

A Brief History of Tuberculosis in Iran during the 19th and 20th Centuries

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Abstract

The history of tuberculosis as a worldwide fatal illness traces back to antiquity, a well-known disease in ancient civilizations. However, its causative agent remained unidentified until the last decades of the 19th century, when discovered by Robert Koch. In due course, preparation of the BCG vaccine, application of the Mantoux intradermal diagnostic tuberculosis test and administration of proper antituberculosis medications eventually controlled tuberculosis. However, despite these significant advancements tuberculosis remained uneradicated, particularly in developing countries after the emergence of both multidrug-resistant tuberculosis and HIV co-infection. Presented here, is a brief review of the history of tuberculosis in the world as well as its historical background in Iran, mainly during the 19th and 20th centuries.

Keywords: history of medicine, Iran, tuberculosis

Introduction

The historical background of tuberculosis (TB), as one of the major causes of mortality in human history,¹ dates back to the previous millennia. Paleopathological investigations revealed evidence of TB in the skeletons of the Neolithic period² as well as in some lesions of the vertebral column of the Egyptian mummies.³

In iconography of ancient Egypt, some cases of hunchbacked spines were noticed, which probably indicated complications of TB.⁴ In Mesopotamia, the Babylonian law code known as the Code of Hammurabi, which dates prior to 2000 BCE, mentioned TB among several other diseases.⁵ The cuneiform clay tablets of Mesopotamia translated by the French scholar, Labat and published in 1951, also contained an accurate description of the clinical picture of pulmonary TB as follows: "The patient coughs continuously. What he coughs is thick and frequently bloody. His breathing sounds like flute. His hand is cold, his feet are warm. He sweats easily and heart activity is disturbed."⁶ In recent decades, Japanese investigators showed that TB bacilli had a long-standing history; around 35,000 years,⁷ and polymerase chain reaction studies in Japan confirmed the presence of mycobacterial DNA in 2000 year-old human skeletons.⁸

Since ancient times, physicians were familiar with TB. According to Edwin-Smith, Papyrus, which dates from 3000 to 2500 BCE, ancient Egyptian surgeons were aware of the TB abscess and believed that it should not be drained and excised; a practice, which is still acceptable in modern surgery. The renowned Greek physician, Hippocrates (460 – 377 BCE), discussed the clinical findings of TB as a chronic disease accompanied by reproductive cough, sweating, and fever. He also mentioned the complications of TB of the spine, but he believed that TB was a hereditary illness worse during autumn.⁶ Later, according to McClelland, Galen (129 – 199 CE) explained the formation of phyma (i.e., tumor) in the lungs of TB patients, probably consistent with the tubercles produced in pulmonary TB.⁹ He considered TB as a transmissible disease.

In Iran, during the Islamic period, the Iranian physicians were

aware of TB. Ali ibn Sahl-e Rabban Tabari (838 – 870 CE) in his book, "Firdous al-Hekmah" ("Paradise of Wisdom", Figure 1) described TB of both the skin (lupus vulgaris) and the lymph nodes (Khanazir or scrofula).¹⁰ Rhazes (865 – 925 CE), reported in "Al-Hawi" that a patient's medical history who had bloody sputum (nafeth-o-damm) was most probably due to pulmonary TB.¹¹ In addition, he described TB of the joints.¹² In the "Canon of Medicine", Avicenna (980 – 1037 CE) devoted a chapter to TB. He said that pulmonary TB should be differentiated from asthma, because both disorders may result in cough and shortness of breath. Avicenna added that in advanced cases of pulmonary TB, a potential danger would be lung hemorrhage and may ultimately lead to death.¹³ Avicenna believed that TB has three stages including pre-inflammatory, ulcerative, and cavernous.¹⁴ In another famous Persian medical text, "Zakhireh-ye Kharazmshahi" (Treasure of Kharazm Shah), Ismail Jorjani (1040 – 1136 CE) expressed TB as a contagious illness with prolonged fever.¹⁵



Figure 1. Up) The front cover of Firdous al-Hekmah (Paradise of Wisdom) published in Arabic (1928, Berlin, Germany). **Down)** Treatment of TB of the lymph nodes (Khanazir in Arabic, scrofula) is discussed.¹⁰

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The global combat against TB during the 19th and 20th centuries

Despite the aforementioned efforts, the battle against TB was not triumphant until the 19th century. In 1804, Rene Laennec (1781 – 1826) was the first physician who improved our understanding of the multifaceted nature of TB when he delivered a lecture regarding his observations on the cadavers of TB victims. The first stethoscope for auscultation of chest sounds was his innovation and in 1819, Laennec described the physical signs of pulmonary TB. However, in the 19th century, TB remained an epidemic disease in Europe and America and the establishment of sanitariums was the only possible solution. Thus, at the end of 19th century, TB sanitariums were founded in America. The next step was experimental investigation of the transmittable nature of TB by Jean Antoine Villemin (1827 – 1892). He was a French army surgeon who suggested the germ theory of disease and published his idea in 1866. Nevertheless, the infective agent of TB remained unidentified until the last decades of 19th century when in 1882 the German physician-scientist, Robert Koch (1843 – 1910) isolated the TB bacillus.³ He initially announced his discovery as the etiology of TB in the Berlin Weekly Clinical Bulletin on March 24, 1882 and then published it on the 10th of April. He won the Noble prize in medicine in 1905 for his discovery of the TB bacillus.

Later, a great innovation was preparation of the Bacillus Calmette-Guérin (BCG) vaccine made of the attenuated live bovine TB bacillus. The BCG vaccine was first used in humans in 1921 and until 1962, around 400,000 children in 46 countries were vaccinated against TB after which, TB vaccination became mandatory in many countries. The Mantoux diagnostic test (also known as PPD or purified protein derivative) was suggested by Charles Mantoux (1874 – 1944) who won the Noble Prize in 1909.¹⁶ Even with these fruitful attempts, TB was not appropriately controlled until the 20th century, when during 1950s, the effective anti-TB drugs were introduced.³

The battle against TB in Iran during 19th and 20th centuries

Data on the prevalence and mortality rate of TB in previous centuries in Iran is scarce, but the history of TB during the 19th and 20th centuries is more informative. The first translated medical texts on TB appeared at the beginning of the 20th century. The following picture shows the front cover of a treatise entitled “Marefatosel” (“TB Cognition”), which was translated into Persian in 1900. In the introduction, the French author has pointed out: “despite considerable progresses, the prevalence of TB has not yet decreased (Figure 2).”

According to the Dutch contemporary historian, W. Floor, at the end of the Qajar period (1796 – 1925) TB was a widespread disease in Tehran and other cities; one of the major causes of death in the 1920s.¹⁷ Dr. Jacob Eduard Polak (1818 – 1891) from Austria was the first European medical teacher of the Dar-al-Fonun School founded in 1851 by Mirza Taqi Khan Amir Kabir, the Chief Minister of Naser-ad-Din Shah, the fourth king of the Qajar dynasty.¹⁸ In his travel book named “Iran and Persians“, published in Germany in 1865, Polak wrote: “Pulmonary TB could not be regarded as an endemic disease of Iran but I have seen nine cases in nine years of my medical practice in Iran, mostly among white women who developed signs of disease, short period after delivery and died soon.” Then, he added that TB was more prevalent in Azarbaijan Province in the northeast and along the Caspian Sea in

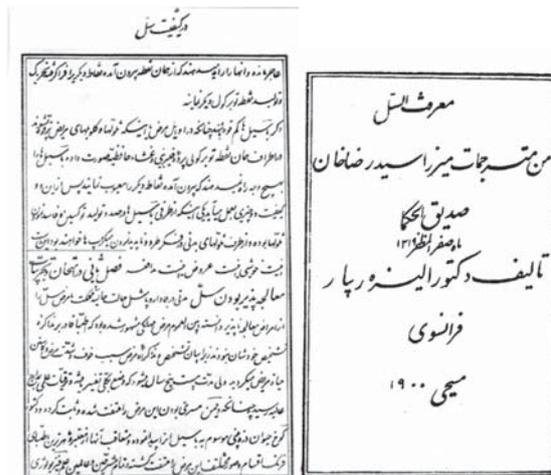


Figure 2. The treatise of Marefatosel (TB Cognition), 1900. A lithographic version is available at the library of Iran’s Parliament (MS No. 9877). It was written by a French physician and translated into Persian by Mirza Seyyed Reza Khan-e Seddiq-o-al-Hokama (Courtesy of Ms. Javadi, Iranian Academy of Medical Sciences).

the north of Iran. He also reported the death of a French man who developed miliary TB in Iran.¹⁹

At the last decade of the Qajar period, in 1921, the Pasteur Institute of Iran was established which in due course played a major role in TB control.²⁰ The first physician who managed TB patients in his private clinic was Dr. Siavash Shaghghi, a Swiss trained physician.²¹ Another pioneer physician in the battle against TB was Dr. Masih Daneshvari (1899 – 1976), a pulmonologist trained in Europe, mainly in France (Figure 3). The first TB sanitarium, known as Shah Abad TB Patients’ Hospital was established in 1937 due to his efforts.²² In 1939 he wrote a letter to the Prime Minster and focused on the expansion of a TB combat program at the Shah Abad TB Patients’ Hospital. The Prime Minster ordered the responsible authorities in the Ministry of Interior to assist him (Figure 4).



Figure 3. Dr. Masih Daneshvari (1899 – 1976).



Figure 4. The letter of the Prime Minister to support Dr. M. Daneshvari for expansion of a program against TB.

In due course in 1944, “the Society against TB and for the Support of TB Patients” (Anjoman-e Mobarezeh ba Sel and Hemayat Az Masloulin) was established. The main objectives of the society were to combat TB, as well as supporting the TB patients and public preventive measures education.²³ Later, the 30 members of this society founded a TB medical center named Bou-Ali Hospital in Tehran in 1945²¹ and in 1946, the society requested the authorities of Tehran Medical School to introduce a faculty member as the representative of the school in the society’s board of trustees (Figure 5). Dr. Sadegh Azizi, professor of internal medicine was introduced.



Figure 5. The letter of the Society against TB and for the Support of TB Patients to the authorities of Tehran Medical School to introduce a faculty member as the representative of the school in the society’s board of trustees, 1946. (Source: National Library and Archives of the I.R. of Iran, Manuscript serial no. 270000055, courtesy of Mr. Farid Ghasemlou and Mr. Ali Akbar Vatanparast, Iranian Academy of Medical Sciences).

In 1942, the first professor of pulmonary diseases was appointed at the School of Medicine in Tehran. Dr. Mohammad Ali Nashroudi (born in 1909, Rasht-Gilan Province), a graduate of the Dar-al-Fonun School went to France in 1929 and graduated from the Paris School of Medicine in 1938. He continued his study on pulmonary diseases and TB, and returned home in 1940 after which he was appointed as an associate professor at the Tehran School of Medicine in 1942. In 1948 he became full professor of pulmonary diseases (Figure 6).²⁴



Figure 6. Dr. Mohammad Ali Nashroudi (b. 1909).

Valuable activities against fatal diseases such as rabies, cholera, tuberculosis, and plague were initiated at Pasteur Institute of Iran. BCG vaccine production began at the institute in 1947, under the supervision of Dr. Mehdi Ghodssi (1900 – 1991; Figure 7), ap-

pointed in 1961 as the director of the institute after Dr. Marcel Baltazard (1908 – 1971) who was the third French Director of the Pasteur Institute of Iran and instrumental in control of fatal infective diseases, including plague, smallpox, and TB.²⁰



Figure 7. Dr. Mehdi Ghodssi (1900 – 1991).

In 1948, under the auspices of the Society against TB and for the Support of TB Patients, the Abu-Hossein Hospital for TB Patients was founded in Tehran and a French-trained chest specialist, Dr. Mohammad Ghazi-Tehrani (b. 1921) became employed at this hospital. In due course, Dr. Anwar Shakki (1913 – 2003), a chest surgeon was employed in the same hospital. Both were pioneer chest specialists.²¹ In 1952, with the support of the World Health Organization (WHO), an effectual battle against TB was started in Iran and the Ministry of Health, the Pasteur Institute, the former Red Lion and Sun Society (now Red Crescent Society) and Tehran Medical School were actively involved in this battle. The TB screening program in Tehran, identification of TB cases and their treatment as outpatients was initiated by Dr. Ahmad Daneshvar, at the clinic known as the “TB Battle Center No. 1”. As a TB expert, he began work in the Ministry of Health and with the cooperation of the former Red Lion and Sun Society, Dr. Daneshvar and his colleagues were the pioneers of the public TB vaccination.²⁰ In 1954, Dr. Daneshvar reported the results of these efforts against TB in a national medical meeting held in Ramsar, northern Iran.²⁵ In addition, at the Pasteur Institute of Iran, a European-trained microbiologist, Dr. Tabatabaei was appointed as the Director of the TB Department. She started her practical and scientific research on TB, and later published the results of her studies.²⁰ At that time, the prevalence of TB was evaluated in 120 cities and districts, and 1071 villages by a team of experts of the Pasteur Institute of Iran in collaboration with WHO. In 845,061 individuals, TB skin tests were performed, of which 4% were positive.²⁵ After Dr. Tabatabaei, Dr. Mostafa Pourtaghva (b. 1936) a specialist in infectious and tropical diseases was appointed as the director of TB department (Figure 8).



Figure 8. Dr. Mostafa Pourtaghva.

In the mid-20th century, TB was still a common disease. For instance in 1943, Professor Charles Oberling (1895 – 1960), the famous French pathologist and Dean of Faculties of Medicine, Pharmacy and Dentistry of Tehran wrote an article on the public health status in Iran and pointed out that: “despite common belief, TB is prevalent in Iran particularly in some regions of Tehran as well as in villages and tribes“. He pointed to the shortage of TB sanitariums in Iran and stated: “in a country with a population of around 15 millions, the only available 100 beds TB sanitarium for the patients ‘care is inadequate and it is necessary to establish more TB medical centers, train TB experts and educate people on the TB preventive measures”.²⁶

Another influential figure who fought against TB for around five decades was Dr. Abolhassan Ziazarifi (1926 – 2010; Figure 9).



Figure 9. Dr. Abolhassan Ziazarifi (1926 – 2010).

He was a graduate of the School of Pharmacy of Tehran University who started his professional career in 1952. His interest was mainly pulmonary diseases, particularly TB. In 1956, he worked at the first TB diagnostic laboratory supervised by Dr. Mehdi Zolriassatian, and later, went to England to study microbiology. On his return, his major achievement was the establishment of the “National Reference TB Laboratory” in 1963 and in that year, Dr. Zia-Zarifi became a member of the International Union against Tuberculosis and Lung Diseases (IUTLD). Later he was appointed as the Director of IUTLD. In 1968, Dr. Zia-Zarifi continued his training at the Pasteur Institute of Paris and in 1971 he completed his studies on medical laboratory management at the University of Maryland as well as the Centers for Disease Control and Prevention founded in USA in 1942. Between 1975 and 1979, Dr. Zia-Zarifi was appointed as the “Director General of Laboratories of the Ministry of Health” and during this period he successfully established over 400 medical laboratories in remote regions of Iran with the support of WHO. Due to his outstanding professional endeavors, he was nominated as a consultant to the WHO in the Middle East, Asia and Africa.²⁶ He wrote several papers and books including one on the “History of TB”.²⁷

The Establishment of the National Research Institute of Tuberculosis and Lung Diseases in Iran

The history of the forerunner of the current National Research Institute of Tuberculosis and Lung Diseases in Iran dates back to Mozzafar-al-Din Shah’s (1853 – 1907) period. He had tuberculosis and according to French physicians’ recommendations, had to spend his recovery period in a place with fresh mountain air. Thus

in 1941, a small palace for the king was built in northern Tehran. After Mozzafar-al-Din Shah’s death, his palace was gradually converted into Shah Abad TB Sanitarium. Consequently, in the 1920s, several new buildings were built by the Ministry of Health of that time and in 1986, it was affiliated to Shahid Beheshti University of Medical Sciences. In 1992, the National Research Institute of Tuberculosis and Lung Disease was established there. In 1998, the Research Institute and hospital were combined and renamed as “Dr. Masih Daneshvari Educational, Therapeutic and Research Center for Tuberculosis and Lung Disease”. Currently, it is a leading educational collaboration center of the WHO Eastern Mediterranean Region, the Middle East Office of the International Union against Tuberculosis and Lung Disease and a reference medical center for TB educational and research programs in Iran.²⁸

The current TB situation in the world

The battle against TB still continues throughout the world and despite brilliant achievements during the 19th and 20th centuries, TB is not yet eradicated, particularly in developing countries. From 1990 onwards, HIV co-infection caused TB outbreaks²⁹ and multidrug-resistant TB (MDR-TB) is another great challenge. According to an estimate by WHO in 2008, 1.8 million people worldwide died of TB, which included 500,000 patients infected with HIV. In 2009, more than 2 billion people were infected with TB bacilli, and 1 out of 10 of those infected developed active TB. Based on data from more than 100 countries, in 2009, 5% of all TB cases were MDR-TB.³⁰ As the 2010 Report of WHO showed, the success rate of treatment for patients with MDR-TB was 60%.³¹

TB in the last two decades in Iran

Between 1992 and 1999, rate of TB at the national level decreased in Iran. In 1997, the TB incidence rate per 100,000 population in Sistan and Baluchistan Province was the highest in Iran (73.5) and the lowest rate at 33 per 100,000 belonged to Semnan Province.³² In 2001, the majority of TB patients in Iran were more than 50 years old and the rate of TB was more in women than men. In 2001, there were over 9000 new cases of TB in Iran, mostly identified in Sistan and Baluchistan Province in southeastern Iran, especially in the city of Zabol, and in Golstan Province in northern Iran along the Caspian Sea (probably because of the immigration of people from Zabol to Golstan Province). In addition, the prevalence of TB in the eastern and western provinces as well as in Gilan Province along the Caspian Sea was more than the average country rate. In 2003, the least detected cases of TB were in Fars and Isfahan provinces.³³ According to the “Administration of Tuberculosis and Leprosy Control” of the Ministry of Health and Medical Education in Iran, in 2010, a total of 10,485 old and new cases of TB were reported in Iran and of these cases, 326 patients (around 2.2%) were HIV positive.³⁴

Finally, as Charles Dickens (1812 – 1870), the popular English novelist, wrote in “The Life and Adventures of Nicholas Nickleby” (1838 – 1839):

“There is a dread disease which so prepares its victims, as it were, for death; which so refines it of its grosser aspect, and throws around familiar looks, unearthly indications of the coming

change. A dread disease, in which the struggle between soul and body is so gradual, quiet, and solemn, and the result so sure, that day by day, and grain by grain, the mortal part wastes and withers away, so that the spirit grows light and sanguine with its lightening load, and, feeling immortality at hand, deems it but a new term of mortal life; a disease in which death takes the glow and hue of life, and life the gaunt and grisly form of death; a disease which medicine never cured, wealth warded off, or poverty could boast exemption from; which sometimes moves in giant strides, and sometimes at tardy pace; but, slow or quick, is ever sure and certain".³⁵ TB should always be remembered as a dreaded disease.

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