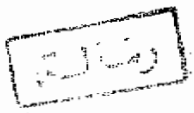
OST SUSCEPTIBILTY LEVELS TO LEISHMANIA MAJOR

EGYPTIAN STRAIN

THESIS SUBMITTED



BY

MAHA ALY GHAREIB

TO

THE FACULTY OF SCIENCE

AIN SHAMS UNIVERSITY

IN

PARTIAL FULFILLMENT OF

THE REQUIREMENTS

FOR

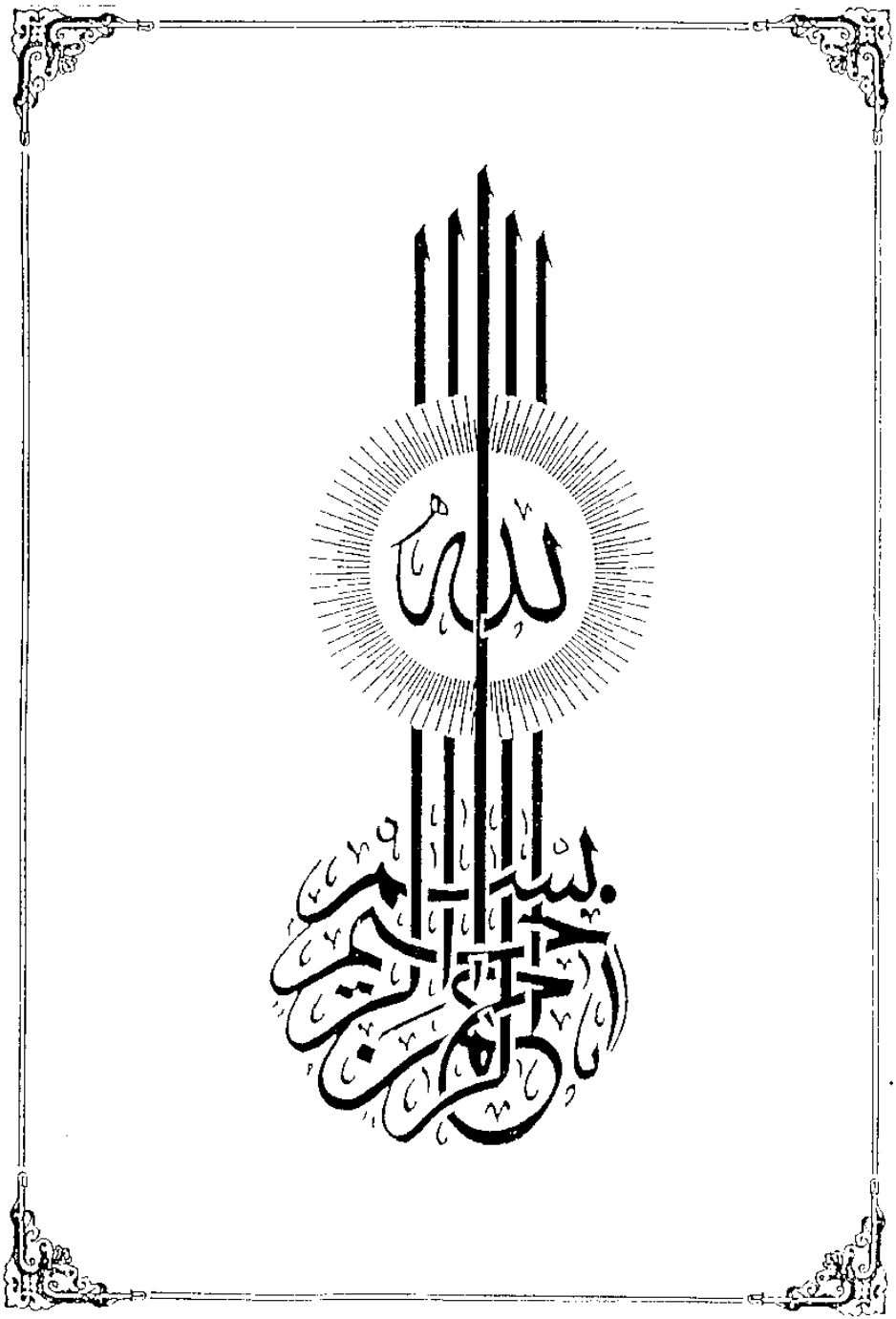
THE DEGREE

OF MASTER OF SCIENCE

1996

Special appreciation is due to Prof. Dr. Bahira M. El Sawaf, Head of Entomology Department and Director of "The Research and Training Centre on Vectors of Diseases", Ain Shams University for her generous assistance and continuous encouragement throughout the whole period of the study.

I am also greatly indebted to the staff members at the Department of Zoology, Faculty of Science, Ain Shams University, particularly Prof. Dr. Abdalla M. Ibrahim, the Head of the Department for their kind support and sincere encouragement.



LIST OF ABBREVIATIONS

BV	Blood vessels
CT	Connective tissue
CV	Central vein
D	Dermis
ED	Oedema
EP	Epidermis
F	Fibrosis
Fc	Fibrocytes
Fb	Fibroblasts
HF	Hair follicles
HS	Hepatic sinusoids
IC	Inflammatory cells
Kc	Kupffer cells
LD	Lower dermal layer
Lym	Lymphocytes
M	Macrophages
N	Nuclei
Pc	Plasma cells
RP	Red pulp
SG	Sweat gland
SL	Sinusoidal lumen
T	Trabeculae
UD	Upper dermal layer
V	Vacuoles
WP	White pulp

LIST OF FIGURES

Histology and Histopathology

MICE

The Skin

The Liver

The Spleen

HAMSTERS

The Skin

ABSTRACT

The present work has aimed principally at detecting the hazardous consequences evoked in some principle body organs of certain mammals as a result of infection with *Leishmania major*. This study had also headed toward defining which one of these mammals could be recommended as a satisfactory model in the field of experimental leishmaniasis. The used mammals comprised mice, hamsters and cats, and the selected organs were the skin, liver and spleen. The animals were injected either intradermally or intramuscularly with the amastigote stage of *Leishmania major*. At the end of the period of treatment, the animals were sacrificed, rapidly dissected, and suitable parts of the aforementioned organs were taken and processed for paraffin sectioning in the usual manner. Sections of 6-8 μ thickness were stained with hematoxylin and counterstained with eosin. The examined specimens have brought into vision consequences pathological alterations comparable to the crossponding normal specimens. In the skin, certain lesions were recorded, including thickening and compactness of the epidermal layer, damage of the dermis and widening, as well as marked injury of the blood vessels. The liver of the infected animals has also suffered from tissues disorganization, cloudy swelling and hydropic degeneration of the liver cells in addition to nuclear pyknosis. Besides, severe inflammatory infiltration was clearly noticed in those tissues. In the spleen, cell proliferation and abundance of necroinflammatory cells were conspicuously prevailing in the *Leishmania* infected animals. The severity of such pathological changes occurred in case of these selected groups of animals were time-dependant. Moreover, such pathological consequences were relatively more stricking in case of intramuscular treatment with the parasite than in case of intradermal infection. Furthermore, the cats' organs had clearly reflected the pathological responses to parasitic infection in a more pronounced manner than other mice or hamsters. In turn such adverse consequences were comparatively more prevailing in hamsters in comparison to mice.

AIM OF THE WORK

This part of work was carried out on three species of mammalian animal comprised mainly of mice, hamsters and cats aiming at finding out which of them is most selective for *Leishmania* infection. Such aspects are of specia importance for any successful experimentation. Needless to recall in thes concern the three varieties of animals were adults.

In view of the aforementioned introductory remarks, the presen investigation was constructed aiming at following the dissemination o *Leishmania major* in some laboratory animals. It is worthy of mentioning in thi respect that this protozoan organism is regarded as the main causative agent o cutaneous leishmaniasis.

Another intended goal in this study has entailed the examination of th adverse affects of the parasite on some essential body organs of such animals.

The animal models selected for this study have comprised mice, hamster and cats. Thus, a conclusion could be obtained regarding the levels c susceptibility of such animals to infection with the parasite, which could be the selected as a successful model in the research areas of experimental infectio induced by the parasite.

Hopefully, the obtained results could be of some value in providing mor information on this injurious parasite, which could in turn help in its control c rather complete eradication for maintaining the health of man and his usefi animals.

INTRODUCTION

Leishmania major is one of the common protozoan parasitesof the Old World. Its vector is the sandfly, *Phelobotomus papatasi*. Man is an incidental host of this parasite in which cases the parasite usually causes straightforward cutaneous leishmaniasis **(Bray, 1974).** The systematic position of the parasite is thereafter represented:

Subkingdom : Protozoa (Goldfuss, 1918 emend. Von Siebold, 1845).
Phylum : Sarcomastigophora (Honigberg and Balamuth, 1963).
Subphylum : Mastigophora (Diesing, 1966).
Class : Zoomastigophora (Calkins, 1909).
Order : Kinetoplastida (Honiberg, 1963).
Family : Trypanosomatidae (Doflein, 1901 emend. Grobben, 1905).
Genus : *Leishmania*
Species : *Leishmania major*

According to **Molyneux** and **Killick-Kendrick (1987),** there are two stages of *Leishmania* which are the amastigote stage (unflagellated form) and the promastigote stage (flagellated form).

The initial stage of the parasite is the amastigote stage which is easily detected in the blood meal of the sandfly. This stage undergoes active division in the midgut of the sandfly; the resulting amastigotes are then transformed into free swimming promastigotes. When these promastigotes reach the thoracic midgut they become infective. Ultimately, these freely moving stages are easily observable in the sandfly proboscis.

Concerning the life cycle of *Leishmania* within the mammalian host; firstly, when the infected sandfly bites the mammalian host, the promastigotes penetrate the macrophages and start to transform from this falgellated promastigote to the unflagellated amastigotes. These stages undergo active division, and thus, become increased in number. Then they migrate to certain organs in the infected mammal such as the skin in case of cutaneous leishmaniasis.

Leishmania designates an acute and chronic tropical infectious disease of humans and animals, prevailing in the old world as a result of infection with sandfly borne protozoal parasites of the genus *Leishmania* **(Adler., 1964)**.

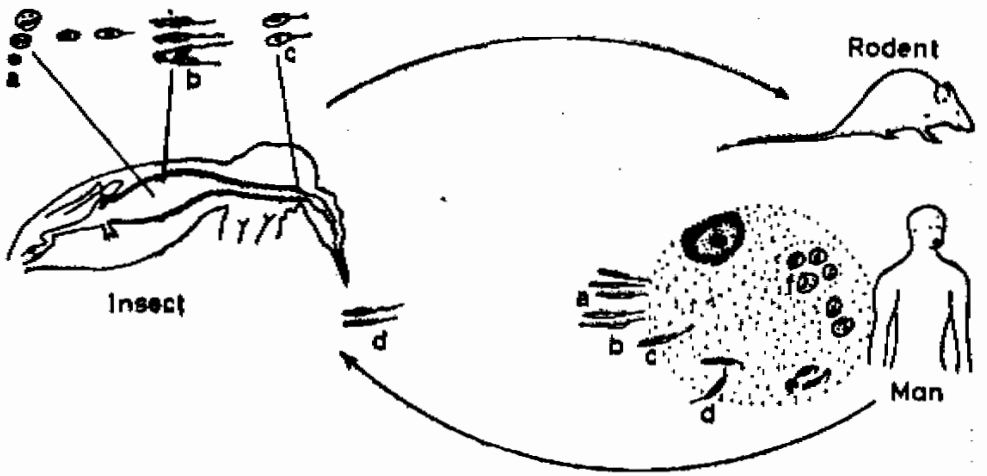
Leishmaniasis was mentioned to provoke a variety of clinical forms in the skin in addition to affection of the mucous membrane of the new world. However, the clinical presentation of cutaneous leishmaniasis was noticed to vary in the different geographic regions of the old world, being correlated with the different infective species of *Leishmania*. In urban areas in the neareast symptoms of leishmaniasis are usually reflected by the appearance of dry skin ulcerations, commonly referred to as "Oriental sore" being particularly produced by *L. tropica*. From another angle, *Leishmania major* is more frequent in rural areas and is borne to ulcerate earlier as indicated in a report issued by **WHO (1990).**

Leishmaniasis may also be present in a systemic lifethreatening form known as visceral leishmaniasis or "Kala azar" produced by *Leishmania donovani*. In the Near East and Mediterranean Basin, a disease of children was discovered, being induced by *L. infantum*.

In a report offered rather recently by **Gramiccia** *et al.* **(1992),** it was mentioned that leishmaniasis has recently been recognized in France, Spain and Italy as an opportunistic infection in patients infected with human immunodeficiency type-I virus (HIV-1) which is the causative agent of the acquired immunodeficiency syndrome (AIDS)

The sandfly vectors, which transmit *Leishmania* species,are also divided into old world and new world types.

According to **Morsi** *et al.* **(1989),** cutaneous leishmaniasis was particularly widespread in the middle east, being recognized with a rather high frequency in Egypt due to infection of returning workers from the near east and Sinai. The same authors added that El-Agamy district in Egypt has been widely attacked by this disease since 1983. Thus, leishmaniasis has been gaining wider spread in human being in different parts of the world especially in Egypt. Worthwhile is that infection with *Leishmania* is closely correlated with irrigation and urbanization in the near east. Thus, a growing interest is marked nowadays concerning the impacts of *Leishmania* infections on the mammalian body organs.


Rodent
b
c
Insect
d
a
b
c
d
Man