

## Could the 'Black Death' Become a Re-Emerging Infectious Disease?

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The discovery in March 2013 of fourteenth century plague pits in London triggered an interesting debate amongst scientists and policy makers: could the plague ever re-emerge on a similar level in the twenty-first century? Due to the potential seriousness of the disease this is a subject worthy of epidemiological consideration and research.

The news that archaeologists had unearthed a so-termed 'Black Death' grave in London, containing more than a dozen skeletons of people suspected to have died from the plague (in the absence of other paleotraumatological evidences), made the global headlines across a number of media outlets [1]. Here builders discovered ravaged skeletons some three metres below the ground in Charterhouse Square when laying the foundations for a train station.

During the optimal time of the 'Black Death', in the fourteenth century, around 75 million people globally perished, mainly through lymphadenitis. This manifestation of the plague continued to be a disease of major importance until the seventeenth century and the main regions affected were Europe (where 30–60% of the European population was wiped out) and Asia [2]. The 'Black Death' is conventionally known within the medical field as the Bubonic plague (named after the buboes commonly found in the armpits, upper femoral, groin and neck region). Together with the septicemic plague and the pneumonic plague, these infections are caused by the bacterium *Yersinia pestis* (formerly described as *Pasteurella pestis*). The bacterium seemingly evolved several thousand years ago from a far more benign, gut dwelling bug called *Y. pseudotuberculosis* (one of a group of relatively benign intestinal diseases). *Y. pestis* is a facultative anaerobic Gram-negative rod-shaped bacterium. It is unknown if *Y. pestis* caused all causes of plague during this period, although it stands as the etiologic agent (many of the skeletons exhumed from 'plague pits') have been tested using a rapid diagnostic test for the detection of *Y. pestis* F1 antigen to confirm the cause of their death.

The bacterium is what is known as a zoonotic disease, indicating its ability to be transferred between different species. In terms of animal to human transmission, the role of rats and fleas (like *Pulex irritans*) and their detailed role in the transmission of plague has been discovered and experimentally verified [3]. The disease affects the lungs and is highly contagious, leading to mass outbreaks across populations. Without treatment, the bubonic plague kills about two thirds of infected humans within four days [4]. Those infected with the bacteria develop symptoms that can include swollen, tender lymph glands, fever, headache, chills, and weakness. Other symptoms may include muscle pain and seizures. The human body is generally unsuccessful in fighting the disease because cells of *Y. pestis* can resist phagocytosis.

Other major plague events have occurred around the world over the past centuries and similar discoveries of the remains of some of the victims have been made. In 2012 an archaeological discovery of the last remnants of a "lazaretto" or "lazaret" was made in the city of Marseille. This was a place equipped with an infirmary and destined to isolate ship passengers quarantined for health reasons. It was a major site of a plague outbreak.

One debate that has arisen from such finds is whether the major plague pandemics simply stand as historic events or whether they could ever re-occur on a similar scale and with similar virulence?

The argument that the plague could re-emerge on a large scale has been made in an article published in the journal *Infection, Genetics and Evolution*. With this study the researchers have analyzed the Great Plague of Marseille, which caused 100,000 deaths between 1720 and 1723. The researchers aimed to highlight issues we are facing with infectious diseases today, to identify the best ways to respond to epidemics and whether we are still at risk of the plague re-emerging again [5].

The results of the analysis show that a number of factors show populations are still at risk of plague today. This is due to several reasons including transport and trade, and threats in developing countries where multi-drug resistant pathogens are currently emerging and spreading rapidly. These global problems would require responses at various intersecting levels of public health and political authority: global, national, and local.

Cases of plague continue to be reported. In 1994 and 2010 cases were reported in Peru; and in the USA cases were reported in Oregon and Colorado. Whilst the last time there was a Bubonic Plague epidemic in the United States was 1924-1925 when the disease hit the city of Los Angeles, there remain an average of 10 to 20 reported cases each year. Globally, most human cases since the 1990s have occurred in Africa. Typically between 1,000 and 2,000 cases each year are reported to the World Health Organization, although this is likely to be an underestimation. Of the reported cases, the fatality rate is around 60%.

Another reason for concern stems from the genetic analysis of the plague causing bacterium [6]. Studies have found that the *Y. pestis* had a similar genetic structure to the bacterium that causes leprosy. Additionally research suggests that *Y. pestis* continues to evolve; the concern is whether this evolutionary trajectory is towards an even more dangerous pathogen or into one and may one day develop into an microorganism that poses no threat to the cells of its host. Currently the main treatment is with the use of fluoroquinolones drug class. There is no reason why, however, the target bacterium should not develop antibiotic resistance should the drug be over-used.

Similar genetic analysis has revealed the possible point of origin of the 'Black Death'. Researchers from Ireland, China, France, Germany and the United States, examined the past 10,000 years of global plague disease events. Their collaborative research traced the roots to somewhere in or around present-day China. It is considered that the plague spread over various historical trade routes in the fifteenth century, with the legendary Silk Road trade route acting as a possible pathway for disease [7].

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The interesting genetic possibilities aside, the more immediate concern is with the potential for global spread. *Y. pestis* is capable of causing catastrophic human epidemics and was certainly responsible for great epidemics in the past. The consequences of global transport network expansion, which include the potential for infectious disease pandemics, vector invasion events and vector-borne pathogen importation. Heightened vulnerability to epidemics may also arise in relation to population growth, unplanned urbanization, antimicrobial resistance, poverty, societal change, and rapid mass movement of people. These factors mean that study of the disease should remain at the forefront of social and medical research.

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