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Review

Small oversights that led to the Great Plague of Marseille (1720–1723): Lessons from the past ☆

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ABSTRACT

In recent decades, the issue of emerging and re-emerging infectious diseases has become an increasingly important area of concern in public health. Today, like centuries ago, infectious diseases confront us with the fear of death and have heavily influenced social behaviors and policy decisions at local, national and international levels.

Remarkably, an infectious disease such as plague, which is disseminated from one country to another mainly by commercial transportation, remains today, as it was in the distant past, a threat for human societies. Throughout history, plague outbreaks prevailed on numerous occasions in Mediterranean harbors, including Marseille in the south of France. A few months ago, the municipal authorities of the city of Marseille, announced the archaeological discovery of the last remnants of a "lazaretto" or "lazaret" (http://20.minutes.fr, March 3th, 2012), a place equipped with an infirmary and destined to isolate ship passengers quarantined for health reasons. More recently, on September 16th, 2012, the anchor of the ship "Grand Saint Antoine" responsible for bringing the plague to Marseille in 1720, was recovered and it will be restored before being presented to the public in 2013 (http://www.libemarseille.fr/henry/2012/09/lancre-du-bateau-qui-amena-la-grande-peste-%C3%A0-marseille.html).

In the light of these recent archaeological discoveries, it is quite instructive to revisit the sequence of events and decisions that led to the outbreak of the Great Plague of Marseille between 1720 and 1723. It comes to the evidence that although the threat was known and health surveillance existed with quite effective preventive measures such as quarantine, the accumulation of small negligence led to one of the worst epidemics in the city (about 30% of casualties among the inhabitants). This is an excellent model to illustrate the issues we are facing with emerging and re-emerging infectious diseases today and to define how to improve biosurveillance and response tomorrow. Importantly, the risk of plague dissemination by transport trade is negligible between developed countries, however, this risk still persists in developing countries. In addition, the emergence of antibiotic resistant strains of *Yersinia pestis*, the infectious agent of plague, is raising serious concerns for public health.

Contents

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1. Plague, a "calamity"/re-emerging infectious disease since the dawn of time

Plague is a deadly infectious disease notorious throughout history (Fig. 1) and it has been spread along trade routes since the beginning of commerce. The symptoms and the different clinical manifestations of plague (bubonic; septicemic; pneumonic) have been known by physicians for centuries. However, it is only since 1894, that the causative agent of this disease is identified as Gram negative bacillus. Indeed, two bacteriologists, the French-Swiss Alexandre Yersin and the Japanese Kitasato Shibasaburö, independently isolated this Enterobacterium in Asia during the "third pandemic" (see below). Yersin who worked at the Pasteur Institute named this bacterium *Pasteurella pestis* in honor of Pasteur; in 1967, this pathogen was renamed *Yersinia pestis* to acknowledge the original observation by Yersin that plague infections in rats were not only observed during epidemics, but were often preceding epidemics in human. During centuries plague was regarded as a roden-borne disease. However, although primarily carried by rodents, plague was shown in 1898 by Paul-Louis Simond to be spread to humans by vector-borne transmission via fleas (*Xenopsylla cheopis*). Depending on sanitary conditions, plague can be spread either by infected fleas bites, by direct contact, by contaminated undercooked food, and/or by aerosol. The transmission of the plague to humans following the bite of infected fleas is the most frequent mode of human infection. Upon flea bite, bacteria migrate to the draining lymph nodes resulting in bubonic plague. Buboes are commonly found in the armpits, groin and neck. Gangrene of fingers, lips and nose, resulting in the black color of necrotized tissues, is a common symptom of this disease in addition to coughing, diarrhea and blood vomiting. In absence of immediate efficient antibiotherapy, bubonic plague evolves toward septicemia, coma and death within a week. When bacteria reach the lungs, they provoke an acute pneumonia. Patients with pneumonia are highly contagious through the spread of contaminated aerosols that cause primary plague, most frequently provoking death within 3 days. Human-to-human transmission of pneumonia plague favors a rapid spread of the disease in heavily populated areas (Kool, 2005).

Fig. 1. Old illustration showing the protection of physicians against plague. "Der Doktor Schnabel von Rom" (Doctor Beak of Rome). The beak is a primitive protection mask, stuffed with natural substances (such as spices and herbs) thought to ward off the plague. It was designed by Charles de Lorme, the first physician to king Louis XIII of France.

Y. pestis, is unique among the enteric group of Gram negative bacteria in relying on blood-feeding insects for transmission. The *Y. pestis* genome is closely related to that of *Yersinia pseudotuberculosis* from which *Y. pestis* diverged 1500–20,000 years ago in Central Africa (Achtman et al., 1999). The flea-borne transmission of *Y. pestis* followed a drastic ecological change from the food-borne and water-borne transmission of *Y. pseudotuberculosis* and *Yersinia enterolitica* (Chouikha and Hinnebusch, 2012; Stenseth et al., 2008). Indeed, the ecological change turned out to be associated with acquisition of plasmids that play a key role in flea-borne transmission (Sodeinde et al., 1992; Hinnebusch et al., 2002a). Moreover, genome sequences of *Y. pestis* belonging to different biovars are available (Parkhill et al., 2001; Deng et al., 2002). Chromosomal segments that carry genes involved in pathogenicity of *Y. pestis* have also been indentified (Buchrieser et al., 1998).

2. The major outbreaks of plague in history

Although plague can currently be treated with antibiotics (i.e., streptomycin; gentamicin, tetracyclines, fluoroquinolones, amynoglycosides) (Mwengee et al., 2006) strongly reducing mortality, it remains etched in the collective subconsciousness of the people as a threat to survival of human societies. This fear, still present in our modern societies, is probably due to the transmission of a memory of the great epidemics that have marked the history of civilization. The most terrible episodes of plague that humanity as experienced in the past 1500 years, are: the devastating plague