

**THE INFANTILE VISCERAL LEISHMANIASIS:
COULD IT ATTACK EGYPTIAN NORTH COASTAL REGION AGAIN?**

By

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Abstract

Visceral leishmaniasis is caused by three species of the *L. donovani* complex: *L. donovani*, *L. infantum*, and *L. chagasi*. Infections with these organisms are often asymptomatic or very mild, but in a minority of individuals there is progression to severe symptomatic disease. This is associated with spread of the infection throughout the reticuloendothelial system. *L. infantum* typically affect children below the age of 5 years. However, IVL can also occur in immunosuppressed adults, such as transplant recipients and patients receiving immunosuppressive chemotherapy or patients suffering from chronic intestinal schistosomiasis.

IVL was encountered in Al-Agamy, Alexandria on 1983 with *Phlebotomus langeroni*. This vector is still abundant with low density away from Al-Agamy. Urbanization of the north coastal area in the vicinity of Alexandria changes the ecological status but how does it affect the behavior of sandflies; mainly the IVL vector *Phlebotomus langeroni*? Many employees and their families return home from Libya with fever with or without other accompanying symptoms. Fever can be a manifestation of a minor, self-limited process or can herald a progressive, life-threatening illness.

The detection of *Phlebotomus langeroni* in El-Hamam City, Sedi Barany City, and Matrooh City and the abundance *P. papatasi* in these three cities in addition to Al Agamy must be taken into consideration of the Public Health Authority.

Key Words: Egypt, Infantile visceral leishmaniasis, Sandflies, Re-emerging?

Introduction

There is a long history of visceral leishmaniasis from Alexandria, Egypt (Panayotatou, 1922), Hassan (1968) reported a case of Kala-azar. However, the disease impact on human health in

El Agamy, Alexandria was not really recognized until 1982 (Tewfik *et al*, 1983). Mansour *et al*. (1984) in Al Agamy characterized the *Leishmania* isolates from children with infantile visceral leishmaniasis. Soliman *et al*. (1984) experimental found that the

Pentostam the drug of choice in the treatment of visceral leishmaniasis in Egypt had side effects mainly on the liver. On the other hand, *Phlebotomus langeroni* was the proven vector of infantile visceral leishmaniasis in El Agamy as it meets all the established criteria for the vectorial competence, essentially its anthropophily and the feeding on the reservoir host (Morsy *et al*, 1983; El Sawaf *et al*, 1989), spatial distribution coincided with the human cases (Beier *et al*, 1986), natural infection by *Leishmania infantum* (Doha and Shehata, 1992) and transmission of disease by bite (El Sawaf *et al*, 2012).

El Sawaf *et al.* (2008) experimentally *L. infantum* and *L. major* in the midgut of infected *P. langeroni* and *P. papatasi* showed difference in flagella mode of attachment to the midgut of their respective sand fly vectors suggested higher adaptation between *L. major* /*P. papatasi* compared to *L. infantum*/*P. langeroni*.

Kassem *et al.* (2012) stated that the epidemiological significance of *P. lan-*

geroni highlighted the importance of entomological surveillance and monitoring measures, especially considering its displacement or migration, allowing the maintenance of the visceral leishmaniasis transmission cycle in the rural environment.

The present objective aimed at the surveying of selected areas in the North Coastal Zone for *Phlebotomus langeroni*, the main vector of the previous documented infantile visceral leishmaniasis in the vicinity of Al-Agamy, Alexandria.

Materials and Methods

The sticky paper traps (N=100) coated with castor oil, were set up randomly around houses 2 hr. before sunset and were collected the next early morning (Morsy *et al*, 1989). Twenty-five standard sticky traps were distributed in each of Abo-Talaat north of Al-Agamy, El-Hamam City, Sedi-Barany City and Matrooh City. The keys given by Morsy *et al.* (1990) and Lane (1993) were adopted for the identification of the collected sandflies in these surveys.

Result

Table 1: Identified sandflies in the different sites

Site	<i>Phlebotomus papatasi</i>	<i>Phlebotomus langeroni</i>
Abo-Talaat	++	-
El-Hamam City	++	+
Sedi Barany City	++	+
Matrooh City	++	++

+ = one female/trap/night

In the present study, the ZCL vector; *P. papatasi* was common abundantly in the four examined sites. On the other hand, the IVL vector; *Phlebotomus langeroni* was trapped from three sites; in a descending order of abundance these

were El-Hamam City, Sedi-Barany City and Matrooh City, but not from Al-Agamy vicinity where it was previously abundant and many proven clinical and parasitological infantile visceral leishmaniasis cases in the 1980s.

Discussion

El Okby *et al.* (1989) in Al Agamy over two successive years found a bimodal or two peaks a year for *P. papatasi* and *P. langeroni*. The blood of *P. papatasi* females was mainly human blood, while that of *P. langeroni* was mainly non-human blood. El Sawaf *et al.* (1989) examined blood meals from 602 *P. papatasi* and 49 *P. langeroni* in El Agamy. Of 597 *P. papatasi* collected indoors, 594 contained human blood and three had mixed blood meals (human-dog, human-rat, and human-avian). Four of five *P. papatasi* collected outdoors contained human blood and one contained avian blood. All 39 *P. langeroni* collected indoors had fed on humans. Six of 10 outdoor-collected *P. langeroni* had fed on human blood, 2 on dog, 1 on cat, and 1 on rat blood. They concluded that feeding on humans and dogs by *P. langeroni* supports the role of this species visceral leishmaniasis at the El Agamy focus. Kassem *et al.* (2012) expected that urbanization has led to the *P. langeroni* displacement to flourish in suitable rural habitats, similar to that previously found in El Agamy.

Cases of feline leishmaniasis have been reported in different countries. Morsy *et al.* (1980) in Jordan parasitologically incriminated stray cats as reservoir hosts visceral leishmaniasis. In Egypt, Michael *et al.* (1982) and Morsy *et al.* (1993) reported anti-leishmanial antibodies in street cats in Ismailia and Cairo Governorates respectively. Trainor *et al.* (2010) in Texas in 5 of 8 cats, *L. mexicana* DNA was amplified from

paraffin-embedded tissue by PCR and sequenced. da Silva *et al.* (2010) in urban endemic areas in Brazil suggested domestic cats as possible alternative reservoirs of *Leishmania (L.) infantum*, the causal agent of visceral leishmaniasis (IVL). They reported *Lutzomyia longipalpis* infected by *L. infantum* from a naturally infected cat by xenodiagnosis. Also, Cadia *et al.* (2013) in Brazil found specific anti-*Toxoplasma* IgG in 63 of 386 (16.3%) cats and IgG against *Leishmania* spp. in two cats' serum samples. Apart from cats, Morsy *et al.* (1987) reported *Leishmania* antibodies in the Egyptian bats.

Morsy *et al.* (1993) studied the seasonal abundance, nocturnal activity and breeding sites as well as other relevant behavior *P. papatasi* (Scopoli) the proven vector of zoonotic cutaneous leishmaniasis. They showed that: (a) the seasonal activity started in April and ended in November or beginning of December. (b) Female outnumbered male indoors (7.4:1) and vice-versa outdoors (0.14:1). (c) Blood fed females were 97.7% indoors and 29.4% outdoors. (d) The nocturnal activity ranged between 6 p.m. to 6 a.m. indoors and 8 p.m. to 6 a.m. outdoors. (e) the immature stages of *Phlebotomus* were successfully recovered from rodent burrows and poultry sheds.

Abdel Badei *et al.* (2012) studied the morphometrics and protein composition of salivary glands of colonised *P. papatasi* and *P. langeroni* sand flies from Egypt. Female glands were dissected at day 1 (D1, unfed), day 2 (D2, sugar-fed), day 3 (D3, blood-fed) and day 7 (D7, blood-digested). *P. papatasi*

had larger lobes and higher protein content than *P. langeroni* ones. *P. papatasi* D1 flies had 15 protein bands that decreased in the D2, D3 and D7 flies to 10 bands in the Sinai flies and 9 bands in the Alexandria flies. All *P. langeroni* flies had 12 protein bands but with different intensities. The results reveal inter-specific variation between *P. papatasi* and *P. langeroni*, while no intra-specific variation between *P. papatasi* strains.

Abroad, Chelbi and Zhioua (2007) experimentally found that the Tunisian strain of *P. papatasi* could reproduce autogenously or anautogenously, depending on the availability of a suitable blood-meal source. Chelbi *et al.* (2008) reported that *P. papatasi* proved to be zoo-prophylaxis. The indoor abundance of *P. papatasi* in houses with rabbit holes in the peri-domestic areas was significantly lower than the indoor abundance in houses without rabbit holes in their peridomestic areas. They strongly suggested that zoo-prophylaxis could be effective in reducing the indoor abundance of *P. papatasi* and subsequently might be used to control the transmission *L. major* in rural areas. Derbali *et al.* (2012) studied the ability of *P. papatasi* to transmit *L. major* under laboratory conditions. The sand flies became infected with *L. major* after feeding on a lesion of needle-inoculated *Meriones shawi*. Previously infected *P. papatasi* transmitted *L. major* to *M. shawi* by bite during a second blood-meal. Two months after the blood-meal, the animal developed a lesion on its ears. The infectivity of *M. shawi* to *P. papatasi* lasted for five

months, period corresponding to winter season in North Africa. They concluded that reservoir hosts surviving winter time are the main source of infection for *P. papatasi* during the following season, and subsequently they play a major role in the persistence and transmission of *L. major* between transmission cycles.

As to the reservoir host; Morsy *et al.* (1983) reported ELISA and IHAT anti-leishmanial antibodies in street and pet in the vicinity of Al-Agamy. Morsy *et al.* (1987) in Al-Agamy typed two leishmanial isolates from dogs serologically and biochemically as *L. major*. This was the second time that *L. major* has been shown to occur in dogs in Saudi Arabia by Elbihari *et al.* (1987) who suggested that dogs were probably victims rather than reservoirs of *Leishmania*. Morsy *et al.* (1988) in Al-Agamy isolated a flagellate parasite from the spleens of two *R. norvegicus* typed serologically by excreted factor serotyping and enzymological by thick starch electrophoresis of four of its enzymes: GPI, G6PD, 6PGD and PGM. The same type of parasite was isolated from two stray dogs from the same vicinity. This flagellate was quite distinct from *Leishmania donovani*, *L. major* and *L. tropica*, the three common Old World species of *Leishmania*; but its exact identity remains uncertain. They concluded that it could be a new leishmanial entity or a flagellate parasite of another genus.

Nowadays, the visceral leishmaniasis (VL) is documented in Egypt mainly in Al Agamy, Alexandria. Other studies all over Egypt (based on the clinical

and/or serological diagnosis rather than demonstration of the parasites) raised the possibility of adult affection with visceral leishmaniasis. The point is that visceral leishmaniasis, shares many clinical manifestations with other diseases known in Egypt as schistosomiasis *mansoni*, hepatic amoebiasis, toxoplasmosis, and malaria (Morsy, 1997). Besides, Feinsod *et al.* (1988) in a focus of IVL in Al Agamy, found adults by radioimmune assay to have leishmanial antibodies. Ten of 16 seropositive individuals were on corticosteroids compared to one of 22 seronegative ones ($P=0.0002$). Two seropositive individuals (a woman and a man) were taking phenylbutazone, and two women were taking female sex hormones. The association between immunosuppressive medication and leishmanial seropositivity suggested that acquired changes in host population immunocompetence might significantly alter age-specific seroprevalence of leishmanial antibodies. Soliman (1992) in El-Max area west of Alexandria reported 6.2% IFAT positivity among 96 pupils.

Apart from Al Agamy, Alexandria, Madwar *et al.* (1985) suggested the possibility of VL in Qalyoubia Governorate. A case of infantile visceral leishmaniasis was identified in an adult farmer (unusual host) in Qalyoubia District the patient suffered from hepatosplenomegaly and who never left his home area (Kabil *et al.*, 1988).

El Mahdy *et al.* (1993) in Dakahlia reported *Leishmania*-positive by IHAT and dot-ELISA in 4/22 hypersplenic patients with *Leishmania* amastigotes were demonstrated in splenic smears of

two patients obtained during splenectomy. One culture grew promastigotes. Morsy *et al.* (1993) in Abo Hamad, Sharkia reported lymphatic leishmaniasis as an indigenous infection in a 30 year old male. Cervical lymphadenopathy was the only clinical sign but no visceral involvement. The patient was successfully treated with sodium stibogluconate as shown clinically and parasitologically. They stated that lymphatic leishmaniasis should be in mind when dealing with lymphadenopathy of unknown etiology. Again, Rosypal *et al.* (2013) examined blood samples from 50 stray dogs in Giza for antibodies to visceralizing *Leishmania* spp. by commercial immunochromatographic strip assays based on recombinant antigen K39. The antibodies to *Leishmania* spp. were found in 5 of 50 (10%) of dogs tested from Egypt. They stated that the stray dogs are exposed to the visceralizing *Leishmania* species in Egypt.

Conclusion

Generally speaking, with rapid international travel, it is very common to diagnose infectious diseases in areas where they were not known before.

Besides, leishmaniasis is an insect-borne zoonotic disease with a worldwide distribution. *Leishmania* spp. infections cause a broad spectrum of the clinical signs, ranging from skin lesions to fatal visceral disease. The dogs are a major reservoir host for visceral leishmaniasis.

The presence of *Phlebotomus langeroni* in some sites west to Al Agamy and the endemicity of infantile visceral

leishmaniasis in Libya very near to the Libyan-Egyptian board as well as travelers returning home must be in consideration.

Besides, one must take into consideration the serologic and parasitological detection of natural leishmanial infection in pet and street cats and signify their role and perhaps other carnivores in the epidemiology of disease; leishmaniasis public awareness of its complications and the importance of early detection could affect its prognosis.

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