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History of Medicine in Iran

Brief Historical Perspectives of Malaria in Iran

Mohammad Hossein Azizi MD¹, Moslem Bahadori MD¹**Abstract**

The history of malaria as a serious human disease dates back to ancient times. For centuries, malaria has been a deadly disease with high morbidity and mortality that profoundly impacted the socioeconomic status of endemic countries. However, its causative agent remained unidentified until the last decades of the nineteenth century. There were no effective synthetic anti-malarial agents until the mid-twentieth century. Currently malaria has been eliminated or pre-eliminated in numerous countries; however, this preventable and curable disease remains a significant global health problem. A major concern is drug resistance. Presented here, is a brief look at the history of malaria in Iran and the rest of the world, particularly during the nineteenth and twentieth centuries.

Keywords: History of medicine, Iran, malaria

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Introduction

Malaria is a vector-borne disease caused by protozoan parasites that belong to the genus *Plasmodium*. The parasites are transmitted from person to person by the bite of infected female *Anopheles* mosquitoes.¹ There are approximately 400 *Anopheles* mosquitoes of which 70 species are potentially malarial vectors; however, only about 36 species are considered significant.² There are four species of malaria parasites that potentially could infect humans, including *Plasmodium vivax* (*P. vivax*), *P. falciparum*, *P. malariae*, and *P. ovale*. Of these, *P. falciparum* is the most hazardous. The symptoms of malaria vary depending on the responsible species, but the initial symptoms generally include lethargy, headache, anorexia, nausea and vomiting. The typical findings are recurrent intermittent fever and chills that last several hours and are accompanied by profuse sweating.³ Most malarial mortalities occur in children and pregnant women.⁴

Global malaria timelines

It has been speculated that *P. vivax* originated approximately two million years ago from a group of malaria parasites in monkeys and apes.⁵ Three factors-wars, spontaneous and forced migrations affected the spread of special strains of parasitic diseases in specific geographic areas. Because of human migration, plasmodia transferred from Africa to the Mediterranean region. However, the actual malarial foci primarily formed following the 'Neolithic Revolution' which included sedentarisation, irrigation and population increase.⁶ In due course, malaria extended from Africa to Europe, India, China and Indonesia through traveling; however its spread to the Americas was doubtful.⁷ The evidence of malaria could be traced in Chinese documents that dated back to 2700 B.C., clay tablets from Mesopotamia (2000 B.C.), Egyptian papyri (1570 B.C.) and Hindu texts from the 6th century B.C. Hippocrates (c. 460–370 B.C.) knew the characteristic malarial fevers and splenomegaly in people who lived in marshy areas.⁸ The word

Authors' affiliation: ¹Academy of Medical Sciences of the I.R. of Iran, Tehran, Iran.

Corresponding author and reprints: Mohammad-Hossein Azizi MD, Academy of Medical Sciences of the I.R. of Iran, Tehran, Iran.

Tel: +98-212-293-98-69, E-mail: azizi@ams.ac.ir

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malaria literally means bad air (mal-aria).⁹ For a long period, it was a popular belief that malaria was an environmental disease caused by bad weather. Thus, it was also called marsh fever.¹⁰ In Hippocratic medicine the miasmatic theory of disease causation was an explanation for the origin of disease outbreaks, in which remittent and intermittent fevers were caused by bad air and bad swamp water. This erroneous theory continued until the end of the nineteenth century when scientists described the transmission mode of the malaria parasite as dependent upon mosquitoes that bred mainly in marshy areas.¹¹

Due to the lack of reliable resources the exact occurrence of diseases such as malaria during antiquity is unknown. However, evidence has shown that during ancient times various micro-organisms, including malaria parasites, were among the main threats to human health.¹²

The etiologic agent of malaria remained undetermined until the last decades of the nineteenth century when in 1880, malaria parasites were detected by the French Army surgeon Charles Louis Alphonse Laveran (1845–1922) who won the Noble Prize for medicine in 1907.¹³ Subsequently in 1897, the role of *Anopheles* mosquitoes as vectors of malaria were initially identified in avian malaria by a British physician, Ronald Ross (1857–1932) and thereafter, between 1898 and 1900, the vectors of human malaria were discovered by several Italian scholars, including Camillo Golgi (1843–1926).^{8,14} Ross won the Nobel Prize in 1902 for his work on malaria.¹⁵ According to F.E.G. Cox, in 1948, Henry Shortt and Cyril Garnham discovered that malaria parasites developed in the liver before entering the blood circulation (known as the pre-erythrocytic phase) and in 1982, Wojciech Krotoski found the final dormant stage of the hepatic lifecycle of malaria parasites^{8,16} (hypnozoites).

Until the 17th century there was no specific treatment available for malaria. Later, an anti-malaria drug known as quinine was extracted from the bark of the cinchona tree. Synthetic quinine alternative drugs were manufactured during the twentieth century. Chloroquine was the most successful antimalarial drug, however in the 1970s, widespread drug resistance occurred.^{17,18}

Up to the beginning of the 20th century, there was no efficient method that control breeding of the *Anopheles* mosquito.¹⁹ Before the 1940s; control of mosquito borne diseases such as malaria was performed mainly by environmental management such as oiling

stagnant waters with petrol products and utilizing larvivorous fish. The use of indoor spraying for malaria by dichloro-diphenyl-trichloroethane (DDT) began around the mid-1940s and in due course, remarkable declines in malaria prevalence occurred.²⁰ In 1955, the World Health Organization (WHO) began the Global Malaria Eradication Program.⁴

A historical background of malaria in Iran

In “Avesta”, the Zoroastrian religious book, the characteristics of a disease that resembled malaria were mentioned (Tab-Larzeh, which means fever and chill).²¹

During the Islamic period, the clinical picture of malaria was a familiar entity to famous Iranian physicians. Ali ibn Sahl-e Rabban Tabari (838–870 C.E.) in his book, “Firdous al-Hekmah” (Paradise of Wisdom) expressed various types of fevers including malaria²² and Ali ibn Abbas Majusi Ahvazi (10th century C.E.), known as Haly Abbas in the West, in his book entitled “Tebb Maleki” (Royal Medicine) described the clinical manifestations of malaria as Tab-e Naeb (paroxysmal fever).²³ Razi (865–925 C.E.) or Rhazes explained in his renowned book, “al-Hawi”, various fevers as well as the fever pattern of malaria.²⁴ Abu ul-Ala Shirazi who lived around the 10th century C.E. also mentioned that arsenic (known as Sam-ol-far or mouse killer poison) could be effective in the treatment of malaria.²⁵ Another physician, Akhawayni Bukhari in the 10th century C.E., who was the author of the oldest known medical Persian treatise named “Hedayat al-Motaallemin fi-Tebb” discussed various patterns of fever and malaria (Figure 1).²⁶

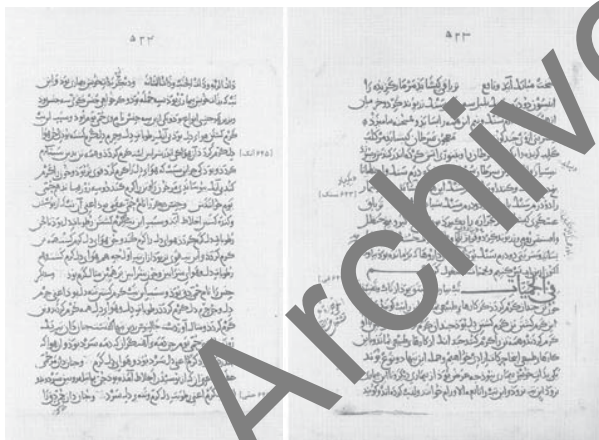


Figure 1. Two pages from the book “Hedayat al-Motaallemin fi-Tebb” which described various fevers (Hammiat) and malaria was written by the Persian physician, Akhawayni in the 10th century C.E. [Akhawayni Bukhari A. Hedayat al-Motaallemin fi Tebb (Edited by Afshar I, Omidisalar M, Motalebi Kashani N). Tehran: Bahram Publication; 2008]

The distinguished Iranian physician, ibn-Sina or Avicenna (980–1037 C.E.) classified fevers including malaria (Tab-e Nowbeh) in his “Canon of Medicine”.²⁷ Later, Ismail Jorjani (1040–1136 C.E.), in “Zakhireh-ye Kharazmshahi” (Treasure of Kharazm Shah) described different types of fever including the fever pattern in malaria.²⁸

Malaria in Iran during the 19th and 20th centuries

No accurate data exists regarding the malaria outbreaks and its true prevalence in Iran in previous centuries; however, the malaria

profile during the 19th and 20th centuries is more informative.

The modern concepts regarding malaria were gradually introduced in Iran after the establishment of Dar al-Fonun School in 1851. As an example, figure 2 shows the pages of a Persian pathology manuscript dates back to 1858, translated from a European textbook which described various patterns of fever and malaria pathogenesis and diagnosis.(Figure 2)

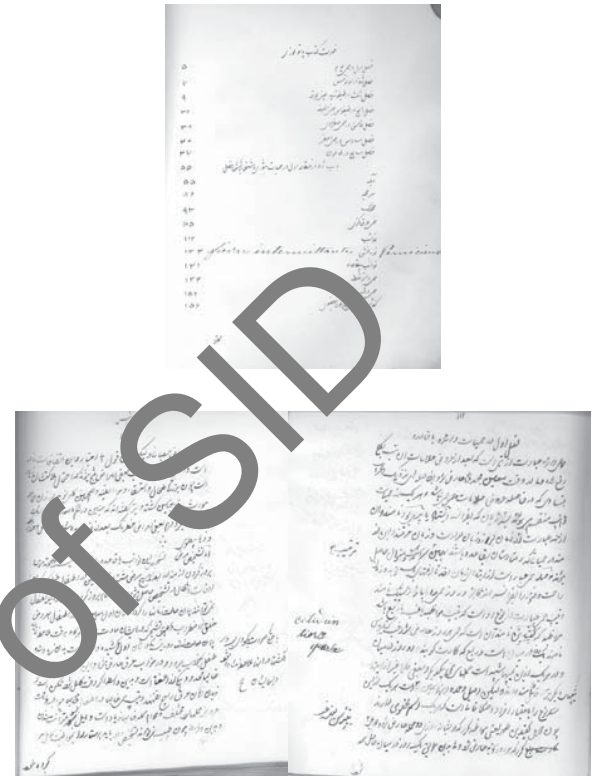


Figure 2. A Persian pathology manuscript written in 1858 discussed various types of fevers and malaria.

Based on historical evidence, during the time of Shah Abbas, a ruler of Safavid dynasty (1587–1629 C.E.), there were approximately 100,000 Armenians that migrated to Northern Iran. Shortly thereafter 20,000 people died of malaria and the survivors transferred to Isfahan, the capital city.²⁹ Subsequently, during the Qajar period (1796–1925) malaria was a major health problem. It was an endemic disease, particularly along the Caspian Sea in Gilan, Mazandaran and Gorgan Provinces; additionally it was common in Khorasan, Azarbiajan, Kurdistan, Kermanshah, Hamadan, and Khuzestan Provinces. The Persian Gulf territories were highly affected. During that time, the main reasons for malaria, particularly in Iranian villages, were lack of adequate sanitation and presence of stagnant waters which were conducive to breeding the *Anopheles* mosquitoes. In certain areas, *Anopheles* mosquitoes were so common that it led to unwanted migration of people who lived in those areas.³⁰ In 1924, malaria killed 2,634 people in Tehran.³¹ Between 1949 and 1953, around half of the workers who were constructing the roads or industrial factories in Northern Iran died from malaria.²⁹

The first official report on malaria in Iran has been written by Gilmour in 1925 which was a part of an inquiry regarding the endemic diseases in Iran and was compiled for the League of Nations. According to his report, in 1921, the estimated total population of Iran was around 12 million, of which 60% resided in high-

ly endemic malaria areas. Gilmour added that each year, between 4 and 5 million people developed malaria, which was responsible for 30% to 40% of all mortalities in Iran, thus at that time, the Ministry of Health had to invest around one-third of its annual budget to purchase quinine for the treatment of malaria-infected patients.³²

Prior to the second world war, the campaign against malaria in Iran was limited and mainly focused on the distribution of quinine tablets (Figure 3), petrol products for spraying stagnant waters, and the promotion of some environmental standards on a restricted scale. However, because of the lack of facilities, budget shortage, lack of expertise and WWII, these measures were ultimately stopped.³³

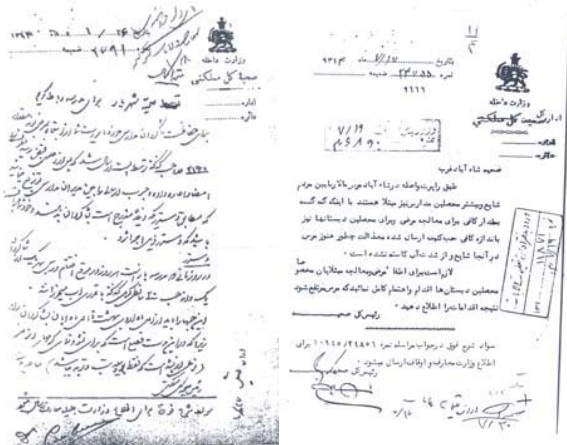


Figure 3. Left) A letter from the Sehhyeh-e Koll-e Mamelekati (Public Health Administration) regarding distribution of quinine tablets among the students who resided in Shahriar, Karaj, near Tehran during 1934. **Right)** Another letter from the Public Health Administration that described an outbreak of malaria in Shah Abad Gharb, Kermanshah Province in Western Iran during 1935.

Between 1943 and 1946, malaria control by the Ministry of Health was undertaken only in the cities of Khoramabad, Sanaddaj, Isfahan and Shiraz.³⁴ However, later in 1949 malaria control measures were reinforced and the government approved the establishment of an organization to combat malaria which was called Edareh-ye Mobarazeh-e Malaria (the Administration for Malaria Campaign). The main objectives of this newly established organization were to study malaria and train the required experts. This organization devoted 55,000,000 Rials for the first year of the program in the areas along the Caspian Sea in Northern Iran, as well as in the southern cities that included Bushehr and Bandar-e Abbas.³⁵

In 1950, following WWII, public health measures to control malaria resumed in Iran; DDT spraying began in small infected areas and eventually the program expanded. Then in 1958, according to a WHO recommendation, the malaria eradication program was approved by the government and continued until 1961, but the program was again stopped due to emergence of *Anopheles* mosquitoes' resistance in Southern Iran. In 1968, an organophosphate insecticide, malathion was used and other preventive measures undertaken such as oiling stagnant waters with petrol products and the introduction of larvivorous fish. Until 1973, malaria was controlled in most areas of the north of the Zagros mountain range, a

major epidemiological malaria zone in Iran. At that time, the total number of malaria patients was 16,000, but in the next two years malaria became epidemic in some parts of Southern Iran, particularly in Hormozgan, Baluchistan and Kerman. Because of travel of patients from infected areas to disease-free regions, some foci of malaria reappeared in Northern Iran.³⁵

In 1949, 'the Point Four Program' as a technical assistance program for developing countries was announced by US President Harry S. Truman.³⁶ In due course, in 1951, the Department of Health Organization Collaboration was established in Iran by cooperation from the Ministry of Health, but after a few years, the aforementioned organization was dissolved and Edareh-ye Koleh-e Behdashaht (General Administration of the Public Health) was founded at the Ministry of Health and then, after launching the Malaria Eradication Program, Edareh-ye Risheh Kani Malaria (General Administration of Malaria Eradication) was established.³⁷

In addition to the establishment of the General Administration of Malaria Eradication, the Institute of Malariology was founded in Iran in 1952 by mutual collaboration of the Parasitology Department of Tehran University Medical School and the Ministry of Health. It was headed by Dr. Naser Ansari, a Professor of Parasitology. The institute was changed to the Public Health Research Institute in 1964 and the first malaria research station was established in Mazeroon, Fars Province in Southern Iran.³⁸ Dr. Naser Ansari (born in 1913 in Isfahan) was sent to Paris in 1930, where he studied parasitology. On his return, he was appointed Associate Professor of Parasitology at Tehran Medical School. He became a full Professor in 1943.³⁹ The Institute of Malariology trained malariologist physicians and technicians. This institute was changed to the Institute of Malariology and Parasitology in 1956 and in 1955 it was expanded and became the Institute of Medical Parasitology and Tropical Health.³⁸ The national program for malaria eradication in Iran was launched in 1958, but because of major technical and administrative difficulties, malaria eradication was officially declined to malaria control in 1987.⁴⁰

Between 1964 and 1965, indoor DDT spraying of 43,896 villages with a population of 878, 414 was performed. In 702 villages with a total population of 298,497 resistance to malaria appeared, therefore malathion spraying was used.³⁸ In 1960s, several stamps were issued to support the malaria campaign in Iran (Figure 4).⁴¹



Figure 4. Stamps issued in Iran between 1960 and 1968 regarding the malaria campaign.⁴¹

In the past few decades, several researchers studied malaria in Iran. The first study on malaria in Iran was carried out by Latchev in 1921 who investigated malaria in Rasht and Bandaranzali, Gilan Province, in Northern Iran.²⁶ Manouchehrian et al. pointed out that other main malaria investigations were performed by Lindberg (1936), Amidzadeh (1941), Zolotarev (1945), and Macan (1950) who studied the epidemiology of malaria in Iran, followed by Jalali (1955), Motabar et al. (1975), Manouchehri et al. (1972, 1974, 1975, 1976), Manouchehri and Janbakhsh (1977), Manouchehri and Yaghoubi-Ershadi (1988), Zaim (1987), and Zaim et al. (1991).³²

Current picture of malaria in the world and Iran

According to the World Malaria Report 2011 by WHO, there were 216 million cases of malaria in 2010; of which 81% were in the WHO African Region. The estimated number of people, who were at risk of malaria in 2010, was 3.3 billion. Around 655,000 persons died of malaria in 2010 and 86% of these victims were children below the age of five; 91% of malaria deaths occurred in the WHO African Region. WHO reported that since 2000, malaria mortality rates have decreased by more than 25%, with the largest reductions in the European (99%), American (55%), the Western Pacific (42%) and African Regions (33%). Drug resistance has been a major concern.⁴²

At present, according to the WHO, malaria in Iran is in the pre-elimination phase.⁴³ For instance, according to a report by the Ministry of Health officials, in 2009 (1388 Shamsi), 3,016 cases of malaria have been detected in Iran; 50% of these patients were immigrants or refugees from neighboring countries.⁴⁴ Currently, most cases of malaria (90%) in Iran are from three endemic regions i.e., Hormozgan, Kerman, and Sistan and Baluchistan Provinces.⁴⁵

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