

ORIGINAL ARTICLE


To the Memory of Mohammad Hanifi, a Prominent Expert on Plague in the Pasteur Institute of Iran

Abstract

Due to the human plague epidemic in some regions of Kurdistan in 1947, research teams of the Pasteur Institute of Iran were sent to these regions for investigations. Such studies are still ongoing. Mohammad Hanifi caught plague during its epidemic, and most of his relatives died of the disease. He began his official collaboration with research teams of the PII in diagnosing and controlling plague reservoir rodents in 1959, and it lasted until his death in 2015. In addition to plague, Hanifi conducted a great number of studies on other diseases such as relapsing fever, rabies and cholera. During his lifetime, he also suffered from plague and relapsing fever, but he was healed. The present paper reviewed his lasting activities during his work at the Pasteur Institute of Iran (PII).

Key words: Pasteur Institute of Iran (PII), Plague, *Borrelia*, Rabies, Medical History

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Introduction

Mirza Mohammad Hanifi was born in Aq Bolagh-e Morshed village in Bijar in 1936. He spent his childhood and adolescence in his hometown and did agriculture. His mother tongue was Turkish and was a little familiar with Persian.

Plague epidemic in Aq Bolagh-e Morshed Village

Aq Bolagh-e Morshed is a village of Bijar in Kurdistan Province. This village was focused on due to the plague epidemic on December 23, 1947. It was near Sooudje-Boulak village which had the plague epidemic causing the death of more than 100 people in 1871¹.

After the epidemic of plague in Aq Bolagh-e Morshed in 1947, missions of PII teams began in the region: Dr. Biouk Seyedian and Dr. Shamseldin Mofidi in 1947, and Dr. Marcel Baltazard², Dr. Rasoul Pouranki and Dr. Mansour Shamsa³, Dr. Pezeshkipour Mostashfi, Dr. Mirhamed Siadat, and Dr. Younes Karimi⁴ in 1948 went to this village to control plague and conduct further studies. These missions continued for the following years. The teams had the mission to hunt rodents around the village and observe patients in the village and surrounding areas. They watched Aq Bolagh-e Morshed village carefully in order to control human diseases in the region, but the disease bacterium still existed in the rodents living in that area. In 1950, the construction of a research laboratory of plague started in Akanlu village of Kabudarahang County in Hamadan in about 40 km of Aq Bolagh-e Morshed village with the responsibility of Dr. Mahmoud Bahmanyar⁵ and continued until 1953. According to the reports from the headquarters of this center, PII teams could conduct their research using more equipment on the plague that was the main disease in the surrounding areas of village. During 9 epidemics of plague in 1947 to 1956 in Kurdistan and East Azerbaijan provinces, a large number of people with plague were saved by the PII teams, and 156 people died of this illness^{6, 7}.

Plague is an old disease that still exists in endemic forms in some regions of the world⁸. *Yersinia pestis* is the bacterium of plague and can be seen in humans in three forms, namely the Bubonic plague, Pneumonic plague and Septicemic⁹. The pulmonary form of plague should be promptly reported to the WHO according to International Health Regulations¹⁰. Wild rodents are disease reservoirs in the nature; and the cause of the disease is transmitted by fleas to various animals and humans¹¹. The most important source of human contamination is the bite of *Xenopsylla Cheops*-contaminated flea. Living in rural areas or hunting animals increases the risk of disease for humans¹². Due to the presence of contaminated rodents and flea vectors in Kurdistan Province, it has remained an

- 1- Tholozan, 1874: 563-569.
- 2- Keypour, 2017: 553.
- 3- Mostafavi, 2017: 326-8.
- 4- Mahdavi, 2017: 1.
- 5- Mahdavi, 2018: 428-433.
- 6- Hanifi, 2013: 9.
- 7- Mostafavi, 2017: 139-158.
- 8- Gage, 1996: 1-15.
- 9- Chin, 2000.
- 10- World Health Organization, 2008: 77.
- 11- Slack, 1989: 641-3.
- 12- Chin, 2000.



endemic region for plague. In the natural center of plague in Kurdistan, there are different rodent species, among which four species have played important roles in preserving this bacterium. These four rodents are from Meriones genus and include Meriones libycus (M. libycus), Meriones persicus (M. persicus), Meriones Vinogradovie (M. Vinogradovie), and Meriones tristrami (M. tristrami). Meriones tristrami (M. tristrami) and Meriones Vinogradovie (M. Vinogradovie) are severely susceptible to the disease and have a relative resistance against the cause of disease than Meriones persicus (M. persicus) and Meriones libycus (M. libycus)¹³. Plague still exists in the wildlife of western regions of Iran¹⁴.

During the plague epidemic in Aq Bolagh-e Morshed in December 1947, Mohammad Hanifi was an 11-year-old teenager who saw the plague epidemic. In this epidemic, 17 of his relatives died, and he also suffered from plague but was saved by the PII research teams. Dr. Marcel Baltazard asked Mohammad Hanifi for cooperation while visiting the region as he could read and write and had a full knowledge of the region. He took charge of finding nests of rodents and trapping them as well as helping the PII research teams to catch rodents and investigate their contamination with plague. Due to his interest, perseverance and skill in diagnosing and catching rodents, he was employed in PII at the age of 23 and worked as the expert of epidemiology laboratory for his enough knowledge of wild rodents and his perseverance in doing his tasks. He was humble, trustworthy, and hardworking in field studies (Figure 1).

13- Karimi, 1976: 166.

14- Esamaeili, 2013: 1549.



Figure 1. The plague-stricken Aq Bolagh-e Morshed village in 1948: Expedition team of the PII to overcome the plague; from right to left (front): Dr. Mirhamed Siadat, Dr. Shamseldin Mofidi, Dr. Marcel Baltazard, Dr. Zare, and Ahmad Karimi

Hanifi continued his learning along with field studies. He



learned Persian and could obtain a high school diploma in 1975. During the years when he worked at the Pasteur Institute of Iran (PII), he was able to attain good knowledge of the epidemiology of wild plague and was not only famous in the diagnosis of wild rodents in the region, but also as an expert in the diagnosis of these animals in the whole Iran. He also obtained valuable information during his work on the ecobiology of animals, the types of rodents in different regions and their residence, and also specifications and architecture of different rodents' nests in terms of depth and branching corridors. This knowledge was obtained by the guidance of outstanding and famous professors worldwide such as Dr. Xavier Misonne from Belgium¹⁵, Dr. Douglas M. Lay from the University of Chicago¹⁶ and Dr. Bechinkev from Russia and their active participation in various missions in the country. For many years, he worked as a strong active technician accompanied by Dr. Mahmoud Bahmanyar¹⁷, Dr. Rasoul Pouranki, Dr. Mansour Shamsa, Dr. Younes Karimi, Dr. Mirhamed Hissein Siadat, and Dr. Mehdi Asmar. In implementing research programs, the PII gained unique experience by removing thousands of nests, observing details of their structures, and molding dozens of nests belonging to different types of desert rodents as an initiative, which was first conducted in Iran, resulting in many points about the epidemiology of plague and the cause of its survival in nature¹⁸ (Figures 2 and 3).

- 15- Misonne, 1975: 47-58.
- 16- Lay, 1967.
- 17- Mahdavi, 2018: 428-433.
- 18- Hanifi, 2013: 85.
- 19- Ibid.



Figure 2. Molding the nest of M. persicus near Aq Bolagh-e Morshed village, 1965

With a regular and hardworking attendance in field operations and the nocturnal hunt of foxes and other wild animals, he played an important role in scientific progress in this field in Iran. He was also involved in the project of recognition of wild plague loci by serum experiments in foxes¹⁹.

With the participation of Hanifi in 1960, the plague reproach group discovered the secret of the survival of plague in nature indicating that the bacilli of the disease could survive in soil for many years and re-cause the disease after years of ex-



tinction²⁰. In 1963, he collaborated with Dr. Marcel Baltazard and Dr. Henri Mollaret, the French physician and biologist²¹ to conduct the terrarium project. In the project, there was a hole to the depth of 1 and a half meters on four sides. It was then surrounded using impermeable cement plates, and the nest was tightened by a metal mesh. To illustrate the concept of survival of plague in the soil, they allowed *Meriones* mice to dig new nests by placing those rodents in the terrarium. The rodents were then infected with the plague bacterium and all died in their nests. Twenty-eight months later, new animals were transported to the terrariums. Some of them died of the plague, and thus the bacteria survival hypothesis in the soil was approved²² (Figure 4).

20- Karimi, 1963: 1183-6.

21- Carniel, 2012: 1-11.

22- Ibid.



Figure 3. Mohammad Hanifi next to the gypsum mold of Fox nest; Bam Khanbaghi in 35 km from the Research Centre for Emerging and Reemerging Infectious Diseases, The Pasteur Institute of Iran, Hamadan, 1970



Figure 4. Jebreil Village: The terrarium Project (Mohammad Hanifi, the second person from the left with white clothing)

In 1973, the first mountainous *Spermophilus fulvus* was reported on the border of Maku and Turkey; and the first *Meriones tristrami* from Jolfa county was observed.



The PII's research attracted the attention of health officials and the World Health Organization (WHO), and they asked for help from the PII for investigating plague in many countries²³. Mohammad Hanifi was active as a leader for field studies in an International Seminar at the Research Centre for Emerging and Reemerging Infectious Diseases in the PII in 1975 (Figure 5).



Figure 5. International Plague Seminar at the Research Centre for Emerging and Reemerging Infectious Diseases, The Pasteur Institute of Iran, Hamadan, 1975

The diagnosis of plague locus in Sarab in 1976 was an important scientific work by him and his colleagues. In July 1976, a new plague locus was introduced with the advent of the plague microbe in Sarab (Mugan plain of Ardabil province)^{24, 25}. In this mission, a dead *Meriones vinogradovi* was in the mouth of a nest that was shown to be of plague according to the infected fleas spreading around it²⁶. In this mission, five dead *Meriones persicus* in a nest and a person with plague were identified. In the East Azarbaijan locus in Sarab, 14 isolated *Yersinia pestis* of wild rodents and fleas were also identified²⁷.

In addition to catching plague in 1947, he caught the relapsing fever due to *Borrelia* and was then treated in 1974, 1975 and 1985 during his mission.

Mohammad Hanifi got retired as the laboratory expert in 1994. He cooperated with several missions with plague research teams of the Pasteur Institute of Iran in transferring knowledge about plague studies during 2011 to 2013. The book "The Plague against People; A Man against the Plague" was a collection of his memoirs during the service. He died on June 26, 2015.

Mohammad Hanifi has a son, Hamed, who was recruited by the Pasteur Institute of Iran in 1985 and continued his father's career for thirty years and then retired in 2013, but he is still active in field missions at the Pasteur Institute of Iran.

In 2012, Mohammad Hanifi donated documents and sam-

- 23- Karimi, 1976: 166 p.
- 24- Ibid.
- 25- Karimi, 1978: 326-2.
- 26- Karimi, 1976: 166 p.
- 27- Karimi, 1980: 28-35.



ples of many animals and birds, which were collected over years, to the Pasteur Institute of Iran. These donated properties constituted a museum that was named Mohammad Hanifi at the Research Centre for Emerging and Reemerging Infectious Diseases in Akanlu Village^{28, 29}.

In 2018, an alley was named Mohammad Hanifi in Akanlu village. (Figure 6)



Figure 6: Naming a passage of Akanlu village Mohammad Hanifi, 2018

Mohammad Hanifi's main activities were studies related to plague although he also conducted studies on other diseases such as rabies, relapsing fever, hemorrhagic purpura and brucellosis.

A review of his scientific activities is presented as follows.

Plague studies

During 1947 to 1950, he detected the contaminated area of Kurdistan and accomplished missions in regions such as Sonqor (1948), Khorramabad (1949), Marivan (1950) and Aq Bolagh-e Morshed (1947 to 1950).³⁰

In 1951, Gazar Darreh village of Sanandaj in Kurdistan province had the plague epidemic; and Hanifi with the PII teams managed to control the epidemic. In 1952, the plague epidemic occurred in Zeynal kedy village of Kurdistan, and 12 out of 300 people of village were infected with plague within six days, and three ones died. In 1960, people of Nurabad village of Sanandaj were infected with plague. In 1963, plague studies indicated that fleas in bird nests were infected with plague and could transmit the disease for kilometers.

In 1963, the mission continued in Bukan, Miandoab, Aq Bolagh-e Morshed village and surrounding areas to investigate the plague. In 1965, on a mission to Kurdistan, a number of village children had bubonic plague.

Hanifi's missions continued in Aq Bolagh-e Morshed village (1964, 1966, and 1968), Khorasan and Golestan (1964), Jask of Chabahar (1964), Khorasan (1965), Qazvin, (1966-1967, 1974), Kerman (1968), Torbat-e Jam and Taybad (1971), Akanlu (1964, 1972, 1974, 1975, 1976, 1977, 1978, 1979, 1982, 1983, 1984, 1986 and 1989, 1993), Mashhad

28- Keypour, 2017: 553.

29- Mahdavi, 2017: 1.

30- Bahmanari, 1995: 25-45.



(1968), Bukan and Miandoab (1972), Ardabil (1972, 1973, 1974 and 1976), Sistan and Baluchestan (1973, 1986), and Dezful and Minab (1973), Maku, Urmia and Bukan (1972, 1973 and 1975), Zabol (1973, 1985, 1986 and 2011), Darab, Jahrom, Lar, Fasa and Neyriz (1974), Maku (1975), Kermanshah (1975), Shiraz, Borazjan, Dogonbadan, Kazerun (1975), Gonabad, Ferdows and Tabas (1978), Tehran (1979, 1989 and 1992), Sarab and Ardabil (1981), Urmia, Piranshahr, Oshtnavieh (1981), Sarakhs (1983 and 1990), Borazjan (1983), Bandar Abbas (1983 and 1994), Zahedan (1984), Bandar Abbas (1984), Bushehr (1985), Parsabad-e Mughan (1985), Mahshahr (1986), Sanandaj (1986), Chabahar (1986), Mobarakeh of Isfahan (1988), Gilan and Mazandaran (1989), and Hashtpar city of Gilan (1991) to study wildlife contamination with diseases such as plague and relapsing fever³¹.

Along with the investigation of the contamination of rodents and other small mammals, the isolation of ectoparasites, and the collection of external and internal parasites and their detection in these missions, rabbits and carnivores such as foxes, jackals, wolves and wild cats were hunted for examining their contamination. The number of studied rodents and fleas was very high in most of these studies; for instance, in a mission in regions around Akanlu in 1989, 8257 fleas and 1354 rodents were examined for the plague contamination.

Study of other diseases

Hanifi's studies were not limited to plague. He studied the antigen of hepatitis in human and livestock samples on missions to Bojnord, Quchan, Shirvan, and Dargaz (1974), Fasa and Jahrom (1974), Akanlu, Ardabil, Mugan plain, and Sarab (1974), and Bandar Abbas and Akanlu (1983) (Figure 7). The mission to Ardabil and Sarab (1974) was accomplished to take the blood samples from patients with cutaneous bleeding manifestations³². The mission to Sarab, Meshkinshahr and Ardabil in 1978 was done to evaluate the hemorrhagic purpura patients (Figure 8). Hanifi also participated in studies on rabies in the wildlife in Gilan province (1966-1967), Sarab (1978), Bandar Abbas (1983), Sanandaj (1987) and Mazandaran (1989). In 1968, he sought to hunt bats around Isfahan, Shiraz, Andimeshk, Shush, Kazerun, the margin of Namvar (Parishan) Lake in order to study rabies.

He also had missions to regions such as Khalkhal (1975), Golestan province including Gonbad-e Kavus, Maraveh Tappeh, Dashli Borun (1976-1977), Mugan plain (1974), Akanlu (1975), Ardabil (1976), Tehran (1979), Firuzkuh (1988), Bandar Abbas (1987), Sanandaj (1987), Mazandaran province (1988), and Talesh and Gorgan (1990) to investigate their fauna in studied regions, and also conducted stud-

31- Hanifi, 2013: 85.

32- Karimi, 1976: 399-404.



ies on Spirochaetes, Relapsing fever, hemorrhagic purpura, Lyme disease, Theileriosis and Babesiosis.

33- Karimi, 1979: 157-68.



Figure 7. Dr. Sabbar Farman-Farmaian (Head of Pasteur Institute of Iran): Standing first from right; and Mr. Mohammad Hanifi: sitting; plague studies around the Research Centre for Emerging and Reemerging Infectious Diseases in Akanlu village of Hamadan, 1975



Figure 8. The region around Tabas in Khorasan province; Mohammad Hanifi is taking care of a girl who has worms in her leg due to the severity of wound, 1978

He also participated in surveillance of Poliomyelitis in Ahvaz (1962).

In a mission to Akanlu village, coincided with the cholera epidemic in 1970, an oral cholera vaccine was used in this region.

He participated in the mission to Ardabil and Sarab (1975) by hunting birds in studies on Arbovirus.

The outbreak of relapsing fever was investigated in a mission to Ardabil in 1974, and about 90% of children caught the relapsing fever. A new species of *Borrelia* called Baltazard *Borrelia* was discovered in the mission³³.

Hanifi collected the black fly in a mission to Kapurchal



(1977) and Borazjan (1983).

He also participated in a study on warehouse mice in Tehran in 1981 with the aim to investigate Toxoplasmosis, *Borrelia parkri*, *Borrelia latyschewii*, Plague, Tularemia and Giardia.

He participated in missions to Zahedan (1983) to evaluate the leprosy, leishmaniasis and Leptospirosis, and missions to Mugan plain, Parsabad-e Mughan and Sarab (1985) to evaluate the Tularemia and relapsing fever.

In a mission to Hormozgan (Bandar Abbas) (1987), a certain microbe called Sodoku Fever was isolated from warehouse mice.

The infection with *Borrelia* was observed in a mission to Farsan in Chaharmahal and Bakhtiari Province (1985).

The missions to Karaj (1988) and Tehran (1991) aimed to investigate the warehouse and desert rodents in terms of *Borrelia* and *Trypanosoma*; and results did not indicate any contamination.

The mission to Tehran (1989) aimed to investigate Brucellosis, and the vicinity of Tehran including the southern part of Damavand and the northern part of Rudehen were investigated in terms of brucellosis.

The mission to Bandar Abbas (1983) was accomplished to investigate the relapsing fever, Toxoplasmosis and fungal diseases.

Life lessons

Mohammad Hanifi was a villager in most remote villages in Iran and could play an active role as an influential person in field teams of the Pasteur Institute of Iran in the following years due to his talent and also collaboration with research teams of the institutes of the Pasteur Institute of Iran during his adolescence (11 years of age).

- Learning: Despite the insufficient facilities for continuing his education after the elementary school, he could get his high school diploma at the age of 39 because of his interest in education and did not cease to study until his final years of life.

- Documentation: The documentation of missions, in which he participated, was an important aspect of his life, and he wrote details of each mission in his notebook. A series of reports of his missions has been published in a book under the title of "The Plague Against People, A Man Against Plague".

- Collection and donation of equipment during service years: In addition to documentation, Mohammad Hanifi also collected and stored animals (Taxidermy or keeping in formalin) and donated them along with other items, which were collected during his services; to the Pasteur Institute of Iran providing the basis for establishing a museum at the Research Institute of the Pasteur Institute of Iran in Akanlu village.



- Self-devotion to the promotion of health in the society: Mohammad Hanifi had understood the importance of Plague as his close relatives all died of it, and thus he devoted himself to fighting the disease. Hanifi's major part of life passed in field missions and sampling in deserts. At the same time, the Iran's research teams also needed people like him who valued such works in order to clarify various aspects of diseases that originated in the wildlife.

- Transfer of knowledge and experiences: Hanifi's field-work experiences were transferred to his son, Hamed, over years. Transferring experience to next generations is an important issue that should not be ignored.

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