The Ecology and Epidemiology of Plague

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Introduction

Throughout history, plague has been made infamous as the ultimate biological killer. The word is now synonymous with any particularly contagious, lethal, and uncontrollable epidemic. However, the true plague, caused by the bacterium *Yersinia pestis*, has largely been ignored in recent years. Many people think of plague as an extinct disease of the Middle Ages, a horrifying tale from history class that has been eliminated from society through time and technology. Of course, this is not the case. Although plague, like many other diseases, has been eliminated from industrial countries, it continues to afflict most parts of the world. In fact, just last month, pneumonic plague killed over 60 people in a recently reopened diamond mine in the northeastern region of the Democratic Republic of the Congo. The situation is even more dangerous because DRC is close to the border of Sudan, where a long civil war and political unrest in Darfur are forcing many refugees to escape to neighboring countries under unsanitary conditions.

The lack of concern about plague in the developed world also presents another complication to preventing its spread; while treatments and vaccines for plague exist, they are not widely distributed, and knowledge about them has decreased considerably. In the Middle Ages, the Europeans were much more susceptible to this newly introduced infection than those in the tropics. The developed world faces the same situation today, since very few people have developed antibodies to fight off the infection. The insidious character of this bacterium, combined with the lack of preparedness to face such an outbreak, might make plague an ideal agent for bioterrorists seeking death and major havoc. Even without this bioweapon potential, plague is still a widely occurring but poorly understood disease. It is therefore important to return to a scientific study of the bacterium, particularly in understanding how it spreads and what measures can be taken to control its threat.

The majority of literature on plague dates back to the Middle Ages, when the disease was much more rampant. While studies of plague were scarce in the 18th-19th centuries, there was resurgence in interest at the turn of the 20th century when a major pandemic hit Asia. Subsequently, though, interest in and literature on the disease has disappeared. There has been virtually no coverage of the topic in major scientific journals, including those in parasitology. The most recent epidemiological works on plague date from the 1970s and early 1980s, but the information in these texts is still considered accurate by most parasitologists today. This paper will therefore concentrate on these books and reports, while occasionally including new information from more recent articles.

The essay will begin with a brief historical analysis of plague outbreaks, and then explore plague's geographical distribution, with the goal of understanding where the disease originated and how this might affect population resistance. Then, the organisms involved in plague ecology will be discussed in detail: the first is the plague bacterium *Yersinia pestis*; next are several of the common flea and other arthropod vectors of the disease; subsequently the small mammalian reservoir hosts of plague will be considered, concentrating on rats but also with a discussion of campestral foci; finally, methods of human infection with the plague bacterium and its effects are investigated. After understanding the ecology of plague, preventative and control measures at each stage of the infectious cycle and their effectiveness are examined. Finally, social and political questions about plague are raised, particularly its threat as a bioterrorist weapon and the role of international health policy in eradicating this disease.

A Brief History of Plague

The bubonic plague pandemic of the 14th century, more commonly referred to as the Black Death or Great Dying, is probably the most well known and documented health disaster in history. It is also suspected to be the first example of bioterrorism. According to historical accounts, the epidemic started in 1348, when Mongol invaders from central Asia started mysteriously dying aboard ships entering the Mediterranean (Norris, 1977). Upon reaching port in Genoa, in the northwestern part of Italy, the Mongols decided to rid themselves of these bodies by catapulting the infected corpses over the fortressed walls of the city. While this story is rather sensational, several important conclusions stem from it. Rats are notorious as stowaways on ships, and it is highly likely that rats native to Asia were able to make their way into Europe aboard these Mongol vessels, and thereby penetrate the city. Along with these rats came their parasites, the Oriental Rat Fleas (*Xenopsylla cheopis*). It is probable that these fleas were still clinging to the human corpses thrown into Genoa, and were able to colonize new rat populations. No matter what its origin, the effects of the Black Death on Europe are irrefutable. It is thought that between 1348-1350, at least 25% of the population of Europe was killed, with estimates ranging as high as 50% in certain cities, such as Florence (Rail, 1985).

The last known pandemic of plague in Europe was the Great Plague of London in 1665. Within a five week period in late August and September, over 38,000 people were killed, and by February 1666 close to 100,000 were dead in London alone (Gregg, 1985). More recently, plague has been found in virtually every part of the world, including North America. In the United States, plague was found in California in the early 20th century, and spread through the desert southwest into Louisiana and Florida. In almost all cases it occurred in rural foci, with

ground squirrels as the reservoir host, and tended to remain in the southern states. In recent years (1980s-90s), isolated cases of plague have been found mostly in New Mexico.

The most recent epidemics of plague have occurred in tropical and subtropical regions of Africa and Asia. India has been particularly susceptible to the disease over the centuries. Plague was endemic in northwest India in the late 1600s, but it gradually seemed to disappear. However, in the early 19th century it once again appeared in northern India, and in 1896, the last great plague pandemic started in Bombay, which had been free of plague for over 200 years (Rail, 1985). At this time, Bombay was a worldwide commercial port city, so the disease was able to spread rapidly to other parts of Asia and beyond through merchant ships and the rats that inhabited them. By the beginning of the twentieth century, plague had spread to Hong Kong, China, the Pacific islands, and finally into western North America, as noted above. Plague also spread to South Africa through the Indian shipping routes during this period, and cases have occurred throughout the continent. In recent years, isolated cases of plague have continued to occur in India and Africa. In 1994, 200 were killed in Surat, India (Gujurat State), and in 2002 16 cases were reported in an isolated village in Himachal Pradesh, in the Himalayan foothills (WHO, 2005). The largest recent outbreaks have occurred in central Africa, starting with 23 cases in Zambia in 2001, then moving northeast with 71 cases in Malawi in 2002 and 130 cases in the Congo in early 2005 (WHO, 2005).

Geographical Distribution

The geographic origin of plague has been controversial. Most epidemiologists believe that the disease emanated somewhere in Asia, though the precise location is still debated. John Norris's seminal treatise on this question argues that there are three distinct strains of plague that

have different distributions (Norris, 1977). These strains are differentiated based on a) whether they can ferment glycerine and b) whether they can produce nitric acid. The strain of *Yersinia pestis* that is suspected to have caused the Black Death and most other medieval epidemics is able to ferment glycerine but does not produce nitric acid. It is postulated that this strain originated in the Tigris River valley, in what are now Iraq, Turkey, and Syria. It then spread north into trans-Caucasian Russia (now Armenia and Azerbaijan), and eastward to Central Asia, where trading routes and Mongol invasions introduced the strain into Western Europe. Meanwhile, the strain that has caused most recent plague outbreaks is one that does not ferment glycerine but does produce nitric acid. This strain started in India and Burma, then spread east into China through trade routes, and eventually to the Pacific coast of North America and to South Africa. The third strain, which has been the cause of the recent outbreaks in Central Africa, is one that can both ferment glycerine and produce nitric acid, and is likely to have evolved from the Middle-Eastern strain.

Glycerine production is significant in the virulence of the plague strain (Norris, 1977). Initially, all rodents in a campestral focus are equally susceptible to infection by the *Y. pestis* bacterium. However, as certain rodents develop antibodies to the bacterium, they no longer serve as suitable reservoir hosts, so the bacterium specializes in the more susceptible hosts. In the Middle East and central Asia, these hosts were hibernating rodents, such as marmots and voles. During their hibernation, these hosts produced large amounts of glycerine, which was then overcome by the development of a glycerine fermentation process in the plague bacterium. However, in south and east Asia rats are the prevalent rodents, and since these creatures do not hibernate, they do not produce glycerine, and this strain of *Y. pestis* therefore did not develop this fermentation process. It appears that the Middle Eastern strain of *Y. pestis* has a higher rate of

proliferation than its counterpart, is more likely to enter the pulmonary system of its host, and is also resistant to penicillin, making it the far more deadly of the two strains (Norris, 1977). It is therefore likely that during the Black Death, the *Y. pestis* had recently made a host switch to non-hibernating rats from hibernating wild rodents.

According to the Centers for Disease Control and Prevention (CDC, 2005), the world distribution of plague between 1970-1998 was as follows: in Asia, countries that reported plague in this period included Burma, Cambodia, China, India, Indonesia, Kazakhstan, and Mongolia, and additional zoonotic foci were found in northern Pakistan, Turkmenistan and Uzbekistan. In the Middle East, no plague cases were reported, but infected animals were found in Saudi Arabia, eastern Turkey, northern Iraq, and western Iran. Almost all countries in Sub-Saharan Africa, from the Democratic Republic of the Congo, Malawi, and Uganda to South Africa, had reported plague, as well as Libya and Madagascar. There were also infected animals reported in Morocco and Western Sahara. Finally, in the New World, cases had been reported in the western United States and in Bolivia, Brazil, and Peru, with animals infected in Argentina and Paraguay.

Except for the strains in central Africa and central Asia, all existing plague cases are of the Indian variety, infecting non-hibernating rodents and lacking a biochemical mechanism for glycerine fermentation (Bahmanyar and Cavanaugh, 1976). This is supported by the fact that all these cases occur in the tropics and subtropical regions, where rodents do not need to hibernate. The medieval strain that caused the Black Death and that infected hibernating rodents in colder climates (such as Europe) has disappeared, except for isolated foci in the Caspian Sea region (Bahmanyar and Cavanaugh, 1976).

The *Yersinia pestis* Bacterium

Yersinia pestis, formerly known as *Pasteurella pestis*, was first isolated and studied independently by Swiss microbiologist Alexandre Yersin and Japanese microbiologist Shibasaburo Kitasato in 1894 during the Hong Kong epidemic (Gregg, 1985). This bacterium is a non-motile, non-sporeforming, Gram-negative coccobacillus (Bahmanyar and Cavanaugh, 1976). *Y. pestis* is very fragile, and can be killed by heat-treatment at 55º C, chemical agents, sunlight, or extreme dryness (Stark *et al.*, 1966). This is why the bacterium is generally not found in extremely arid environments, such as the Saharan Desert and the Middle East. Its optimum growth temperature is 28º C, so it prefers subtropical climates, but it has been found to grow in full nutrient broth at temperatures ranging from -2º C to 45º C (Stark *et al.*, 1966). *In vivo*, where nutrients are available, its optimal growth temperature is 37º C, the body temperature of mammals (Rail, 1985).

Y. pestis grows optimally under 60% or higher humidity, so its incidence in tropical climates like India and Africa is low in the dry winter months and high in the monsoon season in late summer (Rail, 1985). Although studies have been conflicting on the ability of *Y. pestis* to survive outside of a host, it is generally accepted that the bacterium will not remain infective for more than a few months in the open. Bacteria remaining in the feces or carcasses of infected animals, though, can stay viable for a longer period (Rail, 1985). *Y. pestis* also requires certain metallic ions for proper growth. It multiplies faster in the presence of calcium. However, if magnesium concentrations are high, virulent *Y. pestis* requires less calcium to grow, and high concentrations of both calcium and magnesium cause the cells to swell and eventually lyse (Rail, 1985). *Y. pestis* also requires high levels of iron for reproduction, and iron concentrations in the reticulo-endothelial cells involved in pneumonic plague increased after infection (Rail, 1985).

Moderate levels of selenium have been found to promote antibody formation against the plague bacterium in mammals, although high levels are toxic (Rail, 1985).

The Flea Vectors of Plague

The primary vectors of the plague bacterium are arthropods in the order Siphonaptera, the fleas. Fleas are laterally flattened, highly sclerotized, and wingless, with large coxal leg segments to allow them to jump long distances in order to attach to a host (Rail, 1985). Both sexes and most species within this order are blood-feeders of mammals (Rail, 1985). Fleas are holometabulous, with a non-parasitic larval stage that feeds on detritus. Fleas are nidiculous parasites as adults, preferring to live in the environment of a host due to their sensitivity to temperature and humidity (Rail, 1985).

Flea morphology is important in its vector potential for plague. The flea's foregut contains a chamber called the proventriculus, between the esophagus and stomach, where the blood meal is digested. When a *Y. pestis* bacterium enters the proventriculus, it releases a coagulating enzyme which forms a solid blood clot, creating a nutritious environment to facilitate bacterial growth (Gregg, 1985). This mass of dried blood and bacteria eventually blocks the proventricular valve (Stark *et al.*, 1966). When this valve is blocked, the blood meal remains in the esophagus, never entering the stomach. Therefore, the flea feels starved and avidly seeks another blood meal from a new host. Upon feeding, the flea regurgitates the blood that has remained in its esophagus from the previous infected host into the new wound. This mechanism is particularly important in *X. cheopis*, because in most other flea species, particularly those targeting wild rodents, masses either have to cover the entire stomach to produce this effect, or there is no blockage at all (Stark *et al.*, 1966). Sometimes, the bacterial

mass undergoes autolysis and becomes dislodged, so normal feeding resumes (Stark *et al*., 1966). However, if this mass remains, the flea quickly dies from starvation, even as it constantly makes attempts to feed and subsequently infects many hosts with the plague bacterium.

There are two siphonapteran species that are the primary vectors of *Y. pestis*. The original vector is *Xenopsylla cheopis*, the Oriental rat flea of Asia (Rail, 1985). *X. cheopis* is the ideal vector for the bacterium because bacterial incubation is rapid, with blockage of the proventriculus occurring in 12-21 days (Stark *et al*., 1966). *X. cheopis* has optimal survival rates in moderately warm and moist climates, and prolonged heat is unfavorable (Stark *et al*., 1966). The preferred hosts for this species are rats that harbor underground (such as sewer rats). *X. cheopis* feeds many times a day for short intervals, and often lives within the fur of its host (Stark *et al.*, 1966). Despite being an excellent vector, *X. cheopis* has a relatively short lifespan of 376 days (Rail, 1985), and since this lifespan can be further shortened by starvation, this flea can be more easily contained than some other species. A closely related species, *Xenopsylla brasiliensis*, is an even more efficient carrier of plague that occurs in temperate regions of Brazil and East Africa (Gregg, 1985).

The primary plague vector in the cooler areas of Europe and North America is the European rat flea *Nosopsyllus fasciatus*. It probably became a vector of plague through interactions with *X. cheopis* fleas that were introduced into southern Europe through trade routes to the Orient. *N. fasciatus* is about 1/3 as effective in transferring plague as *X. cheopis* (Gregg, 1985). However, several other characteristics make it a more lethal vector than *X. cheopis*. Its lifespan of 680 days is nearly twice as long as that of *X. cheopis* (Rail, 1985). Also, while it feeds for longer intervals, it also tends to stay off the host for longer periods (Stark *et al.*, 1966),

making it more difficult to control. This species is also amenable to feeding on hosts other than *Rattus*, and may serve as a link between urban and campestral foci of plague (Stark *et al*., 1966).

Other fleas can also be vectors for plague, although they are not as efficient as *X. cheopis* and *N. fasciatus*. The human flea *Pulex irritans* cannot readily transmit the plague bacterium individually. However, if large numbers of these very common fleas attack a host, transmission is much more likely (Stark *et al*., 1966). These fleas do not require rats or other rodents as reservoir hosts, and are considered an important interhuman transmitter of bubonic plague (before the disease reaches its contagious pneumonic form) (Stark *et al*., 1966). *Ctenocephalides felis*, the abundant 'cat flea' of domestic animals, also effectively transmits plague in large groups (Stark *et al*., 1966). These fleas are important in campestral settings, where domestic animals that get infected from wild rodents can bring the bacterium to human households. Finally, the sticktight flea *Echidnophaga gallinacea* is a relatively efficient transmitter of plague, with a similar infection rate to *N. fasciatus* (Stark *et al*., 1966). However, this parasite of poultry and rodents is relatively sessile, so it functions primarily to keep enzootic plague active in a campestral focus, and is not an important vector to humans.

Several other arthropods, including lice, bedbugs, and dipterans, are able to carry the plague bacterium in laboratory settings. However, these arthropods have never been shown to transmit the bacterium (Stark *et al*., 1966). The proventriculus of the flea is essential in *Y. pestis* transmission. The flea is already a much more active host-seeker than other arthropods, and blockage of the proventriculus and subsequent starvation of the flea makes it feed constantly. Also, the bacterium most efficiently enters the reservoir host through regurgitation by the flea during feeding, and this requires that the bacteria remain in the esophagus. While bacteria can remain viable in flea feces, even heavy fecal contamination of soil does not result in high human

infection rates (Rail, 1985). Finally, fleas are more mobile than other arthropods, which are usually permanent or long-term ectoparasites of their hosts.

Mammalian Reservoir Hosts

Almost all fleas are parasites of warm-blooded mammals, though a few also parasitize birds. While all mammals can be targeted by plague-carrying fleas, carnivores (such as dogs and cats) are resistant to the bacterium (Stark *et al*., 1966). Small rodents, though, are highly susceptible to flea attacks. There are two environments where plague cycles can occur: urban and campestral settings. Research has suggested that plague originated in wild rodent reservoirs, and later moved to rats (Stark *et al.*, 1966). The plague cycle is thought to have survived for millions of years in prairies, steppes, and meadows throughout the world (Gregg, 1985). In this cycle, fleas infected by the plague bacterium feed on wild rodent hosts. The rodent hosts die from the bacterium, but fleas that are still on the dead host move on to other hosts before they are killed by starvation. Since campestral fleas tend to be relatively non-host specific, they can move to several species, ensuring the continuation of the cycle even if a certain host species dies out. There are many wild reservoir hosts of plague, but only a few will be discussed here.

Mammals in the Family Sciuridae include marmots, squirrels, prairie dogs, and chipmunks (Stark *et al*., 1966). These animals are particularly important reservoirs in North America. Ground squirrels (*Citellus* sp.) are not very social, and therefore are not naturally likely to be found near human habitations. However, they form vast underground networks and are widespread over large areas in the western U.S. *Citellus townsendii*, the sage squirrel, is distributed in the grasslands of the northwest in Idaho, Montana, and Wyoming. Farther south, into western California, Utah, Arizona, and New Mexico, the striped and spotted ground

squirrels (*C. tridecemlineatus* and *C. spilosoma*, respectively) are found (Stark *et al.*, 1966). On the Pacific coast and into the Rockies, rock squirrels of the subgenus *Otospermophilus* are the primary reservoirs. All these species are heavily infected by fleas, particularly *Diamanus montanus*, which efficiently transmit plague. This genus has been implicated in most cases of plague that occurred in the western US in the 20th century.

Another important reservoir host in the US is the prairie dog (*Cynomys* sp.), which lives in the Rocky Mountains and desert southwest. These rodents are extremely susceptible to plague, with almost all individuals in a colony being killed by an epizootic that was probably initiated by the prairie dogs' common contact with ground squirrels (Stark *et al.*, 1966) Since they are popular pets in the western states, white-tailed prairie dogs are important in spreading plague to children (Stark *et al.*, 1966).

The second important family of campestral reservoir hosts is Cricetidae, the New World mice and rats, voles, and muskrats (Stark *et al.*, 1966). Particularly important species in this family are *Onychomys* sp., the grasshopper mice, *Peromyscus maniculatus*, the deer mice, and *Microtus* sp., the meadow voles. Grasshopper mice are carnivorous, feeding on anything from insects to other mice. They also enter ground squirrel and prairie dog habitations to search for food, and are therefore likely to get bitten by the same fleas (Stark *et al.*, 1996). Deer mice seem to have evolved immunity to the plague bacterium, and are in close contact with other rodents, so they effectively circulate *Y. pestis* through shared fleas. Finally, meadow voles have extremely high reproductive potential, and their numbers can actually increase in an epizootic of plague (Stark *et al*., 1966). They also can come near human habitations, and several species have been responsible for plague outbreaks in Tacoma, Washington, and Mexico City (Stark *et al*., 1966).

While campestral rodents have been responsible for most recent cases of plague in the US and around the world, the far more important rodents historically are those in urban environments, the Old World commensal rats and mice. These species, responsible for the Black Death, are still the primary reservoir hosts in plague transmission in Asia. Particularly important are two species in the genus *Rattus*: *Rattus rattus*, the black or roof rat of India and southeast Asia, and *Rattus norvegicus*, the brown or Norway rat of Russia and Central Asia. *R. rattus* is smaller and less aggressive than its cousin, and resides in tropical climates (Stark *et al*., 1966). It also is a climber, and tends to live in the roofs of buildings and ships. *R. norvegicus* likes to live close to the ground, and is also not as adaptable, making it easier to expel or exterminate from buildings (Stark *et al.*, 1966). Rats are not capable of maintaining an epizootic cycle on their own, since they die quickly from plague, and their fleas (such as *X. cheopis*) are usually species-specific. However, if rats interact with campestral rodents, fleas such as *N. fasciatus* would be able to transfer the infection to rats. A large number of rats and fleas, such as can occur on ships and in densely populated cities, can then maintain the plague cycle for a significant period.

Human Infection with Plague

In most cases, the information detailed above is simply reference material, as the plague bacterium continues to circulate only between fleas and their rodent hosts. However, humans can be infected with *Y. pestis* in several ways (Scott and Duncan, 2001). The first and most important is cohabitation with rats and their fleas. *X. cheopis* is rather host-specific, but it does occasionally bite humans, particularly in situations where people regularly come into contact with rats. When rats are infected with plague, they quickly expire from the disease. When the flea senses the carcass getting cold, it will leave its host and seek a new one. The blockage of the proventriculus

of *X. cheopis* makes it even more eager to find a new blood meal. As more rats die, a vicious cycle is created where starved fleas become more cosmopolitan in their host selection, eventually biting a person. A human could also be infected from plague directly from wild reservoir hosts. This is particularly the case with hunters who are bitten by the fleas of a small rodent that they have killed and eaten.

In both cases, there are situations that place people at a higher risk of contracting plague. The most important is when movement into new, untrodden campestral regions brings humans into direct contact with enzootic plague, particularly in situations of war or mass migration (Christie, 1969 in Scott and Duncan, 2001). Also, unsanitary conditions can lead to higher densities of rats, which may feed on detritus and fecal matter or the insects that inhabit them. Finally, in certain cultures, particularly in India, it is sinful to harm rats, so they are often allowed entry or habitation in dwellings, making plague infections much more likely. It is unknown what factors might make a person more susceptible to contracting plague, but it has been found that about 65% of human subjects develop protective antibodies following inoculation with formalin-killed, agar grown suspensions of *Y. pestis* (Stark *et al*., 1966).

Once an infected flea has bitten a person, the individual will be afflicted with symptoms of plague. These include a rapid fever, reaching 105º F within a day, headache, nausea, pain, and restlessness (Stark *et al*., 1966). In the bubonic form, inflammation of the lymph nodes (called buboes) occurs. If *Y. pestis* reaches the bloodstream, it multiplies and releases toxins into the blood, causing the rapidly fatal septicemic plague. The first two cases both result in death in 3-5 days in most people, but neither is contagious, and can only be spread through flea bites (Stark *et al*., 1966). However, the third form, pneumonic plague, is contagious. This form occurs in about 5% of infections, where the *Y. pestis* enters the respiratory system, and it can be passed on

through inhalation of airborne saliva droplets containing the bacterium (Scott and Duncan, 2001). Contact with salivary secretions from infected rats or other animals can also result in plague infection (Rail, 1985). Those that survive past a week with the disease are generally able to recover, and develop antibodies to the bacterium.

Without treatment, about 30-50% of bubonic plague cases and nearly all septicemic or pneumonic plague cases are fatal (Scott and Duncan, 2001). Treatment of plague is possible if it is detected early. Pharmaceuticals used to treat plague include sulfonamides and the antibiotic streptomycin. However, the *Y. pestis* might become resistant to streptomycin within 4-5 days of treatment (Stark *et al*., 1966). Treatment presents its own problems; large doses of drugs may cause sudden destruction of many bacteria, which would then release large amounts of toxin into the bloodstream, hastening death (Stark *et al*., 1966). Therefore, the best medication for plague is prevention of *Y. pestis* from infecting a human through parasite control measures.

Preventative and Control Measures

In its 1976 Plague Manual, the World Health Organization offered several suggestions to local governments to control the spread of the disease. The first and primary objective was to control flea populations. Ever since World War II, pesticides such as DDT had been pronounced miracle treatments for parasite extermination. However, this 'miracle' was short-lived. In areas where DDT was used for malaria eradication, which also happened to be areas at high risk for plague epidemics, fleas and most other parasites had developed resistance to the chemical. Therefore, more powerful insecticides had to be formulated. This presented several problems: the first one was the cost of such a measure, which most developing countries could not afford and most western manufacturers would not make cost-effectively. The second was the safety of the

local population. Most people in these areas survived on agriculture, and the accidental poisoning of crops with insecticide could have disastrous results. The use of 'bait boxes' presented a more effective option. These boxes would contain foods for rodent consumption, as well as an insecticide dust. When attracted to these boxes, the rodents would get covered with the dust, which would kill the fleas both on their fur and later in their nest (Bahmanyar and Cavanaugh, 1976). There would have to be care taken not to kill the rodents as well, though, because dead rodents often made the likelihood of fleas biting people higher and therefore more dangerous.

The second goal was rodent control. The WHO noted that the most popular reaction to a plague outbreak was the attempted extermination of all rodents in the area. However, this approach presented some major setbacks, including the lack of funding, personnel, and equipment to institute such a large-scale extermination, and the likelihood that the destruction of a limited population of rodents would only lead to faster reproduction among the survivors and a rapid increase in rodent density over the earlier population (Bahmanyar and Cavanaugh, 1976). Instead, it was recommended that improvements in sanitation, proper waste disposal, proper storage of grains and foodstuff, and ratproofing of structures would yield better results in a much more cost-effective manner (Bahmanyar and Cavanaugh, 1976). If rodent extermination was found to be necessary, it had to be preceded by flea elimination, because as stated previously, dead rats and live fleas would only lead to an epidemiological nightmare. Furthermore, since most rodenticides were also toxic to humans and other animals, such fumigation campaigns could only be undertaken in areas away from human habitations. This makes sense, because rats only get attacked by plague-carrying fleas when they enter non-human campestral settings where wild rodent reservoir hosts reside.

The final part of the cycle that could be affected by control measures was the prevention of the spread of pneumonic plague (Bahmanyar and Cavanaugh, 1976). The most important solution was early detection and treatment of bubonic plague, before it could reach its pneumonic form. If the disease became contagious, it would require quarantine of all individuals who were in contact with the infected individual, and in densely populated regions, such as in Africa and Asia, such a process would be extremely difficult. Furthermore, quarantine would have to take place inside the house, since pneumonic plague patients would be unable to travel to a hospital and would put in danger everyone encountered on the way there. Since adequately equipped public health officials would not be available on an individual basis, such an approach would only be effective if only a small number of infected people and households were involved. Even if pneumonic plague in a single village was treated or controlled, the cycle would likely continue in nearby areas. Therefore, even after attempting all available local measures, there would still have to be larger national and international changes in order to truly prevent plague infection, and this would require a high level of social and political cooperation that is difficult to build and maintain.

Social and Political Questions

All epidemiologists agree that the most important preventative and control measure for any disease is international cooperation and peace. In the current climate of tension and conflict, it has been increasingly difficult for international organizations like the WHO or NGOs to obtain the financial and personnel support from the developed powers that is so desperately needed to address epidemics. While all attempts have been made to control the plague outbreak in the Democratic Republic of the Congo, the huge influx of refugees from Sudan into DRC and

neighboring countries puts thousands of people at higher risk for infection in unsanitary campestral conditions. The only effective remedy for this situation is neither scientific nor epidemiological, but political and moral: a declaration of peace by the Sudanese government and the permission of Sudanese refugees to return to their homes in Darfur. In order for this outcome to occur, the WHO and United Nations must take the initiative, enlisting the aid of thus far uncooperative developed powers in return for better relations with other nations.

A final question that can be asked is whether plague is a practical biological weapon, and if so, the best way to prevent its use by hostile actors. In discussing the ecology of *Y. pestis*, it has been found that the simple introduction of plague bacterium into a city will not immediately cause mass death. The bacterium must first embed itself in the parasitological cycle by infecting a rodent host and getting ingested by a flea. As long as proper sanitary and parasite control measures are maintained, the bacteria would be likely to die out naturally or only survive in campestral foci without debilitating effects on humans. Regardless of this low likelihood of the purposeful use of plague as a weapon, the second question of preventing its use is just as important. The best solution here is ensuring that no actor would ever be justified in having hostile intentions against another state or individual. By maintaining peaceful and open relations with all classes of people throughout the world, the work undertaken by so many epidemiologists over the decades would finally accomplish its goal, the assurance of the world's health and well being.

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