Introduction

The history of the human plague dates back to antiquity. Literally, the term plague is derived from a Latin word ‘plaga’ which means ‘to blow’. Ancient Romans supposed that plague resulted from a blast originating from the Gods’ anger. Ancient Greeks called Apollo the God of medicine a mouse-killer, and they probably were aware of the association between the plague and mice. They believed that Apollo could stop the plague outbreaks by killing mice.

Despite enormous fatality, the secret of this lethal enemy of mankind remained unidentified up to the end of the 19th century when in 1894, a Swiss-born French bacteriologist, Alexander J. E. Yersin (1862 – 1943), discovered the infective agent of the human plague, a bacillus that became known as Yersinia pestis in his honor. The plague was an acute disease of rodents, mostly rats, transmitted from their fleas to man. In humans, plague had three distinct clinical presentations: bubonic, pneumonic, and septicemic varieties. The bubonic variety was more common, but the pneumonic and septicemic types were more severe with higher mortality rates. Nowadays, the human plague is regarded as a curable disease, which with prompt treatment mortality rates would decrease from 60% to less than 15%.

Three major plague pandemics occurred from the 6th century CE until the 19th century: i) the so-called ‘Justinian plague’ occurred in Constantinople (Byzantine Empire) in the 6th century CE and spread to the Middle East and Mediterranean regions with limited outbreaks in Europe. This plague caused substantial depopulation and according to William H. McNeill in ‘Plagues and Peoples’ (New York, 1976), around 25 million people died.

ii) The second bubonic type pandemic began in India, China or the steppes of Russia and reached Western Europe in 1347 CE. In less than three years it spread to most of Europe and was later called the ‘Black Death’. At that time, for the first time, early
quarantine measures in addition to some preventative precautions were started, however, despite these efforts around 42 million people died worldwide, of which 25 million were Europeans. Due to the incalculable number of deaths, people believed that the world was over.7

iii) Thirdly, the Hong Kong epidemic started in 1855 CE in Yunnan Province, China and continued for three successive cycles. The third cycle began in the 1890’s and reached Hong Kong in 1894. It spread rapidly to other countries through transoceanic shipping.6,8

History of the human plague in Iran

The plague was one of the oldest illnesses known to Iranian physicians. For instance, Abu Sahl Massihi (a Persian Christian physician in the 10th century CE) wrote a treatise on the plague (Maghaleh /g191 Tauon) and Ali Ibn Abbas Majusi Ahvazi (10th century CE) also known as Haly Abbas in the West described it in his medical book entitled ‘Tebb Maleki’.9 In addition, Ibn-Sina or Avicenna (980 – 1037 CE) the renowned Iranian physician in the ‘Canon of Medicine’ pointed out the clinical presentation of the bubonic plague10 and Esmael Jorjani (1042 – 1137 CE) mentioned a sign of the bubonic plague, e.g., the enlargement of lymph nodes in the inguinal area.11

There is insufficient data on human plague outbreaks in Iran in previous centuries, but its history between the 19th and 20th centuries is more informative. According to H. Tadjbakhash, several outbreaks of the human plague occurred during the Safavid period (1495 – 1735 CE), which included Gilan Province, Tabriz, Ghazvin, and Ardabil. In Ghazvin and Ardabil, around 30,000 people died. Another outbreak occurred in Qom, which continued for five years with 12,000 mortalities. During Shah Abbas’ reign (1587 – 1628 CE), the cholera and plague epidemics occurred concurrently and in Shah Safi’s reign (1628 – 1642 CE), an outbreak of severe plague occurred in

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Mortality number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1829 – 1833</td>
<td>Caspian Sea littoral Khorasan Province</td>
<td>?</td>
</tr>
<tr>
<td>1871*</td>
<td>Kurdestan Province</td>
<td>?</td>
</tr>
<tr>
<td>1877</td>
<td>Caspian Sea littoral Khorasan Shoshtar in Khuzestan Province +</td>
<td>? 1800</td>
</tr>
<tr>
<td>1899</td>
<td>Persian Gulf region ++</td>
<td>?</td>
</tr>
<tr>
<td>1906**</td>
<td>Sistan</td>
<td>1,409</td>
</tr>
<tr>
<td>1910</td>
<td>Bushehr Port</td>
<td>66</td>
</tr>
<tr>
<td>1911****</td>
<td>Bushehr Port</td>
<td>98</td>
</tr>
<tr>
<td>1912*****</td>
<td>Bushehr Port</td>
<td>725</td>
</tr>
<tr>
<td>1913******</td>
<td>Torbat-e Jam in Khorasan, Kurdestan</td>
<td>?</td>
</tr>
<tr>
<td>1917*******</td>
<td>Khorramshahr (former Mohammareh) in Khuzestan Province</td>
<td>?</td>
</tr>
<tr>
<td>1921</td>
<td>Torbat-e Jam and Kariz in Khorasan</td>
<td>?</td>
</tr>
<tr>
<td>1923*****</td>
<td>Khorramshahr in Khuzestan Province Abadan in Khuzestan Province</td>
<td>43 409</td>
</tr>
<tr>
<td>1924</td>
<td>Khorramshahr, Abadan, Bushehr Bandar-e Abbas</td>
<td>?</td>
</tr>
</tbody>
</table>

*The Italian doctors Castaldi and Cabuzzi came from Istanbul in 1871 to help with the plague epidemic in Persia. (Floor: 178)
++The quarantine measures caused the public protest in June. (Elgood P:577)
+++Down ward effect on trade, migration of the residents due to poor economy.***The most important epidemic in Sistan in South Eastern Iran entered from India probably due to old clothing imported by an Indian Merchant.
****In Bushehr, 4000 people were vaccinated. Of 965 cases, 725 patients or 75% died.
*****Karimi, P:15
******In former Mohammareh (Khorramshahr) of 79 patients, 43 died, and in Abadan, of 481 patients, 409 expired.
Ghazvin and spread to other cities, including Abhar, Tarom, Khalkhal, Zanjan, Azarbaijan, and Gilan. In Ghazvin 20,000 people died. After the collapse of the Safavid Dynasty and Iran’s occupation by the Afghan invaders, another plague outbreak occurred in Gilan Province in 1727 with a high mortality rate. Again it reoccurred in 1731 and around 20,000 expired in Hamadan and western Iran.12

During the Qajar period (1794 – 1925), the most common recorded epidemics were cholera and plague.13 Since public health conditions were poor, therefore the occurrence of outbreaks of fatal diseases was not surprising.14 In 1871, in Saghez and Baneh (two cities of Kurdestan Province in western Iran) an outbreak of the human plague occurred and several Iranian and foreign physicians, which included the Dutch Dr. Johan Louis Schlimmer (1819 – 1881) who was the medical teacher of Dar al-Fonun School, were assigned to control the outbreak. Dr. Schlimmer noted his observations on the outbreak of plague in Kurdestan as part of his French-Persian book entitled “Terminologie Medico-Pharmaceutique et Anthropologique francoise-Persane”, which was published in 1874.15

In 1913, another plague epidemic began again in both Kurdestan Province and Torbat-e Jam, Khorasan Province and another outbreak appeared in 1921.15

It seems that the first Iranian physician who wrote a modern medical book on the plague was Mohammad Razi Tabatabai, the chief of military physicians during the Naser al-Din Shah period. His book, ‘Tauon’ (plague), was published lithographically in 1876 and included five chapters and an addendum that contained the writings of Dr. Joseph Desire Tholozan (1820 – 1897) on the prevention and treatment of plague.16 Dr. Tholozan was the special physician to Naser al-Din Shah and the first President of the Sanitary Council (Majles Hefz-o-Sehheh) in Iran, which was founded during Naser al-Din Shah’s Era.14 He made a scientific investigation on the human plague in Kurdestan and Khorasan provinces and published the results of his study.14 Between 1870 and 1882, Tholozan studied the natural plague foci in Kurdestan Province in western Iran and precisely described the foci of the disease in some villages of Kurdestan Province.17,18 His writing on the history of plague in Iran was published in Tehran in 1876.13

Several outbreaks of the human plague occurred in Iran during the Qajar Period (Table 1).

Figure 1 shows the report of an outbreak of a plague-like illness in 1921 in a village in Kermanshah Province, western Iran.

Due to the increase in international trade, transoceanic shipping and episodes of fatal epidemics, quarantine was considered as a significant tool for epidemic prevention. After a plague outbreak in 1877, the idea to establish quarantine stations in Iran was recom-

Figure 1. Left) the report of the outbreak of a plague like illness in 1921 in a village in Kermanshah Province in Western Iran sent by Vezarat Sehhyeh va Omur Kheiryeh (Ministry of Health and Welfare) to the Ministry of Interior. Right) the second report (a telegram) from the Department of Public Health of Kermanshah regarding the vanishing the mentioned outbreak. (Courtesy of Mr. Farid Ghasemlou and Mr. Ali Akbar Vatanparast, Iranian Academy of Medical Sciences, Source: National Library and Archives of the I.R. of Iran)
mended, but their foundation was delayed until 1899, after a severe plague outbreak in the Persian Gulf region. In 1899, a quarantine station was founded in the port of Bushehr. Then, in 1905, a conference was held in Paris on quarantine and it was suggested to the Iranian officials to establish quarantine stations in Bandar-e Abbas, Bushehr, Bandar-e Lengeh, Abadan, and Bandar-e Jask. Thus a quarantine station in Bushehr was founded and managed by English staff until 1928, and in due course, Iranian personnel supervised it.19 In 1927, the Public Health Administration Office wrote a letter to the Ministry of Interior to allocate a budget for the establishment or reconstruction of quarantine stations in Julfa, Ghasr-e Shirin, Bandar Anzali, and Astara. The total requested money was 145,000 tomans, which was allocated by the Ministry of Interior.20 Although the quarantine stations of Bandar-e Anzali and Astara were built in 1912, the Astara Quarantine Station was destroyed during the First World War.14 In 1923, some preventive measures to control the plague epidemic in Abadan, Khuzestan Province were applied. A total of 4,534 people were vaccinated against the plague, patients were quarantined and death certificates became mandatory for better detection of the plague victims.20

The Pasteur Institute of Iran was founded in 1921 and it was connected scientifically to the Paris Institute of Pasteur. In 1946, Dr. Marcel Baltazard (1908 – 1971) was appointed as the director. He remained in Tehran as the director until 1961. Dr. Baltazard was a great researcher, particularly in the field of epidemic diseases including the human plague.15,21

In 1947, in Kurdestan Province (Table 2), an outbreak of pneumonic plague occurred in the villages of Sameleh and Aghbolagh-e Morshed. The Iranian research team of the Pasteur Institute of Iran supervised by Dr. Baltazard went to Kurdestan to begin scientific investigation into this plague outbreak. The research team of the Pasteur Institute established a research plague center in a village called Akinlo, Hamadan Province (100 km from Hamadan and approximately 200 km from Aghbolagh-e Morshed village). The activities of the Akinlo Research Plague Center continued for about 20 years. Dr. Baltazard and his Iranian colleagues, including Dr. Mansour Shamsa and Dr. Younes Karimi, eventually found the plague bacilli infected reservoirs among the rodents in Kurdestan Province as well as the natural plague foci in the region15 (Figures 2 and 3). They published several scientific papers on the human plague in Iran. In an article published in 1960, Baltazard and his Iranian colleagues (M. Bahmanyar, P. Mostachghi, M. Efthari, and Ch. Mofidi) pointed out that this co-operative effort led to the identification of four species of rodents, of which two (Meriones libycus and Meriones persicus) were highly resistant to plague and the other two (Meriones tristrami and Meriones vinogradovici) were extremely susceptible.22

Figure 2. The investigative team of the Pasteur Institute of Iran evaluating plague bacilli infected reservoirs among the rodents in Kurdestan Province, Iran22

Figure 3. A map showing the natural plague foci in northwestern Iran, including Azerbaijan, Kurdestan, Kermanshah, and Hamadan provinces based on four different studies (Source: Plague Research in Iran, 1960)22
At that time, an active and prominent researcher of the human plague was Dr. Younes Karimi (1929 – 2009; born in Darreh-Gaz, Khorasan Province) (Figure 4) who graduated from the Tehran School of Medicine and became a specialist of infectious diseases. Dr. Karimi later continued his studies in microbiology and immunology at the Pasteur Institute of Paris.

On his return to Iran, he was employed at the Pasteur Institute of Iran and investigated various epidemic diseases, particularly the human plague. He studied this fatal disease for around 25 years in Iran including Kurdestan and Azarbaijan provinces as well as in Brazil and Zaire, as an expert of the World Health Organization (WHO). Between 1963 and 1978, Dr. Karimi published 16 original papers on the human plague in Iran in sound international journals, which included WHO publications (the list of papers and names of his colleagues are available at Pub Med). He also wrote a comprehensive Persian book entitled ‘Plague and its Epidemiology’ which was published by the Pasteur Institute of Iran in 1977. His book contained the latest data at the time on plague endemic foci in the world and Iran, as well as valuable data on the species of rodents responsible for human plague outbreaks in Iran (Figure 5). Dr. Karimi died at age 80 in Tehran and his memorial ceremony was held at the Pasteur Institute of Iran in 2009.

Table 2 shows the death toll of the human plague in Kurdestan and Azarbaijan provinces between 1947 and 1966 based on Dr. Karimi’s book. Total mortalities were 156.15

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Mortality number</th>
<th>Type of plague</th>
</tr>
</thead>
<tbody>
<tr>
<td>1947</td>
<td>Kurdestan</td>
<td>73</td>
<td>Pneumonic</td>
</tr>
<tr>
<td>1951</td>
<td>Kurdestan</td>
<td>2</td>
<td>Bubonic</td>
</tr>
<tr>
<td>1952</td>
<td>Kurdestan</td>
<td>53</td>
<td>Bubonic, septicemic</td>
</tr>
<tr>
<td>1958</td>
<td>Western Azerbaijan</td>
<td>6</td>
<td>Bubonic, septicemic</td>
</tr>
<tr>
<td>1961</td>
<td>Kurdestan</td>
<td>7</td>
<td>Pneumonic</td>
</tr>
<tr>
<td>1963</td>
<td>Kurdestan</td>
<td>14</td>
<td>Pneumonic</td>
</tr>
<tr>
<td>1966</td>
<td>Kurdestan</td>
<td>1</td>
<td>Bubonic, septicemic</td>
</tr>
</tbody>
</table>

*This table is designed based on information compiled by Dr. Y. Karimi*15

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**Figure 4.** Dr. Younes Karimi (1929 – 2009), a prominent Iranian researcher of the human plague

**Figure 5.** The front cover of the Persian book entitled “Plague and its Epidemiology,” written by Dr. Y. Karimi. The Pasteur Institute of Iran published it in Tehran, 1977.15
The Bacteriology Department of the Pasteur Institute of Iran was established in 1953 and was a pioneer in research on epidemic diseases, including the human plague. An international plague seminar was held at the Pasteur Institute of Iran in 1970 (Figure 6).

Figure 6. A picture of the International Seminar of the Human Plague, Pasteur Institute of Iran, 1970. Right to left: Dr. Mahmoud Bahmanyar (the seminar President), Dr. S. Moghaddami (Chancellor of Tehran University), Dr. A.M. Sardari (Chancellor of the Ministry of Health) and Dr. M. Namvari (Director of the Pasteur Institute).

In the 20th century, great outbreaks of the human plague with high mortality continued, especially in India. Despite the discovery of the etiologic agent of the human plague, the introduction of antibiotics for patients' treatment and worldwide hygienic improvement, outbreaks of the human plague continued during the last decades of the 20th century. Between 1980 and 1986, in total, 4,522 cases from 17 countries (Iran was not included) were reported to the WHO. Of these patients, 431 died.

According to some experts, outbreaks of the human plague in the future are still possible due to the known and probable plague transmission foci in the world. Therefore we should always remember the allegorical statement of the renowned French writer and philosopher, Albert Camus (1913 – 1960) in his novel “The Plague” (Fr. La Peste) published in 1947: “The plague bacillus never dies or disappears for good; that it can lie dormant for years and years in furniture and linen-chests; that it hides its time in bedrooms, cellars, trunks, and bookshelves; and that perhaps the day would come when, for the bane and the enlightening of men, it would rouse up its rats again and send them forth to die in a happy city.”

Acknowledgment

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References

20. Ghodssi M. *The History of the Fifty Years of the Services of the Pasteur Institute of Iran* [in Persian]. Tehran: Pasteur Institute of Iran; 1971.

![Alamut, around 100 km from present-day Tehran - Qazvin Province -Iran](Photo by Mr. Arash Hamidi)