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PLAGUE; A MEDIEVAL KILLER IN THE PRESENT WORLD: A REVIEW

ABDUL BARI AND ALI ABBAS QAZILBASH

Department of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

CONTENTS

Abstsract: Plague as a disease was known in the sixth century, but it was not till the fourteenth century that it became pandemic resulting in the ove 14 million deaths in Europe between 1348 and 1400. Unlike smallpox, plague can never be eradicated, as is evident from -the recent outbreak of the disease in India. Plague is a disease of the earth, of creatures that run and burrow and of the fleas that live on them. It is found mainly in the wild, often far from man. Plague bacterium need not attack man in order to persist, for it finds all that it needs in wild places. In India, between 1898 and 1919 there may have been more than ten million deaths due to plague. According to WHO between 1961 and 1970 a total of 26,262 cases and 1,887 deaths have been reported worldwide and from 1971-80 there were 16,480 cases and 932 deaths due to plague. During the recent outbreak of plague in India an estimated 55 individuals died of the disease. The plague pathogen is known as *Yersinia pestis* and its host is black rat, its vector being the flea *Xenopsylla cheopis* which lives on the rat. Plague is perpetuated by 3 cycles, (1) natural foci among commensal rodents with transmission by fleas (wild plague), (2) urban rat plague, which is transmitted by the rat flea (domestic plague), and (3) human plague, which may be acquired by contact with either of the former cycles and which may be transmitted by pneumonic spread, or, rarely by the bite of a human flea. Plague is now recognized as a well marked disease caused by a Gram-negative facultative anaerobic bacterium. It comes in three forms, all of which are fatal if not properly treated, a) bubonic plague, producing bubos/swellings of the lymph glands, b) pneumonic plague, attacking primarily the lungs; and c)septicemic plague, killing the patient rapidly by poisoning the blood. In bubonic plague the incubation period is 2-8 days. If left untreated the infection spreads to other parts of the body through the blood stream eventually infecting the lungs- leading to pneumonic plague. This type is highly contagious as the patient's sputum contains the bacillus and droplets of the sputum can spread the disease from person to person, resulting in localized outbreaks, or devastating epidemics. Incubation period is 1-6 days after exposure and the patient experiences fever, headache, vomiting and a marked clouding of consciousness. Pneumonic plague is the most fatal, as well as the most directly infectious form of the disease. Treatment of plague involves a variety of antibiotics, namely streptomycin, tertracycline, chloramphenicol and sulfonamides-dosages also vary. A vaccine has also been developed using the killed or attenuated pathogen, but is useless in rapidly developing localized outbreaks-such as the recent outbreak in India. Control measures are the key methods for curbing the outbreaks of plague and they include those required during an outbreak to bring it to an end and long term action to prevent the spread of infection from the wild to human population.

INTRODUCTION

Plague is now recognized as a well-marked disease caused by bacillus, *Yersinia pestis*. There are three forms of the disease: a) bubonic plague, producing buboes, or swellings of the lymph glands, b) pneumatic plague, attacking primarily the lungs, and c) septicemic plague, killing the patient rapidly by poisoning the blood.

All types are fatal, if not properly treated. Plague is transmitted to man by fleas from black rats and other rodents' such as wild squirrels, gophers and gerbils. It produces high fever, agonizing pain and prostration (complete physical and mental exhaustion). Plague was frequently accompanied by outbreaks of typhus and `English fever', which was a deadly form of influenza.

Plague was known as a disease in the sixth century Roman Empire and even earlier in North Africa, but it was not till the 14th century that plague became pandemic-- the European epidemic.

It was first thought that the black rat was brought to Europe by the Crusaders returning from the Middle East, but this seems unlikely as prehistoric sites of rats have been found in Switzerland.

The 14th century pandemic started in 1348 from the Italian ports, apparently from merchant ships from the Middle East region. During the next two years, plague swept across Spain, France, England, Central Europe and Scandinavia.

It was a slow yet unrelenting advancement of the disease striking with deadliest effect in crowded, unsanitary towns. Each year the epidemic rose to a peak in late summer and subsided in the winter months only to return in spring. The 1348-50 A.D. pandemic was followed by long series of recurrent outbreaks all over Europe at intervals of ten years or less. For example, in London at least 20 attacks of plague were reported in 15th century. In Venice the black death struck 23 times between 1348 and 1576. It has been generally accepted that 25% of Europe's population was wiped out in the first epidemic between 1348-50. Over the next 50 years, mortality rose to more than 33% of the population-totalling over 44 million deaths, although the rate and occurence varied in various regions.

In 1665 A.D., England was afflicted with bubonic plague epidemic which killed over 40,000 people in London alone. Afterwards plague mysteriously disappeared. Some scientists thought that the larger brown rat had killed off the smaller black rats but this was not the case. Something must have happened to the fleas, the bacillus, or the living conditions of the human host. Probably the better living conditions and personal hygiene had something to do with the subsiding of the plague epidemic. In Florence, Italy, 45,000 died out of a population of 90,000, people, in Sienna, France, 27,000 died out of a population of 42,000 people, while in Hamburg, Germany, 66% of the population perished.

In Venice the local Board of Health kept accurate counts of the deaths due to plague outbreak of 1576-77 A.D. totalling 46,721 out of 160,000 people. In Marseilles, (1720 A.D.) 40,000 people died out of a population of 90,000 and Messina lost 58% of its population in the 1743 A.D outbreak of plague. In India, between 1898 and 1919, there may have been more that 10 million deaths from plague, but the numbers have fallen greatly since then. According to WHO, between 1961 and 1970 a total of 26,262 cases and 1887 deaths have been reported worldwide; the corresponding figures for 1971-80 were 16,480 with 932 deaths.

Eighty percent of all those who came in contact with this disease died within 2-3

days usually in agonizing pain. Prevention and cure was not known at that time. It was interpreted as being God's way of punishing humans for their sins.

Plague epidemic of the 14th and 16th century frightened many people to migration from towns. Emperors, kings, princes, clergy, merchants, lawyer, professors, judges, students, even physicians rushed away, leaving behind the sick to die. In the 1563 plague epidemic, Queen Elizabeth I took refuge in Windsor Castle and errected gallows to hang anyone who had the gall to enter Windsor from plague ridden London. Entire streets were closed off by chains and the sick quarantined. French surgeon Pane, in 1568 wrote that husbands and wives deserted each other and parents abandoned their children. People went mad with terror and often committed suicide.

The disease and causative agent

Unlike smallpox, plague can never be eradicated, for it is a disease of the earth, of creatures that run and burrow, and of the fleas that live on them. It is found mainly in wild regions, often far from man -- in dry deserts or in wet rice fields, in treeless steppes or dense forests, on foothills, on the higher slopes of mountains, or across wide lowland plains. Plague needs not attack man in order to persist, for it finds all it needs in wild places. If man steps into the wild, as a hunter, trapper, or even tourist, he can catch palgue and then carry it far away from the source before the disease takes hold.

The host of plague bacillus is commonly a rodent and a vector, commonly the flea *Xenopsylla cheopis*. They interact and, if conditions are favorable, all three persist together in nature. Their numbers rise and fall over the years under thre influence of both internal and external factors. The internal factors include differences in the susceptibility of the host to the plague bacillus, or in the efficiency of the vector in transmitting it. External factors are the conditions in the environment in which the interactions take place, such as temperature, humidity, season, the availibility of food and shelter for hosts etc.

There are not just one, or, two hosts to consider, *i.e. Rattus rattus* and *Rattus norvegicus*, but over three hundred rodents and other species are known hosts of the plague bacillus, and not just one or two fleas, such as *X. cheopis* and *Pulex irritans*, but at least 30 of the 3000 or more known species are capable of transmitting the organism. The plague bacillus may vary in virulence under the influence of slight environmental changes.

Three species of the genus *Yersinia* are primarily animal pathogens, but also produce human disease. *Y. pestis* is the cause of plague, while in humans *Y. pseudotuberculosis* and *Y. enterocolitica* are most commonly associated with G.I. tract diseases. Previously this organism was classified in the genus *Pasteurella*, now the pathogen has been placed in the family *Enterobacteriaceae*. It expresses the enterobacterial antigen and its physiological characteristics and lipid composition is similar to the other species of this family.

The causative agent, *Y. pestis* is a Gram-negative, non-motile coccobacillus. It shows marked bipolar staining, especially in tissue impressions, bubo aspirates and pus

stained with Giemsa's stain. The cells have a safety-pin appearance with the polar bodies staining blue and the remainder staining light blue to reddish. Freshly isolated virulent organisms are enveloped. *Yersinia* are facultative anaerobes or anaerogenic and usually do not ferment lactose. They are oxidase negative and produce catalase.

Culture characteristics and strain identification

Y. pestis can grow over a wide temperature range; from 0°C to 43°C, the optimal temperature of growth being 28°C. Several phenotypic characteristics are best expressed at room temperature. It can grow on ordinary laboratory media even from small inoculate. On nutrient agar plates, small mucoid colonies apperar in 1-2 days.

Three bio-types have been detected on the basis of their ability to reduce nitrate to nitrites and to ferment glycerol. These bio-types have been designated *orientalis*, *mediaevalis*, and *antigua* and are characterized by the differences in their geographical distribution. *Orientalis* is the usual bio-type of western North America.

Y. pestis strains are also characterized by quantitative differences in their antigens. At least twenty different antigens have been identified on the basis of gel diffusion and biochemical analysis, many of which are shared with *Y. pseudotuberculosis* and *Y. enterocolitica*.

Determination of virulence

Yersinia are facultative intracellular parasites. Virulence is thus assumed to reflect an ability of the organisms to proliferate within mammalian cells. Most of the virulence factors that have been defined are largely associated with resistance to mechanism of intracellular killing and with invasive abilities to gain access to favored sites of replication in fixed phages.

Among the factors associated with virulence are (1) Ca^{++} ions; (2) V and W antigens; (3) F-I (envelope antigen); (4) Pesticin, coagulase and fibrinolysin production; (5) Pigment absorption.

The V and W antigens develop early in infection and appear to confer on *Y. pestis* the ability of small numbers of bacilli to establish infection in animals. Once the infection is established the F-I (envelope) antigen, pesticin, coagulase and fibrinolysin contribute to the rapid extension of the disease process.

V and W antigen: The V and W antigens are always produced together. *In vivo*, the V and W antigen correlate with pathogenicity and with the ability of *Y. pestis* to rapidly proliferate and to cause overwhelming septicemia.

Envelope antigen: F-I antigen,. or envelope antigen is a soluble antigen contained within the bacterial envelope. It consists of two immunologically identical complexes; (a protein complexed with polysaccharides).

Envelope antigen appears to be antiphagocytic and prevents pagocytosis by

professional phagocytes, thus potentiating the rapid evolution of septicemia that characterized the clinical disease. It is highly immunogenic and may constitute as much as the 7% of the dry weight of the organism. Antibody to F-I appears to be protective in both humans and experimental animals.

Pesticin I, coagulase and fibrinolysin: The production of pesticin-I, coagulase and fibrinolysin is always correlated. Pesticin I is a bacteriocin produced by *Y. pestis* that inhibit the growth of *Y. pseudotuberculosis*, as well as some strains of *E. coli* and *Y. enterocolitica*.

Strains of *Y. pestis* lacking these enzymes are infectious for the mouse, or guinea pig. But, lethality is significantly attenuated. Augmentation and persistence of the infectious process in organs correlate with these properties.

Pigment absorption: In virulent strains unidentified surface components are present that result in the absorption of hemin and basic aromatic dyes to form colored colonies.

Other virulence-associated factors: Two additional factors that have been proposed as virulence factors are murine toxin and endotoxin. For rats and mice the lethal dose of murine toxin is less than 1 μg, but for other animals it is relatively a toxic-hence the name murine toxin.

Epidemiology

Plague was introduced into the United States from China in 1900, when the first human case of the disease was reported in San Fransisco. In 1907-08, a major epidemic of 167 cases occured in San Fransisco. Permanent foci of plague now exist that involve at least 57 wild rodent species and their fleas. These extend as far east as Kansas, Oklahoma, and Texas and to approximal areas of Canada and Mexico.

Plague is perpetuated by three cycles, (1) natural foci among commensal rodents with transmission by fleas (sylvatic plague, wild plague, (2) urban rat plague weich is transmitted by the rat flea (domestic plague, urban plague), and (3) human plague, whicy may be acquired by contact with either of the former cycles and which may be transmitted by pneumonic spread or, rarely, by the bite of a human flea.

Flea related factors

In nature, the flea is essential for perpetuation of plague. At least four flea-related factors influence the epidemic potential of plague;

1) Fleas vary greatly in their vector efficiency. Most wild rodent fleas are relatively inefficient in the transmission of disease to humans. However, the Oriental rat flea, *Xenopsylla cheopis*, is highly efficient and has been the classic vector in urban rat-borne epidemics. 2) The restricted feeding habits of most wild rodent fleas limit their threat to humans. Human occasionally have been infected when wild rodent death during an epizootic left hungry fleas in search of a new host. Dog and cat fleas are very poor vectors and have been associated with individual cases of human plague, but not with

outbreaks. 3) Some infective wild rodent fleas survive in burrows for long periods of time, even after the rodent hosts have died. Survival of fleas for as long as 15 months has been shown. 4) The development of dichloro-diphenyl-trichloromethane (DDT)-resistant fleas in some areaas may influence the epidemic potential of plague. This occured in some instances with widespread DDT spraying during malarial control programs.

Transmission of plague by flea may occur in several ways. The most efficient involves ingestion of the organism by the flea during a blood meal from a bacterimic host. In the flea stomach, the infected blood is coagulated by coagulase that is produced by *Y. pestis* in the presence of an enzyme from the flea stomach. Bacteria are thus trapped in a matrix of fibrin, which fixes them to the spines of the flea proventriculus. As the bacteria multiply, the proventriculus is occluded, which causes blockage. The time between ingestion and blockade is the extrinsic incubation time, and usually for *X. cheopis* it is about 2 weeks. During subsequent attempts to obtain a blood meal, regurgitation of the infected material results in the infection of the new host. The hungry flea also becomes less fastidious about its host and will readily attack humans. Hot, dry weather adversely affects all stages in the life cycle of the flea, which explains the subsidence of many epidemics at the beginning of the hot and dry season. Blockage is enhanced at temperatures below $26^{O}C$. Above $27^{O}C$ the fibrinolytic factor of *Y. pestis* and the trypsin-like activity of the flea stomach enzyme are activated, thereby destroying the fibrin meshwork needed for blockage. Decreased blockage results in decreased vector efficiency.

Mechanical transmission by contaminated mouth parts of the flea are important in the transmission of plague, especially in wild plague.

The host

The facts that were established about the spread of plague in rats are as follows:

1). Unless fleas are present, plague is not spread from infected rats, even from those that die of palgue, to susceptible rats in close contact with them; it does not spread from infected females to their sucklings; 2). Plague does not spread through the air from infected rats, nor from soil contaminated with infected feces, urine or food; 3) A rat can be infected by being fed contaminated food of pieces of a rat that died of plague, but the pathological findings -- mesenteric lymphadenitis and intestinal lesions -- are not encountered even once in necropsies of 5000 rats that died from the natural disease; auch animals showed cervical lymphadenitis and lung congestion, but no intestinal lesions; 4) Plague spreads from one infected rat to another, or from contaminated soil, if fleas are present, and the spread from such sources to a new host is limited by the distance, or the height that a flea can jump. Without fleas, infection does not spread.

Plague infection and spread

In man: Infection may be maintained for years in such a focus without the overt appearance of plague, unless some outside host intrudes. A man may stray into the focus as a hunter and be bitten by a flea searching for a host, or by one that jumps from

a dead rodent; or he may skin a small animal for its pelt or for food. The hunter usually catches plague by direct contact with the infected flesh of an aimal. So also does the cook who handles refrigerated meat in which *Y. pestis* has survived. Man may unknowingly enter a focus as a tourist, be bitten, and become ill a few days later after having traveled far from the source of infection. Much more important, however, are massive human migrations into untrodden areas, such as occur durig a war. These migrations bring man close to the earth, to fleas and rodents, and to unsuspected enzootic plague.

In dogs: As man can intrude into a wild focus so too can domestic animals. Serological surveys in rural areas have shown that dogs are often infected, though usually they remain well and do not spread infection. They can be regarded as sentinel animals, their seropositivity indicating that plague is in the area and may spread to man. There were 19 cases of human plague in western US in 1982, at a time when serotesting of dogs and other animals had demonstrated the presence of the disease i the area.

In cats: Cats too may be infected, but they tend to become ill and some die. They may have buboes, or abscesses in the thigh, and some develop respiratory symptoms and die of pneumonic plague.

In goats, sheep and camels: Some of man's other domestic animals, sheep and goats for example, may stray into wild focus, become infected, and then carry the infection to man. In one outbreak in Lybia, six shepherds died, five of them having slaughtered ailing or morbid sheep a day or two earlier. Again in Libya, a peasant farmer developed plague meningitis two days after killing a goat; the illness spread in his family, and goats of the area proved to be seropositive.

Perhaps more impórtant is the camel, which travels over vast areas yet is constantly close to man. Camels have been infected experimentally with *Y. pestis*, albeit with some difficulty. In one study, two of the four camels inoculated subcutaneously died, as also did each of the six infected by aerosol; but the feeding of contaminated hay produced only a mild illness, with buboes in the neck, from which the animals recovered. In libya, four men who killed and skinned an ailing camel with swellings in its neck all died within three days; plague also affected a further ten persons, two fatally, who handled or ate the camel meat. In another outbreak in Libya, sudden unexplained deaths in children were followed by three sudden deaths in adults, one of whom had slaughtered a sick camel two days earlier, sharing the meat with the other two. Human plague related to contact with camels has also occured in Saudi Arabia in the form of septicemic and meningitic infections, but nothing has yet been published on these occurence.

Local escape: Infections resulting from the intrusion of man or his domestic animals into a plague focus are in a sense accidental. They are not the result of any change within the focus. True active spread, however, occurs when infected hosts leave the focus to forage or explore outside it. They carry their infected fleas with them, and if they come near a dwelling place of man they encounter `peridomestic' rodents such as *R. norvegicus*, and infected fleas then pass from one to the other. *R. norvegicus* comes into contact with the `commensal' rat *R. rattus*, and fleas again pass from one to the

other. *R. rattus* and flea again pass between the species. *R. rattus* lives close to man, in the walls or roof-spaces of his house or hut. Being highly susceptible, the rat dies of plague, and its fleas must then find another host. The new host may be man, infected in his home. Thus a new focus is established within an area of human habitation.

The type of outbreak varies according to local circumstances. For example the commensal host may be *Bandicota bengalensis* (mole-like burrowing rat of south and south-east Asia) instead or *R. rattus*; the flea may be a poor transmitter, such as *X. astia* instead of an effective one such as *X. cheopis*. Temperature, humidity and other environmental circumstances may also play a role. In a newly formed focus the interaction between host, flea and organism is once again delicately balanced.

Worldwide escape: Man may interfere with nature and disrupt a wild plague focus. He may, for example, harvest a field, driving out the rats and their fleas to seek new shelter, perhaps nearer to human habitations. He may empty a grain store, carting loads of grain to some distant village or town; rats in the grain may then mingle with the local rats, passing on infected fleas. Many rats die, and soon plague breaks out among the human inhabitants. There is no limit to the scale of man's interference. He may send his cargo, together with rats, fleas and plague, by train into a continent, or by ship across the ocean. Thus plague can leap from one part of the world to another.

Disease in man

Bubonic plague: In this type of plague the incubataion period is two to eight days. A small lesion occurs at the site of the infected flea bite with the adjoining lymph glands becoming swollen and painful, followed by high fever, vomiting, intense thirst and some patients may have diarrhoea. The spleen and liver are usually enlarged. The lymph gland or bubo enlarges and becomes soft, bursts and discharges pus. If left untreated the infection progresses to other parts of the body through the blood stream and eventually infects the lung resulting in pneumonic plague.

Pneumonic plague:

Pneumonic plague is highly contagious as the patient's sputum contains the plague bacillus and droplets of this sputum can spread the disease from person to person thus resulting in localized outbreaks or devastating epidemics. The incubation period for pneumonic plague is one to six days after exposure. In pneumonic plague the patient is very ill, with fever, headache, vomiting and marked clouding of consciousness from the beginning. The sputum is thin, watery and bloodstained. If the disease is left untreated it can prove fatal by the fourth, or fifth day. Pneumonic plague is most fatal as well as the most directly infectious form of plague.

Diagnosis and treatment

In animals: Plague in rodents is strongly suggested by the presence of a bubo, and aspirates from this may reveal bacteria of characteristic morphology. Specimens, including rodents and fleas, must be sent to a laboratory recognized by WHO. Requirements for the final diagnosis of *Y. pestis* infection include confirmation of

typical microscopic and colonial morphology, lysis by specific bacteriophage, staining with flourescent-antibody conjugate for *Y. pestis* fraction 1, and production of characteristic lesions in laboratory mice or guinea pigs. During widespread outbreak, when the diagnosis of plague in an area has already been confirmed, the passive hemagglutination test, which is rapid and inexpensive, may be used for the examination of rodent sera.

In man: The initial diagnosis, which must be made on clinical grounds, is of great importance because, although mortality is high, early treatment is very successful. Swollen inguinal or axillary lymph nodes may suggest staphylococcal or other septic infection, lymphogranuloma, tularemia, filariasis and so on. But if the patient has contact with the wild the doctor should think of plague. If, on the other hand, the infection appears overwhelming, he must think of septicemia due to Meningiococci, or other Gram-negative bacteria, typhus, malaria and hemorrhagic fever as well as plague. If there are already cases of plague in the area, the treatment should include anti-plague drugs untill onother diagnosis is established. So-called peripatetic plague is particularly difficult to recognize because the patient may have traveled thousands of miles since becoming infected from an unsuspected source. A positive result on microscopic examination strengthens the clinical diagnosis and reinforces the urgency of the need of specific treatment. Should the bubo yield pus, rubbing this into the shaved abdominal wall of a guinea-pig will usually succeed in separating plague bacilli, which will penetrate the skin, from other pyogenic organisms, which will not do so.

For final diagnosis, bubo aspirat, blood, sputum and in meningitic cases, cerebrospinal fluid should be inoculated on to blood and MacConkey's agar, and into infusion broth. Material may also be injected into rats, guinea-pigs or mice. After their death *Y. pestis* is easily demonstrated in smears from lymph nodes, blood and other organs. After a patient's death, material for diagnosis is best obtained from buboes, or spleen. If opening of the body is not permitted, specimens can be obtained by means of viscerotomes, organ puncture or finger amputation. Alternatively, sternal bone marrow, venous or heart blood, blood-stained nasal discharge may be examined.

Hemagglutinating antibodies appear towards the end of the first week of illness. Serological testing is therefore useless in the early stages of the disease, when a diagnosis is urgently needed, but it is very useful for retrospective or confirmatory diagnosis. In the passive hemagglutinin test, *Y. pestis* fraction 1 is used as the antigen. It is virtually specific for *Y. pestis*. A titer of sixteen, or a four-fold rise in titer, is very suggestive of plague.

The persons who are in close contact with patients of plague should be given a course of antibiotics, not because the patient in infections, but because the contacts have probably also been exposed to the danger of flea-borne infection. Tetracycline in doses of up to 500mg four times a day for one week is suitable treatment for an adult. For children, doses of 25-40 mg/kg/day are suitable, the risk of dental damage being minute compared with the risk of plague. In a small isolated village, it may be advisable for everyone to have a course of antibiotics, but massive dosing in a widespread outbreak is useless.

Hospital staff will probably bot be familiar with plague and the risks must therefor be explained to them. A patient with bubonic plague is not infectious if there are no fleas on him, but a patient with pneumonic plague, or with septicemic plague and terminal respiratory symptoms, is very infectious until after several days of antibiotic treatment. If there are only one or two patients, hospital staff should take a course of antibiotics while looking after them, but if there is a succession of cases they should, instead, take their own temperature every six hours and have treatment at once if it rises. Laboratory staff unaccustomed to handling plague specimens should be made aware of the risks and precautions.

Antibiotics for the patients: Response to antibiotics is dramatic provided these are given early enough, and certainly before the patient is collapsed and moribund (near death); treatment must not await the outcome of laboratory tests. The specific drugs are streptomycin, tetracycline, chloramphenicol, and to a lesser extent, sulfonamides. Penicillin is useless and must not be given alone for any obscure febrile disease that might be plague.

Steptomycin - loading dose 1g intramuscularly; 0.5g/4h until the temperature falls, then 0.5g/6h for several days.

Tetracycline - loading dose 3g orally; then 3g daily in divided doses for one week; but in late or severe cases a first dose of 0.75-1.0g is given intramuscularly.

Chloramphenicol - similar doses.

Perhaps the best treatment is a combination of streptomycin and tetracycline. Sulfonamides, may be used if antibiotics are unavailable, in doses of up to 4-6g/day together with 2-4g of sodium bicarbonate to keep the urine alkaline; useless against pnrumonic plague.

Vaccination: Killed virulent, or live virulent (attenuated) vaccines both cause sharp reactions; only killed vaccines are in common use. Two doses at an interval of 1-3 months followed by a third after a further six months are recommended. Vaccine is useless in rapidly developing localized outbreaks, but should be given to those whose work exposes them to plague such as staff in plague laboratories, plague control teams, and hospital workers in known plague areas.

Protection is probably short-lived, and booster doses are therefore required every six months. Moreover, the degree of protection is limited and varies with the degree of exposure. Thus vaccination would not necessarily protect against exposure to pneumonic plague. A vaccinated person, even if known to have formed anti-plague antibodies, must be given antibiotics when exposed to a definite risk, especially of pneumonic plague.

Prognosis

Untreated bubonic plague has a mortality of about 50%, while untreated primary pneumonic plague is invariably fatal.

Plague can be cured, and lives saved, by informed and urgently applied treatment

Plague pandemics may now be a thing of the past, but in the wild the disease will continue and in developing countries, such as India and southeast Asia, epidemic can and sometimes do arise.

Control of plague

Measures to control plague includ,: 1) those required during an outbreak, to bring it to an end, 2) long-term action to prevent the spread of infection from the wild to human population.

Control of outbreaks: For control of the epidemic education is of great importance. The local people must be told: a) How plague spreads; b) The importance of personal hygiene in avoiding flea infestation; c) The need to keep their houses free of dirt and debris in which fleas can linger; d) The need to seek medical advice if they are bitten by fleas; e) Dogs and other pets should, if possible, be treated weekly with insecticide; f) A local control team should carefully spray the inside of dwellings and other buildings with an insecticide to which local fleas are sensitive; g) No attempt should be made to kill commensal rats unless insecticide spraying has been first done, otherwise the fleas will jump from the carcasses to man; h) Villagers should be warned not to hunt, or trap in dangerous areas.

Long term control: Anything that keeps rats away from man lessens the risk of human plague; a) Good sanitation and waste disposal; b) Houses made rat-proof, also warehouses, stores, airports and railway stations, trucks, containers, trains, ships and planes must also be made secure against rats; c) Rat escape routes must be blocked; d) Proper storage of food; e) Protection of population and health workers; f) Use of gloves, masks while handling bodies of persons dying of plague; g) Isolation and treatment of individuals showing symptoms of plague; h) Quarantine of persons coming from plague affected areas.

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