspects of plague and non-plague Yersinia infections. European Journal of Clinical Microbiology and Infectious Diseases.1999; 12: 1-15.

[12] Sun W, Singh AK. Plague Vaccine: recent progress and prospect. Nature Partner Journals (npj) vaccines. 2019; 4.

[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] Andersson J. Combating Plague: Fighting a War on Two Fronts Through Vaccine Design and New Therapeutic Intervention. Doctoral Dissertation. UTMB Health: UTMB Health. 2017.

[15] National Department of Health. 1998. Report on plague surveillance in South Africa with special reference to activities between 1993 and 1998. Unpublished.

[16] Hull HF, Montes JM, Mann JM: Plague masquerading as gastrointestinal illness. Western Journal of Medicine.1986; 145:485.

[17] Isaacson, M. 1972. Human plague in southern Africa during period 1965-1969. Thesis. University of Witswatersrand.

[18] Known 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 Security. 2018; 16(4): 224-238.

[19] Rabaan AA, A1-Ahmed SH, Alsuliman SA, Aldrazi FA, Alfouzan WA, Haque S. The rise of pneumonic plague in Madagascar: current plague outbreak breaks usual seasonal mould. J Med Microbial. 2019; 68(3):292-302.

[20] Hu Wang YC, Zuyun Wang, Xiaoyi Wang, Zhaobiao Guo, Yanfeng Yan,, Chao Li BC, Xiao Xiao, Yonghai Yang, Zhizhen Qi, Guajun Wang, Baiqing Wei,, Shouhong Yu DH, Hongjian Chen, Gang Chen, Yajun Song and Ruifu Yang. A Dog-Associate Primary Pneumonic Plague in Qinghai Province, China. Clinical infectious disease. 2010; 52(2).

[21] John M. Doll PSZ, Paul Ettestad, Ann L, Bucholtz, Ted Davis, Kenneth Gage. Cat- Transmitted Fatal Pneumonic Plague in a Person Who Traveled from Colorado to Arizona. The American Journal of Tropical Medicine and Hygience. 1994; 51(1):109-114.

[22] Gage KL and Beard CB. Plague Ch 126. In: Cohen J, Powderly WG and Opal SM (eds) Infectious diseases 4th Ed. Vol 2. Section 6 International medicine: Major tropical syndromes: Systemic infections. Amsterdam: Elsevier. 2017;2: 1078-84.

[23] Munyenyiwa A, Zimba M, Nhiwatiwa T, Barson M (2019): Plague in Zimbabwe from 1974 to 2018: A review article. Public Library of Science Neglected Tropical Diseases 13(11):e0007761. doi: 10.1371/journal.pntd.0007761.

[24] National Department of Health. 2002. Draft strategy for Disease Outbreak Response and Epidemic Management in South Africa.

[25] Narayanan N, Lacy CR, Cruz JE, et al. Disaster preparedness: biological threats and treatment options. Pharmacotherapy.2018; 38(2): 217-234.

[26] Centers for Disease Control and Prevention: Biological and chemical terrorism: Strategic plan for preparedness and response. Recommendations of the CDC Strategic Planning Workgroup. Morbidity and Mortality Weekly Report (MMWR) 49:1, 2000.

[27] WHO. 1999. Plague Manual: Epidemiology, Distribution, Survillance and control. WHO/CDS/CSR/ED/99.2. Geneva. Downloaded from http://WWW.Who.int/enc.

[28] Watson AK, Ellington S, Nelson C, Treadwell T, Jamieson DJ, Meaney – Delman DM. Preparing for Biological Threats: Addressing the Needs of Pregnant Women Birth Defects Research. 2017;109(5): 391-398.

[29] Titball RW, Williamson ED, Dennis DT: Plague. In Plotkin SA, Orenstein WA (eds): Vaccines, 4th ed. Philadelphia, WB Saunders. 2004; Page No. 999.

[30] Byard RW.A Forensic evaluation of plague- a re-emerging infectious disease with biowarfare potential. Medicine, Science and the Law. 2020; 60(3): 200-205. doi :10.1177/0025802420908483. Epub 2020 Mar 19.

[31] Byard RW. Lethal dengue virus infection – a forensic overview. American of Journal of Forensic Medicine and Pathology. 2016; 37: 74–8.

[32] Centers for Disease Control and Prevention. Prevention of plague. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report (MMWR) 45:1, 1996.

[33] World Health Organization: Technical guide for a system of plague surveillance. Weekly Epidemiological Record.1973; 14:149.