A Brief Report on Pubonic Plague (The Black Death) and its Origin

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1. Abstract

1.1 Objectives
This article reviews and updates the epidemiological information, global distribution and prevention of bubonic Plague. Also discusses the origin and the possibility of disease occurrence/re-emergence in Egypt.

1.2 Material and methods
The available published reports and several internet-based articles on Plague globally and in Egypt (geographical distribution, historical epidemics and present situation) were reviewed.

1.3 Results and conclusions
Plague which is a zoonotic bacterial disease caused by Yersinia pestis and transmitted by fleas mainly Xenopsylla cheopis has been responsible for a number of high-mortality epidemics throughout human history. Evidence indicated that the plague may have begun in Egypt rather than Central Asia. Despite no available reports on present situation of plague disease in Egypt, however historically, the country had suffered from several epidemics. Moreover, Egypt is under risk of disease re-emergence and transmission due to the existence of potential foci in the neighboring countries mainly Libya.

2. Abbreviations
BC: Before Christ; CDC: Centers for Disease Control and Prevention; P.: Pulex; WHO: World Health Organization; X.: Xenopsylla; Y.: Yersinia

3. Introduction
Plague "Black death" is an acute, contagious, febrile illness, primarily of rodents caused by the bacteria, Yersinia (Pasteurella) pestis (Family: Yersiniaceae, Order: Enterobacteriales) which can accidentally transmits to humans by the bite of infected fleas of which the oriental rat flea, Xenopsylla cheopis (Family: Pulicidae, Order: Siphonaptera) is the most important vector. The name "Black death is due that the disease frequently leads to gangrene and blackening of various parts of the body and hemorrhages in the skin which also results in black patches. The disease follows urban and sylvatic cycles and is manifested in humans in three main clinical forms: bubonic, septicaemic and pneumonic [1]. Bubonic plague is the most common form of plague which can be a very severe disease in people, with a case-fatality ratio of 30% to 60% [1]. As the epidemic of bubonic plague develops (especially under conditions of severe overcrowding, malnutrition, and heavy flea infestation), it eventually shifts into a predominately pneumonic form, which is far more difficult to control and which has 100 percent mortality when left untreated [2, 3].

Plague has been responsible for a number of high-mortality epidemics throughout human history and is still endemic in some parts of the world. The natural foci of Plague are found in the tropical, sub-tropical and warmer
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parts of the globe, between the parallels 55 North and 40 South [4], and are found on all continents except Australia [5]. Plague has recently been recognized as a re-emerging disease and remains a serious problem for international public health, especially in Africa [6-9].

It was considered that central Asia as the birthplace of the deadly epidemic of the bubonic plague [10], which originated in or near China and spread by way of the Silk Road or by ship [4]. However, studies [11,12], indicated that the disease may have arisen thousands of years earlier in ancient Egypt. Eva Panagiotakopulu [10], found plague bacillus in fossilized flea remains in ancient ruins in the workmen’s village at el Amarna, Egypt. So that she believed that the plague may have begun in Egypt rather than Central Asia and thought that the Plague epidemics originated in Egypt, where the Nile rat, was the natural host of the flea. The black rats, which came into contact with the Nile rats in the dirty cities, spread the flea and the plague throughout much of the ancient world. In almost all cases, plague epidemics strike areas with poor and cramped living conditions, much like the “Workmen’s Village” section of Amarna where Eva Panagiotakopulu carried out her research [13]. She is the first to look at fossilized insect remains of the ancient city and found a very high frequency of fossilized human fleas, bedbugs and other insects and parasites that “present a picture of squalid living conditions” in and around the workers’ houses [14].

This article reviews and updates the epidemiological information, global distribution and prevention of bubonic Plague. Also discusses the origin and the possibility of disease occurrence/re-emergence in Egypt.

4. Materials and methods

A review of the available published reports on Plague globally and in Egypt, (geographical distribution, historical epidemics and present situation) was performed on PubMed, Research Gate, WHO (World Health Organization) publications, CDC (Center for Disease Control and Prevention) documents and internet-based articles. As much as possible, several articles related to Plague outbreaks (patterns, prevalence and mortality), flea vectors and reservoirs were searched and reviewed. In addition, several related web pages were accessed. The past situation of Plague in Egypt was added and discussed. A total of 43 articles concerning different aspects of Plague epidemiology, distribution, outbreaks, prevention and control and vectors were included in this review.

5. Results and discussion

5.1. Involved Organisms in Plague Transmission

5.1.1. Causative agent

The zoonotic plague bacillus, Yersinia (Pasteurella) pestis [15], is a non-motile, non–spore-forming, gram-negative, rod-shaped bacterium. It is a facultative anaerobic organism that can infect humans and other animals via the oriental rat flea, (Xenopsylla cheopis) and which undergoes an obligate flea–rodent–flea life cycle, causes bubonic Plague [16]. Also, Y. pestis has gained attention as a possible biological warfare agent [4].

5.1.2. Vectors

Various species of Xenopsylla fleas are found throughout Africa and central and southern Asia, coinciding with the distribution of gerbils or rats of which the important vectors [9,17] include:

(a) the oriental rat flea, X. cheopis (nearly worldwide in moderate climates) which is the most important vector of urban plague

(b) X. brasiliensis (Africa, India, and South America) is an effective vector, especially in rural environments and is characteristically found in buildings parasitizing Rattus rattus, R. norvegicus and other rodent species,

(c) X. astia (Indonesia and Southeast Asia), a parasite of gerbils and rats

(d) X. vexabilis (Pacific islands). In addition to the northern rat flea, Nosopsyllus fasciatus (nearly worldwide in cool, temperate climates) which plays a weaker or unimportant role as plague vector [9].

Oropsylla montanus is the most important flea vector in the USA [18]. The human fleas (Pulex irritans) may play an important role in human- to- human Plague transmission [8]. Also, ticks and human lice (Pediculus humanus corporis) have been proved as efficient vectors [19,20].

5.1.3. Reservoirs

Rodents mainly domestic and urban rats are the most important reservoirs. Field mice, cats, camels, chipmunks, prairie dogs, rabbits, and squirrels can be important animal reservoirs as well [19].

5.2. Life Cycle and Transmission of Y. pestis

Both male and female fleas feed on blood and can transmit the infection [4]. Fleas become infected with Y. pestis after taking blood meals from septicemic animals. Within the flea, Y. pestis cells grow to high density in the midgut (stomach) [16]. After three days, bacteria, will continue to reproduce and sticking together until a brownish large plug is formed in the midgut attached to the proventriculus (a valve-like chamber between the midgut and esophagus). During the first week of infection, Y. pestis eventually blocking the proventriculus and the blocked flea [21] (Figure 1) becomes starved for blood, which no longer can reach the midgut, and thus the insects attempt to bites a host several times. Consequently, the flea vomits infected blood back into the...
wound from the bite. The bacterium then infects a new victim, and the flea eventually dies from starvation [4,16]. There are two cycles for transmission of the disease (Figure 2). The first is the Sylvatic Cycle, or pre-human cycle, which occurs in wild rodents and fleas. This cycle continues until either all the wild rodents are dead, or the fleas find a new food source, usually domestic rats. Once a domestic rat or another domestic animal bitten, the Urban Cycle starts [4]. If a flea that carries Y. pestis happens to bite a human then that human is infected [22]. Humans can be infected through the bite of infected fleas, direct contact with infected tissues, and inhalation of infected respiratory droplets. A person usually becomes ill with bubonic plague 2 to 6 days after being infected [23].

5.3. Risk Factors
The main risk factors [19] are:
(a) Flea bite
(b) Contact with a patient, a potential host, or sick animals or rodents
(c) Exposure to dead rodents or rabbits
(d) Travel to or residing, camping, hiking, hunting and fishing in endemic areas of Plague
(e) Presence of a food source for rodents in the immediate vicinity of the home (f) Occupational exposure (e.g., researchers and veterinarians) as direct handling of contaminated tissues or of tissue fluids or inhalation of infected vapors.

5.4. Geographic Distribution
Plague is worldwide in distribution, endemic in many countries in Africa (10 countries), the Americas (5) and Asia (3) [2]. Over the past decade, 76.2% of the cases and 81.8% of the deaths were reported from Africa [1]. Shahraki, et al. [24] reviewed the status and outbreaks of plague in countries of the Middle East and north Africa (Iran, Afghanistan Bahrain, Iraq, Jordan, Lebanon, Saudi Arabia, Syria, United Arab Emirates, Yemen, Egypt, Libya, Morocco, and Tunisia) and stated that “In the last 50 years, human plague outbreaks have been reported in Saudi Arabia, Afghanistan, Libya, Morocco, Algeria, and Jordan”. Currently, the three most endemic countries are the Democratic Republic of the Congo, Madagascar and Peru [1,25] (Figure 3). Plague persists in rodent populations in many parts of the world in an enzootic (asymptomatic) form. Occasionally, the disease is transmitted by fleas from these enzootic hosts to several species of susceptible squirrels, chipmunks, wood rats, marmots and prairie dogs, which may then suffer epizootic plague and die in vast numbers. The urban rat-borne plague remains a potential threat wherever commensal rat species come into contact with either the enzootic rodent species or the epizootic plague-susceptible rodent species in urban or peri-urban areas. The transfer of Y. pestis organisms from the native rodent species to the domestic rat species is the initial step in the urban plague cycle that begins with the bite of an infected flea on a domestic rat [4].
to the commensal rats by exchange of fleas occurs rather easily. Once commensal rodents become infected, the risk of human infection is greatly increased [17].

5.5. Global status and trends
The Black Death was one of the great epidemic scourges of mankind. It swept across Europe and Asia in a series of large-scale epidemics, and may cause historical changes in many nations. Historically, plague was responsible for widespread pandemics with high mortality causing more than 50 million deaths in Europe. The first pandemic was believed to have started in Africa and killed 100 million people over a span of 60 years. In the early twentieth century, plague epidemics accounted for about 10 million deaths in India (1994) [19]. For unknown reasons, bubonic plague ceased to be an important pandemic disease [2]. Outbreaks in people, however still occur in rural communities or in cities. Almost all of the cases reported in the last 20 years have occurred among people living in small towns and villages or agricultural areas rather than in larger towns and cities [26]. These are usually associated with infected rats and rat fleas that live in the home. Globally, the World Health Organization (WHO) reports 1,000 to 3,000 cases of Plague every year [27]. In 1999, 14 countries reported 2,603 cases to WHO (including 212 deaths). These figures are comparable with the annual average figures (2,547 cases, 181 deaths) for the previous 10 years (1988-1997) [1]. From 2010 to 2015 there were 3248 cases reported worldwide (Figure 4), including 584 deaths [1,28]. As with many primarily zoonotic diseases, where the disease is transmitted from vertebrate animals to humans, plague is a very severe disease in people, with a case-fatality ratio of 50%-60% if left untreated [1]. With appropriate antibiotics and supportive therapy, the mortality rate is reduced to 5% [19].

Figure 3: Areas with potential plague natural foci based on historical data and current information (WHO/PED 2016) [43]

5.6. Origin of plague
It was reported that most researchers consider central Asia as the birthplace of the deadly epidemic of the bubonic Plague [10] which originated in or near China and spread by way of the Silk Road or by ship [4] but the disease may have arisen thousands of years earlier in ancient Egypt [11,12]. Although, the plague was not an epidemic disease in ancient Egypt, the Ebers papyrus manuscripts from around 1500 BC (Before Christ) describe patients suffering from diseases with similar symptoms of Plague, such as buboes and black spots. Moreover, one of the recipes of this papyrus recommends sprinkling of houses with natron water in order to expel the fleas [29]. Panagiotakopulu [11] suggested that the bacillus Y. pestis was primarily a disease of the Nile rat, Arvicanthis niloticus, which only achieved epidemic proportions when its vector, the tropical rat flea, Xenopsylla cheopis, was able to make the jump to a new host, the black or ship rat, Rattus rattus, introduced from India or indirectly via Mesopotamia during the Pharaonic period. Synanthropy and a high death rate in the new host lead to frequent transfer to human populations and stochastic waves of
pandemics. During her study, Eva Panagiotakopulu found plague in fossilized flea remains in ancient ruins in workmen's village at el Amarna and believed that the plague may have begun in Egypt rather than Central Asia, as has long been believed [13]. The workmen’s Village at Amarna (Figure 5) located at 270 km south of Cairo, had a very short occupation period (20-25 years, 1350-1323 BC) and consists of a group of well-preserved structures apparently built to house the workers involved in the construction and building of the tomb of Akhenaton [29,30]. The insect study from Amarna [29], produced a wide range of specimens, among which are 35 human fleas which provided clear evidence for the early dispersal of human fleas and the earliest examples of the so-called human flea. *Xenopsylla cheopis*, is thought to have originated in Egypt and during the 19th century spread to all parts of the world as parasite of rats infesting ships’ cargos [31]. The flea was collected and described in Egypt by Rothschild [32] and was named *cheopis* after the Cheops (Khufu), an ancient Egyptian Pharaoh.

### 5.7. Plague outbreaks in Egypt

It was reported [11], that Plague existed in Egypt since the Pharaonic era. Lotfy [4], and Shahraki, et al. [24] summarized the different outbreaks that occurred in Egypt since 1347, when the disease reached Alexandria, probably through the port’s trade with Constantinople, and ports on the Black Sea. Subsequently, Several outbreaks occurred during the period from 1899 to 1947 in different parts of Egypt mainly the portal areas (Alexandria, Port Said and Suez). As a result of rat control program introduced in 1941, no cases were reported from inland areas (1941-1945) despite an outbreak in the Suez Canal Zone (Port Said, Suez and Ismailia). Using DDT and other control measures during Alexandria epidemic of 1946–1947, resulted in a sharp decrease in flea indices [33] however, resistance to DDT was detected in *P. irritans* and *X. cheopis* flea populations [31]. Although, no available reports on recent epidemics (except in 1984 [34]) nor present situation of Plague disease in Egypt, the country is under risk of disease transmission from the neighboring countries mainly Libya and Israel. Libya which experienced several plague outbreaks during the period 1913-1920, 1972, 1976, 1977, 1984, 2009 and 2011 [4,24,35,36] and Israel due to its activity in research and development of biological weapons [4,37] using the plague bacilli. The re-emergence of plague in Egypt should not be excluded [24] due to the presence of suspected natural foci in Libya, environmental conditions, and the prevalence of flea vectors and rodent reservoirs [38,39,40]. Moreover, climate change, including global warming, which is expected to significantly affect many countries of the world, including Egypt [4] which affects all components of the plague cycle (host, vector, and pathogen) in various ways [41].

![Figure 5: Location of Amarna (Minya Governorate) in Upper Egypt where Eva Panagiotakopulu, University of Sheffield carried out her excavations at Workmen’s village](image)

5.8. Prevention, Surveillance and control
Plague prevention is directed toward reducing the threat of infection in humans in the high-risk areas. Several Preventive measures were reported [1,42] and include: (a) Public health education: informing people when zoonotic plague is present in their environment and advising them to take precautions against flea bites and not to handle animal carcasses, (b) Find and stop the source of infection: (i) Identify the most likely source of infection in the area where the human case(s) was exposed, and (ii) Eliminating food and shelter for rodents in and around homes, using insecticides to kill fleas during wild animal plague outbreaks, and weekly treatment of pets for fleas, (c) Protect health workers: they must wear protective clothing and receive a chemoprophylaxis with antibiotics for the duration of seven days or at least as long as they are exposed to infected patients, (d) Ensure correct treatment: verify that patients are being given appropriate antibiotic treatment which is effective against plague bacteria, so early diagnosis and early treatment can save lives Also, antibiotics are often recommended in the event of close exposure to a person or pet with suspected pneumonic plague and (e) Isolate patients with pneumonic plague.

Surveillance and control requires investigating animal and flea species implicated in the plague cycle in the region and developing environmental management programmes to limit spread of the natural zoonosis of the disease cycle [1]. Moreover, identify and monitor close contacts of pneumonic plague patients and give them chemoprophylaxis and obtain specimens for laboratory testing.

6. Conclusion
Plague which is a zoonotic bacterial disease has been responsible for a number of high-mortality epidemics throughout human history. Evidence indicated that the plague may have begun in Egypt rather than Central Asia. Despite no available reports on present situation of plague disease in Egypt, however, historically, the country had suffered from several epidemics. Moreover, Egypt is under risk of disease re-emergence and transmission due to the existence of potential foci in the neighboring countries mainly Libya.

7. References