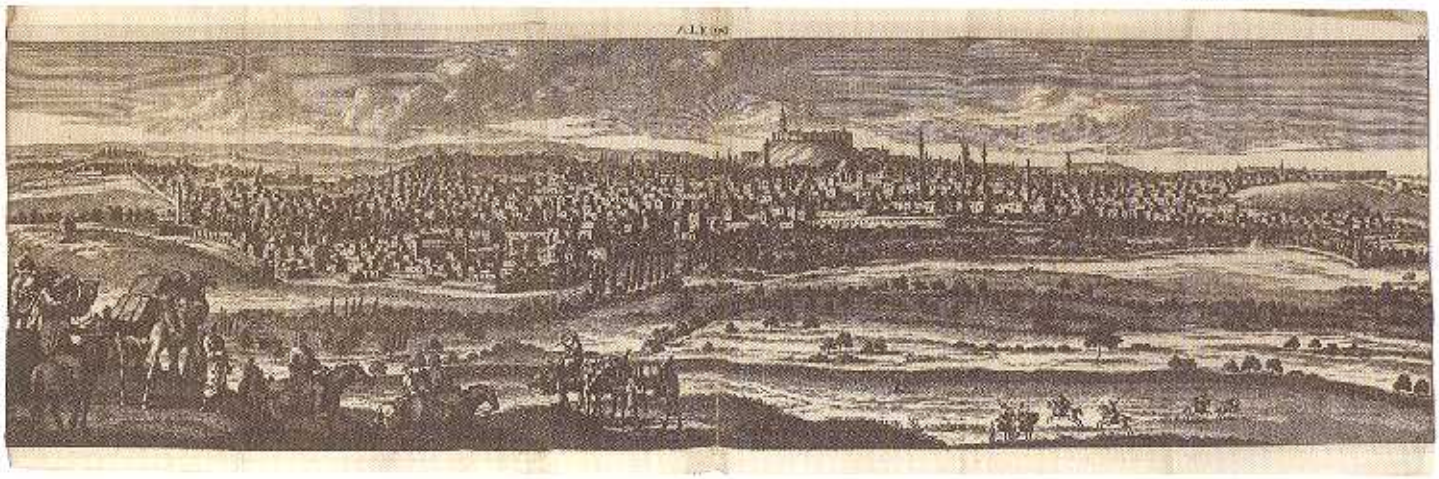

Oriental sore

An ancient tropical disease and hazard for European travellers

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One of the commonest souvenirs for Europeans travelling in Asia or North Africa in the 18th and 19th centuries was an Oriental sore or bouton d'Orient. These were often named according to the place they were acquired, such as Aleppo evil, bouton d'Alep, Haleb choban (Turkish for Aleppo ulcer), clou de Biskra, clou de Mila, Delhi boil, Baghdad boil, Jericho boil, bouton de Crète, Caniotica (also in Crete), Balkh sore (in Afghanistan) and Penjdeh sore (in Turkmenistan).

Other names gave ideas of the nature of the infection, such as the time to spontaneous cure or the time sores appeared. Examples are Elizabethpol godovik (Elizabethpol is a town in the Caucasus and godovik means annual; anthroponotic cutaneous leishmaniasis usually heals about one year after infection), bouton d'un an (sore of one year), and Habt il senne (in Aleppo – again referring to the duration of one year) and Habb Mta el Tmar (date sore – because, in Algeria, the lesions appeared as the dates ripened). In Turkmenistan it was called Sart sore (from the name of a tribe) and, in Arabic countries of the Middle East, Al Okht (the little sister – because everybody has one).

Above: Panorama of Aleppo. From Corneliis de Bruyn's *A voyage to the Levant*, 1702.

A thousand years ago, the great Persian physician Ahū 'Alī al-Ḥusayn ibn 'Abd Allah ibn Sina (981–1037), better known in western Europe as Avicenna, gave what is arguably the best early clinical description of cutaneous leishmaniasis. From that time onwards, there were several accounts in Farsi or Arabic of skin infections that were almost certainly leishmaniasis. Most of these early accounts describe dry lesions that suggest urban anthroponotic infections caused by *Leishmania tropica* (Wright), rather than the rural, wet zoonotic form caused by *L. major* (Yakimoff and Schokhor). An exception is a remarkable clinical description of both forms of the disease published in 1756 by Alexander Russell (1715–1768), a Scottish doctor who practised in Aleppo in the days of the Ottoman Empire. In *The Natural History of Aleppo and Parts Adjacent*, he gives an account of how the local people differentiated between a 'male' form, which must have been the zoonotic infection, and a 'female' form, which must have been the anthroponotic infection. The descriptions of the lesions and the time to spontaneous healing are the most important distinguishing features. He describes treatment with a mercury ointment but concludes: "from what I have observed, it is infinitely better to apply nothing, than any of the numberless medicines they make use of". Some physicians of today would agree.

Although the disease was well known, nobody had any idea of its cause or how it was transmitted. Then, in 1885, D D Cunningham saw the parasite in sections of a Delhi boil in India. Shortly afterwards, in 1891, R H Firth also reported the presence of parasites in a lesion, but both misinterpreted what they saw. A Russian army doctor, P F Borovsky, was the first to realise the bodies in lesions were protozoa but his observations, published in an obscure Russian journal in 1898, remained unknown outside his country until C A Hoare translated his paper in 1938. In 1903, an American doctor, J H Wright,

published three papers on the discovery of *L. tropica* in a lesion of a child from Armenia and the parasitic nature of the infection became universally accepted. But how were people infected? K Schulgin, a Russian colleague of Borovsky, influenced by the new knowledge that malaria was transmitted by the bites of mosquitoes, gave the first clue when, in 1902, he wrote a paper entitled 'The question of the aetiology of Penjdeh sore', in which he suggested the disease was transmitted by a nocturnal biting insect. His report went unnoticed until Nobel Laureate Alphonse Laveran drew attention to Schulgin's speculation in his classic book on the leishmaniases published in 1917. But tucked away in an earlier book (on the prevention of malaria) published by A Prassat in 1905 was the first suggestion that sand flies could be the vector of Oriental sore (in Egypt).

Edmond Sergent at the Pasteur Institute in Algiers was also puzzling over the transmission of Oriental sore and, like Schulgin, concluded that the infection must be by the bite of a nocturnal haematophagous insect. He knew of Prassat's suggestion about sand flies and suspected the vector was *Phlebotomus papatasi* (Scopoli), an abundant phlebotomine in Biskra, an infamous focus of Oriental sore 330 km south-east of Algiers. In 1921, he asked the Institute's entomologist, Louis Parrot, to collect sand flies there and send them to Algiers. Of more than 2000 caught by Parrot and identified as *P. papatasi*, only 561 survived the journey: they were enough. On arrival, they were ground up in lots and suspensions were scarified on the skin of four volunteers, one of whom (A Donatien) developed a small papule with a crust seven weeks later at the site of scarification on his arm with a suspension from seven flies. The papule increased in size, reaching a diameter of 6 cm, before healing spontaneously seven months after infection. Numerous parasites were seen in stained smears of the lesion. The identity of the sand fly and the fact that the lesion healed without treatment in less than a year strongly suggest the parasite was *L. major*. But the results of this experiment were not accepted as proof that sand flies are the vectors of Oriental sore. C Wenyon, the doyen of British protozoology of the day, insisted that proof required experimental transmission in the laboratory. Other workers pointed out that there are many monoxenous trypanosomatids parasitic in numerous species of insects and the lesion could have been a transient infection by one of these. Nevertheless, even today Sergent is sometimes credited with the discovery that sand flies are vectors of cutaneous leishmaniasis.

Saul Adler, a British worker in Jerusalem, finally produced overwhelming evidence of the role of sand flies that satisfied everyone, even Wenyon. He repeated Sergent's experiments with the same species of sand fly (*P. papatasi*) and parasite (*L. major*, mistakenly called *L. tropica*) and then struggled for years to transmit it by bite. He fed 253 heavily infected sand flies on 12 men and a puppy, but only one man (himself) developed a lesion where flies had fed. He did not accept this as proof of transmission by bite because he had lived for several months in a place where he could have been infected naturally.

The proof was eventually obtained 20 years after Sergent's experiment, when Adler and Ber managed "with remarkable ease" to infect five volunteers with 27 lesions from the bites of 26 sand flies bred and infected experimentally in the laboratory. Since that time, other workers have transmitted various species of *Leishmania* by the bite of different sand flies and their vectorial role is no longer questioned. But many travellers to the Middle East still return home with the same souvenir as the travellers of the 19th century.

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Above: The sand fly, implicated in the spread of leishmaniasis. *Swiss Tropical Institute/R Knechtli*

Right: Avicenna, who provided an early description of cutaneous leishmaniasis.