

History of Medicine

An Overview of Epidemic Typhus in the World and Iran during the 19th and 20th Centuries

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Abstract: The present article provides a concise historical review on classical epidemic typhus (*exanthemata typhus*) in the world as well its outbreaks in Iran mainly during the 19th and 20th centuries. Typhus is still a potential public health threat under certain conditions, despite the fact that nowadays, efficient antibiotics are accessible and sanitary conditions which lead to typhus outbreaks have improved significantly.

Key words: Epidemic typhus, history of medicine, Iran

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Introduction

Several diseases are caused by the Rickettsiae microorganisms. They include epidemic typhus (louse-borne typhus, *exanthemata typhus*) caused by *Rickettsia prowazekii*, Brill-Zinsser disease (recrudescence form); a relapsed mild form of typhus that appears as sporadic cases many years after the initial infection, scrub typhus (bush typhus or tsutsugamushi fever) caused by the *Orientia tsutsugamushi*, transmitted by mite and murine typhus (endemic typhus) caused by *Rickettsia typhi* which is flea-borne, related to rodents such as household rats and mice.^{1,2} *Rickettsia prowazekii* infection is not limited to humans and since 1975, it is known that *Rickettsia prowazekii* infection in humans may also occasionally occur after contact with the southern flying squirrel (*Glaucomys volans*) in the United States.³

The word typhus is derived from the Greek origin *typhos*, meaning stupor associated with fever.⁴ The onset of epidemic typhus is frequently abrupt, with chills, high fever, severe headache, prostration, malaise and delirium. The skin eruptions develop on the patient's entire body except the face, palms and soles.¹

Epidemic typhus is the only rickettsial disease that can cause sudden outbreaks. The case mortality rate of epidemic typhus varies from 1% to 20%.⁵ The human body louse (*Pediculus humanus corporis*) is the vector of several fatal infectious diseases including epidemic typhus.⁶ Head lice have no role in typhus transmission.⁵ Human body lice live and proliferate in clothes under unhygienic conditions in cold weather.⁷ In refugee camps, lice proliferate rapidly. Infected lice excrete Rickettsiaceae.⁵

Epidemic and endemic typhus may be misdiagnosed as typhoid fever due to their similar clinical patterns. Thus, high clinical suspicion is essential.

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Typhus in the world

Throughout history, typhus outbreaks have had a major impact on human civilizations.⁸ The information about epidemic typhus was scanty up to the first decade of the 20th century.⁹ An accurate clinical description of epidemic typhus was provided in 1546 by an Italian physician, Hieronymus Fracastorius, in a book entitled "On Contagion and Contagious Diseases".¹⁰

The typhus causative agent remained unidentified until the early 20th century. The role of louse as a vector of infection was detected in 1909 by the French bacteriologist, Charles Nicolle (1866–1936) at the Pasteur Institute. Nicolle won the Nobel Prize of medicine in 1928 for this discovery. In 1910, typhus microbiological isolation was performed by Howard Ricketts and Stanislaus von Prowazekii (1875–1915), the Czech zoologist and parasitologist. Howard Ricketts (1871–1910) was an American pathologist and the Rickettsiaceae family is named after him. Ricketts died of typhus at the age of 39. Prowazekii also passed away of typhus at the age of 40 while investigating typhus. The etiologic agent of epidemic typhus was named in honor of Ricketts and Prowazekii.^{9,11}

Effective synthetic anti-typhus antibiotics were unavailable until the mid-twentieth century. The tetracyclines were introduced in the late 1940s to the early 1950s.¹² The tetracyclines were particularly helpful in the treatment of several infectious diseases, including typhus.¹³ Advent of tetracyclines significantly declined the fatality rate of typhus. In subsequent years, doxycycline was introduced in 1967.¹⁴ At present, typhus cases are treatable and a single dose of 200 mg of doxycycline, irrespective of patients' age, is effective.⁵

At the end of the 20th century, the complete genome sequence of *Rickettsia prowazekii* was determined at the Uppsala University in Sweden.¹⁵

In the past, diagnosis of typhus was confirmed by Weil-Felix test, an agglutination test which was first described in 1916,¹⁶ but recently it has been replaced by more sensitive and specific serologic tests.¹⁷

For centuries, epidemic typhus outbreaks occurred in crowded and unsanitary situations and accompanied war, famine, and

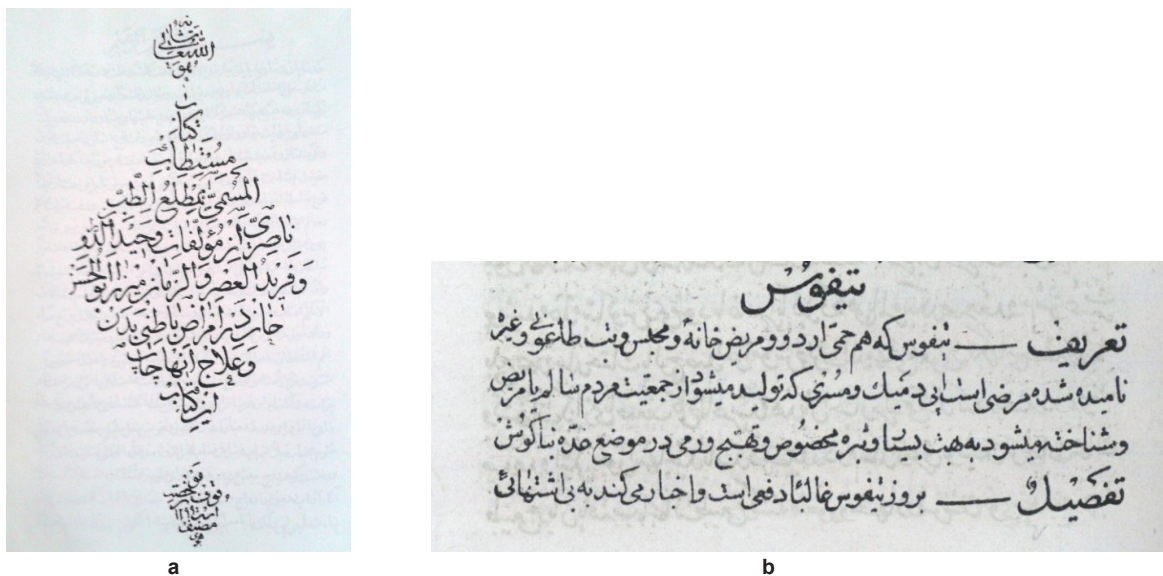


Figure 1.a) The front cover of a Persian medical book entitled *Matlaol-tebb Nasserī*; 1882. The lithographic version is available at the Majlis library (the Parliament Library). The book was compiled by a medical teacher of the Dar al-Fonoun; Mirza Abolhassan Khan Doktor based on European resources. **b)** The beginning of the chapter on typhus in *Matlaol-tebb Nasserī* in which the abrupt nature of typhus and its epidemicity are described.

poverty. Between 1500 and 1831, typhus played a significant role during the wars in the Europe.¹⁸

In June 1812, Napoleon attempted to invade Russia; however, his huge army was defeated due to wartime shortages and mainly of typhus outbreak, which killed thousands of French soldiers.¹⁹ In World War I (1914–1918), typhus became a widespread disease. The worst outbreak of typhus occurred between 1917 and 1921. In Russia, around 25 million people contracted typhus of whom 3 million died.¹⁸

During World War II (1939–1945), typhus outbreaks reappeared mainly in the French North Africa, Egypt and Iran.¹⁰ Accordingly, a vaccine with nearly 90% effectiveness was produced in 1940 and from 1942 onwards, most of the Allied soldiers were vaccinated. When WWII ended, mass delousing was carried out with DDT in Germany and Eastern Europe and typhus was quickly controlled.²⁰ After WWII, massive outbreaks of typhus arose in Africa, mainly in Burundi, Ethiopia and Rwanda.²¹

History of typhus in Iran

Killing harmful insects including the lice has been advised in the Avesta, the religious text of Zoroastrians.²² Typhus, as a clinical concept has appeared in the medical works of well-known Persian physicians as ‘*Homay-e mohregheh*’ (typhus fever). The clinical manifestations resembling the picture of typhus are described in Abu Bakr Moḥammad Ibn Zakariyā’ Rāzi’s (865–925 C.E.) *al-Hāwī*, Avicenna’s *Qānun fi’l-tebb* (Canon of medicine), and Esmā’il Jorjāni’s *Daḳīra-ye k̄ārazmšāhi* (Treasure of k̄ārazmšāh).²³ In the latter, Jorjani portrayed the clinical profile of the disease including skin rashes as well its fatality and he recommended to wash the patient’s body with cold water. He called typhus *mohregheh* and typhoid fever *motabhbegheh*.²⁴

Razi (Rhazes) precisely documented 33 medical cases including

the clinical appearance of a patient who contracted a febrile illness which is highly compatible with typhus. He reported that the patient had high fever, chills, and then developed black urine, nose bleeding, insomnia, irregular breathing, thirst and finally delusion.²⁵ Various aspects of fevers including typhus are also discussed in Aḳawayni Boḳāri s’ *Hedāyat al-mota’allemīn fi’l-tebb*, the oldest known medical Persian treatise most probably written prior to 983–4 C.E.^{25,26}

During the 19th and 20th centuries

Historically, typhus has been one of the main health problems with economic impact in Iran; however, limited published data exists on typhus outbreaks in previous centuries. The history of typhus outbreaks during the 19th and 20th centuries is more informative. Typhus has been an endemic disease in Iran, but its outbreaks have been rare.²⁷

In the Qajar period (1796–1925), infectious diseases, including typhus, were prevalent. Modern insight of fatal diseases was gradually introduced into Iran after the foundation of the Dār al-Fonun School in 1851 (Figure 1).

Dr. Jacob Eduard Polak, the Austrian teacher of medicine and surgery at the Dār-al-Fonun mentioned that between 1851 and 1859, typhus became epidemic.²⁸ According to Joseph Désiré Tholozan, Naser al-Din Shah’s special physician, between 1864 and 1865, severe typhus outbreaks reoccurred.²⁷ Frequent outbreaks of typhus occurred in Iran during the 20th century. In November 1909, in Bandar-e Gaz, in current Golestan province in northern Iran, a typhus outbreak appeared.²⁹

For long periods of time, physicians were confused about clinical differentiation of typhus from other similar infectious diseases, in particular typhoid fever. Thus, in 1918, the authorities of the Sanitary Council suggested the word *mohregheh* for typhus and



Figure 1. The front covers of two successive issues of the *Nameh Mahaneh-ye Daneshkadeh-ye Pezeshki* (the Monthly Letter of School of Medicine) affiliated to Tehran University Faculty of Medicine, which were devoted to typhus, 1943.

motahbegheh for typhoid fever to avoid misdiagnosis.³⁰

According to John Gilmour, during the famine of 1917–1918 in Iran, typhus outbreak resulted in high mortalities.³¹ As Neligan, the British Representative on the Persian Sanitary Council pointed out, an extensive outbreak of typhus occurred in Iran between 1917 and 1918.³⁰ In 1918, a typhus outbreak happened in Qom.³¹ Around 1920, it is reported that various infectious diseases including typhus were common in the rural areas of Hamadan. At that time, typhus occurred mostly in fall and winter, and children were more affected.²⁷ In 1922, typhus outbreak appeared in Azerbaijan province in northwestern Iran. Between 1922 and 1923, typhus killed 163 people in Tehran and from 1923 to 1924, 121 people died.³²

There are many medical documents at the National Library and Archives of Iran, such as the letters of the Ministry of Health regarding typhus outbreaks in Iran. In 1936, in rural areas of Toos in current Razavi Khorasan province in northeastern Iran, a typhus outbreak appeared.²⁹

During WWII, typhus was regarded as one of the most dangerous epidemic diseases which were expected to occur during and after the war. Before 1939, in some countries including Morocco, Algeria, Tunisia, Egypt, Iran, Yugoslavia, and probably Poland, typhus had appeared each winter as a small-size outbreak, but during WWII, these regions experienced large outbreaks.³³ In 1941, despite Iran's declaration of neutrality, it was occupied by the allied forces and at that time, typhus became epidemic in Tehran and other major cities.²⁹ Many people, including health workers, died of typhus. For instance, Dr. Abolghasem Sheikh-ol-Eslami, the chairman of ENT department at the Farabi Hospital in Tehran died in 1944.²⁹ Reported cases of typhus in Iran between 1940 and 1950 were respectively 256, 115, 907, 12, 885, 6,436 and 826 (in total: 21,425).³³

In an investigation by Sachs which was published in 1946, he affirmed the lower incidence of typhus in March, April and May among the troops in west central Iran as compared to the troops in southern Iran. He also noticed that the causes of death in 55% of the patients who died of typhus in the northern Iran were

circulatory collapse or pulmonary edema. In addition, hypostatic congestion was also much higher in the patients in northern Iran. On the other hand, cyanosis of fingers and toes in patients was more common in southern Iran. Among the cases treated in Teheran, 100 were under 12 years of age, of whom two patients died.³⁴ The tick-borne and flea-borne typhus were both present in Iran. Immunization against typhus was recommended when an outbreak occurred.³⁵

When Iran was occupied by the allied forces during WWII, the Russian troops entered Mashhad in northeastern Iran on August 25, 1941. In due course in March 1942, around 700 Polish refugees entered the Khorasan province through Bajgiran near the Iran-Turkmenistan border and were settled temporarily in some cities of the Khorasan Province. A typhus outbreak appeared in Khorasan province in 1943 with high mortality.³⁶

In 1943, a committee for fight against typhus was established in Iran.³⁷ The first Persian academic medical journal in Iran was published in 1943 by Tehran University Medical Faculty.³⁸ Two successive issues of the journal were devoted to typhus (Figure 1) in which various aspect of typhus were discussed. Dr. Mohammad Ali Hafizi wrote a comprehensive review on the history of typhus published in the journal.

During WWII, approximately 120,000 Polish refugees entered Iran between 1942 and 1943.³⁹ The first cases of typhus appeared when the Polish army was organized in Tockoje in Russia. However, the typhus outbreak occurred shortly after when the army moved to southern Russia and its peak took place in February of 1942 and in total 7,346 became ill, of whom 1,290 died. Then, after the evacuation of the first of the Polish refugees to Tehran, many civilians also contracted typhus.⁴⁰

To sum up, the health care authorities and physicians should always consider the potential risk of typhus outbreaks occurring under special situations. These include natural disasters, famine and overcrowded camps. The health professional should always

remember that according to the WHO, typhus is still classified as a “disease under surveillance”.⁴¹

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