STUDIES ON TYPHOID MICROORGANISMS

A Thesis

Submitted for the Degree of Doctor of Philosophy

(Botany: Microbiology)

Presented by

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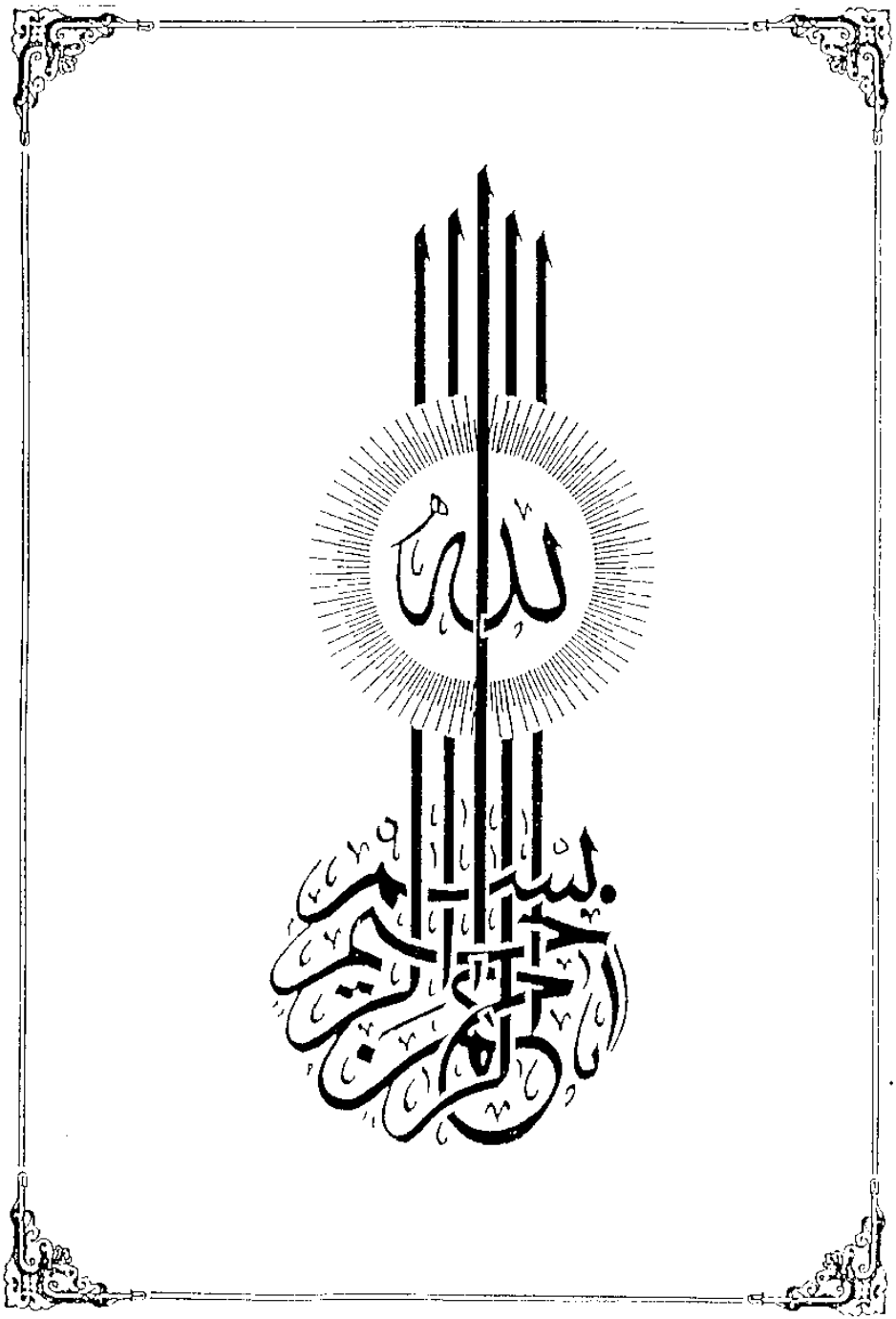
1979

DEDICATED TO MY LATE FATHER



ACKNOWLEDGMENT

I do feel deeply indebted to Prof. Dr. Sabry H. Elwan, Head of Botany Dept., Faculty of Science, Al-Azhar University for his supervision, suggestions and his help in presenting this thesis and discussion of the results.

I wish also to thank Dr. Sohair, A. Moustafa, Assist. Prof. of Microbiology, Department of Botany, Women's College, Ain Shams University for her encouragement and help.

My thanks are also due to Dr. Khodair, A.A., Head of Botany Dept., Faculty of Education, King Abdel Aziz University, Saudi Arabia for his encouragement.

I would like to express my deepest gratitude and sincerest thanks to Prof. Hoda Hakim, Head of Botany Dept., Women's College for her great help.

I wish also to thank Dr. Gene I. Higashi, M.D., Sc.D., Head of Immunology Dept., NAMRU-3, to whom I shall be forever grateful for his kind and patient supervision of all the details of the work and for enriching me with his vast experience.

Sincere thanks and appreciation are due to Dr. Noshy S. Mansour, Head of Parasitology Dept., NAMRU-3, for his continous generous assistance while accomplishing the work.

I wish also to express my thanks to Dr. Nabil I. Girgis, Research Investigator and the late Dr. John W. Mikhail, Assoc. Investigator, Parasitology Dept., NAMRU-3, for their great help in technical guidance.

The author wishes to express her sincere appreciation to Dr. David E. Edman, and Dr. John E. Sippel, the successive Heads of Bacteriology Dept., NAMRU-3, for the willing instructions extended by them.

Thanks are also to Prof. Refaat Hablas, Clinical Pathology Dept., Al-Azhar Faculty of Medicine, for his great help in studying the phage types.

My thanks are also to Dr. Philip, T. LoVerde, Assist. Prof. Department of Biological Sciences, Purdue University, West Lafayette Indiana, for his micrographs.

I am grateful also to Mrs. Basma and Mr. Fathy, library staff, NAMRU-3, for their help.

I would also feel grateful to Mr. Soliman A. Aly, Bacteriology Dept., NAMRU-3, for his sincere aid.

Credit for photographs is due to Mr. Tony, Head Graphic Art Dept., NAMRU-3.

The author also acknowledges with thanks the great help of Miss Sona Atchoukian for typing the manuscript.

The author is greatly indebted to the Director, NAMRU-3 for the help and facilities put at her disposal to accomplish this study. This work was supported by the U.S. Navy Work Unit No.M0095-PN-002-5025.

Last but not least, I wish to thank my husband for his understanding.

CONTENTS

ABSTRACT

Chronic *Salmonella paratyphi* A bacteriaema associated with schistosomiasis is clinically well-known in Egypt. Since the mechanism is unknown, an *in vivo* model system in schistosome infected hamsters (SIH) was developed. *Schistosoma mansoni* infection enhanced and prolonged the growth of *S. paratyphi* A in hamsters. Animals with dual infections had "increased mortality" in comparison to bacterial infection alone during the 8 weeks of study. Normal hamsters (NH) and SIH were given approximately 2×10^7 *S. paratyphi* A intracardially. Over the first 3 days, SIH cleared the bacteria from their blood as well as NH. Over the next days SIH blood remains positive with increasing numbers of bacteria up to termination at 9 days. Further studies showed that bacteria persisted in various organs (liver, spleen, lung, kidney, mesenteric lymphnodes) for up to 8 weeks post infection. Worms recovered from SIH had a 100-fold increase in bacteria when compared to blood. *S. paratyphi* A were consistently found colonizing the schistosome tegument (and gut ?) up to 8 weeks after bacterial infection. No lethal effect on worms was noted. *In vitro*, *Schistosoma mansoni* alive worms were found to activate or stimulate the growth of *S. paratyphi* A in worms culture medium. Fresh serum from NH or SIH equally inhibited bacterial growth, but heat inactivated serum had no inhibitory effect on bacterial growth. In contrast, *Leishmania donovani* infection had no effect on *S. paratyphi* A infection. These findings suggest that *S. mansoni* facilitated the establishment and growth of *S. paratyphi* A *in vivo*. A general discussion of results has been given and a claim of salmonella protection against the immune host mechanism through a new surface combination between the pathogen and parasite justifying reported chronic salmonellosis in association with history of schistosomiasis in Egypt.

PART I

General Preface

Introduction

Materials and Methods

GENERAL PREFACE

Indications of an intimate relation between the development of the chronic enteric carrier state and the schistosomal infection have been repeatedly reported. In Egypt chronic salmonellosis (*Salmonella paratyphi* A relative more than *S. typhi*) has been reported to be associated with schistosomiasis (Hathout *et al.*, 1967; Higashi *et al.*, 1975). It was felt of interest to throw light on the nature of this association in a model system close to what would happen in human. In preliminary work, hamsters have been found suitable as a model system for schistosome - salmonella association. Certain experiments have been designed in an endeavors to elucidate certain aspects of this association. This thesis represents the results obtained from these experiments with a general discussion in view of the findings of the other investigators. It will be shown that a type of protection of *S. paratyphi* A, against the immune host mechanism resulting in a prolonged infection in the hamsters. The aspects investigated limit the scope of the thesis to the following:

1. The distribution of *Salmonella paratyphi* A T_{1341} in the

organs of normal and Schistosoma mansoni - infected hamsters (Mesocricetus auratus).

2. Effect of Salmonella paratyphi A T_{1341} on Schistosoma mansoni adult worms in hamsters (Mesocricetus auratus).

3. The interaction of Salmonella paratyphi A T_{1341} on different organs of normal hamsters and of hamsters infected with either Schistosoma mansoni or Leishmania donovani.

4. Studies on the nature of defense against salmonella:

a. In vivo recovery of Salmonella paratyphi A T_{1341} from the blood of Schistosoma mansoni - infected hamsters and normal hamsters.

b. In vitro reaction of Schistosoma mansoni - infected hamsters serum and normal hamsters serum on the growth of Salmonella paratyphi A T_{1341}.

5. The effect of live Schistosoma mansoni adult worms on the growth rate of Salmonella paratyphi A T_{1341}.

INTRODUCTION

Chronic Salmonella paratyphi A bacteremia associated with schistosomiasis is clinically well known in Egypt. Similar concurrent infections have been reported from China and Brazil.

The main concern in this thesis is to investigate the distribution of Salmonella paratyphi A T_{1341} in a model animal infected with Schistosoma mansoni, the effect of this salmonella on the adult worms of the latter schistosoma developed in this animal, the role of the microbe on the organs of the animal, the recovery of the microbe, and the effect of the adult worms on the growth of the microbe. It was thought that this would reveal certain considerations regarding schistosoma - salmonella interaction. In view of the above aim, this review will be given according to the following sequence:

1. Relation between the chronic enteric salmonellae carriers and their infection with schistosomes.
2. Distribution of enteric microbes in animals both normal and infected with schistosomes.

3. Effect of salmonellae and other enterics on the adult worms of schistosomes.

4. The interaction of salmonellae and other microorganisms on animals infected with schistosomes compared to other parasites in infected animals.

5. Nature of defense against salmonellae.

6. Metabolic activities of schistosome adult worms.

Before dealing with the above points, it was found suitable to outline the life cycle of schistosomes in the following manner:

The life cycle comprises the passing of the ovum from the definitive host, its hatching in water with the liberation of a free-swimming miracidium, the penetration of a suitable species of snail by the miracidium, the metamorphosis of the larva into primary and secondary sporocysts and cercariae in the snail, the eruption of free-swimming cercariae into the water, the penetration of the skin of man by the cercariae; and the migration and growth of the immature worms in the liver and blood vessels. The damage to the tissues is caused by the migrating immature worms, the adult worms, and the extruded ova.

Three species of the genus Schistosoma produce serious human disease viz. Schistosoma haematobium (bilharziasis), Schistosoma mansoni (intestinal schistosomiasis) and Schistosoma japonicum (Asiatic intestinal schistosomiasis). These three diseases have long been recognized, but the parasitic species have been clearly differentiated only since about 1915 (Belding 1964).

Since the present work deals with investigations in the relationship between schistosomiasis and salmonellosis it is felt of value to give a short account of schistosomiasis which is one of the serious medical problems of the tropics and sub-tropics.

Schistosomiasis is a chronic infection lasting, if not treated, for many years often for life and it brings about numerous serious complications as to hepatosplenic syndrome, portal hypertension and others.

1. Relation between the chronic enteric salmonella carriers and their infection with schistosomes.

In Egypt, it has been suggested by Abdalla (1946) that the presence of a high incidence of urinary salmonella carriers is closely associated with urinary schistosomiasis. Neva (1949) in Cairo studied 76 cases of salmonellosis. Fourteen failed to respond to treatment and continued for many months as chronic carriers of salmonella in the urine. Out of these 14, eight had Schistosoma haematobium infection and three gave a history of bilharziasis. Morton (1949) demonstrated that enteric fevers are common in the canal zone of Egypt, where many of the native population are urinary bacterial carriers. He suggested that this is probably due to the prevalent urinary bilharzial infections. Walton, in the same year (1949) reported that in a population, such as that of Egypt, relatively immune to the enteric fevers in adult life, a symptomless transient carrier state is not uncommon. He suggested continuing work to find out whether such carriers are a fact transient or intermittent chronic carriers and also to ascertain what other factors affect the chronicity of carriers such as age, infection of the urinary