PLAGUE AS A BIOLOGICAL WEAPON OF MASS DESTRUCTION

Dewi Kartikawati Ningsih

Lecturer at Emergency Nursing, Department of Nursing Science, Faculty of Medicine

ABSTRACT

Background: Indonesia is an archipelago country lies on the pacific ring of fire, which has a greater risk for disaster due to its geographic location. Indonesia had experienced both natural disaster and man made disaster. However, now days man made disaster often occurred that lead towards destruction of human mankind. Modern weapon of mass destruction are either nuclear, biological or chemical can bring a huge damage to societies and civilization.

Methods: The method used in this literature review was collected and analyzed the article of biological weapon of mass destruction. Articles collected through electronic databases such as CINAHL; ScienceDirect; Center for Disease Control (CDC); American Medical Association (AMA); National Institute of Allergy and Infectious Diseases (NIH) and textbook of emergency preparedness response. The criteria of articles have full text and published in the period of time between 2004-2014.

Result: In this article mainly focused on explaining plague as a biological weapon of mass destruction that including description of the agents, historical background occurring plague as a biological organism, historical use plague as a weapon of mass destruction (WMD), transmission/dispersion/incubation, diagnosis and treatment, detection, responder safety consideration, environmental impact, medical surge consideration and future implications.

Discussion and recommendation: The huge number of casualties due to sudden event can cause increasing demand for health care resources including facilities, health care providers, hospital resources, infrastructures and other resources. Preparing for medical surge are always in the first priority and can be consisting medical services facilities, medical care providers, hospital resources as well as infrastructures. During tremendous outbreak health care center will probably run out of space, furthermore it is essential to establish the alternate care facilities such as school, mosque, churches, community center, mall, government building, stadium, medical professional offices and so forth to deal with large casualties. In addition, totally eliminating plague is less possible, and so improving prophylactic and therapeutic antibiotic regimen as well as rapid diagnostic and technical laboratory microbiology standards are essential to response plague outbreak.

Key word: plague, biological weapon of mass destruction, bioterrorism-related epidemics.

Jurnal Ilmu Keperawatan, Vol : 1, No. 2, Nopember 2013; Correspondence : Dewi Kartikawati Ningsih University of Brawijaya Jl. Veteran Malang 65145. Email address: kartika.karso@ub.ac.id Mobile phone: 0821 8687 7361

Description of the Agent

Plague has known as a biological warfare that has been recognized to causing destruction human mankind (Kapur& Smith. 2011; Inglesby et all. 2000; Rotz et all. 2002; Rosenbloom et all. 2002; Casadevall&Pirofski. 2004). This is because a small amount of this agent may create sufficient damage among inhabitants (Rosenbloom et all. 2002). Thereby as a biological weapon plague has been killed populations over millions in Siege of Caffa known as *the blackdeath* (Wheelis. 2002; Ligon. 2006; Kool. 2005; Casadevall&Pirofski. 2004; Inglesby. 2000).

Plague is an infectious disease caused by *Yersinia pestis*, gram-negative bacillus, which hosted in rodents as well as fleas. It's also may be transmissible to human if plague-infected fleas bite them or by handling an infected animal (CDC. 2004; Gani& Leach. 2004; Inglesby. 2000). Human who are exposed this agent may get infections called bubonic plague. The bubonic plague may develop into pneumonic plague if the infections disperse to the lungs known as pneumonic plague. This infection can be easily spread to human by inhalation and that can be contagious (Gani& Leach. 2004; Inglesby. 2000).

Plague has three forms which are bubonic plague, pneumonia plague and septicemia plague. The first one is the most common plague and transmitted to human by fleas bitten or substances contaminated *Yersinia pestis* (CDC. 2004; Kool. 2005). When the bacteria disperse to the lungs, it will develop pneumonic plague afterwards (Kool. 2005). These type of plagues will only occur when infections spreads person to person, and so it has been recognized as a biological weapon since it can be transmitted as an aerosol agents (Gani& Leach. 2004; Kool. 2005; Josko, D. 2004). Whereas the last one, which is septicemia plague, it could encounter if both plagues have less treatment in which bacillus have been circulated into blood stream and resulted on exacerbation throughout the body (CDC. 2004).

Historical background occurring plague as biological organism

Naturally plague occured arise mostly as bubonic plague that common happened through fleas bitten from infected rodents. From that way, it may develop into pneumonic plague through blood stream if the victims are well untreated. The pneumonic plague is dangerous since it can be dispersed through air (Begier et all. 2006).

Plague historically as epidemic diseases started when it devastated human mankind appeared in period of 1300 - 1000 BCE and became outbreak in the city of Ashdod (Ligon, B.L. 2006; NIH. 2007; Riedel, S. 2005). Then, it's followed by the original report of plague called *"Great Plague of Justinian"* in Egypt around AD 532 and being transmissible to Middle East and several countries surrounding the Mediterranean year after (Riedel, S. 2005). During an epidemic, roughly forty percent residents in Constantinople were death (Ligon, B.L. 2006). The tremendous victims due to plague infections known as *"The Black Death"* occurred in Siege of Caffa, Eastern Europe thatwas approximately 25 million populations died. It, moreover, has recorded as the greatest epidemic of civilization (Wheelis, M. 2002; Ligon, B.L. 2006). Since then, plague dispersed around Europe, Middle East and North Africa (Riedel, S. 2005).

The next epidemic plague struck China in 1894 and resulted over ten thousands people died (Begier et all. 2006; Josko, D. 2004). It, also, lead spreads across China continent, which was overwhelmed especially in both Canton and Hongkong where large epidemic had found. After China, the incidence of plague appeared in Bombay around 1898 and 1908 where almost 6 million civilizations were deceased (Josko, D. 2004). Since then, plague remained spread to almost all Asian continents except for Australia. On one hand, in the year between 1900 and 1924 the smaller outbreak plague happened in the US especially along the Pacific and Gulf coasts (Riedel, S. 2005), then followed between 1924 and 1925 the outbreak of plague announced in Los Angeles due to undomesticated rodent population (Josko, D. 2004). Moreover, in the year 1994 it has been reported pneumonic plague outbreak hit city of Surat, India. Lastly, the recent suspected cases of pneumonic plague occurred in the Uganda and the Republic of Congo during 2004 and 2005 respectively (Begier et all. 2006).Since then, both of National and International had focused to deal with combating plague.

Historical use plague as a weapon of mass destruction (WMD)

Historically plague as biological weapon started in Siege of Caffa from 1346 to 1347 resulted on severe devastating civilization called by *the Black Death*. It was nearly 20 to 30 millions people around Europe died which meansthat approximately one third of the European population (Inglesby et all. 2000; Wheelis, M. 2002; Ligon, B.L. 2006). This occurred once the Mongolian army, The Tartar, thrown plague-infected

corpse surrounded Crimean city of Caffa (Riedel, S. 2005; Wheelis, M. 2002). It, thus, created spreading of plague in the city and caused an outbreak. However, in fact, what was actually found is that it wasn't the infected corpse that caused the epidemic, but the fact that the fleas moved to the local rodent population. Because of that, plague remained disperse in a county or even a nation which had enormous effect on livelihood and it ended up within one and half century (Inglesby at all. 2000)

During World War II (WW II) plague being used as a biological weapon by Japanese army. A Japanese army through secret research unit (Unit 731) experienced on plague as biological weapon agents (Ligon, B.L, 2006; Riedel, S. 2005). The Japanese physician leader relied on plague, which was devastating agents to cause tremendous serious accident among populations. Thereby, they tried to study plague and had many experiments on that. Finally, at the end of their study, they found that clay bombs were one of the ways to address their mission (Ligon, B.L. 2006). Following on October 4, 1940 Japanese army had spread of plague into step food at Chuhsien and that resulted 21 people killed. In addition, on October 29 the Japanese flight released plague at Ningpo and two days later 99 people were death within 34 days due to bubonic plague infections. Furthermore, on November 1941, the Japanese dropped mixture materials and other particles at the business center of Changteh in the province of Hunan and two weeks later, it found that a small outbreak occurred which led to people died (Ligon, B.L. 2006).

Transmission/Dispersion/Incubation

Plague need reservoir to carrying on human. The natural host of *Yersinia pestis* that can be found in rodents, squirrel, prairie dog and it usually dispersed through fleas (Josko, D. 2004). Human may get exposed plague by fleas bitten, contacts with an infectious animal and throughout a droplet (UPMC. 2011). The most cases occur in human due to infected bite animals or fleas and handling infectious animal. Those transmissions may towards bubonic plague rather than pneumonic plague, which can be spread only through droplets (UPMC. 2011; NIH. 2009). However, septicemia plague could be happened once the patientwas well untreated that lead to getting worst. Neither bubonic or septicemia plague are transmitted through human to human, whereas, both of bubonic and pneumonic plague may develop into septicemia plague when it left untreated (UPMC. 2011; Stenseth et all. 2008).

The incubation period of plague, overall, need approximately 2-10 days (Rosenbloom et all. 2002). The incubation of plague itself differs from the route of infection: bubonic, septicemia and pneumonic which require 1 to 8 days following exposure towards infected animal or flea bites, 2 to 6 days after symptoms arise due to untreated bubonic and pneumonic plague and 2 to 4 days after exposure respectively (UMPC. 2011)

In conjunction with the clinical of manifestation, plagues are divided into three forms associated with the routes of infections: bubonic, septicemia and pneumonic (Stenseth et all. 2008). For the bubonic plague may have causing immediate fever, weakness, chills, headaches, nausea, vomiting. Quite often time, it will occur buboes, which is very painful, and usually can be found in the neck, axillary and inguinal. On the other hand, the septicemia plague appears when if it is untreated and that lead to getting worst than bubonic and pneumonic. Sometime it followed by blood coagulation and gangrene. Lastly, the pneumonic plague are being dominated by respiratory problem that turns into the light sign such as cough, muscle aches, headache and fever to severe condition like chest pain, short of breathing and hemoptysis (UPMC. 2011). One thing that should be remembered is about the key to diagnosing pneumonic plague, which is hemoptysis since there are only two infections that cause bloody sputum and the other one is tuberculosis.

Diagnosis/Treatment

Establishing diagnosis and faster treatment are an important waysto reduce the number of morbidity and mortality (Stenseth et all. 2008). Establishing diagnosis is derived from the patient's history including environmental exposure (Josko, D. 2004). Based on the guideline from CDC (2012) after specimen had been taken, then, it followed by drug therapy. If the patients are indicated towards pneumonic plague, it should be placed into isolation room to avoid droplet transmission (Stenseth et all. 2008).

Diagnostic testing is adapted from CDC (2012) that consist of:

- Lymph node aspirate: an affected bubo should contain numerous organisms that can be evaluated by microscopically and blood culture.
- Blood cultures: organisms may be seen in blood smears if the patientssuffer from septicemia.

Blood smears were taken from suspected bubonic plague. In the early of the illness, it is usually a negative for bacteria throughout microscopic examination, however it may be a positive by blood culture. Then, if the result of blood culture is a negative and the plague still remained exist thus required serologic testing to establish the diagnosis.

- Sputum: culture is a possible that can be found on sputum to pneumonic patients; however, blood is usually a culture-positive as well. Bronchial/tracheal washing may be taken from suspected pneumonic plague patients.
- In cases of living organisms are unculturable such as lymphoid, spleen, lung, and liver tissue or bone marrow, samples may yield evidence of plague infection by direct detection methods for instances*direct fluorescent antibody* (DFA) or PCR.

Treatment should be performed as soon as possible to reduce the risk of complication and death. Treatments are extremely effective if administered within 24 hours (Rosenbloom. 2002). Antibiotics are initially given in 24 hours after the first of symptoms appeared and it should be administered for minimum ten days (Josko, D. 2004). The recommended antibiotic treatment for plague can be seen in **Table 1**. Furthermore, the history of treatment towards vaccine to combat plague hasbeen recorded in the US around 1998, but it has been no longer available (Inglesby et all. 2000; Josko, D. 2004). Research had done and showed that the vaccine was used to prevent bubonic plague instead of pneumonic plague. In addition, the development of vaccine finally used in certain condition such as laboratory towards microbiologists and researcherswhoworking with *Yersinia pestis.*However, recently research about*Yersinia pestis* was in progress in order to be able to access and to utilize combating pneumonic plague (Inglesby et all. 2000).

Table 1. Treatment of patients with pneumonic plague in the contained

	Preferred agents	Dose	Route of administration
Adults	Streptomycin1	1 g twice daily	IM
	Gentamicin1	5 mg/kg once daily, or 2 mg/kg loading dose followed by 1.7 mg/kg every 8 hours	IM or IV
	Alternative agents	**Dose**	**Route of administration**
	Doxycycline	100 mg twice daily or 200 mg once daily	IV
	Ciprofloxacin	400 mg twice daily	IV
	Chloramphenicol2	25 mg/kg every 6 hours	IV
Children	**Preferred agents**	**Dose**	**Route of administration**
	Streptomycin1	15 mg/kg twice daily (maximum daily dose, 2 g)	IM
	Gentamicin1	2.5 mg/kg every 8 hours	IM or IV
	Alternative agents	**Dose**	**Route of administration**
	Doxycycline (for children ≥ 8 years)	Weight < 45 kg: 2.2 mg/kg twice daily (maximum daily dose, 200 mg) Weight ≥ 45 kg: same as adult dose	IV
	Ciprofloxacin	15 mg/kg twice daily (maximum daily dose, 1 g)	IV
	Chloramphenicol2 (for children > 2 years)	25 mg/kg every 6 h (maximum daily dose, 4 g)	IV
Pregnant women	**Preferred agent**	**Dose**	**Route of administration**
	Gentamicin1, 3	Same as adult dose	IM or IV
	Alternative agents	**Dose**	**Route of administration**
	Doxycycline4	Same as adult dose	IV
	Ciprofloxacin4	Same as adult dose	IV

Mass casualty setting and post-exposure prophylaxis

	Preferred agents	Dose	Route of administration
Adults	Doxycycline	100 mg twice daily	PO
	Ciprofloxacin	500 mg twice daily	PO
Children	Doxycycline (for children ≥ 8 years)	Weight < 45 kg: 2.2 mg/kg twice daily (maximum daily dose, 200 mg) Weight ≥ 45 kg: same as adult dose	PO
	Ciprofloxacin	20 mg/kg twice daily (maximum daily dose, 1 g)	PO
Pregnant women	Doxycycline1	100 mg twice daily	PO
	Ciprofloxacin1	500 mg twice daily	PO

Adapted from: Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

Detection

Early detection is mandatory to provide appropriate response that consisting of prophylactic medicines, vaccine or antidotes (CDC. 2000). According to CDC in the MMWR (2000) surveillance will be established through developing new standards to detect, evaluate and report dubious incidence that can be led to terrorist action. Because of this, CDC establishing cooperation between state and local health institution including hospital, emergency physician staff, poison control center and other institutions to improve quality of surveillance for any suddenly event which create to unexpected injury and disease, develop statistical methods as well as establish the criteria of investigating and evaluating suspect agents (CDC. 2000).

Additional information's that should be considered as a key to detect special condition are important. Firstly is size including how agent is virulence, mode of transmission and people affected. Secondly, is population dispersion todiseaseswhether it happensin concentrated or cluster area. Third is health care quality personal that may provide promptly treatment to suspectvictims. The last oneis season in which it should be distinguished between bioterrorism attack and natural occurring diseases, as it may be challenges to detect if it happens in seasonal natural diseases (AMA. 2012; Buehler et all. 2003)

Detecting specific biological warfare like plague depends on how fast identification causative agent and specific diagnosis (AMA. 2012). Especially for pneumonic plague, it should be determined from the incubation periods, which is range from two to four days. This case has short prodromal and increase progressively during an epidemic episode. The procedure of clinical laboratory doesn't enough to establish suspected diseases and so, microscopic investigation of sputum may provide promptly result to deliberate diagnosis. Then, it has to be followed by treatment as earlieras they could to avoid risk of complication and fatalities (Buehler et all. 2003).

Responder Safety Consideration

Health care professional should stick on personal protective equipment (PPE) once handling transmissible disease to extenuate spread of diseases (AMA. 2012). In this way, it'sneeded specifics requirement to handling biologic casualties as compare to hazardous material contamination, specifically for contagious diseases that highly recommend to use protective equipment (Siegel et all. 2007).

Once it's dealing with the plague victims, the responder should follow standard precautions which includinghand washing before and after contacted with victims and their stuffs, wearing gloves, coat and eye protection. In addition, patient with pneumonic plague must be equipped with respiratory protection (*N-95, N-100 particulate respirator*) or *Powered Air Purifying Respirator* (PAPR) and surgical mask (DHSS. 2007).

Plague, as a biological agent, can cause tremendous catastrophic event in public health setting. It is because the period of incubation and contagious doses are associated with mortality. Therefore, it is paramount to perform decontamination to decrease number of casualties after following exposure (Raberet all. 2001). In addition, the rescuer must be wearing protective equipment and certain clothing to dismiss substances while working on decontamination. The process of decontamination applied water and soap, but sometime are also used 0.5% hypochlorite solution, even though there is out there still actually don't use bleach anymore while doing decontamination. Furthermore, all equipment may have taken off and the rescuer allowed to shower with abundant of water and soap (DHSS. 2007).

Environmental Impact

Study showed that following plague outbreak there was no residual impact on environment and there wasn't founded spore of *Yersinia pestis.* So, it can be said that contaminated environment due to plague aerosol is far away. In addition the *Yersinia pestis* can't life prolonged under sunlight and heating as well as outside host (Inglesby et all. 2000). According to WHO in the poorest condition plague aerosol will remained stay in the air and can be contagious and spreadable for less than one hour. Because of that study, it isn't required to establish environmental decontamination in the area where plague aerosol has been released (Inglesby et all. 2000).

Medical Surge Consideration

In public health emergency, the huge number of casualties are due to sudden event create increasing demand for health care resources including facilities, health care providers, hospital resources, infrastructures and other resources. Once plague aerosol released and created large casualties, it's needed lot of resources to deal with it. So, during tremendous outbreak health care center will probably run out of space, then it is essential to establish the alternate care facility (AFC) such as school, churches, community center, mall, government

building, stadium, medical professional offices and so forth (AMA. 2012).

Preparing for medical surges are always the first priority. That can be consisting medical services facilities (number, type, location, and total physical beds of hospitals in the region); medical care providers (physicians, physician assistants, nurse practitioners, registered nurses, licensed practical nurses, and respiratory therapists); and hospital resources as well as infrastructure (including personal protective equipment, negative airflow isolation rooms, isolation beds, and decontamination capability) (AHRQ. 2006).

Future Implications

Totally eliminating plague is less possible since it's can spread over rodent populations. Human may have high risk because the dynamic of rodent is as natural host. Recently study showed that climate change particularly, moderate hot during spring and humid summer, can be precipitated plague outbreak in the future years. The weather condition tends to increase plague in its main reservoir (Stenseth et all. 2008). In addition *Yersinia pestis* acquire some antibiotic resistance, apparently disperses of multi-resistance strains of *Yersinia pestis* could delineate serious threat to human health (Stenseth et all. 2008). Therefore, improving prophylactic and therapeutic antibiotic regimen would provide benefits to determine optimal antibiotic. In the same time, improving rapid diagnostic and technical laboratory microbiology standard are essential to response plague outbreak promptly (Inglesby et all. 2000)

REFERENCES

Agency for Healthcare Research and Quality (AHRQ). 2006. Bioterrorism and Health Care Preparedness. Retrieved: http://archive.ahrq.gov/news/ulp/btbriefs/btbrief11.pdf

American Medical Association (AMA). 2012. Basic Disaster Life Support. Biologic Disaster: Situational Awareness and Detection.

American Medical Association (AMA). 2012. Advance Disaster Life Support. Personal Protective Equipment and Casualty Decontamination: PPE for Biologic Casualties.

American Medical Association (AMA). 2012. Advance Disaster Life Support.Health System Surge Capacity for Disasters and Public Health Emergencies.

Begier, E. M., Asiki, G., Anywaine, Z., Yockey, B., Schriefer, M. E., Aleti, P., . . . Bearden, S. W. 2006. Pneumonic plague cluster, uganda, 2004. Emerging Infectious Diseases, 12(3), 460.

Buehler, J. W., Berkelman, R. L., Hartley, D. M., & Peters, C. J. 2003. Syndromic surveillance and bioterrorism-related epidemics. Emerging Infectious Diseases, 9(10), 1197.

Casadevall, A., &Pirofski, L. 2004. The weapon potential of a microbe.Trends in Microbiology, 12(6), 259-263.

Center for Biosecurity of UPMC. 2011. Yersinia Pestis. Retrieved:http://www.upmc-biosecurity.org/website/our_work/biological-threats-and-epidemics/fact_sheets/plague.pdf

Center for Diseases Control (CDC). 2004. Facts about Pneumonic Plague. Retrieved: http://emergency.cdc.gov/agent/plague/factsheet.asp

Center for Diseases Control (CDC). 2012. Resources for Clinician.Retrieved: http://www.cdc.gov/plague/healthcare/clinicians.html

Center for Diseases Control (CDC). Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response. 2000. Retrieved: http://www.cdc.gov/mmwr/PDF/RR/RR4904.pdf

Delaware Health and Social Services (DHSS). 2007. Emergency Medical Services : Plague. Retrieved: http://dhss.delaware.gov/dph/files/plagueems.pdf

Gani, R., & Leach, S. 2004. Epidemiologic determinants for modeling pneumonic plague outbreaks. Emerging Infectious Diseases, 10(4), 608.

Henderson, D. A. 1999.The looming threat of bioterrorism.Science, 283(5406), 1279-1282.

Inglesby, T. V., Dennis, D. T., Henderson, D. A., Bartlett, J. G., Ascher, M. S., Eitzen, E., . . . Koerner, J. F. 2000.Plague as a biological weapon. JAMA: The Journal of the American Medical Association, 283(17), 2281-2290.

Josko, D. 2004. Yersinia pestis: Still a plague in the 21st century. Clinical Laboratory Science : Journal of the American Society for Medical Technology, 17(1), 25-29.

Kapur& Smith. 2011. Emergency Public Health : Preparedness and Response. Jones & Bartlett Learning : USA.

Kool, J. L., & Weinstein, R. A. 2005. Risk of person-to-person transmission of pneumonic plague.Clinical Infectious Diseases, 40(8), 1166-1172.

Ligon, B. L. 2006. Plague: A review of its history and potential as a biological weapon. Seminars in Pediatric Infectious Diseases, , 17(3) 161-170.

National Institute of Allergy and Infectious Diseases (NIH). 2007. *Plague*.Retrived :http://www.niaid.nih.gov/topics/plague/Pages/Default.aspx

National Institute of Allergy and Infectious Diseases (NIH). 2009. *Transmission ofPlague*.Retrived :http://www.niaid.nih.gov/topics/plague/Pages/transmission.aspx

Raber, E., Jin, A., Noonan, K., McGuire, R., &Kirvel, R. D. 2001. Decontamination issues for chemical and biological warfare agents: How clean is clean enough? International Journal of Environmental Health Research, 11(2), 128-148.

Riedel, S. 2005.Plague: From natural disease to bioterrorism.Proceedings (Baylor University. Medical Center), 18(2), 116.

Rosenbloom, M., Leikin, J. B., Vogel, S. N., &Chaudry, Z. A. 2002. Biological and chemical agents: A brief synopsis. American Journal of Therapeutics, 9(1), 5-14.

Rotz, L. D., Khan, A. S., Lillibridge, S. R., Ostroff, S. M., Hughes, J. M., Rotz, L., . . . Hughes, J. 2002. Public health assessment of potential biological terrorism agents. Emerging Infectious Diseases, 8(2), 225.

Stenseth, N. C., Atshabar, B. B., Begon, M., Belmain, S. R., Bertherat, E., Carniel, E., . . . Rahalison, L. 2008. Plague: Past, present, and future.PLoS Medicine, 5(1), e3.

Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007. Healthcare Infection Control Practices Advisory Committee: Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Retrieved :http://www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf

Wheelis, M. 2002. Biological warfare at the 1346 Siege of Caffa. Emerging Infectious Diseases, 8(9), 971.