

The Return of the Beast: Modern Black Death?

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Introduction

Pandemics have played an important role in shaping the human history. By the Oxford definition; the noun pandemic refers to a globally prevalent disease affecting large numbers of populations. Pandemics were from the main causes by which civilizations flourished or fell to their doom. They caused the decline of populations and aided greatly in the process of “natural selection”. Two of the deadliest pandemics in history have been the Justinian Plague and The Black Death. They both caused great reductions in the populations by more than 50%. Both epidemics were caused by the same bacteria; *Yersinia pestis*. *Y.pestis* is known to be transmitted primarily through flea bites carrying infected blood from rodents and secondarily through inhaling cough or sneeze droplets from infected humans. *Yersinia pestis* has been evolving ever since its discovery and it has the ability to take huge leaps in its evolution to form new unexpected strains. The plague is still found in multiple cases yearly across the globe. It never failed to make an appearance throughout history. Fortunately, antibiotics were developed for the plague and the mortality rate dropped significantly. Even though, it seems that the world is currently immuned against the viciousness of *Yersinia pestis* and the plague, scientists cannot help but wonder about the possibility of another Black Death occurring in the modern world. Through investigation of the evolutionary characteristics and behaviours of *Y.pestis* along with understanding the plague transmission conditions and such, it can be concluded that there is a huge possibility of the return of a modern Black Death genocide.

History: the Treasure Chest¹

History recorded three main pandemics in the old, middle and modern ages; the Justinian plague, Black Death and Indo-Chinese plague respectively. The Justinian Plague is said to be one of the main causes in the fall of the Roman Empire and Black Death was one of the main factors which aided in the emergence of the Renaissance and Protestant Reformation in Europe.

The first pandemic was the Justinian Plague which originated at around the year 532 AD in Northern Africa and from there it spread throughout the Mediterranean basin. Another theory claims that the first pandemic rather originated in China and then was transferred to Africa. It is said that by the year 565 AD, half of the Byzantine Empire was wiped out¹. The causes of the Justinian Plague were unknown to physicians at that time; but some claims were that the plague was caused by the inhalation of putrid air coming from “contaminated” sources or by an imbalance of the four bodily fluids (phlegm, blood, cholera and yellow bile). The second pandemic was the Black Death which occurred in Europe in around 1347 AD, it is believed that the plague came to Europe from China through rats on trade ships. After three years of its first occurrence, it killed an estimated 15 to 23.5 million Europeans representing one fourth to one third of the European population at that time. The causes of the plague and its methods of transmission were again mind boggling to all citizens at that time; precautions (some extreme) were taken to prevent the spread of the disease; such as wearing masks to prevent the “foul smells” of the disease, burning fires using aromatic substances, quarantines and even self-flogging to ask God for mercy. Finally, the last pandemic was the Indo-Chinese plague which originated in China in the year of 1855 AD and from there it spread across the whole continent and then the whole modern world. This plague is considered the most important of the three

historical plagues because by the end of it Alexander Pestis, a Swiss bacteriologist, uncovered the causative agent of the Plagues: *Yersinia pestis*¹.

One of the main characteristics of the Black Death was its rapid spread and that is due to the abundance of the disease's transmission conditions and its very sophisticated life cycles.

Life Cycles and Transmission Factors of *Y.pestis*

Studies show that *Yersinia pestis* maintains its existence through cycles involving the rodents and their fleas. *Y.pestis* is usually found in areas where there is a high density of rodents in semi-arid grasslands and forests². Scientists believe that there are two life cycles for *Y.pestis*. The first one is called the enzootic cycle in which the bacteria circulates in low levels amongst rodents without causing high numbers of deaths². The second cycle is called the epizootic cycle in which the bacteria becomes epidemic. Humans catch the disease mainly during the epizootic cycle. Studies have shown that epizootic cycles are found more during cool summers following wet winters and they are more prominent in places where there is large rodent populations². It was also concluded that the existence of *Y.pestis* for long periods of time is due to mobilization and drift⁵

Transmission of the plague from animals to humans happens by flea bites carrying the bacteria; or by handling infected tissue or fluids. These methods of transmission give rise to the bubonic and the septicemic forms of the plague and if they are left untreated they will give rise to the pneumonic plague which then can be transmitted from human to human. The pneumonic form is the only form which allows the bacteria to spread amongst humans by close contact with the infected patients.⁷

There are three forms of the plague; bubonic, septicemic and pneumonic plagues. They do not necessarily occur together or in order but they may lead to each other if they are left untreated.

The Three Plagues: Symptoms, Progression and Treatments²

Yersinia pestis is the causative agent in the three plagues: Bubonic, Septicemic and Pneumonic plagues. The Bubonic plague is the most prominent form of all three and it was the main cause of the Black Death in the 1300's Europe. The symptoms of the Bubonic Plague consist of fever, headache, chills, painful and tender lymph nodes (called buboes; hence "Bubonic") (see figure 1). This form usually results from bites of infected fleas; the bacteria then multiplies in the lymph nodes closest to where the bacteria entered the body and if it is left untreated the bacteria travels to other parts of the body. As for the Septicemic plague, it has multiple symptoms such as fever, chills, weakness, abdominal pains, shock and bleeding under the skin or internally. Skin and tissue may turn black and die especially in fingers, toes and nose (see figure 1). This form of the plague may result from untreated bubonic plague or from handling an infected animal. Finally, the Pneumonic plague is the most dangerous of all and its symptoms may include fever, headache, weakness and development of pneumonia with shortness of breath and cough with bloody or watery mucous (see figure 1). This form may develop from inhaling infected droplets; or from untreated Bubonic or Septicemic plagues which have spread to the lungs. Pneumonic plague may cause shock and death and it is considered the most serious form of the plagues because it is the only one that can be transmitted from one person to another by inhaling infected droplets.

Bubonic plague can be diagnosed by the presence of a bubo occurring in the cervical, axilla and groin nodes which can be very painful that the patient has restricted movement in the affected area. Pneumonic plague can be diagnosed by the pneumonia-like symptoms such as cough and fever as well as the presence of bloody sputum. Septicemic plague can associated with gastrointestinal symptoms such as nausea, vomiting, diarrhea and abdominal pain. Overall, the diagnosis cannot be valid without blood samples, lymph nodes aspirates or sputum samples sent to the laboratory for testing and verification. Once the plague is verified, health authorities have to be notified immediately because the plague is a threat to the national security, patient needs to be isolated completely and medication should be administered as soon as possible².

Currently, there is no vaccination in North America although many studies and models have been submitted². The only effective treatment/ protection is antibiotics, but unfortunately by time *Y.pestis* develops resistance against antibiotics.



Figure 1: Symptoms from the three plagues (www.cdc.gov/plague/)

Antibiotic Resistance

Y.pestis is known to be sensitive against any gram-stain negative bacterial antibiotic⁸.

Antibiotics given for treatments from the three plagues can be streptomycin or gentamicin².

The dose depends on age, medical history and allergies. Method of treatment is usually through

muscular injections and after some improvements oral administrations may be allowed².

Streptomycin is the main effective drug against the plague but gentamicin is also used when there is little availability of streptomycin in some countries⁸. The antibiotics were able to drop the mortality rate to 8% after it was approximately 70% when there was no treatments.

Unfortunately, though, for the past decade, the mortality rates have been constantly and slowly rising; which caused scientists to classify the plague as a re-emerging disease. The rise is most likely contributed to current *Y.pestis* strains gaining resistance against antibiotics.

Y.pestis usually affects the lymphoid nodes, dermis and the blood which are considered as sterile environments, but in later stages of the disease when the bacteria reaches the gastrointestinal systems, it will form aggregates for easier disease transmission. Due to the non-sterile environment in the digestive tract, *Y.pestis* is in closer contact with other pathogens⁸. This close proximity between an antibiotic-sensitive strain of *Y.pestis* and an insensitive strain of another pathogen such as *E.coli* will cause the insensitive genes to transfer to the *Y.pestis* strain in a horizontal gene transfer; immunizing *Y.pestis* against antibiotics⁸. This discovery was made through a study by Marc Galimand *et al.* during a Madagascar outbreak. Through the study it was discovered after four weeks, 95% of the fleas were carrying the antibiotic resistant gene acquired from the *E.coli* strains.

Along with antibiotic resistance, *Y.pestis* is known for its rapid and sudden evolution which cause the rise and fall cycle of the plague's appearance.

Yersinia pestis: Discovery and Evolution

The discovery of the specific features of the plague and the causative agent has been an ongoing process. The science behind fully understanding the plague and fully grasping the capabilities of *Yersinia pestis* is evolving rapidly. New discoveries are added by the day and new scientific insights are uncovered by the hour.

The Swiss bacteriologist, Yersin, uncovered the plagues' causative agent during the Indo-Chinese plague. His discovery marked the first milestone in the journey of "unearthing" the mysteries hidden in the plagues. *Yersinia pestis* was discovered to be a gram negative, rod-shaped facultative bacterium. *Y.pestis* was found to be closely related to *Y.pseudotuberculosis*; a gastrointestinal pathogen. It is believed that *Y.pestis* is a clone of *Y.pseudotuberculosis* and it evolved around 15000 to 20000 years ago. Thus, it appears that *Y.pestis* was able to evolve from a gastrointestinal pathogen found widely in the environment to a mammalian blood-borne pathogen that is able to parasitize insects as well²

Studies, later, have shown that there were "Big Bang" events before each of the last two historical epidemics in regards to *Y.pestis* diversity; and that was due to the emergence of multiple extant lineages during short periods of time. The reason of the sudden booms in diversity is due to the fact that replication cycles occur more frequently during epidemics than during the enzootic periods, which will in turn cause an amplification of mutations in the populations and that will cause the rise of new strains.³

The latest study known to science regarding the evolution of *Yersinia pestis* investigated the strains of *Yersinia pestis* from the Justinian plague. By matching the phylogeny trees and

likelihood trees of both strains of the first pandemic's and the second pandemic's *Y.pestis*; it was discovered that the Justinian Plague was caused by an independent strain of *Y.pestis* and it did not give rise to any further stains; meaning that the strains which occurred during the Black Death were a completely separate emergence of different *Y.pestis* strains. It was further discovered that the Black Death's strain was the ancestor of all future strains, therefore this means that the third strain evolved directly from the second strain while the first one was an isolated currently extinct/ undetected strain. The study lastly inferred that over history *Y.pestis* emerged from rodent reservoirs independently to cause independent plagues with the same devastating symptoms and results.⁵

Modern Day Plague

Plague, unfortunately, still exists in various parts of the modern world. Over the last documented 15 to 20 year period, approximately 38310 cases and 2845 deaths have been reported to WHO from 25 countries^{6,8}. It is suspected that these numbers are underestimated due to the unreported cases and the lack of education in rural areas to catch and treat a plague case. Important to note that all patients inhabited rural or semi-rural areas where agriculture is prominent. The latest serious endemic, according to World Health Organization, was in 2006 in the Republic of Congo, where more than 50 people died out of 1174 suspected cases from a serious pneumonic outbreak⁶. In the twenty-first century; Zambia, India, Malawi, Algeria, Democratic Republic of Congo, China and Peru reported cases to WHO⁶ (see figure 2 for plague distribution map). Due to all of these characteristics, the plague has been labelled as a re-emerging disease after a period of quiescence

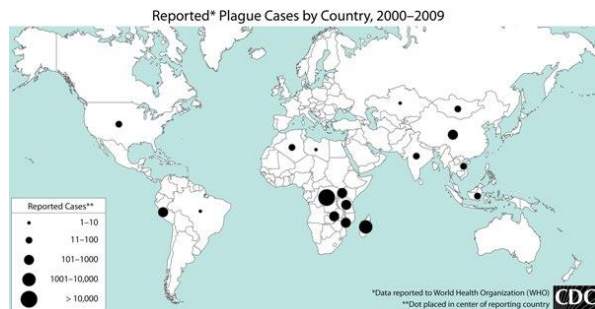


Figure 2: Plague distribution map in 2010 (source: <http://www.cdc.gov/plague/maps/>)

Conclusion

The puzzle of whether the Black Death may return or not has always bothered scientists. The plague never failed to make an appearance in various parts of the world through times.

Understanding symptoms, ecology, methods of transmission and evolution of *Yersinia pestis* is needed to present any clear hypothesis regarding the reoccurrence of the Black Death.

Currently, all evidence and data are supporting the high possibility of the resurrection of the Black Death in the modern world.

Firstly, it was discovered that there happens a boom in the diversity of *Y.pestis* strains prior to any plague and that is due to the increased number of replication cycles which intensify mutations causing them to become more noticeable in the population. From this discovery, we can conclude that *Yersinia pestis* is always evolving at a very high rate to give rise to different strains. Not forgetting to mention its amazing ability to evolve from *Y.pseudotuberculosis* to *Y.pestis* (two completely different pathogens) which means that when conditions required, it was able to evolve from a totally different pathogen and may give rise to a totally different pathogen in the future likewise. Secondly, it was discovered that *Y.pestis* evolved at various

times in history giving rise to independent deadly epidemics each time, therefore, there is a huge possibility in the future that *Y.pestis* will evolve to a new strain which we currently have no antibiotic or natural resistance against. Along with its ability to acquire new genes from other pathogens; it may gain antibiotic resistant genes easily and rapidly. Given global warming and climatic instability worldwide, conditions of the continuous successful evolution of *Y.pestis* are found excessively.

All of the evidence combined point towards the possibility of a new *Y.pestis* strain evolving along with the possibility of the reoccurrence of a modern Black Death. The Beast is simply Returning!

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