

THE BLACK DEATH

DMSJ;19(2) 4-8

<http://dx.doi.org/10.4314/dmsj.v19i2.2>

Ferdinand. S. Matemu MD2;

Institution: Hubert Kairuki Memorial University

ABSTRACT

Introduction

Bubonic plague is a deadly bacterial disease that causes fever and painful swollen lymph nodes called buboes. The disease also causes spots on the skin that are red at first and then turn black. The Black Death was one of the most devastating pandemics in human history, peaking in Europe between 1348 and 1350. Although there were several competing theories as to the etiology of the Black Death, it has been conclusively proven via analysis of ancient DNA from plague victims in northern and southern Europe that the pathogen responsible is the *Yersinia pestis* bacterium that causes bubonic plague.

Objectives

The aim of this paper is:

1. To describe the risks of getting the disease (Bubonic plague)
2. To describe the magnitude and impact of Bubonic Plague
3. To describe the pathogenesis of bubonic plague
4. To describe different ways of managing and controlling the disease clinically

Methodology

This paper is a product of literature review from journals, books and Internet search.

Results

From 1987-2001, the World Health Organization reported an annual average of 38,876 cases of the plague with 2847 deaths worldwide. The number of actual cases was probably much higher, given the failure of many countries to diagnose and report plague. Most cases occur in the developing countries of Africa and Asia. Recent outbreaks of plague have occurred in Vietnam, India, Algeria, Madagascar, and the northeastern part of the Democratic Republic of the Congo. [2] During 2000-2001, 95% of the world's cases occurred in Africa. Bubonic plague has a 1-15% mortality rate in treated cases and a 40-60% mortality rate in untreated cases.

Conclusions

Bubonic plague is a threat to man. This disease is very virulent due to its rapid nature of transmission and very high mortality rate if untreated.

Correspondence to: Ferdinand. S. Matemu, Hubert Kairuki Memorial University; fesakeba@hotmail.com

INTRODUCTION

Bubonic plague is a zoonotic disease circulating mainly among small rodents and their fleas, ^[1] and is one of the three types of infections caused by *Yersinia pestis* (formerly known as *Pasteurella pestis*) which belongs to the family Enterobacteriaceae. Without treatment, the bubonic plague kills up to two out of three infected humans within 4 days. 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 animals.

The risk factors for Bubonic Plague include:

- Camping, hiking and hunting
- Contact with an infected person
- Contact with sick animals or rodents
- Flea bite
- Occupational exposure: researcher, veterinarian

- Presence of a food source for rodents in the immediate vicinity of the home
- Residing in areas exposed to plague

HISTORY OF BUBONIC PLAGUE

Bubonic plague has been responsible for at least 3 great pandemics and multiple epidemics in history. The first pandemic occurred from the Middle East to the Mediterranean basin during the 5th and 6th centuries AD, killing approximately 50% of the population in these areas. The 2nd pandemic afflicted Europe between the 8th and 14th centuries, destroying nearly 40% of the population. The 3rd pandemic started in approximately 1855 in China, and, although it has been mostly controlled, it is still ongoing. In 1894, Alexander Yersin discovered the causative bacterium of this disease, which was named *Yersinia pestis* after him^[2].

BUBONIC PLAGUE AS A BIOLOGICAL WEAPON

Plague is currently considered to be one of the most serious bioterrorism threats. *Y. pestis* was developed as an aerosol weapon by several countries in the past.

Plague was used during the Second Sino-Japanese War as a bacteriological weapon by the Imperial Japanese Army. These weapons were provided by Shirō Ishii's units and used in experiments on humans before being used on the field. For example, in 1940, the Imperial Japanese Army Air Service bombed Ningbo with fleas carrying bubonic plague. During the Khabarovsk War Crime Trials, the accused, such as Major General Kiyashi Kawashima, testified that, in 1941, some 40 members of Unit 731 air-dropped plague-contaminated fleas on Changde. These operations caused epidemic plague outbreaks.^[11]

EPIDEMIOLOGY

Wild rodents in certain areas around the world are infected with plague. Outbreaks in people still occur in rural communities or in cities. They are usually associated with infected rats and rat fleas that live in the home. In the United States, the last urban plague epidemic occurred in Los Angeles in 1924–25. Since then, human plague in the United States has occurred mostly as scattered cases in rural areas (an average of 10 to 15 persons each year). Globally, the World Health Organization reports 1,000 to 3,000 cases of plague every year. In North America, plague is found in certain animals and their fleas from the Pacific Coast to the Great Plains, and from southwestern Canada to Mexico. Most human cases in the United States occur in two regions: 1) northern New Mexico, northern Arizona, and southern Colorado; and 2) California, southern Oregon, and far western Nevada. Plague also exists in Africa, Asia, and South America (see maps below)^[3].

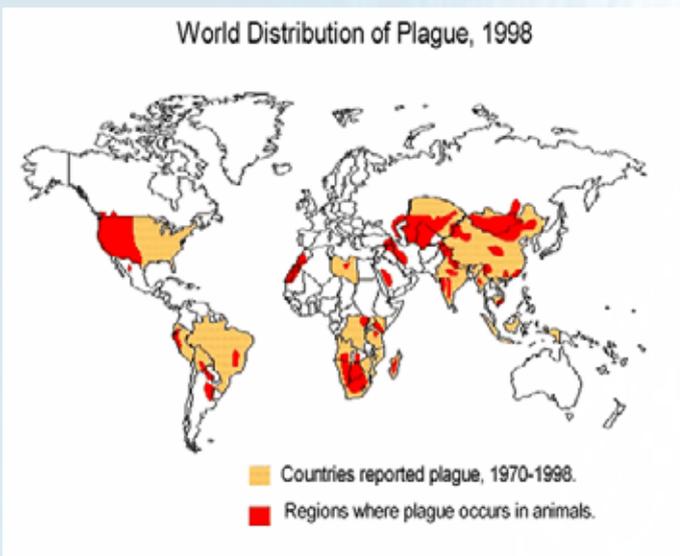


Figure 01a: The world map showing distribution of plague from 1970 to 1998

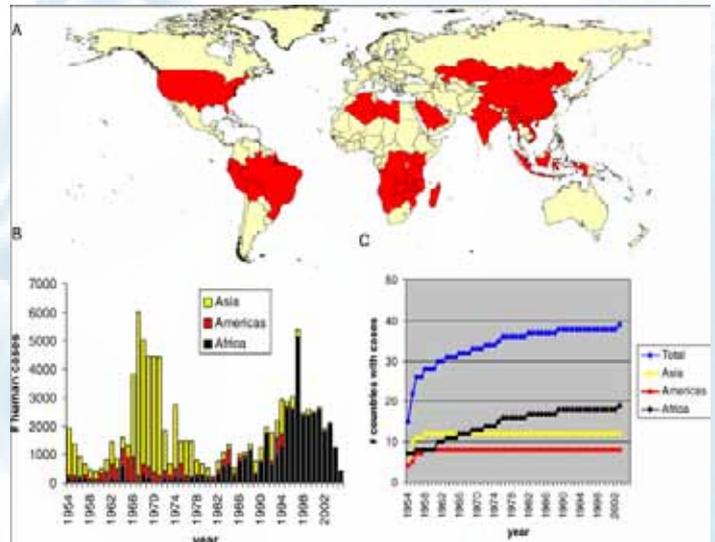


Figure 01b. The Global Distribution of Plague ^[12,13,14]

(A) Map showing countries with known presence of plague in wild reservoir species (red) (after ^[12]). For the US, only the mainland below 50° N is shown. (B) Annual number of human plague cases over different continents, reported to WHO in the period 1954–2005. (C) Cumulative number of countries that reported plague to WHO since 1954.

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^[4].

Scientific classification

- Domain: Bacteria
- Kingdom: Eubacteria
- Phylum: Proteobacteria
- Class: Gammaproteobacteria
- Genus: *Yersinia*
- Species: *Y. pestis*
- Binomial name: *Yersinia pestis*

PATHOGENESIS

• *Yersinia pestis* is primarily a rodent pathogen, with human beings as accidental hosts when bitten by infected rat fleas. The flea draws viable *Y. pestis* organisms into its intestinal tract. These organisms multiply in the flea and block the flea's proventriculus.

• Some *Y. pestis* in the flea are then regurgitated when the flea gets its next blood meal thus transferring the infection to a new host. While growing in the flea, *Y. pestis* loses its capsular layer. Most of the organisms are phagocytosed and killed by the polymorphonuclear leukocytes in the human host. A few bacilli are taken up by tissue macrophages. The macrophages are unable to kill *Y. pestis* and provide a protected environment for the organisms to synthesize their virulence factors.

• The organisms then kill the macrophage and are released into the extracellular environment, where they resist phagocytosis (*YopH* and *YopE*; *Yersinia* outer membrane protein) by the polymorphs. The *Y. pestis* quickly spread

to the draining lymph nodes, which become hot, swollen, tender, and hemorrhagic. This gives rise to the characteristic black buboes responsible for the name of this disease.

- Within hours of the initial flea bite, the infection spills out into the bloodstream, leading to involvement of the liver, spleen, and lungs. The patient develops a severe bacterial pneumonia, exhaling large numbers of viable organisms into the air during coughing fits. 40 to 60 percent of untreated patients will die if untreated. As the epidemic of bubonic plague develops (especially under conditions of severe overcrowding, malnutrition, and heavy flea infestation), it eventually shifts into a predominately pneumonic form, which is far more difficult to control and has a 100 percent mortality^[5].

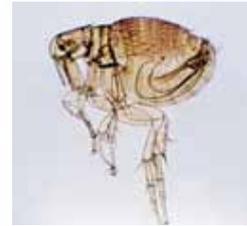


Figure 04: a picture showing a rodent flea.

2. Transmission by ingestion of infected animals.
3. Transmission through contact with body fluids from infected animals^[6].

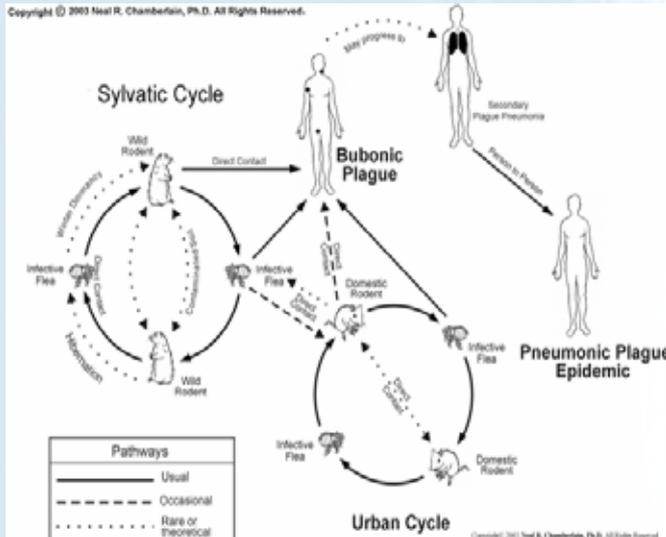


Figure 02: a diagram showing the cycle of the plague.

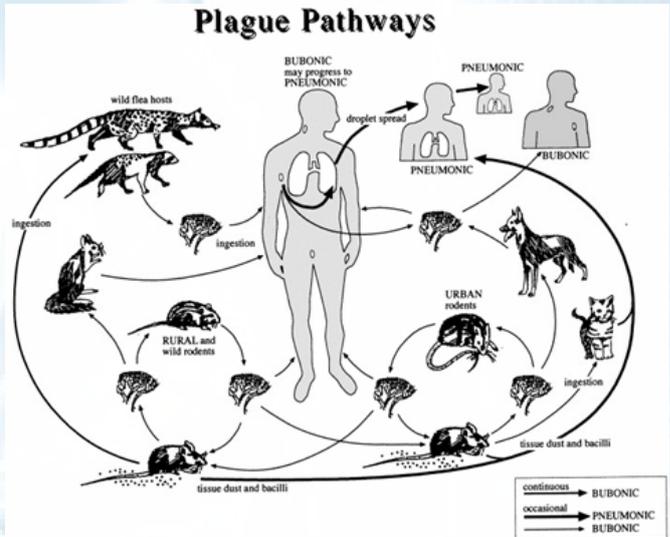


Figure 05: a diagram showing the plague pathway.

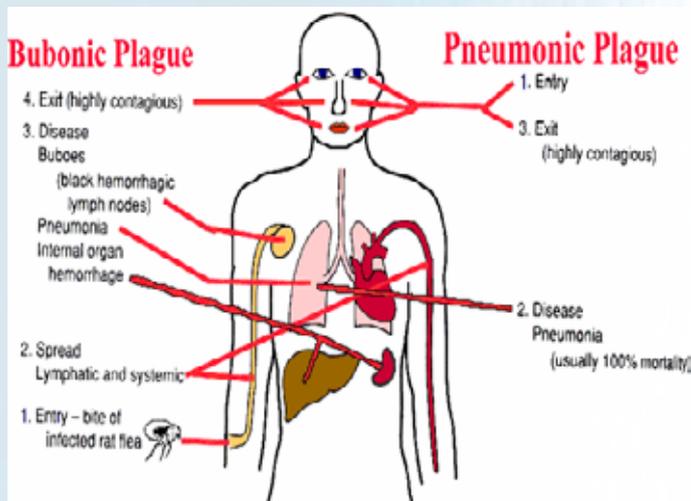


Figure 03: a diagram showing pathophysiology of plague.

CLINICAL PRESENTATION

Transmission

Yersinia pestis is transmitted through three major ways as follows:

1. Transmission via fleas:
 - a) The primary reservoir for *Y. pestis* is rodents. Transmission among rodents, other wild animals, domestic animals and humans occurs via flea bites.

Signs and symptoms

Bubonic plague normally presents with the following signs and symptoms^[7]:

- I. Acral gangrene: Gangrene of the extremities such as toes, fingers, lips and tip of the nose
- II. General ill feeling (malaise)
- III. High fever (39 °Celsius; 102 °Fahrenheit), Muscle Cramps and Seizures
- IV. Smooth, painful lymph gland swellings called buboes commonly found in the groin but may occur in the armpits or neck
- V. Bleeding out of the cochlea will begin after 12 hours of infection
- VI. Chills, Myalgias, Sore throat, Headache and body weakness
- VII. Abdominal pain:

May occur as an only presenting symptom more commonly in a patient with septicemic plague (primary blood-borne plague) than in one with bubonic plague
- VIII. Nausea, vomiting (bloody at times)
- IX. Constipation, diarrhea, and black or tarry stools
- X. Gastrointestinal complaints (may precede a bubo)
- XI. Cough, which may be productive of bloody sputum

Diagnosis (laboratory studies)

Laboratory techniques used to diagnose bubonic plague include the following:

- 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 or Arterial blood gas level may reveal hypoxia and/or 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 coccobacillus. Gram stain can be performed on bubo aspirate, sputum, and blood.

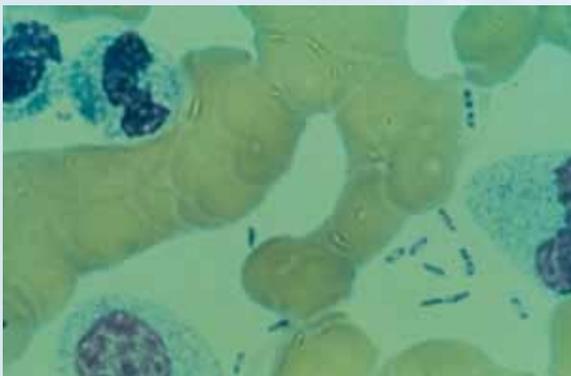


Figure 06: Wright stain peripheral blood smear of a patient with septicemic plague demonstrating bipolar, safety pin staining of *Yersinia pestis*

Cultures of blood, sputum and bubo aspirate

- The plague bacillus grows readily on most culture media (at 28°C) and takes 48 hours before identification of colonies.
- Blood culture results are positive in 85-96% of patients while bubo aspirates are positive in 80-85% of patients.

Treatment and management [8, 9, 10]

- Medical management of plague involves antibiotic treatment and a myriad of supportive medications, including crystalloids, colloids, medications used for intubation, vasopressor agents, and antiulcer and antipyretic agents.
- 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. The antibiotics include the following:
 - Gentamicin (Garamycin, Jenamicin). Aminoglycoside antibiotic for gram-negative coverage. Drug of choice (DOC) with consideration of use as a secondary agent.
 - Streptomycin. Alternative DOC in combination with consideration of use with a secondary agent. Drug often not commercially available.
 - Chloramphenicol (Chloromycetin). DOC to be used as a secondary agent in plague meningitis (better CNS penetration), profound hypotension, and pleural and/or pericardial involvement.
 - Doxycycline (Doryx, Vibramycin, Bio-Tab) Inhibits

protein synthesis and thus bacterial growth by binding to 30S and possibly 50S ribosomal subunits of susceptible bacteria. May be considered as a secondary agent or for post-exposure prophylaxis.

- Ciprofloxacin (Cipro). Fluoroquinolone that inhibits bacterial DNA synthesis and, consequently, growth, by inhibiting DNA gyrase and topoisomerases, which are required for replication, transcription, and translation of genetic material. Co-trimoxazole (Bactrim, Septra)
- DOC for prophylaxis of pregnant women and children < 8 years; inhibits bacterial synthesis of dihydrofolic acid by competing with PABA, inhibiting folic acid synthesis and resulting in the inhibition of bacterial growth.

CONTROL

The basic objective is to reduce the likelihood of people being bitten by infected fleas, having direct contact with infective tissues and exudates, or of being exposed to patients with pneumonic plague. [11]

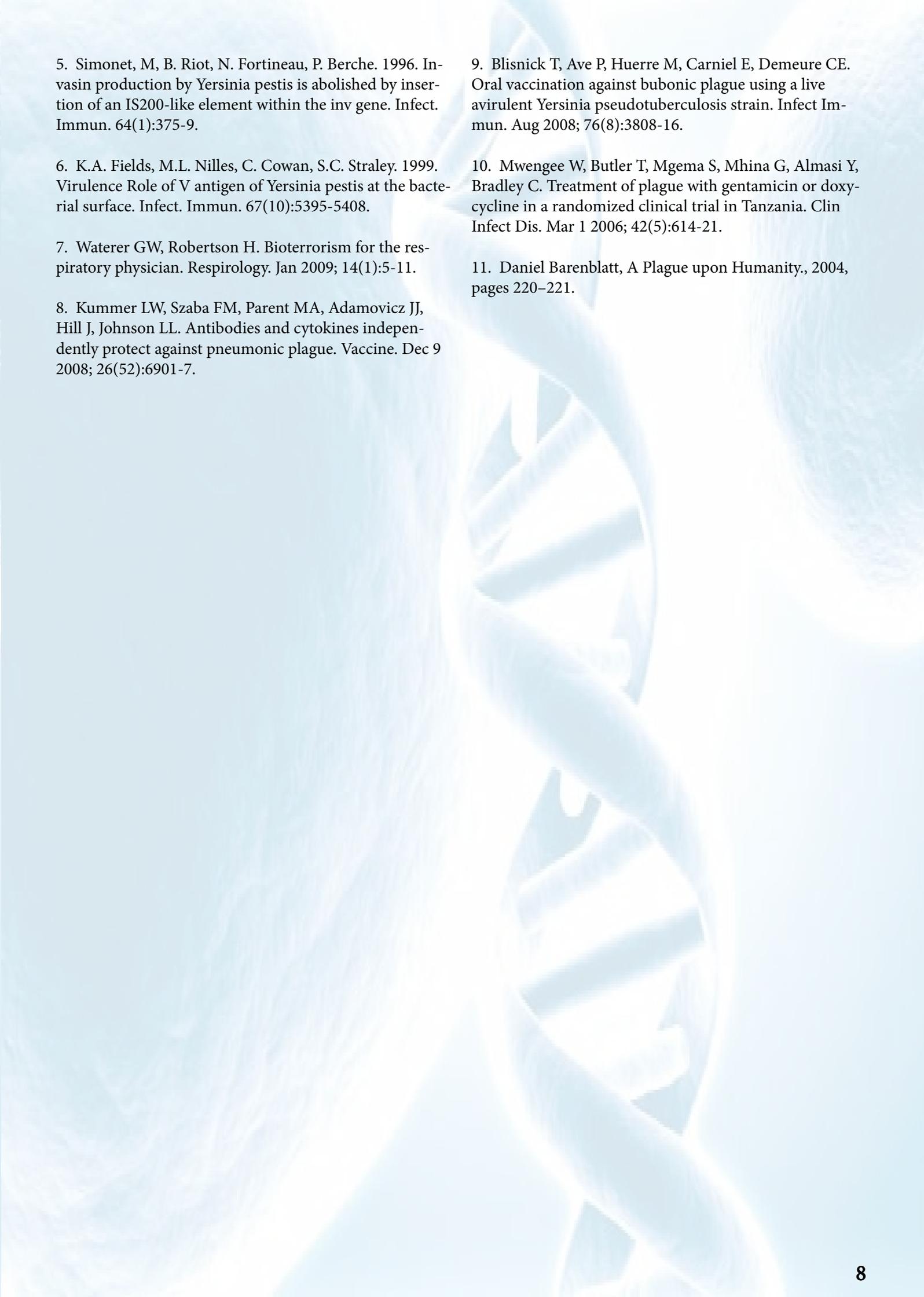
1. Educate the public in enzootic areas on the modes of human and domestic animal exposure.
2. Survey rodent populations periodically to determine the effectiveness of sanitary programs and to evaluate the potential for epizootic plague.
3. Collection and testing of fleas from wild rodents and their nests or burrows may also be appropriate.
4. Control rats on ships and docks and in warehouses by rat proofing or periodic fumigation.
5. Wear gloves when hunting and handling wildlife.
6. Active immunization with a vaccine of killed bacteria confers some protection against bubonic plague.

CONCLUSION

Bubonic plague is a threat to many lives on earth, especially in this modern world of science and technology in which powerful countries use the plague as a mass destructive war weapon. The disease, however, is a threat to developing countries especially in Africa due to poor Health environment control. Therefore it is our task as professional medical personnel to educate our society on how to prevent plague and conduct environment control programs to fight against the causative agent of plague.

REFERENCES

1. Kman NE, Nelson RN. Infectious agents of bioterrorism: a review for emergency physicians. *Emerg Med Clin North Am.* May 2008; 26(2):517-47, x-xi.
2. Prentice MB, Rahalison L. Plague. *Lancet.* Apr 7 2007; 369(9568):1196-207.
3. Centers for Disease Control and Prevention. Prevention of plague. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*, 1996; 45(RR-14):1-15.
4. Ryan KJ, Ray CG (editors) (2004). *Sherris Medical Microbiology* (4th Ed.). McGraw Hill. pp. 484-488. ISBN 0-8385852-9-9.

- 
5. Simonet, M, B. Riot, N. Fortineau, P. Berche. 1996. Invasin production by *Yersinia pestis* is abolished by insertion of an IS200-like element within the *inv* gene. *Infect. Immun.* 64(1):375-9.
 6. K.A. Fields, M.L. Nilles, C. Cowan, S.C. Straley. 1999. Virulence Role of V antigen of *Yersinia pestis* at the bacterial surface. *Infect. Immun.* 67(10):5395-5408.
 7. Waterer GW, Robertson H. Bioterrorism for the respiratory physician. *Respirology.* Jan 2009; 14(1):5-11.
 8. 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.
 9. Blisnick T, Ave P, Huerre M, Carniel E, Demeure CE. Oral vaccination against bubonic plague using a live avirulent *Yersinia pseudotuberculosis* strain. *Infect Immun.* Aug 2008; 76(8):3808-16.
 10. 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.
 11. Daniel Barenblatt, *A Plague upon Humanity.*, 2004, pages 220–221.