Endorsement

Title of thesis

Risk Assessment of Cutaneous Leishmaniasis
in Jericho City-Palestine, 1994-1999

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ABSTRACT

In this study 471 referred individuals for the diagnosis of CL from Jericho District between 1994 – 1999 showed that the direct smear (parasitological) prevalence was 32%, with males constituting (60%) of the exposed cases. CL showed seasonal pattern in which 57% of the cases were diagnosed in the months between October to January. During the six-year-study, 1995 was shown to be the peak year.

75% of the cases (114/152) were mapped. 52% were in Jericho City, 17% in Aqbat-jber refugee camp and 31% in other Jericho District areas. 45% of the cases were in clustered the southern parts of the city periphery.

Sera from 201 individuals were examined for the presence of anti-leishmanial antibodies by ELISA. The sero-prevalence was 26.3%.

The case -control study which included 37 households in Jericho City and Aqbat-jaber refugee camp showed that the level of education of the household head and the children sleeping in nets were significantly related to CL incidence rate.

Chapter 1

INTRODUCTION

"What we call the beginning is often the end.
And to make an end is to make a beginning.
The end is where we start from."

T.S.ELIOT

1.1. GENERAL BACKGROUND

Jericho in the Jordan Valley is the centre of a region where simple cutaneous leishmaniasis (CL) caused by *Leishmania major* is an endemic (Naggan, 1970; Schlein *et al.*, 1982, 1984; Greenblatt *et al.*, 1985). In fact, "Jericho Boil" is the vernacular name of the skin lesion that develops as the infection progresses. De Beurmann (1910) appears to have been the first to describe a parasitologically confirmed case from the region. The next published record describing parasitologically confirmed cases was by Huntemuller (1914). He was shown two cases by two local physicians, Dr. Mastermann and Dr. Canaan, from Jerusalem. From that time on, CL has become an ever-increasing public health problem. This is compound by the fact that CL is a vector borne zoonotic disease.

The zoonotic nature of the disease was exposed by the Soviet scientists during the 1940's, who showed that desert rodents are the natural animal reservoir of CL caused by *L. major,* referred to as *L. tropica* (var. *major*) at that time (Latyshev & Kriukova, 1941). The primary and, apparently, the only animal host species in the Jordan Valley is the rodent *Psammomys obesus*, the fat sand rat, which was

discovered as such by Gunders *et al.* (1968). In other foci, more than one species of host can exist as in the Negev and northern Sinai where *P. obesus* and *Meriones crassus* are both hosts (Schlein *et al.*, 1982).

Female phlebotomine sandflies are the vectors of all the leishmaniases, and where originally shown to be so by Shortt *et al.* (1931) and Adler and Ber (1941). In the Jordan Valley, sandflies of the species *Phlebotomus papatasi* are the vector. They live in the rodent burrows in a very close association with the sand rats. This ensures high rates of infection in the vectors (Naggan *et al.*, 1970; Schlein *et al.*, 1982), maintaining effective transmission of the parasite among the primary hosts. Female *Ph. papatasi* are zoophilic, transmitting the parasite efficiently from rodent to rodent, and anthropophilic, from rodent to humans (Ashford, 1996). It is the abundance of vectors living in very close association with highly susceptible reservoir rodents and also their equal readiness to feed on human hosts that accounts for the hyperendemicity of CL in humans in the Jordan Valley (Schlein, 1982).

Despite their medical importance, humans are only incidental, secondary hosts with infections rarely, if at all, playing a part in further transmission of the parasite in the case of *L. major* (Schlein and Jacobson, 1996). However, some of the other species, *e. g., L. tropica*, are anthroponotic, transmission being from person to person, where humans

are the primary hosts and the reservoir for new human infections of CL (WHO, 1984).

1.2. THE PARASITE LIFE CYCLE: (Figure 1)

The life cycle of all species of *Leishmania* is essentially the same. The parasite exists in two morphological forms, the non-flagellated amastigote found living intracellularly in macrophages of the mammalian host and the flagellated, motile promastigote, living extracellularly in the digestive tract of the female sandfly vector. Transformation from one form to the other occurs shortly after transfer from the mammlian host to vector and vice versa. Both forms of the parasite, essentially, reproduce asexually by binary fission. Figure 1 presents the life cycle of *L. major*, the main cause of CL in Jericho and its vicinity.

1.3. CLINICAL FEATURES

The leishmaniases are a group of diseases, each having its own distinctive clinical features. The mode of transmission is essentially the same in all cases, through the bite of an infected female sandfly. However, different species of sandfly transmit the different species of *Leishmania* implicated in causing disease. The clinical manifestations associated with and defining the different leishmaniases are: inapparant, asymptomatic, sub-clinical manifestations; either single or multiple self-curing cutaneous lesions; persistent muco-cutaneous lesions; persistent

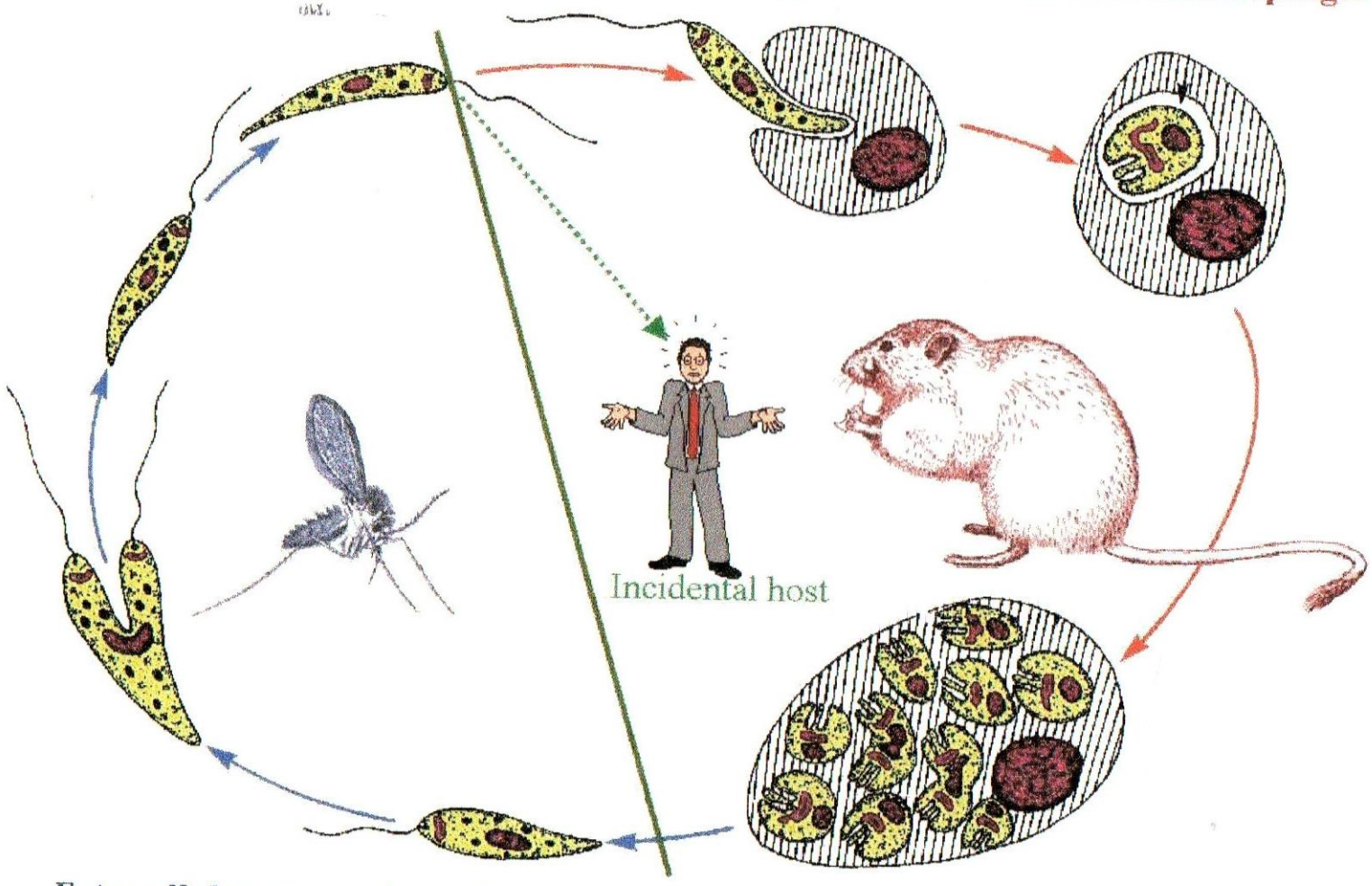

Figure 1. Life cycle of *L. major*, the causative agent of CL in the Jordan Valley

diffuse cutaneous lesions; persistent recurrent cutaneous lesions; and systemic fatal disease (Klaus and Frankenburg, 1999; Klaus, 1999; Schnur and Greenblatt, 1995). Depending on the species of *Leishmania* and host cellular immune response, one or more of these clinical conditions and combinations of some of them can result but no one species is known to cause them all (Sacks *et al.*, 1993). Thus, a series of clinical syndromes are presented that are associated with different species of *Leishmania*. For example, *L. tropica* is associated with simple CL, recurrent leishmaniasis recidivans (LR) and occasional visceral leishmaniasis (VL), *L. aethiopica* with simple CL and persistent diffuse cutaneous leishmaniasis (DCL) and *L. braziliensis braziliensis* with simple CL muco-cutaneous leishmaniasis (MCL) (Schnur and Greenblatt, 1995).

In the case of Jericho and its vicinity, the causative agent is *L. major*, which invariably causes simple, self-curing CL, with one recorded exception of a 12-year old girl who developed disseminated CL, owing to the co-existence of AIDS after receiving a contaminated blood transfusion (Gillis *et al.*, 1995).

Classically, leishmaniases were classified into three types: CL, MCL and VL (Klaus and Frankenburg, 1999). However, other clinical types have also been described that are often ignored by reviewers of the

leishmaniases and the writers of textbooks. In the context of cutaneous leishmaniasis (CL) these are: leishmaniasis recidivans (LR) caused by *L. tropica*; diffuse cutaneous leishmaniasis (DCL) caused by *L. aethiopica,* East Africa, and *L. mexicana amazonensis*, Latin America; muco-cutaneous leishmaniasis (MCL) caused by *L. aethiopica,* East Africa, and *L. braziliensis braziliensis*, Latin America; oronasal and nasopharyngeal leishmaniasis caused by *L. donovani donovani* in Sudan. In the context of visceral leishmaniasis (VL) they are post-kala-azar dermal leishmaniasis (PKDL) caused by *L. donovani donovani* in India and East Africa and asymptomatic leishmaniasis caused by *L. donovani infantum* in the Old World (Schnur and Greenblatt, 1995). However, in the geographical region encompassed by this thesis only simple CL has ever been recorded and only this type of leishmaniasis will be described further.

1.4. CUTANEOUS LEISHMANIASIS (CL)

In the Palestinian Authority, two species of *Leishmania, L. major* and *L. tropica*, are known to cause CL. *L. infantum* also occurs in the area (Schnur and Le Blancq, 1986). It is usually described as one of the agents causing VL and in particular infantile VL. However, it has also been isolated from cutaneous cases devoid of visceral symptoms in many parts of its global range (Schnur and Greenblatt, 1995). No cases of CL caused by *L. infantum* have been recorded in the Eastern Mediterranean Region so far.

بسم الله الرحمن الرحيم

خلاصة

شملت هذه الدراسة 471 شخصا تم تحويلهم من محافظة أريحا لتشخيص داء الليشمانيات في الفترة الواقعة بين الأعوام 1994 و 1999. أظهرت الدراسة أن معدل انتشار المرض طفيليا هو 32% من بين الأفراد المحولين. وقد تبين أن الذكور كانوا أكثر عرضة للإصابة (60%) من الإناث. كما واتضح أن داء الليشمانيات يتخذ نمطا فصليا للإصابة، حيث أن 57% من الإصابات تم تشخيصها في الأشهر ما بين تشرين أول وكانون ثاني. كما وأظهرت الدراسة بأن عام 1995 شكل الذروة في عدد الحالات.

شكلت نسبة الحالات التي تم تحديدها على الخريطة 75%(152/114) من الحالات، ظهر منها 52% من مدينة أريحا، 17% من مخيم عقبة جبر للاجئين الفلسطينيين و 31% من بقية مناطق المحافظة.

تم فحص أمصال 201 شخصا للتحري عن الأجسام المضادة لداء الليشمانيات باستعمال ELISA.حيث تبين أن معدل انتشار المرض مصليا هو 26.3%.

من خلال دراسة مقارنة لتقدير الخطورة شملت 37 حالة بيتية في مدينة أريحا ومخيم عقبة جبر، تبين أن المستوى التعليمي لرب البيت و نوم الأطفال داخل الناموسيات هما عاملين مرتبطين إحصائيا بمعدل الإصابة.