

## CHAPTER 1

# BUBONIC PLAGUE

## THE PROTOTYPE OF PANDEMIC DISASTERS

**A**LL EPIDEMICS OF DEADLY DISEASES IN HUMAN HISTORY have been called *plagues* to stress how devastating these outbreaks are. However, whenever actual bubonic plague appears, panic develops, quarantine measures are instituted, and people flee the area. Although primarily a disease of rats and other small mammals, and their fleas, bubonic plague is spread from place to place by human commerce and travel, an excellent route for the migration of the animal vectors of the disease.

Formally known as *bubonic plague* because of the enlarged, painful, abscessed lymph nodes, or *buboes*, it produces, bubonic plague was also called the Black Death during a devastating pandemic in the mid-fourteenth century. The name most likely arose because patients with severe disease develop septicemia, a widespread contamination of the blood system. This, in turn, leads to a syndrome formally known as disseminated intravascular coagulation (DIC), in which multiple hemorrhages and patches of gangrene develop in the skin, turning large areas of the body black.

Like most other epidemic infectious diseases, war has played an important role in the spread of plague and, as early as 1347, plague was successfully employed as a form of biological warfare. As recently as World War II, the Japanese used airplanes to spread infected fleas over several Chinese cities, as discussed earlier.

Plague does not readily spread directly from person to person; its transmission depends on small animal hosts, especially rats and their fleas. Hungry fleas feed on infected rats and, when these rats die, the fleas may move on to a human

host. Plague can be spread directly from person to person when it causes pneumonia and, although the same organisms that cause the bubonic form of the disease can cause pneumonia, severe lung disease does not occur frequently enough to rely on airborne pathogens to purposely spread the disease.

The septicemia that occurs in extremely sick plague patients can spread the disease without the help of rats. A flea directly feeding on the contaminated blood of a septicemic patient could pick up sufficient numbers of organisms to infect another person with its bite.

Sporadic cases of plague still occur in the United States, primarily in the Southwest, where small wild mammals and their fleas serve as a reservoir for the disease. When a couple from a rural area near Santa Fe, New Mexico arrived in New York early in 2003 they were unknowingly incubating bubonic plague. Their hospitalization led to alarming news reports. The husband barely survived after developing septicemic disease with DIC and gangrenous changes in his legs that required bilateral below-the-knee amputations. No further cases occurred, however, and public concern (and news media interest) quickly waned. The two cases that startled New Yorkers were no surprise to people of the Southwest, where a few cases occur almost every year.

**BUBONIC PLAGUE IN HISTORY.** Bubonic plague has caused major epidemics since ancient times, with huge mortality rates. Some historians suspect that the Plague of Athens, described by Thucydides during the Peloponnesian War (in the fifth century BCE, with outbreaks occurring in 430, 429, and 427), was actually bubonic plague. Epidemiologists disagree; Thucydides does not describe buboes, and mortality among doctors was the highest of all groups, suggesting human-to-human spread (contagion). Such spread does not occur unless the plague victim has developed pneumonia (pneumonic plague), and this form of infection usually primarily affects family members.

Thucydides reported that when human remains were left lying unburied because of the number of deaths, scavengers avoided them or, if they did taste the flesh died soon afterward. Such spread of bubonic plague could occur if the deceased person had infected fleas still on his body, but it has not been described in other epidemics that were more likely plague. Thucydides also mentioned that second attacks occurred, a very unlikely occurrence in plague, which gives its victims immunity; however, he points out that the second attacks were never fatal, suggesting some degree of increased resistance to the infection.

The disease reportedly spread to Athens from Egypt; Athens was a busy commercial city with a nearby port, whereas its enemy, Sparta, was inland, which might explain why it was spared the epidemic. The extremely high mor-

tality in Athens, which claimed Pericles and his two sons among its victims, crippled its defenses. Sparta eventually won the Peloponnesian War, thus ending the Golden Age of Athens. (One author wrote that more ink has been spilt trying to explain this fateful plague than blood spilt during the war itself.)

In its early years, Rome was attacked by many severe epidemics of uncertain nature. Plague has been suggested as an explanation for many of them, but no descriptions of cases suggest that disease. The Antonine Plague of 164–180 CE, described by Galen, was spread rapidly by the return to Rome of infected soldiers in 166. Marcus Aurelius died of it. Galen's description is not recognizable to us, and some authors think this epidemic was more likely smallpox than plague; others favor typhus. In 251–266, the Plague of Cyprian, or the Aurelian Plague, in which half the population of Alexandria perished, also seems more likely to have been smallpox than plague. This epidemic also affected the invading Goths, who often gathered into crowds.

Many severe epidemics that occurred in the interval between the Justinian Plague of 542 and the Black Death of the fourteenth century have been labeled bubonic plague, but this identification is questionable. The high mortality rate of some of these epidemics suggests plague, but more persuasive evidence is lacking. The evidence for the Plague of Justinian having been bubonic plague is more convincing. Procopius clearly describes buboes during that epidemic. He also wrote, "There was a pestilence, by which the whole human race came near to be annihilated ... And this disease always took its start from the coast and from there went up into the interior." He added that, "at Pelusium [on the Mediterranean coast near the present-day entrance to the Suez canal, the plague] then moved to Alexandria and reached Constantinople in 542." Notably, the historical record of many devastating epidemics affecting the ancient world includes observations of the disease beginning in Egypt, or in Ethiopia and spreading to Egypt, then traveling down the Nile to cities in the delta and to other ports in the Mediterranean. Spread by human movements, and specifically by commerce, is a prominent feature of these and later epidemics.

**T**HE BLACK DEATH. The most famous pandemic of bubonic plague was the Black Death of the mid-fourteenth century. The history of its appearance and spread illustrates how human activities, especially commerce, can cause the dissemination of a devastating disease, even one that primarily affects an animal species. The history of the Black Death and how it was spread is a model for the spread of many major epidemic diseases, since bubonic plague goes where travelers go. And, it is a history that starts with an attempt at biological warfare.

The story of the Black Death begins in 1338–1339, in the vicinity of Lake Issyk-Kul, in southern Russia near the Crimea, where a cemetery contains an unusual number of burials. Inscriptions state that the deaths were due to the plague. The disease spread from there along the main caravan routes from the Far East toward Western Europe and the Middle East. Even before the great pandemic traveled from the Crimea to the Mediterranean and other parts of the world, there is evidence of plague in southern Russia. For example, in 1346, outbreaks of plague accompanied traders along the Silk Road in Astrakhan (at the mouth of the Volga River) and Sarai (farther up the Volga). Records reveal the presence of the disease at caravan stations on the lower Volga River and, in 1347–1348, Ibn Battata, an Arab traveler and scholar returning along the Spice Route from India, reported hearing about the plague when he reached Aleppo in northern Syria. He noted that it had not been seen there before that year.

In this area of Central Asia, marmots were trapped for their fur, which was then sold to various traders who transshipped them along these caravan routes. Hunters and trappers always were happy to find sick or dying animals that they could catch easily, and around this time many untrapped marmots were found dead; trappers skinned these animals and sent the furs to be shipped to buyers in the West. Bales of marmot fur probably contained living fleas that became very hungry without a live animal on which to feed. Reports of illness in trappers were ignored. The furs reached Astrakhan and Sarai first and, when the bales were opened, the hungry fleas jumped out.

The area north of the Crimea, in what is now Russia, the Ukraine, and Rumania, was controlled by Mongols, descendants of the Golden Horde of Genghis Khan. The Russians called these people Tartars. The ports of the Crimea were used by rival Genoese and Venetian traders, who each allied themselves with rival Khans. The Tartar prince Janiberg Khan, who ruled the area known as Western Kipchak, became allied with Venice in 1340. His forces attacked the Genoese and their allies near the ports of the Crimea, forced them behind the walls of the fortified city of Kaffa (now Feodosia in the Ukraine), and besieged them there.

Gabriel De Mussis (1280–1356) left an account of the progress of the plague from the Crimea to his home in Piacenza in 1348. He described how, among the besieging forces of the Khan, “infinite numbers of Tartars and Saracens suddenly fell dead of an inexplicable disease....” They developed buboes in the groin and “putrid fever,” and many died. “Tartars, fatigued by such a plague and pestiferous disease, ... observing themselves dying without hope ... ordered cadavers placed on their hurling machines and thrown into the city of Kaffa, so that by means of these intolerable passengers the defenders died widely. Thus there were projected mountains of dead.... And soon all the air was infected and the water

poisoned, corrupt and putrefied, and such a great odor increased....” Thus we have a record of an early form of intentional biological warfare.

Because fleas leave cadavers to parasitize living hosts, it has been suggested that the corpses catapulted over the walls of Kaffa may not have been carrying competent plague vectors. Rats were not catapulted, but the city must have had its own supply. The cadavers may still have had infected fleas on them (either human or rat fleas, or both) and could thus have spread the disease inside the besieged city, or the infection could have been spread by rats migrating into and out of the city despite the siege. Either way, sickness made Kaffa uninhabitable during the winter of 1347–1348. The survivors fled to their boats and returned to the Mediterranean, spreading plague as they went, probably assisted by the ships’ rats. Plague first appeared at Constantinople, the exit from the Black Sea and the capital of the Byzantine Empire; then it appeared in the Mediterranean ports of Egypt and the Near East.

When the Genoese ships from Kaffa arrived at Constantinople, crewmen were lying dead at the oars. Similar reports emanated from other port cities. Byzantine Emperor John VI [Ioannes VI Contacuzenus (1292?–1383)] wrote a history of his empire from 1320–1356 (he abdicated in 1352), stressing the Black Death “which ... attacked almost all the sea coasts of the world ... and all the islands, ... and spread throughout almost the entire world.” He reported outbreaks on the Greek Islands of the Aegean and along the coast of Anatolia. In all, about sixteen galleys brought plague into Italian ports in 1348. Three made it to Genoa. One carried Venetians to their home port.

Twelve ships from the Crimea reached Messina in Sicily. When the citizens of Messina realized that ships were bringing plague, they drove them out of the ports. One ship went to Marseilles and carried the disease westward from there to Barcelona; the plague then spread throughout Spain and Portugal.

The Genoese realized that the ships from Kaffa brought plague with them and drove them away, but it was too late. The routes of the ships and of the refugees fleeing the affected cities illustrate how people spread the disease. It spread throughout Italy, northward into to Switzerland and Bavaria, and east to the Balkans. From Marseilles it spread by ship along the Mediterranean coast and up the Rhone River to Avignon, then the seat of the papacy. Because there were too many bodies to bury, Pope Clement VI (1300–1368) consecrated the river, so that dead bodies might be dumped in it. Plague also spread along the Mediterranean coast from Marseilles to Toulon and either down the Garonne River or by ship to Bordeaux. In August 1348, boats from Bordeaux carrying claret to Great Britain brought the disease there.

There is a record of a wool-carrying ship with full crew that left London bound for Bergen, Norway, in May 1349. Some days after leaving, the ship was

found drifting off the coast of Norway with the entire crew dead. The disease then appeared in Norway and spread by ship to the rest of Scandinavia and to Germany; it reached Poland in 1351.

Plague reached into the depths of Russia in 1351 or 1352, not by spreading north from the region around the Crimea where the outbreak began, but via Sweden and Poland, because that was the direction in which trade flowed. The disease followed the trade routes and thus came back to Russia by ship via the Mediterranean, the Atlantic, and the Baltic Sea.

Boccaccio (1313–1375), whose father died of plague in 1348, described the disease in some detail. He mentioned buboes appearing in the groin and armpits, and added that, “the mere touching of the clothes or of whatever other thing had been touched or used of the sick appeared of itself to communicate the malady to the toucher.” Air was “tainted by the scent of dead bodies” and people went about “carrying in their hands, some flowers, some odoriferous herbs, and other some divers kind of species, which they set to their noses.” This practice, intended to ward off poisonous miasmas and disgusting, sickening odors, continued as a preventive measure until near the end of the nineteenth century. According to some sources, it is the origin of the practice of sending flowers to funerals.

Plague may have reached the Mesopotamian area independently of the Crimean ships, via caravans from Samarkand, in Turkestan, that traveled the southern route, south of the Caspian Sea, along the silk and spice routes, reaching Baghdad, Damascus, and then the Mediterranean coast. Ships carrying silks, slaves, and furs to Alexandria brought plague as early as 1347. From there it spread to Cairo, Gaza, and Beirut.

Inhabitants of seaports realized the danger of the plague and drove ships away, trying to institute a form of quarantine, but it was too little and too late. By the spring of 1348, Black Death was well established in Italy. *Quarantine*, derived from the Italian word for *forty*, lasted forty days, a period long enough for any incipient disease to become manifest and run its course. Quarantine became a standard practice whenever plague or any other feared disease appeared until well into the twentieth century. Facilities were established outside city walls for travelers to spend their period of quarantine before being allowed to enter the city. On land, quarantine was primarily designed to keep people outside the city, but infected rats and their fleas could still escape and infect a city. Keeping ships away from a port was more effective, but usually incomplete. There were few pockets of freedom from the Black Death.

It is estimated that the Black Death killed 25 million people during the years 1348–1350, a loss of one-third of the population of Europe and the Middle East. It has also been estimated that no less than 70 percent of those who contracted

the disease died. In France, towns lost an estimated 50 percent and rural areas 30 percent of their inhabitants. The Black Death was followed by widespread famine because of insufficient labor to raise food. Malnutrition resulted in deaths from a variety of other diseases, probably including smallpox and typhus. "Sweating sickness" hit Britain at this time, with considerable mortality, but its nature is uncertain.

Severe epidemics of plague continued to occur in parts of Europe after the mid-fourteenth century. An outbreak began in Germany in 1356. As late as 1630–1631, 1.5 million people are thought to have died of plague in Italy, largely in Lombardy. In 1709, epidemic plague killed 300,000 people in Prussia. In 1720–1722, a severe epidemic in France affected Marseilles and Toulon, where 50 percent of the entire population died; in other cities, including Avignon, the death rate ranged between 30 and 50 percent. Napoleon's troops encountered plague when they invaded Egypt and the Middle East in 1801.

Beginning early in the eighteenth century, Europe was protected from the spread of plague from Ottoman areas by a barrier erected by Austria (the Habsburg-Ottoman frontier), primarily running through Hungary. Over 100,000 men manned it, with quarantine and checkpoint stations. This "Sanitary Cordon" limited human traffic and trade, and thus the spread of infectious diseases such as plague. The term *cordon sanitaire* has been used since for any attempt to wall off and prevent disease (or unwanted political influences).

Plague was endemic in England from fourteenth through the seventeenth centuries, with numerous outbreaks in the seventeenth century, some of them shutting down Shakespeare's theater. Severe epidemics occurred in London from 1604 to 1610, and 1640 to 1649, with at least four milder epidemics between those two larger ones. Outbreaks of plague in London ended with great fire of 1666.

The gradual ascendance of brown rats over black rats has been suggested as a factor in the subsidence of plague epidemics. Black rats tend to live in inhabited areas of houses, whereas brown rats prefer dark cellars and sewers, in less close contact with people. Because the rat flea can jump only 90 mm (3.5 inches), proximity to people may be important. However, the theory weakens, when we consider that brown rats had replaced black rats in Moscow before a particularly severe epidemic of plague struck during the 1770s, and brown rats did not reach England until 1727, over 60 years after the last "bout of the plague." Plague is not very particular about which species it affects. Rabbits, ferrets, dogs, and cats were also involved in other outbreaks, with the pattern of disease similar regardless of the original source.

Plague reappeared in England in 1902–1903, and again in 1906–1918, when twenty-four cases were described in a rural area of Suffolk. Six cases recovered

(four bubonic and two pneumonic). Only four cases were confirmed bacteriologically; the rest were considered likely to be bubonic plague. Investigators found infected rats and rat fleas—*Ceratophyllus fasciatus*, not the usual tropical rat flea—and a couple of infected rabbits, but no black rats were found in Suffolk during the period of that outbreak. To control the outbreak, rat catchers were used, and all 15,332 of the rats caught were dissected. Infected rats were found in twenty-seven areas. A key town in this outbreak was a port on River Orwell, where ocean-going traffic tied up. Investigators concluded that the most likely source of the disease was infected rats coming ashore. In subsequent years, investigators found infected ferrets, rabbits, and rats in rural areas.

Another theory about the history of plague is that a new, less pathogenic form of the causative organism, *Yersinia pestis*, may have evolved, or that resistance appeared in rats and man, decreasing the amount of plague in rats. The appearance and spread of a closely related organism, *Y. pseudotuberculosis*, may have been a factor—human infections with that organism are mild and give rise to cross resistance to *Y. pestis*. This observation is compatible with the theory of a famous parasitologist, Theobald Smith, who postulated that parasites evolve to less virulent forms that become able to co-exist with their hosts. Genetic studies have shown that two genes play an important role in the pathogenic differences between *Y. pseudotuberculosis* and *Y. pestis*. A mutation in one or both of these genes may account for the emergence of less virulent organisms, and these organisms may have replaced *Y. pestis* in rat populations, thus accounting for the subsidence of the disease.

*The Plague of the 1890s.* During the 1890s, a major epidemic of plague developed in Hong Kong and mainland China. It was spread by maritime commerce, as plague usually is, and appeared in major port cities around the world. Ports in Thailand, Indo-China, and Java were affected, as were Manila, Sydney, Capetown, Buenos Aires, Oporto, Honolulu, Glasgow, Mauritius, and Auckland. It returned to China, where a severe epidemic occurred in Yunan. Plague also appeared in Manchuria and Japan. Some cases of plague occurred in Australia and on the Essex-Suffolk border near the coast of England. The progress of this epidemic illustrates the role of human maritime commerce in spreading plague.

**FINDING THE CAUSE OF PLAGUE.** In 1894, the causal agent of plague was identified simultaneously by two physicians who had participated in the epochal early studies of the germ theory of disease in Europe: Dr. Alexandre Yersin, who

had worked with Louis Pasteur in Paris, and Dr. Shibasaburo Kitasato, who had worked in the other main site of discovery of disease-producing agents, the laboratory of Dr. Robert Koch in Berlin. (By that time, after millennia of speculation about disease-producing miasmas, causative agents of the major infectious diseases of the era were being identified at the rate of one a year.) When the plague broke out, Dr. Yersin had left France to go to Hanoi, capital of French Indo-China, and Dr. Kitasato had returned to his native Japan. During the 1890s, public health authorities in various countries became concerned, even alarmed, by reports of outbreaks of plague in the Far East, knowing how it spread by sea to commercial ports worldwide. The French government set up a commission to study the disease and asked Yersin to head it. Concerned for their own safety, the Japanese took a similar step, sending Kitasato to China. The plague bacilli turned out to be relatively easy to observe, stain, and culture. Almost simultaneously, both investigators identified the organism that became known as *Pasteurella pestis*. Kitasato apparently was the first to make the observation but published his findings in Japanese and English. Yersin found the same organism and recognized its role, but he published in French in a leading scientific journal of the time that quickly published short reports. Thus, his results appeared first. Yersin's priority of publication prevailed, and in 1970, the bacillus was renamed *Yersinia pestis*.

Although the role of the rat flea was not yet known, insect vectors were suspected. In 1894, Yersin found that the flies in his Hong Kong plague laboratory died in great numbers, their bodies "crowded with the specific bacillus." He injected tissues from the dead flies into guinea pigs, which developed plague and died of it. Later in 1894, Simond identified the tropical rat flea, *Xenopsylla cheopis*, as the vector in an article in the journal of the Pasteur Institute. This theory had been put forward previously by Ogata, a Japanese investigator, but disregarded. Since then, a wide variety of small mammals, including marmots and rabbits and their fleas, have been shown to be capable of carrying plague bacillus.

*Twentieth Century Epidemics of Bubonic Plague in the U.S.* A series of plague epidemics occurred in California between 1900 and 1924. In 1899, two cases of plague were known to have occurred on a ship from Hong Kong bound for San Francisco. Although the victims had recovered by the time it arrived, the ship was quarantined on Angel Island and searched. Eleven stowaways were discovered. The next day two of them were missing; later, their bodies were found in the Bay. The plague bacillus, identified during the outbreak in the Far East a few years earlier, was relatively easy to culture, and it was recovered from the two

bodies. Although officials were worried that the disease would spread in California, no further cases appeared at that time. However, nine months later, on March 6, 1900, plague bacilli were found in an autopsy of a Chinese man, and California officials felt that some action was needed to prevent an epidemic of the disease.

At that time, despite earlier observations establishing the relationship of the disease to rats and their fleas, the most likely means of spread was thought to be contaminated food or water, or direct acquisition of the organism through defects in the skin. During the previous decade, such mechanisms of infection were shown to occur in other major diseases, including typhoid fever, dysentery, cholera, diphtheria, and wound infections. Disinfection campaigns were instituted, including pouring carbolic acid into sewers, which actually hastened the spread of the disease by flushing out infected rats and their fleas. Strong anti-Chinese sentiment led to efforts to quarantine Chinatown. The Chinese objected, as did the business community, believing it was bad for business for people to think there was plague in the city. The quarantine of Chinatown was lifted, but health officials conducted house-to-house inspections of the area. Despite resistance to the inspectors, two more plague victims were discovered.

When the Board of Health finally admitted that plague was present in the city, the governor refused to believe it and rejected suggestions that he do something about it. However, the denials of the existence of plague by some officials were not convincing, and more and more states began to avoid trading with California. The Surgeon General of the U.S. Public Health Service finally got permission from President McKinley to enforce standard anti-plague regulations. Commissions and boards were formed, disbanded, and reformed, continually fighting with the governor, who persisted in denying the existence of the disease, still fearing what he felt would be needless alarm. A prominent epidemiologist from the Rockefeller Institute in New York, Simon Flexner (1863–1946) headed one commission responsible for a massive cleanup campaign of the houses and shops in Chinatown. In 1903, a new governor took office and vowed to help the boards of health in every way. Despite little having been done, new cases stopped appearing, and the last victim of this outbreak died on February 29, 1904. The known cases totaled about 120, of whom all but eight died; the high mortality rate probably meant that most nonfatal cases were not discovered.

In 1906, plague reappeared in San Francisco after the devastating earthquake and fire. Rats, as well as people, were made homeless by the destruction and both took up residence in refugee camps. This time, officials launched a new kind of campaign that was based on the scientific knowledge that had been accumulated about the plague: They offered a bounty on rats. A similar rat-

catching campaign had been used successfully a few years earlier to fight an outbreak of plague in New Orleans, and it helped in San Francisco. Although this second epidemic was larger than the first, it was brought to halt in 1909 and was the last urban outbreak of plague in the United States. Scattered cases continued to occur in rural areas, however, with marmots apparently the main reservoir of the disease.

**RATS AND PLAGUE.** Despite the success of rat-catching campaigns, it is worth noting that decreasing the rat population could have increased the spread of plague, at least temporarily. Eliminating rats minimizes the reservoir of infection, but leaves hungry fleas looking for a new source for their blood meals. Humans are a satisfactory alternate source of nutrition. Therefore, the infected fleas are more likely to bite and infect humans as a result of the depletion of the rat population, at least until the population of infected fleas dies off. In many medieval epidemics, the records show that the finding of large numbers of dead rats in a community was shortly followed by outbreak of human cases of plague. (The New Mexican couple who recently became ill with plague in New York City had found a dead rat on their property just before leaving for New York, but they were not aware that they had been bitten by its fleas.)

The fact that rats were associated with the disease was noted long before the role of their fleas was elucidated. In Manson's *Tropical Diseases* (1898), he pointed out, "Many observers have remarked the great mortality among rats and other animals which sometimes precedes and accompanies outbreaks of plague in man." He quotes a report that, in a Himalayan town where plague was epidemic in 1864, "the rats quitted the various villages in anticipation of the advent of the disease; the people, taught by experience, on seeing this exodus recognized it as a warning." During an epidemic in Canton in the 1890s, "from districts of the city where the plague had been raging for some time the rats entirely disappeared, whilst they kept on dying in other quarters to which the disease afterward spread."

Recent studies have elucidated the complexities of the relationship between rats and people and help us to understand the history of this disease. When fleas feed on an infected rat, the fleas become infected. When the infected rat dies, its fleas leave and search for a new host. The fleas usually find other rats, infect them, and spread plague through the rodent community. The spread in rats is slow: When the density of rats is low, as it is when rats die in large numbers, fleas are forced to find alternative hosts such as humans, and a human epidemic begins. Rarely, person-to-person spread of pneumonic plague occurs, usually after a human epidemic has already begun. Studies of the disease in recent years

suggest that if the infection rate in a given rat population is low (e.g., 25–50 percent), human infection is rare or unlikely. If over 80 percent of a given rat population is infected, human infection occurs. Thus a rat epizootic can smolder for long periods without the appearance of human cases.

Once the disease appears in humans, control of the rat population can actually be deleterious. If the rat population is kept at a permanently low level, then the risk of a large rodent outbreak is low, and therefore the risk of human cases is reduced. However, if a cull is brought into effect after the first human cases have been reported, it can create a far larger pool of infection for humans, since a cull releases many infected fleas that seek human hosts. Any area with a rat population density of about 3,000 per sq km exceeds the threshold and is at risk for appearance of the disease. Areas with rodent reservoirs of plague include the United States, southern Africa, southern Asia (including Vietnam, where American servicemen encountered the disease), and South America.

Cases of bubonic plague continue to be reported from many parts of the world, sometimes with long intervals between outbreaks in a given area. In the 1990s, bubonic plague was observed in Madagascar, Mozambique, and Surat. These modern outbreaks suggest that the disease can exist in animals as an epizootic that later starts to infect people, or that it can be reintroduced from other areas, probably by commercial trade.

**V**ACCINATION TO PREVENT PLAGUE. Infection can be prevented in individuals through vaccination, but vaccination cannot eliminate plague. Because of its rodent reservoir, the infection can reappear whenever unvaccinated people appear in a given vaccinated area. One hundred percent of a population must be vaccinated to prevent any cases of the disease. The vaccination of American troops in Vietnam prevented the infection in the troops, but it did occur in the native population.

**SUMMARY.** With its tragically high mortality and seemingly inexorable spread, bubonic plague remains the prototype of severe outbreaks of disease. Although the plague is primarily a zoonosis—a disease of rats and other small animals, especially rodents and their fleas, its effects on humans are legendary. It has been spread by humans through the inadvertent transport of rats and their fleas. It has been purposely induced as a form of biowarfare since the first appearance of the Black Death in the Crimea, through World War II, and it may be used again in the future.

Although thought of as an ancient disease, severe human outbreaks still occur in areas where animal reservoirs exist, and people traveling into those areas can be infected. A vaccine exists, but because it is not possible to immunize the entire population in affected areas, the disease will undoubtedly continue to appear in humans because of its persisting animal reservoirs.

## ADDITIONAL READING

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