History of Contemporary Medicine in Iran

A History of Leishmaniasis in Iran from 19th Century Onward

Mohammad Hossein Azizi MD•[1], Moslem Bahadori MD[1], Shahriar Dabiri MD[2], Simin Shamsi Meymandi MD[3], Farzaneh Azizi DVM[4]

Abstract

The history of leishmaniasis dates back to the distant past; however, its etiologic agent was unidentified until the mid-19th century. Here is an overview of some historical aspects of leishmaniasis in Iran mainly focused on the cutaneous form, from the mid-19th century onwards. In addition, short biographies of several contemporary researchers and experts of leishmaniasis and their achievements in the past decades are presented.

Keywords: Cutaneous leishmaniasis, Kala-azar, history of medicine, Iran

Cite this article as: Azizi MH, Bahadori M, Dabiri S, Shamsi Meymandi S, Azizi F. A History of Leishmaniasis in Iran from 19th Century Onward. *Arch Iran Med*. 2016; 19(2): 153 – 162.

Introduction

Leishmaniasis is a vector-borne protozoan disease caused by more than 20 *Leishmania* species. Through their bites, the infected female sandflies transmit the *Leishmania* parasites from reservoirs (humans, desert rats, and dogs) to humans.[1] Leishmaniasis was formerly classified as cutaneous, visceral and mucocutaneous forms. However, recently they are categorized into localized (acute) cutaneous, diffuse (acute) cutaneous (disseminated anergic cutaneous), chronic cutaneous (including lupoid leishmaniasis), post-Kala-azar dermal leishmaniasis, mucocutaneous leishmaniasis, visceral leishmaniasis and viscerotropic leishmaniasis.[2] Cutaneous leishmaniasis (CL) is the most widespread form, usually appearing as skin ulcer on uncovered body parts. Visceral leishmaniasis (VL) or Kala-azar is the most severe form and generally involves the spleen, liver and bone marrow and untreated cases are fatal. Mucocutaneous leishmaniasis (MCL) is the most destructive variety, leading to partial or total damage of the nasooropharyngeal mucosa.[1] The nose, mouth, pharynx and larynx are respectively involved[3]; hence, it is essential for otolaryngologists to be aware of MCL, particularly if there is a history of travel to endemic areas.[4] The WHO report estimates that each year, around 1.3 million new cases of leishmaniasis occur globally with a total mortality of 20,000–30,000.[5] Leishmaniasis is seen in some parts of Asia, Middle East, Africa, Latin America and Southern Europe.[6] In total, leishmaniasis is seen in over 98 countries as an endemic disease. CL chiefly occurs in Afghanistan, Iran, Pakistan, Algeria, Syria, Saudi Arabia, Brazil, Colombia and Peru and over 90% of cases of VL occur in Bangladesh, India, Ethiopia, Sudan and Brazil. Approximately 90% of MCL cases are from Bolivia, Brazil and Peru.[7]

Authors' affiliation: [1]Academy of Medical Sciences of the I.R. of Iran, Tehran, Iran. [2]Pathology Department, Afzalipour Kerman University of Medical Sciences, Kerman, Iran. [3]Dermatology Department, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran. [4]School of Veterinary Medicine, Azad University, 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
Accepted for publication: 25 December 2015

The discovery of the leishmaniasis etiologic agent

The etiologic agent of leishmaniasis was unidentified until the mid-19th century. The discovery of the causative agent of CL has been attributed to the American pathologist James Homer Wright (1869 –1928); but it was originally detected in 1885 by David Cunningham and in due course, by the Russian surgeon, P. F. Borovsky (1863–1932), who described it in 1898 in a local military journal. The causative agent of human visceral leishmaniasis (*L. donovani*) was recognized in the spleen of patients with Kala- azar independently in 1903 by a Scottish physician, William Leishman (1865–1926) as well as Charles Donovan (1863–1951), Professor of Physiology at the Madras University in India. The sandflies were identified in 1921 and the actual transmission mode of disease was confirmed in 1941.[8] There are two types of VL: human type (anthroponotic) caused mainly by *L. donovani* and animal VL (zoonotic) caused by *L. infantum*.[9] For centuries, dogs - the most important reservoir of *L. infantum (L. chagasi)* and humans have been close companions.[10] *L. infantum, L. tropica, L.major, L.aethiopica and L.donovani* are etiologic agents of the Old World CL[11] [The Old World (Afro-Eurasia) refers to Africa, Europe, and Asia].

Leishman-Donovan bodies (Figure 1) are small round or oval shaped intra-cellular forms of the *Leishmania* parasite.[12] Progression of the leishmaniasis diagnosis and identification of causative agents has been a significant achievement from direct smear examination to the advanced DNA extraction and amplification through PCR technique.

A look at the history of leishmaniasis in ancient times

Leishmaniasis is an ancient disease.[13] CL was a familiar skin disease in vast sections of the world, from India to the Eastern Mediterranean and North African countries. It was known as the Oriental sore, Baghdad Boil, Basra Button (in Iraq), Delhi Boil (in India)[14] and Balkh sore (Balkh; an ancient city and the former center of Zoroastrianism now in northern Afghanistan). Other names of CL were: Aleppo boil (a city of northwest Syria near the Turkish border), Jericho boil (a city located near the Jordan River in

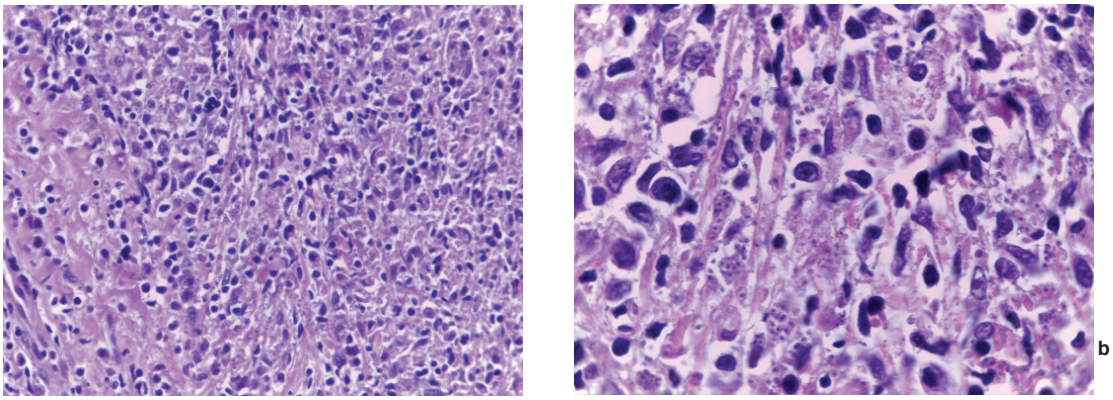


Figure 1. Light microscopy of CL: **a)** Diffuse proliferation of histiocytes containing intracytoplasmic parasitophorus vacuoles of many Leishman- Donovan bodies in the dermis (H&E staining, magnification ×400), **b**)High power shows many intracytoplasmic Leishman - Donovan bodies in the histiocytes rimming by lymphocytes and other mononuclear cells.(H&E staining; magnification ×1000, oil immersion) [From the Pathology Department, Afzalipour Kerman University of Medical Sciences, Kerman-Iran, prepared by the third author].

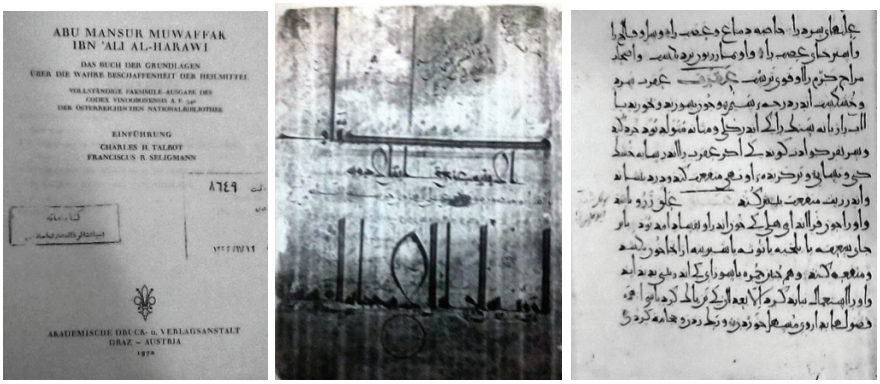


Figure 2. The Book of Remedies (*Kitab al-Abnyia an Haqaiq al-adwiya*). A copy of this Persian manuscript is available in Vienna, Austria.

the West Bank), Bouton de Crete, and Bouton d'Orient. Bray addressed a tablet in the library of King Ashurbanipal of Assyria in Nineveh (Mosul, Iraq), with description of a painless ulcer resembling CL.[15] In several studies, the investigators tried to detect protozoan material from paleontological fossils by PCR technique.[16] In a report, investigators described the DNA of *L. donovani*, the causative agents of VL (Kala-azar), in the mummies of ancient Egyptians.[17] However, the term "Kala-azar" used for the first time in 1883 , consisted of "Kala" meaning "black" (in Hindu) and "Azar" (in Urdu) which is the equivalent of disease.[18] "Azar" is originally a Persian word with several meanings including illness.

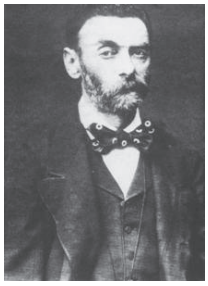
Historical aspects of leishmaniasis in Iran

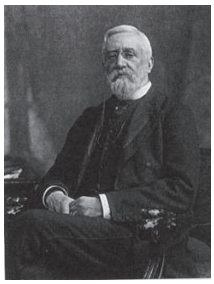
The history of CL in Iran is unknown in antiquity. To the knowledge of the authors, VL seems to be absent in the old Persian medical texts, although there are some data on CL in medical works of Iranian medieval physicians. The current Persian term for CL is *Saalak* or "one-year sore".[15] However; in the 9th century C.E. in the Middle East it was called "Balkh sore".[19] Dr. Cyril L. Elgood (1892–1970) was a physician at the British Embassy in Tehran between 1925 and 1935. He wrote two books on the history of medicine in Iran and several historical articles including one on the early history of CL in Iran.[20] He stated that in the past, CL was a known disease in north-eastern parts of Iran and after the Mongolian invasion of Iran (between 1219 and 1221), the disease was transferred from Khorasan in north-eastern Iran to Baghdad (Iraq).[21] As Elgood indicates "Abu Mansur Muvaffaq Hervai"; the 10th century physician living during the Samanid period, described CL as "Balkh sore".[15] He wrote the oldest Persian pharmacological book named "the Book of the Remedies", in Arabic: *Kitab al-abnyia an Haqaiq al-adwiya*[22] (Persian language was banned for over 300 years, therefore Persian scholars had to write in Arabic, which has given rise to the misunderstanding that these scholars were Arab) (Figure 2). In this book, he mentioned various remedies including antimony. Antimony compounds have been known since antiquity.[23] Antimony-containing compounds including Meglumine antimoniate (Glucantime) are still used to treat leishmaniasis.[24]

The Persian physician, Ibn Sina or Avicenna (980–1037 C.E.), in the first book of "the Canon of Medicine" called CL the "Balkh sore".[25] As Elgood stated, Avicenna was probably aware of the association between mosquito bite and CL. *Zakhireye-Kharazm Shahi* (the Treasure of the Kharazm Shah) is another famous Persian medical book written by Ismail Jorjani (1042–1136 C.E.), the Persian physician of the 12th century C.E.[26] According to Tajbakhsh, Jorjani mentioned that CL was prevalent in Balkh and around Gorgan in northern Iran. It was called "*Pashegazidegi*" (sore of mosquito bite).[15] In *Kholasat-ol-Tajarob* (Summary of Experiences), written by Baha-o-Dowleh Razi during the Safavid period (1501–1722 C.E.) in Iran, he pointed out that there was a frequent skin ulcer in Balkh region called "Balkh sore". [27]

History of leishmaniasis in Iran in the 19th and 20th centuries

During the Qajar period (1785–1925), Iran suffered from a broad range of diseases including leishmaniasis. According to Nadim *et al*. from the beginning of 20th century, several studies were started on CL in rural areas of Tehran. In 1913, Neligan carried out a study of stray dogs in Tehran and detected their skin ulcers and visceral lesions. He also performed autopsy on 21 dead bodies of stray dogs in 1915 and found 15 cases of leishmaniasis. From 1941 onwards, Iranian researchers performed investigations on the epidemiologic and laboratory features of the *Leishmania* parasite as well as the species of sandflies. Accordingly, these investigators noticed that CL is seen in several parts of Iran.[28]


Dr. Jacob Eduard Polak


Dr. Joseph Desire Tholozan

The Dar al-Fonun School was the first modern educational center which was founded in 1851 and its establishment was considered a major turning point of propagation of modern medicine in Iran. The first European medical teacher of Dar al-Fonun, the Austrian physician Dr. Jacob Eduard Polak (1818–1891), wrote several medical books.[29] W. Floor stated that according to Polak, CL was quiet prevalent in Qom, Kashan and Isfahan. He also pointed out that in Sistan, in the south east of Iran, it was a common disease and called it *Dana-i-daghi*.[30] In addition, Dr. Polak described the cases of CL as Aleppo boil (in Persian: *Dokmay-e Halab*).[31]

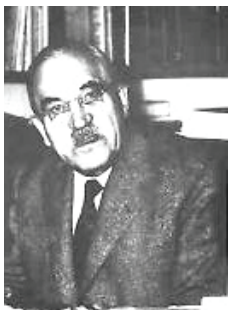
After Polak, the Franco-Mauritian physician, Joseph Desire Tholozan (1820–1897) was the special physician to Nasser al-Din Shah Qajar. He arrived in Iran in 1858 and remained there until his death in 1897. During his long stay in Iran, he studied the endemic diseases of Iran such as the plague, cholera and leishmaniasis[32] and between 1847 and 1892, published several articles and books, mainly on infectious diseases and their epidemiology.[33]

In the last decades of the 19th century, CL was an endemic disease in certain parts of Iran and facial leishmaniasis scars were commonly seen. Isabella Bird (married name Mrs. Bishop, 1831–1904) was a British traveler. In her travel book entitled "Journeys in Persia and Kurdistan" published in 1891 in London, she concentrated on these facial scars of women.[34]

Pioneer physicians and researchers at Tehran Medical School and School of Public Health

After the establishment of the School of Medicine in Tehran in 1934 and the foundation of new medical schools in some major cities of Iran in subsequent years and the establishment of the Public Health School at Tehran University in 1966, some of the pioneer physicians and researchers worked on various aspects of leishmaniasis in Iran. These investigators were:

Professor Charles Oberling (1895–1960), the famous French pathologist, who came to Iran in 1939 and was appointed as the Dean of Faculty of Medicine, Pharmacy and Dentistry in Tehran.[35] He was a prolific researcher and published several articles. One of the earliest recoded scientific papers on pathological aspects of CL in Iran dates back to 1950 which is written by Oberling and entitled, "Remarks on pathology in Iran with special consideration of cutaneous leishmaniasis".[36]


Professor Charles Oberling

Dr. Mohammad Mojallal (b.1898) was a professor of tropical diseases at Tehran University Medical School who authored a textbook on leishmaniasis for the medical students published in 1951.[37]


Dr. Mohammad Mojallal

Dr. Mostafa Habibi-Golpayegani (1904–1948), known as the founder of modern pathology in Iran, was a Professor of Pathology at Tehran Medical School. He wrote several articles including one on CL. In 1942, he reported the histopathologic results of 200 cases of CL in the Medical Journal of Beirut University. Dr. Habibi made a new classification of CL that was subsequently recorded in the French pathology texts.[38]


Dr. Mostafa Habibi-Golpayegani

Habibi-Golpayegani's article on CL was also published in the first issue of the Persian journal known as the Monthly Letter of School of Medicine (*Nameh Mahaneh-ye Daneshkadeh-ye Pezeshki*) in 1943 (Figure 3). In that paper, he mentioned that according to the information collected by the Ministry of Health over a three-year period, CL was common in the central, eastern and south eastern parts of Iran and it was endemic in Tehran, Qom, Mashhad, Semnan, Neishabour, Amol, Isfahan, Kashan, Ferdous, Yazd, Kerman, and occasionally seen in Qasr-e-Shirin, Birjand, and Shahroud. In addition, the name of the former physicians who worked on CL are stated. They included: Dr. Mohammad Hossein Adham (titled Loghman-o-Dowleh) and Dr. Gholamreza Sheikh who wrote their MD dissertations on leishmaniasis in the Paris Medical School in 1917 and 1935, respectively, and Dr. Mohammad Zanganeh, who wrote his MD thesis on the same subject at Tehran Medical School, as well as Dr. Sheikh Mohammad Khan and Dr. Alam-o-Dowleh Saghafi who wrote on leishmaniasis vaccination.[39]

Dr. Yahya Pouya (b.1894) was a French trained specialist of tropical diseases and the director of laboratory of Razi Hospital and faculty of Tehran Metical School who delivered a lecture in

صفحه ۱۸ نتیجه ۲۰۰ بافت برداری در سالك شمارهٔ اول و دوم

٤

آسیب شناسی

نتیجه ۲۰۰ بافت برداری در سالك

نگارش

آقای دکتر مصطفی حبیبی و آقای دکتر ع. ثابتی

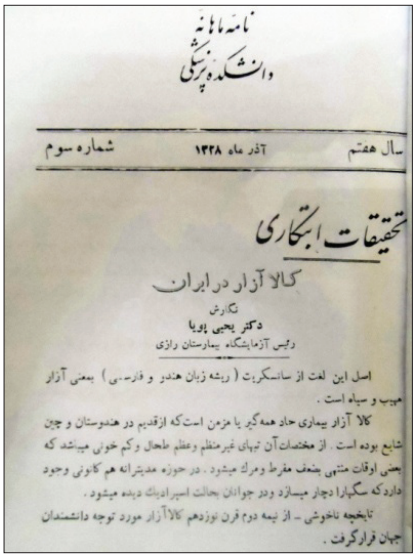
سالك یکی از بیماریهای پوستی است که در اغلب ممالك اروپا کیاب میباشد و بدین سبب علمای باختر زمین بدان گنتر توجه کامل نموده واز آن بویژه ازلحاظ آسیب شناسی اطلاع کافی دردست ندارند . آنچه هم که موجود است باهم متفاوت میباشد و علمای فن درآن باب با یکدیگر توافق نظر کامل ندارند .

تشخیص آسیب شناسی سالك در برخی موارد فوق العاده مشکل است و یافتن مشکل است آترا پاسل و کوفت وحتی چنگرهای (سرطان) پوستی اشتباه نمود. نگارنده در بدو امر بهمین اشکال دچار گردید وبنقض کار خویش پی برد ودرصدد تکمیل آن برآمد و نتیجه کار مقاله ایست که اینك بعرض همکاران گرام میرساند :

تا کنون چندین بار اتفاق افتاده است بیمارانی مثلا زخمهای وسیع جوانه دار ویا تومورهائی بردست ویا ولب فجیره بوده اند که آزمایش بالینی و ظاهر بیماری و سن بیمار و غیره کاملا پزشك را بسوی تشخیص چنگرهای پوستی برده واقدام بیافت برداری آنها نیز برای تعیین نوع چنگر بوده است ولی در آزمایش بافت شناسی سالك تشخیص داده شد و با درمانهای معمولی سالك بیمار بهبود کامل یافت ومتحمل اعمال جراحی قطع دست ویا وغیره نشد .

ضمن بررسی پنجساله سالك درنظر داشت تحقیقات دیگری راجع باین بیماری در

Figure 3. The histopathologic results of 200 cases of cutaneous *Leishmania* [In Persian] reported by Dr. Habibi-Golpayegani and Dr. A Sabeti in the first issue of the journal 'the Monthly Letter of School of Medicine (*Nameh Mahaneh-ye Daneshkadeh-ye Pezeshki*)' in 1943.



نامه ماهانه دانشکده پزشکی

سال هفتم آذر ماه ۱۳۲۸ شماره سوم

تحقیقات ابتکاری

کالا آزار در ایران

نگارش

دکتر یحیی پویا

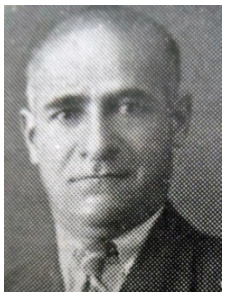
رئیس آزمایشگاه بیمارستان رازی

اصل این لغت از سانسکریت (ریشه زبان هندو و فارسی) بمعنی آزار مهیب و سیاه است .

کالا آزار بیماری حاد همه گیر یا مزمن است که ازقدیم در هندوستان و چین شایع بوده است . از مختصات آن تبهای غیرمنظم وعظم طحال و کم خونی میباشد که بعضی اوقات منتهی بضعف مفرط ومرگ میشود . در حوزه مدیترانه هم کانونی وجود دارد که سگهارا دچار میسازد ودر جوانان بحالت اسپرادیك دیده میشود .

تاریخچه ناخوشی - از نیمه دوم قرن نوزدهم کالاآزار مورد توجه دانشمندان جهان قرارگرفت .

Figure 4. Kala-Azar in Iran, written by Dr. Y. Pouya-1949.



Dr. Yahya Pouya

Dr. Mohammad Ali Maleki

Dr. Naser Ansari

Paris about his experiences on Kala-azar in Iran. It was published in France in 1951.[37,40] The paper was originally published in Persian in 1949, in '*Nameh Mahaneh-ye Daneshkadeh-ye Pezeshki*' (the Monthly Letter of School of Medicine).

In his paper, Dr. Pouya reported three cases of Kala-azar (Figure 4). The first case was a 20-year-old chef from Shahsavar (now Tonekabon), presenting with generalized weakness and splenomegaly, anemia, leukopenia and monocytosis. The Leishman bodies were detected in splenic aspirate. The second case was a 10-year-old girl with lethargy, abdominal protrusion, and fever, as well as hepatosplenomegaly, anemia and monocytosis and the splenic aspiration confirmed the diagnosis. The third case was a 5-year-old child from Tehran, who was admitted to the Razi Hospital in 1949 and the Leishman bodies were detected in her splenic aspirate by Dr. Armin, Professor of pathology. Pouya also mentioned that Kala-azar is an endemic disease in the littoral of the Caspian Sea.[41] In 1953, he used the aspiration technique after skin ulcer aspiration, and the Giemsa staining was performed to detect the Leishman bodies in the macrophages in the cases of CL.

Dr. Mohammad Ali Maleki (1903–1991) graduated from Tehran Medical School in 1928 and continued his training in dermatology in France. He was the founder of the first department of dermatology in Iran. He became a professor of dermatology at Tehran University Medical School In 1949[37] and in April 1949, he attended the 7th congress of French-speaking dermatologists held in Brussels-Belgium and delivered a lecture on common clinical forms of leishmaniasis and their treatment with antimony derivatives in Iran.[36] In 1967, Dr. Maleki published a paper in French, entitled: "Epidemiological, clinical forms and treatment of cutaneous leishmaniasis in Iran."[42]

The Department of Medical Parasitology and Mycology at Tehran Medical School was established in 1940. In due course in 1965, the name changed to the "Institute of Public Health Researches". One year later in 1966, the institute transformed to the 'School of Public Health and Institute of Public Health Researches'.[43] The following researchers at the School of Public Health had a prominent role in the study of leishmaniasis in Iran:

Dr. Naser Ansari (b. 1913) was a graduate of the Dar al-Fonun School. In 1930, he went to Paris and studied parasitology. On his return, he became associate professor of parasitology at Tehran Medical School and a full professor in 1943.[37] He investigated various parasitic diseases, including leishmaniasis. He wrote three papers from 1951 to 1953, including: "CL in *Rhombomys opimus* caused by *L. tropica* (now *L. major)*; a new culture medium for *Leishmania* and *L. tropica* culture in chick chorioallantois"[44,45,46] [*Rhombomys opimus* or great gerbil is a rodent and *L. major* (earlier called *L. tropica,* or *L. tropica* major) is the causative agent of zoonotic cutaneous leishmaniasis (ZCL). Great gerbils are the main reservoir hosts in Iran.[47]]. Dr. Ansari was the advisor of Division of Parasitology (1954), later, the first Director of Parasitic Disease Program of WHO until his retirement in 1975.[48]

Dr. Shams ad -Din Mofidi (1921–2014), Professor of Parasitology at Tehran University Medical School and after Dr. Ansari, Dean of the School of Public Health and Director of Institute of Public Health Research. Mofidi was the Vice Chancellor in charge of Research at the University of Tehran for nearly 20 years. His interest included research on various parasitic diseases of Iran, including leishmaniasis.[37] His thesis under Dr Ansari's mentorship was on experimental leishmaniasis. He infected hundreds of outbred laboratory white mice and noted the different forms of diseases in groups of mice. This was an indication that showed the form of the disease in mice may be genetically controlled.

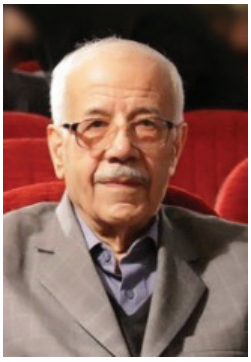
Dr. Mofidi was internationally known and respected for promoting the concept of public health and roles of schools of public health as different from those of schools of medicine for medical education. He was highly respected in International forums and was elected and served as the President of the Executive Board of WHO in the 1970s.


Dr. Shams ad-Din Mofidi

Dr. Abolhassan Nadim (b.1928) is a graduate of Tehran Medical School who continued his training in London in epidemiology and medical parasitology. He became a Professor of Epidemiology and Medical Parasitology at Tehran Medical School. He was the former Dean of School of Public Health, and Director of Institute of the Public Health Research. He started collaborations with the WHO since its establishment.[49] His main academic interests were malaria, zoontic diseases, and leishmaniasis. He is a member of the Academy of Medical Sciences of Iran. His leading efforts during the Iran – Iraq war to protect Iranian forces against CL using leishmanization is exemplary and was globally recognized. He is the author of 5 books and published over 100 papers in Persian and English including several articles on leishmniasis.[48]


Dr. Abolhassan Nadim

Dr.Gholamhossein Edrissian (b.1931) is a graduate of the School of Pharmacy of Tehran University who continued his training on clinical laboratory sciences at the Tehran School of Medicine between 1962 and 1965. He received his MSc in Medical Parasitology from London School of Hygiene and Tropical Medicine in 1969. During 1956–1963, he was a research assistant at the Department of Medical Parasitology, Institute of Public Health Research at Tehran University School of Medicine. He was Assistant Professor of Medical Parasitology and Associate Professor between 1964 and 1968, and Director of Protozoology Unit in the aforementioned department between 1969 and 1975. He became Professor and Director of Protozoology Unit in the Department of Medical Parasitology and Mycology, School of Public Health and Institute of Public Health Research during 1976–2001. His research works mainly focused on the protozoan infestations including leishmaniasis in the endemic areas of Iran. He published 91 articles in English and Persian.[48] Dr. Edrissian and his colleaques introduced the application of Direct Agglutination Test (DAT) for diagnosis and Seroepidemiological studies of VL in Iran.


Dr. Gholamhossein Edrissian

Dr. Farrokh Modabber (b.1940) received his Bachelor in Bacteriology (1964) and PhD in Microbiology/Immunology from the University of California (1968), and continued his fellowship training at the Harvard Medical School in 1969–1972, and then joined the faculty of Harvard School of Public health as assistant professor. He initially joined the Faculty of Medicine of Shiraz University and between 1973 and 1974, he was an Associate Professor of Immunology. Then in 1975, he became Associate Professor of Immunology at Tehran University, School of Public Health and was appointed the Chairman of Pathobiology Department between 1976 and 1980. From 1978 to 1979, he was appointed the Director General of the Pasteur Institute of Iran, while keeping his university appointment. He is a creative researcher and has devoted most of activities to leishmaniasis during the past 3 decades, in particular, promoting leishmaniasis research in Iran from his International positions. While at Tehran, for the first time he established the genetic control of leishmaniasis in mice by importing different inbred strains of mice to Iran and then it distributed to various institutes such as Pasteur, Razi, etc. His group at the School of Public Health in Tehran described the natural history of infection in different strains of mice and in particular developed the BALB/c - *L. major* model which has become widely used globally for vaccine and drug development studies against leishmaniasis (Nasseri and Modabber). Later at Pasteur Institute, Paris, as a visiting scientist, he showed that cutaneous leishmaniasis is always associated with a generalized infection and that live *Leishmania* persists long after the skin lesion is cured. Hence, if the immune response is compromised, i.e. following HIV infection, a generalized leishmaniasis develops; otherwise, a protective immunity prevents disease for life.


Dr. Farrokh Modabber

He was responsible for leishmaniasis research at The Special Program for Research and Training on Tropical Disease of WHO (1984–2000), he brought numerous projects to Iran on *Leishmania* vaccine and drug trials. The first ethical review committee for clearing clinical trials in Iran was established in the early 1980s for vaccine trials under the auspices of the Ministry of Health, during the tenure of Dr. Sadrizadeh as Deputy Minister of Health. He served as a member of The Iran Ministry of Health Committee for National Guidelines on Clinical Studies. Until 2015, he has authored 15 book chapters as well as 85 articles including about 50 on leishmaniasis. His main scientific interest is *Leishmania* vaccine. He is a member of the WHO Expert Advisory Panel on Parasitic Diseases (Leishmaniasis) from 2009 until now and Senior Advisor for Leishmaniasis at Drugs for Neglected Diseases Initiative.

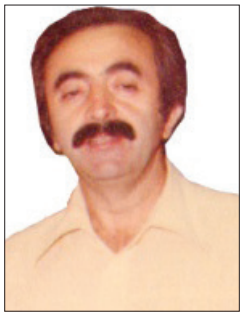
Researchers of other medical schools

Shiraz School of Medicine

The "Shiraz Medical Auxiliary Training School" as the forerunner of Shiraz Medical School was founded in 1946.[37]

Dr. Kamal Dana Haeri

Dr. Sadraddin Mohseni Ardehali



Dr. Hamid Reza Rezaei

Dr. Hossein Farid

Dr. Kamal Dana Haeri (1909-1976) was the medical graduate of Sorbonne University- France who continued his training in London and came back to Iran in 1946. He was a specialist of tropical diseases and hygiene who was appointed as the Associate Professor of Microbiology and Parasitology at the Shiraz Medical Auxiliary Training School in 1946 and then joined the faculty of Shiraz Medical School. [50]

Shiraz Medical School was founded in 1952. The Parasitology Department of Shiraz Medical School was initially a part of the Microbiology Department. The main researches at this department had been immunological aspects of experimental leishmaniasis and development of immunodiagnostic tools for VL through studies carried out by Dr. Hamid Reza Rezaei, Dr. Sadraddin Mohseni Ardehali, and Dr. Mehdi Kabiri. The Parasitology and Mycology Department became independent in 1996 and the studies on leishmaniasis have continued until the present time.[51]

Dr. Sadraddin Mohseni Ardehali (1941–2002) received his PhD of Microbiology and Immunoprotozoology from the School of Hygiene and Tropical Medicine, London, England in 1974. He was Assistant Professor Department of Microbiology, at Shiraz University Medical School between 1974 and 1978 and became full professor in 1991. He carried out several researches on leishmaniasis including on acquired and innate immunity in experimental leishmaniasis, the effect of humoral factors on *Leishmania* organisms, immunology and immunodiagnosis of the parasitic diseases prevalent in Iran including leishmaniasis, production and partial characterization of monoclonal antibodies against *Leishmania* organisms[48] and performed a study on the immunology of leishmaniasis. In total, Dr. Ardehali has published 43 original papers on leishmaniasis. His first study on leishmaniasis was published in 1980.[52] He authored a Persian book on *Leishmania* parasite and leishmaniasis in collaboration with Dr. Rezaei and Dr. Nadim which was published in 1985.[53]

Dr. Hamid Reza Rezaei (b.1937) was a graduate of Tehran Pharmacology School who went to the USA and continued his training at the University of California, Davis, and then returned to Iran and joined the Microbiology Department of Shiraz Medical School to be later appointed as its director. He worked with Dr. Ardehali on immunological aspects of leishmaniasis. Dr. Rezai is known for describing the serological response in guinea pigs to *L. enriettii* and evaluating serum antibodies by immunofluorescence test. He described the *in vitro* anti-leishmanial activity of normal animal sera and developed a serological test for VL using cross immune-electrophoresis.

Dr. Bahram Azadeh at the pathology department of Shiraz School of Medicine and his co-authors worked on immunohistochemical CL and localized *Leishmania* lymphadenitis (LLL) in the 1980s.[54, 55]

Pathologic and electron microscopic study of the VL (Kala-azar) were also carried out by Dr. Khosrow Daneshbod in the pathology department of Shiraz School of Medicine, and the results were published in 1972.[56] Dr. Abdolvahab Alborzi, the Professor of Pediatrics at the Shiraz Medical School also worked on Leishmaniasis, mainly Kala-azar in southern Iran.

Mashhad School of Medicine

The Parasitology Department of the Mashhad School of Medicine became independent in 2003. Before that time, it was a part of the Laboratory Sciences Department. The founders of the department were Dr. Mirdamadi, Dr. Issi and Dr. Azim Ouskoueean. Later, three parasitologists had a major role in the progress of parasitology in Mashhad University. They included Dr. Manouchehr Motakef, Dr. H. Rezvani and Dr. Hossein Fouad Nejati (from Egypt).[57] CL is endemic in North Eastern Iran, thus several investigations have been carried out there.[58] One recent study showed that the seroprevalence rate of canine leishmaniasis in the owned and stray dogs from Mashhad is relatively high.[59]

Isfahan Medical School

In 1968, a pathobiology group was founded in Isfahan Medical School by Dr. Kambiz Hazeghi. In 1991, it was divided into two independent groups, one named microbiology, virology and immunology, and the other mycology and parasitology group.[60]

Dr. Tahmoors Jalayer (b.1931) is a DVM graduate who completed his training in tropical diseases in Liverpool University–UK and on his return to Iran, he initially joined the Parasitology Department of Shiraz Medical School, and then in 1971, became an associate professor at Isfahan Medical School. He collaborated with Dr. Momeni and others in the TDR/WHO *Leishmania* vaccine project.[48]

Dr. Hossein Farid (b.1935), a PhD of parasitology and professor of Isfahan School of Medicine who worked on Leishmania.[48]

Dr. Parviz Dabiri (1921–2012) was professor of pathology at the Isfahan Medical School who investigated various subjects including CL (wet form) and VL since 1953 in Isfahan.[61]

Tabriz Medical School

The forerunner of the parasitology department at the Tabriz Medical School was founded in 1953 and it became independent in 1998.[62] In 1961, a paper was published in the WHO Bulletin entitled, "Observations on phlebotomine sandflies in Iran" and according to the authors, the search on sandflies was carried out in Tabriz and Sarab in Azarbaijan Province, as well as in the Caspian Sea regions, Tehran and Kazeroun. [63]

Ahvaz School of Medicine

Parasitology, Mycology and Entomology Department at the Ahvaz School of Medicine was founded in 1957. The first Director was Dr. Behin and then in 1971 Dr. Ebrahimzadeh became its director. Parasitology investigation was also performed at this department.[64]

Other Researchers

Dr. Ahmad Mesghali (b.1912), a MD graduate of Tehran Medical School who worked on *Leishmania* vectors.[48]

Dr. Mohammad Ali Seyedi Rashti (b.1930), a professor of entomology and parasitology at the Public Health School and advisor of WHO on leishmaniasis who went to Saudi Arabia in 1978 to control leishmaniasis and in 1985, he was WHO educational advisor in Pakistan.[48]

Dr. Ezzat-o-Din Javadin (b.1931) a graduate of Tehran Veterinary Medicine School in 1954 who became a parasitologist in 1960 and worked on leishmaniasis.[48]

Dr. Reza Fesharaki (b.1936), a graduate of Tehran Veterinary Medicine School in 1961, who worked at the Parasitology Department of the Razi Vaccine and Serum Institute, Hessarak, Alborz Province, Iran between 1966 and 2002. He worked on the production of the killed *Leishmania* vaccine in collaboration with TDR/WHO.[48]

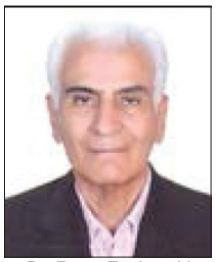
"The Center for Research and Training in Skin Disease and Leprosy" was founded by Dr. Yahya Dowlati (b.1934) in 1992. He is a graduate of Tehran Medical and an American trained dermatologist who returned to Iran in 1972. Dr. Dowlati was the Director of the National Research Committee of Leishmaniasis between 1992 and 1996. In a recent interview, he pointed out that from the beginning of the foundation of the Center for Research and Training in Skin Disease and Leprosy, several researches on leishmaniasis including the immunity to CL, *Leishmania* vaccine and promoting the leishmaniasis therapeutic modalities were carried out in this center.[65–67] Dr. Dowlati was recipient of grants from TDR/WHO for development of a first generation vaccine and for clinical trials of the vaccine. He and his colleagues (Drs A. Firooz, A. Khamesipour, M. Nassiri-Kashani, etc.) at the institute have been highly influential in promoting GCP training in various universities in Iran and performing numerous clinical trials on drugs and the first generation vaccine against leishmaniasis. He has edited a monogram on CL which has become a reference for investigators.

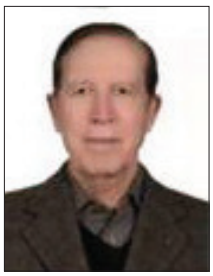
Dr. Mehdi Mohebali (b.1958) is a graduate of the Faculty of Veterinary Medicine of Tehran University in 1985. He received his MPH and PhD in Medical Parasitology from the School of Public Health and Institute of Public Health Researches, Tehran University of Medical Sciences. He currently is the full Professor at Department of Medical Parasitology and he was the Director of Leishmaniasis Laboratory in the Department of Medical Parasitology at the School of Public Health and Institute of Public Health Researches from 2001 until now. His research works mainly focus on parasitic infections, particularly cutaneous and visceral leishmaniasis. He published around 200 articles in Persian and English including 94 papers on leishmaniasis in PubMed database from 1996 to 2015.


Dr. Ahmad Mesghali


Dr. Mommad Ali Seydi Rashti


Dr. Ezzat-o-Din Javadin


Dr. Reza Fesharaki


Dr. Yahya Dowlati


Dr. Mehdi Mohebali

Current status of leishmaniasis in Iran

According to data of the Ministry of Health published in 2012, around 20,000 cases of leishmaniasis are annually reported in Iran, however, the real incidence is 4 or 5 times more. CL in Iran is of two types: the rural form (called wet) and the urban form (dry). The wet form is common in the rural areas of 15 provinces in Iran. The dry form is endemic in the most cities. Over 90% of cases occurred in 88 cities of 17 provinces of Iran.[68]

Published Articles on leishmaniasis

There are 793 articles on leishmaniasis in Iran at PubMed indexing system and 526 papers are devoted to CL, between 1950 and 2014. From 1968 to 2014, 207 papers appeared on PubMed are published on VL in Iran.[69] The first paper is written by Dr. M. Ziai, a pediatrician in Nemazee Hospital in Shiraz and J.E. Bowman, C.W. McMillan and M. Tabatabaei dated 1968.[70]

In recent years, several researchers have worked on leishmaniasis in Iran. According to Mohbali, ZVL occurs sporadically in all geographical zones; however, it is endemic in northwest and south of Iran.[71]In a recent study published in 2015, geographic information of ZCL in Golestan province in northeastern Iran, the investigators detected that most cases of ZCL were related to areas with altitudes low-

Figure 5. Three photos of patients with CL. (from the Dermatology Department, Afzalipour Kerman University of Medical Sciences by the fourth author). **a)** A 2-year old boy with non-painful nodule on his lip for 8 months He received intralesional Glucantime with complete improvement (Cutaneous type, not mucocutaneous). **b)** A 12-year girl with two ulcerative facial plaques for 15 months. She was treated with intralesional Glucantime associated with liquid nitrogen. **c)** A 15-year old girl from Bam with history of leishmaniasis from three years prior to referral. She received Glucantime and cryotherapy with complete improvement, but developed papular lesions around scar after two years. Cryotherapy, intralesional Glucantime plus steroid were started and she improved (Lupoid type).

er than 725 meters above sea level and mostly dry and semi-arid climates.[72] In a study of 11,517 primary school children, between 1994 and 1995 in the city of Bam in Kerman province, in south-eastern Iran, Sharifi *et al.* found that 1.3% of the children developed acute CL and 14.3% had post-leishmaniasis cutaneous scars [73] In another article (2011), the authors reported the emergence of a new focus of anthroponotic CL (ACL) in rural areas of Bam district in Kerman Province after the earthquake of December 26, 2003. In 2006, the number of cases of ACL in Bam increased significantly and an outbreak occurred[74] (Figure 5).

LLL is a rare clinical form of leishmaniasis with lymph node involvement but no systemic manifestations and favorable prognosis. It has been reported a number of times from south-eastern Iran, including from Kerman and Fars provinces. *L. tropica* was the responsible organism which was detected by the real- time PCR technique[75] (Figure 6).

In the last decade, the annual incidence of CL increased in Khouzestan Province in south–western Iran. According to Ghasemian *et al.* and major outbreaks occurred in 2003 and 2004 mainly caused by *Leishmania* major (and *L. tropica*). In their study, the leishmanial DNA were detected by PCR technique.[76]

In a study by Daneshbod *et al.* reported in 2010, the authors described the results of bone marrow aspiration of 204 patients with Kala-azar and concluded that bone marrow aspiration is helpful in correct diagnosis, avoidance of unnecessary workups and prevention of fatal outcomes in untreated or non-diagnosed cases of VL.[77]

In another study in 2013, the investigators reported that in rural areas of Mirjaveh, Chabahar, and Konarak in Sistan and Baluchistan Province in south eastern Iran, ZCL is a major health problem and a rodent known as Indian desert jird (*Meriones hurrianae*) serves as natural reservoir host for ZCL and is responsible for continuation and transmission of ZCL to humans.[78] In 2002, a new endemic focus of CL caused by *L. tropica* in Yazd City in Central Iran was reported in which humans were considered as the main reservoir and transmission from human to human probably occurred by *Phlebotomus sergenti*.[79]

Recent efforts to prevent leishmaniasis in Iran

According to Noazin *et al*., it was known from antiquity that after CL recovery, immunity to the disease occurs. Accordingly, inoculation of the exudate of the active cutaneous ulcer into part of the body of healthy children was carried out to prevent occurrence of CL in exposed parts of the body including the face. This

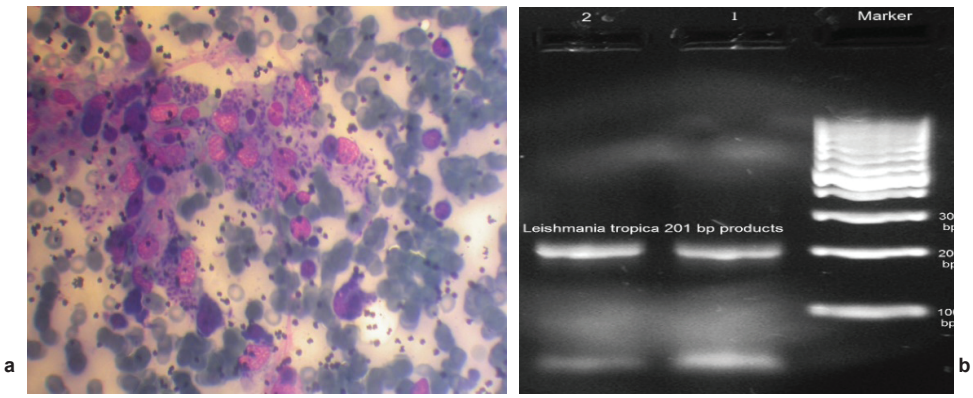


Figure 6. a) Direct smear shows many intracytoplasmic in the histiocytes and extracytoplasmic Leishman bodies with their diagnostic kinetoplasts (Giemsa staining, magnification ×400). **b)** Electrophoresis of PCR end product confirms diagnosis of *L. tropica* [Prepared at the Pathology Department, Afzalipour Kerman University of Medical Sciences, Kerman, Iran, by the third author]

method was called "leishmanization". Afterwards, live virulent promastigotes, (the morphologic stage in the development of *L. major*) substituted inoculation method and in the 1980s, a massive prophylactic *Leishmania* vaccination program started and covered over two million people during the Iran-Iraq war of 1982–1986. However, it was stopped after the war and a national vaccine development program was started at the Razi Vaccine and Serum Institute, Hessarak, Iran to develop a killed *Leishmania* vaccine.[80] The investigation on *Leishmania* vaccine is still continuing in Iran.[81] In recent years, Dr. Sima Rafati, Head of Laboratory of Molecular Immunology and Vaccine Research of Pasteur Institute of Iran has been actively investigating new biotechnological approaches to develop new vaccines to prevent Leishmaniasis.

Dr. Rafati isolated the genes of cysteine proteases of *L. major* and was the first scientist to upload the sequences in International Gene Banks. She has also developed *L. tropica*- mouse model using recombinant *Leishmania* carrying genetic markers such as luciferase and /or EGFP genes to follow parasite loads.[82] In a recent paper, published in 2014, the investigators pointed out that the most infected people with *Leishmania* parasites eventually have power over parasites growth without developing severe disease; in addition, the immune responses needed for killing the parasite and the immunological reactions suppressing the immunity to leishmaniasis are identified; therefore, developing vaccines against leishmaniasis is a reasonable aim.[83]

Acknowledgment

The authors wish to thank Dr. Farrokh Moddaber for sending his CV and photograph, Dr. Seyed Mahmoud Sajjadi, Professor of Parasitology for sending the CV and photograph of Dr. S.M. Ardehali, Dr. Abbas Ghaderi, and Professor of Immunology for sending Dr. H. Rezaei's CV and photo, and Dr. Jila Dana Haeri for sending the biography of her father, Professor Haeri. We would also like to express our gratitude to Dr. Abolhassan Nadim and Dr. Touraj Nayernouri for reviewing the paper and their valuable comments.

References

1. Costa DC, Palmeiro MR, Moreira JS, Martins AC, da Silva AF, de Fátima Madeira M, Quintella LP, et al. Oral manifestations in the American tegumentary leishmaniasis. *PLoS One*. 2014; **1:** 9 – 11.
2. Sellheyer K, Haneke E. Protozoan diseases and parasitic infestations. In: Elder DE. *Lever's Histopathology of Skin*. 9th ed. USA: Lippincott Williams & Wilkines; 2005: 635.
3. Marra F, Chiappetta MC, Vincenti V. Ear, nose and throat manifestations of mucocutaneous Leishmaniasis: a literature review. *Acta Biomed*. 2014; 85(1): 3 – 7.
4. Leishmaniasis. Available from: URL: http://www.who.int/leishmaniasis/about_disease/en/ (Accessed in 26.12.2014)
5. Leishmaniasis. Fact sheet No.375 WHO. Updated Jan 2014. Available from: URL: http://www.who.int/mediacentre/factsheets/fs375/en/ (Accessed in 26.12.2014).
6. Leishmaniasis. Available from: URL: http://www.cdc.gov/parasites/leishmaniasis/ (Accessed in 26.12.2014)
7. Leishmaniasis, Burden and Distribution. Available From: URL: http://www.who.int/leishmaniasis/burden/en/ (Accessed in 26.12.2014).
8. Cox EG. History of Human Parasitology. Discovery of the Parasitic Protozoa. *Leishmania* and Leishmaniasis. *Clin Microbiol Rev*. 2002; 4: 595 – 612.
9. Hotez PJ, Savioli L, Fenwick A. Neglected Tropical Diseases of the Middle East and North Africa: Review of Their Prevalence, Distribution, and Opportunities for Control. Available From: URL: www.plosntds.org/ (Accessed in 2012: 6: 2: e1475).
10. World Health Organization Control of the leishmaniases. World Health Organ Tech Rep Ser. 2010; 949: 186.
11. Bailey H, Bishop WJ. Leishman-Donovan Bodies and Donovaniasis, Sir William Boog Leishman (1865–1926), Charles Donovan (1863–1951). *Brit J Vvener Dis*. 1959; 35: 8.
12. Leishmaniasis in humans. Control of the leishmaniasis, WHO, Geneva, 2010:8.
13. Oumeish OY. Cutaneous Leishmaniasis Historical Perspective. *Clin Dermatol*. 1999: 17(3): 249 – 254.
14. Elgood C. The Early History of the Baghdad Boil. *Journal of the Royal Asiatic Society of Great Britain & Ireland (New Series)*. 1934; 66(3): 519 – 533.
15. Rafati S, Modabber F. History of Cutaneous Leishmaniasis. In: McDowell MA, Rafati S, eds. *Neglected Tropical Diseases -Middle East and North Africa*. Berlin, Germany: Springer. 2014: 118 – 120.
16. Tuon FF , Neto VA, Amato VS. Leishmania: origin, evolution and future since the Precambrian. *FEMS Immunol Med Microbiol*. 2008; 54(2): 158 – 166.
17. Zink A R, Spigelman M, Schraut B, Greenblatt CL, Nerlich AG, Donoghue HD. Leishmaniasis in Ancient Egypt and Upper Nubia. Emerging Infectious Diseases. 2006: 12: 10. Available from: URL: www.cdc.gov/eid (Accessed in 22.1.2015).
18. Kala-azar. The Merriam-Webster Dictionary. Available from: URL: http://www.merriam-webster.com/dictionary/kala-azar (Accessed in 20.1.2015).
19. Hayani K, Dandashli A, Weisshaar E. Cutaneous Leishmaniasis in Syria: clinical features, current status and the effects of war. *Acta Derm Venereol*. 2015; 95: 62 – 66.
20. Elgood C. *A Medical History of Persia and the Eastern Caliphate: From the Earliest Times until the Year A.D. 1932*. UK: Cambridge University Press; 1951.
21. Elgood C. The early history of cutaneous leishmaniasis. *J Roy Asia Soc*. 1934; 3: 519 – 533.
22. Physician 2004: 69: 6. Available from: URL: www.aafp.org/afp (Accessed in 14.1.2015).
23. Leishmaniasis. Medline Plus. Available from: URL: http://www.nlm.nih.gov/medlineplus/ency/article/001386.htm (Accessed in 27.12.2014).
24. Markel WH, Makhoul K. Cutaneous Leishmaniasis: Recognition and Treatment. American Academy of Family Physicians; 2004.
25. Abu- Ali Sina. *The Canon of Medicine*. Book 1, Translated into Persian by A. Sharafkandi (Hajar). Tehran: Soroush Press; 1985: 182.
26. Jorjani SA. Zahkirye-KharzmShahi [In Persian]. First ed. Edited by Dr. M. R. Mohhareri. Tehran: Academy of Medical Sciences of I.R. Iran; 2002: 162.
27. Razi B. Kholasat ol-Tajarob [Persian]. The Institute for Medical History-Islamic and Complementary Medicine, Tehran University of Medical Sciences, Tehran; 2000.
28. Nadim A, Javadin A, Mohbali M, Zameni M, et al. *The Leishmania Parasite and Leishmaniasis* [in Persian]. Tehran: The Academic Publication Center. 2008; 213 – 217.
29. Adamiyat F. Amir Kabir and Iran, Tehran [in Persian]. 5th ed. Tehran: Kharazmi Publication; 1978.
30. Floor W. *Public Health in Qajar Iran*. Washington, DC: Mage Publishers; 2004: 35.
31. Polak JE. *The Polak's Travel book; Iran and Iranians*. Persian translation by K. Jahandari. Tehran: Kharazmi Publication; 1982.
32. Ebrahimnejad H. *Medicine in Iran: Profession, Practice and Politics, 1800–1925*. NY: Palgrave Macmillan; 2013: 99.
33. Théodoridès J. A great Franco-Mauritian epidemiologist: Joseph Desire Tholozan (1820–18970) [in French]. *Bull Soc Pathol Exot*. 1998; 91(1): 104 – 108.
34. Bosworth CE. Isabella L Bird. In: *Encyclopedia Iranica*. Available from: URL: http://www.iranicaonline.org/articles/bird-isabella-l (Accessed in: 1.1.2015).
35. Azizi MH. In memory of the late Professor Charles Oberling. *Arch Iran Med*. 2005: 8(4): 336 – 338.
36. Oberling C. Remarks on pathology in Iran with special consideration of cutaneous leishmaniasis. *Pathol Gen*. 1950; 50(617): 306 – 316.
37. A Guide to the Schools of Medicine, Pharmacy, Dentistry, Hospitals and Affiliated Schools of University of Tehran [in Persian]. Tehran: Tehran University Press; 1951: 56 – 57.
38. Azizi MH, Bahadori M. In commemoration of Dr. Mostafa Habibi-Golpayegani (1904–1948): pioneer of modern pathology in Iran. *Arch Iran Med*. 2006; 9(4): 438 – 441.

39. Habibi-Golpayegani M, Sabeti A. The histopathologic results of 200 cases of CL [in Persian]. *The Monthly Letter of School of Medicine (Nameh Mahaneh-ye Daneshkadeh-ye Pezeshk)*.1943: 1.
40. Pouya M. Kala-Azar in Iran. *Sang*. 1951; *22*(2): 162 – 165.
41. Pouya Y. Kala-Azar in Iran [in Persian]. *The Monthly Letter of School of Medicine (Nameh Mahaneh-ye Daneshkadeh-ye Pezeshki)*. 1949: 7(3): 118–121.
42. Maleki MA. Epidemiological, clinical forms and treatment of cutaneous leishmaniasis in Iran. *Dermatol Int*. 1967: 6(3): 152 – 153.
43. History. School of Public Health. Tehran University of Medical Sciences. Available from: URL: sph.tums.ac.ir/page.php?slct_pg_id=2096&sid=6&slc_lang=en.
44. Ansari N, Faghih M. Cutaneous leishmaniasis in *Rhombomys opimus* Caused by *Leishmania tropica*. *Ann Parasitol Hum Comp*. 1953: 28(4): 241 – 246.
45. Ansari N, Faghih A. New culture medium for *Leishmania*. *Bull Soc Pathol Exot Filiales*. 1952; 45(1): 43 – 45.
46. Oberling C, Ansari N. *Leishmania* tropica culture in chick chorio-allantois. *Bull Soc Pathol Exot Filiales*. 1951; 44(9-10): 542 – 545.
47. Najafzadeh N, Sedaghat MM, Sultan SS, Spotin A, Zamani A, Taslimian R, et al. The existence of only one haplotype of *Leishmania major* in the main and potential reservoir hosts of zoonotic cutaneous leishmaniasis using different molecular markers in a focal area in Iran. *Rev Soc Bras Med Trop*. 2014; 47(5): 599 – 606.
48. The Final Report of Research Project of the Medical Parasitology Information Bank of Iran [in Persian]. The Iranian Academy of Medical Sciences, Tehran; 2014: 190 – 191.
49. Available from: URL: http://isp.tums.ac.ir/Staffs/ (Accessed in 1.1.2015).
50. Dana Haeri J. In Memory of Professor Kamal Dana-Haeri (1909–1976). In: Azizi MH, ed. A *Collection of Essays on the History of Shiraz Medical School;* In *Honor of Professor Faramarz Ismail-Beigi*. Tehran: Mirmah Publication; 2015.
51. Shiraz University of Medical Sciences, School of Medicine, Department of Parasitology and Mycology, Historical Perspective. Available from: URL: http://home.sums.ac.ir/~parasito/ (Accessed in: 21.1.2015).
52. Ardehali S, Sodeiphy M, Haghighi P, Rezai H, Vollum D. Studies on chronic (lupoid) leishmaniasis. *Ann Trop Med Parasitol.* 1980; 74(4): 439 – 445.
53. Ardehali S, Rezaei HR, Nadim A. *Leishmania Parasite and Leishmaniasis* [in Persian]. Tehran: Academic Press; 1985.
54. Azadeh B, Samad A, Ardehali S. Histological spectrum of cutaneous leishmaniasis due to Leishmania tropica. *Trans R Soc Trop Med Hyg*. 1985; 79(5): 631 – 636.
55. Azadeh B. Localized *Leishmania* lymphadenitis: a light and electron microscopic study. *Am J Trop Med Hyg*. 1985: 34(3): 447 – 455.
56. Daneshbod K. Visceral leishmaniasis (kala-azar) in Iran: a pathologic and electron microscopic study. *Am J Clin Pathol*. 1972: 57(2): 156 – 166.
57. The History of Parasitology Department of the Mashhad University of Medical Sciences. Available from: URL: http://www.mums.ac.ir/paramycoldept/fa/Group_history (Accessed in: 1.1.2015).
58. Heidarpour M, Pourtaghi M, Khoshnegah J. Prevalence and risk factors for canine leishmaniasis in Mashhad, North-East of Iran. *Iranian Journal of Veterinary Science and Technology*. 2012: 4(1): 37 – 46.
59. Vaeznia H, Dalimi A, Sadraei J, Pirstani M. Determination of *Leishmania* species causing cutaneous leishmaniasis in Mashhad by PCR-RFLP method . *Archives of Razi Institute*. 2009: 64(1): 39 – 44.
60. Available from: URL: http://med.mui.ac.ir/index.php 61 (Accessed in: 21.1.2015).
61. Dr. Parviz Dabiri Biography [in Persian]. Isfahan Medical School. Available from: URL: http://med.mui.ac.ir/index.php.html (Accessed in 11.1.2015).
62. The History of Parasitology Department, Tabriz Medical School. Available from: URL: http://medfac.tbzmed.ac.ir/?PageID=142 (Accessed in: 11.1.2015).
63. Lewis DJ, Mesghali A, Djanbakhsh B. Observations on Phlebotomine Sandflies in Iran. *Bull World Health Organ*. 1961; 25: 203 – 208.
64. History of Ahvaz School of Medicine. Available from: URL: http://fmedicine.ajums.ac.ir/HomePage.aspx?TabID=15326&Site=fmedicine.ajums.ac&Lang=fa-IR (Accessed In: 17.2.2015).
65. Available from: URL: http://hakimemehr.ir/news/show_detail.asp?id=2626 (Accessed in 23.1.2015).
66. A Short interview with Dr. Yahya Dowlati, the Founder of the Center for Research and Training in Skin Disease and Leprosy [in Persian]. *Teb va Tazkiyeh J*. 2013: (21): 1: 69 – 77.
67. Available from: URL: http://www.ams.ac.ir/index.php/cv/411 (Accessed in 23.1.2015).
68. Shirzadi MR. The guide for care of the patients with leishmaniasis [in Persian]. Ministry of Health and Medical Education. Tehran, Iran; 2012.
69. Available from: URL: http://www.ncbi.nlm.nih.gov/pubmed/?term=cutaneous+leishmaniasis+in+iran (Accessed in: 27.12.2014).
70. Ziai M, Bowman JE, McMillan CW, Tabatabaei M. Leishmaniasis in southern Iran: the occurrence of the three varieties in the same area. *Trans R Soc Trop Med Hyg*. 1968; 62(5): 668 – 671.
71. Mohbali M. Visceral leishmaniasis in Iran: review of the epidemiological and clinical features. *Iran J Parasitol*. 2013; 8(3): 348 – 358
72. Mollalo A1, Alimohammadi A, Shirzadi MR, Malek MR. Geographic information system-based analysis of the spatial and spatio-temporal distribution of zoonotic cutaneous leishmaniasis in Golestan Province, north-East of Iran. *Zoonoses Public Health*. 2015; 62(1): 18 – 28.
73. Sharifi I , Fekri AR, Aflatoonian MR, Nadim A, Nikian Y, Kamesipour A. Cutaneous leishmaniasis in primary school children in the south-eastern Iranian city of Bam, 1994-95. *Bull World Health Organ*. 1998; 76(3): 289 – 293.
74. Sharifi I, Poursmaelian S, Aflatoonian MR, Ardakani RF, Mirzaei M, Fekri AR, et al. Emergence of a new focus of anthroponotic cutaneous leishmaniasis due to *Leishmania tropica* in rural communities of Bam district after the earthquake, Iran. *Trop Med Int Health*. 2011: 16(4): 510 – 513.
75. Dabiri S, Safavi M, Shamsi Meymandi S, Yousefi K, Shamsi Meymandi M, Fotouhi Ardakani R, et al. Molecular pathology and histopathological findings in localized *Leishmania* lymphadenitis. *Arch Iran Med*. 2014; 17(2): 122 – 126.
76. Ghasemian M, Maraghi S, Samarbafzadeh AR, Jelowdar A, Kalantari M. The PCR-based detection and identification of the parasites causing human cutaneous leishmaniasis in the Iranian city of Ahvaz. *Ann Trop Med Parasitol*. 2011: 105(3): 209–215.
77. Daneshbod Y, Dehghani SJ, Daneshbod K. Bone marrow aspiration findings in kala-azar. *Acta Cytol*. 2010: 54(1): 12 – 24.
78. Kassiri H, Naddaf SR, Javadian EA, Mohebali M. First report on isolation and characterization of *Leishmania major* from *Meriones hurrianae* (Rodentia: Gerbillidae) of a rural cutaneous leishmaniasis focus in south-eastern Iran. *Iran Red Crescent Med J*. 2013: 15(9): 789–793.
79. Yaghoobi-Ershadi MR, Hanafi-Bojd AA, Javadian E, Jafari R, Zahraei-Ramazani AR, Mohebali M. A new focus of cutaneous leishmaniasis caused by *Leishmania tropica*. *Saudi Med J*. 2002: 23(3): 291 – 294.
80. Noazin S, Modabber F, Khamesipour A, Smith PG, Moulton LH, Nasseri K, et al. First generationleishmaniasis vaccines: a review of field efficacy trials. *Vaccine*. 2008: 26(52): 6759 – 6767.
81. Khamesipour A, Rafati S, Davoudi N, Maboudi F, Modabber F. Leishmaniasis vaccine candidates for development: a global overview. *Indian J Med Res*. 2006: 123(3): 423 – 438.
82. The Laboratory of Molecular Immunology and Vaccine Research of Pasteur Institute of Iran. Available from: URL: http://en.pasteur.ac.ir/Pages.aspx?Id=839 (Accessed in 19.2.2015).
83. Kumar R, Engwerda C. Vaccines to prevent leishmaniasis. *Clinical & Translational Immunology*. 2014; 3: e13.