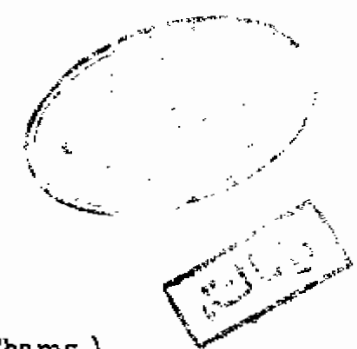
STUDIES ON CELLULAR IMMUNITY AND INTRADERMAL SKIN TEST IN CASES OF SCHISTOSOMIASIS USING SPECIFIC ANTIGENS

Thesis Submitted For Ph. D. Degree in

Medical Science

(Parasitology)



By

Adel M. G. El Missiry

M. B. Ch. B., D. M. Sc., (Ain Shams)

Parsitology Department,

Faculty of Medicine, Ain Shams University

Cairo, A.R.E.

1980

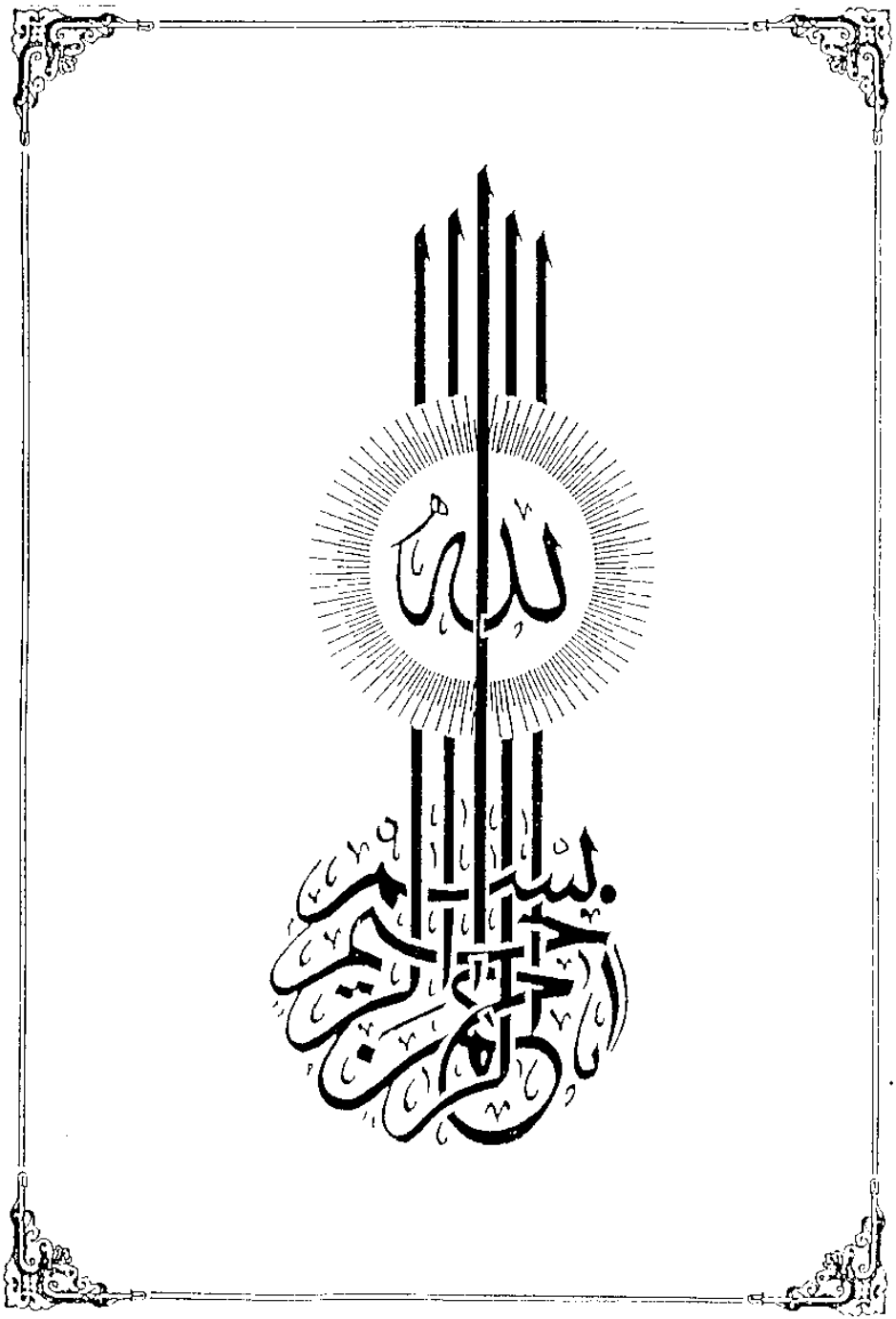
ACKNOWLEDGEMENT

I wish to express my eternal idebtedness to Prof. Dr. Hamed M. Khalil, Professor of Parasitology, Faculty of Medicine, Ain Shams University, and the Principal Investigator of Skin Schistosomiasis Immunology Unit , Sponsored by Grant Agreement No. 03 - 329 C - 1975 between C.D.C., PHS., Atlanta, Georgia, U.S.A. and Ain Shams University, for his advice, guidance, Consultation and encouragement, his material contribution by a wealth of reference has expended my views greatly, and all research facilitis throughout the work .

I must extend my gratitude to Prof. Dr. Kouka S.E. Abdel Wahab, Professor of Bacteriology Department, El-Azhar Faculty of Medicine, for her extreme patience and kind supervision and help to accomplish the work. I would like to express my sincere appreciation and eternal indebtedness to Dr. Mohamed Khairy Makled, Assistant Professor of Parasitology and Senior immunologist, Faculty of Medicine, Ain Shams University, for his untiring effort and his personal enthusiasm and careful supervision, encouragement, he gave me much of his time and experience which helped me throughout the work.

I wish to thank Prof. Dr. Hussein S. El Nahal, consultant of Parasitology, Military Medical Academy, for his help in the start of this work with his constructive criticism.

I am especially extend my deepest gratitude to Dr. M. Fathy Abdel-Wahab, physician and Assistant Professor, Ain Shams University Hospitals, for his valuable help and for his careful supervision of human subjects investigated in this study and admitted as inpatients and for his accuracy in giving treatment and help in correlation of results.



In particular the work would never have been completed without the help of Prof. Dr. Taheia Abdel Aal, Professor of Parasitology, Faculty of Medicine Ain Shams University, for her help in preparation of Schistosome antigens used in this work.

Also, extend my gratitude and a preciation to Dr. Fathy Abdel Ghaffar for his patienceand help in the conduction in the work of cell mediated immunity.

Also, may thanks to Prof. Dr. Mohamed Sadek, Professor of Parasitology Faculty of Medicine, Ain Shams University for his valuable help

Many thanks for Prof. Dr. I.G. Kagan, head Parasitology Section, C.D.C., P.H.S., Atlanta, Geogria, Project officer to the above agreement for his valuble critisism and guidance help and support during his visit to the unit.

Many thanks to Dr. S.E. Maddison for her valuable consultation and guidence during her visits to cairo.

Thanks to all the personal of Parasitoloty Department, Faculty of Medicin Ain Shams University for their cooperation during the performance of this work.

C O N T E N T S

REVIEW OF LITERATURE

I N T R O D U C T I O N

A country can not usefully think of economic and social development without considering health.

Though bilharziasis is a world wide proplem, it is for us the prime health problem related to our socioeconomic progress, hence it affects millions at an early age reducing productivity and exerting a significant socio-economic impact. The reduction of the total economic production due to bilharziasis has been estimated to be about 30 % (Mousa et al, 1969). Since Egypt is a developing country, this problem must be urgently solved.

There is strong evidence that the construction of the High Dam and the progressive increase of cultivated land had contributed to further increase of the disease prevalence in our country (Khalil et al, 1976).

Since four thousand years, the disease is endemic in Egypt and it was described in Ebers papayrus, moreover calcified ova were found in tissues of some ancient Egyptian mummies (Loose, 1911).

Immunological research in schistosomiasis has made important progress during the last years. But in spite of all the information that has been gathered, the overall pattern of immunity in schistosomiasis remains obscure, full of apparent anomalies and unanswered questions. Even if it is not certain that schistosomiasis will take benefit from the immunological studies, the theoretical interest is so great that immunology has already and will continue to take more and more advantage of the study of schistosomiasis (Capron, 1978).

Introduction to concepts of Immunology

The study of immunology began in the 19th. century. Immune is a term derived from latin word immunis which originally means exemption from military service or paying taxes.

The first effective immunization was performed by Edward Jenner (1749 - 1823) who observed that persons who got well after infection with cowpox, were protected against small pox.

* The subject of immunology can be considered under four general headings :-

I - Immunity :- Dealing with the adaptive response to infective agents.

II- Immunochemistry:- Concerned with the chemical nature of antigens and antibodies.

III- Immunobiology :- Deals with the activity of the cells of immune system and their relationship to each other and their environment.

IV- Immunopathology :- This is the study of tissue alternations that result from immune reactions.

* Immunity is divided into two main types :-

I - Non specific or innate immunity.
II- Specific or acquired immunity.

I- Non specific or innate immunity :-

Innate immunity also termed natural immunity, genetic immunity and constitutional immunity. It depends on a number of very effective mechanisms present from birth, which do not depend upon having previous experience of any particular antigens.

Factors Regulating innate Immunity :-

The body has a number of factors that make it capable of reacting to foreign substance and to body cellular debris, for example:-

1- Mechanical barriers and surface secretion :-

a) The skin, with its keratinized surface cell, provides a tough and dense covering layer interrupted occasionally by glands and hair follicles. Some of the fatty acids secreted by the glands of the skin have an anti-microbial effect (Weir , 1977, and Herbert and Wilkinson, 1977).

b) The mucous membranes are covered by a viscous slimy secretion that entrops foreign material.

c) Antimicrobial factors such as white blood cells in the mucinous layer and lysozymes which are found in relatively high concentration in polymorpho-nuclear leucocytes as well as in most tissue fluids except C.S.F., sweat and urine. Lysozymes are synthesized in the parotid gland, mucosa of the respiratory and gastrointestinal tract and in the spleen and lymph nodes. Lyzozyme acts as a mucolytic enzyme, splitting sugar off gluco-peptides of the cell wall of many gram-positive bacteria, and plays a role in intracellular destruction of some Gram-negative bacteria (Foster,1970 and Boyed, 1977).

d) The acidity and movement of food prevents colonization of the stomach with microorganisms (Foster, 1970, and Boyed, 1977).

e) The filtering action of the hair of the nares and the cilia of respiratory tract, and the flushing action of

the saliva and urine exmplify other resistance factors that prevent penetration of tissue by foreign substance.

f) A variety of basic proteins, derived from the tissue and blood cells damaged in the course of infection and inflammation, this variety of basic proteins called basic polypeptides, found in the tissue of animals, these basic polypeptides have ability to destroy bacteria.

g) The normal microflora :-

The normal microflora of the oral cavity, the lower gastrointestinal tract, the skin, and the vagina attack the easy establishment of new arrivals.

h) Prostatic secretion :-

It contains spermine & a polyinine which is a potent inhibitor of gram positive micro-organims at concentration normally encountered in semen.

2- Inflammation and phagocytosis

Inflammation, a common host response to injury, can be induced by antigen-antibody reactions that activate the complement system. Intact skin is not easily infected and most infections begin at mucosal surfaces.

Acute inflammatory responses, induced by antibodies or other agents, involve a rapid set of events at the site of injury. Local vessel dilation allows influx of plasma proteins and phagocytic cell into the tissue spaces.

Chronic inflammatory responses are characterized by an infiltration of lymphocytes and cells of the monocyte-macrophage lineage, these responses may be induced by immunological injury initiated by effector T cell.

Both acute (antibody-induced) and chronic (T-cell induced) inflammation may occur in the skin. These responses are called immediate and delayed hypersensitivity (Broyton et al, 1970 and Rood, 1977).

Micro-organisms or inert particles such as colloidal carbon entering the tissue fluid or blood stream are very rapidly engulfed by various circulating and tissue fixed phagocytic cells, these cells are of two types :

a) Polymorphnuclear neutrophil leucocytes, also called microphages, and concerned with the micro-organisms which perish once ingested, these micro-organisms are considered extra cellular pathogens.

b) Mononuclear phagocytes, these cells are distributed throughout the body both circulating in the blood (monocytes), and fixed in the tissue (macrophage) (Dannenberg, 1975).

These cells are concerned principally with the control of micro-organisms which are able to survive intracellular residence and against which neutrophils are ineffective, these cells are much more important in chronic infection (Ranifin and Eline, 1970).

Phagocytosis :- (Figure: 1)

Bacteria and cellular debris are primarily removed from the injury site by phagocytosis. Many micro-organisms particularly encapsulated ones, resist phagocytosis and hence have enhanced pathogenicity. The phagocytosis by neutrophil is composed essentially of 4 interrelated phages these are :

a) Chemotaxis : It is the process whereby phagocytic cells are attracted to vicinity of invading pathogens.

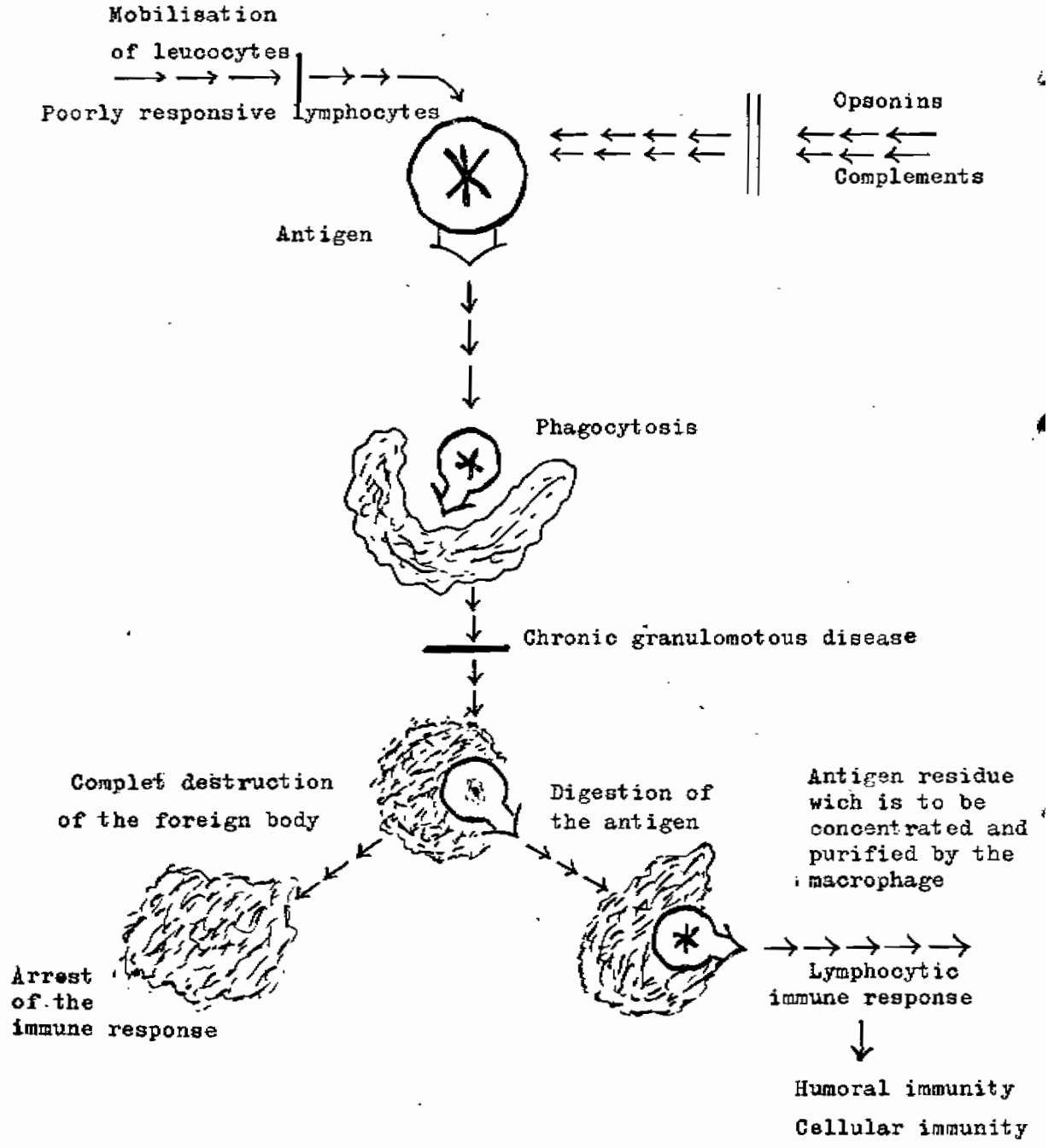


Fig. (1)
PHAGOCYTOSIS

(The initial response in the normal immunological system)

b) Opsonization :- The function of serum opsonin is to react with microorganisms and makes them more susceptible to ingestion by phagocytes.

c) Ingestion :- Polymorph-nuclear leucocytes are actively phagocytic, the energy for this process is derived from glycolysis.

d) Killing :- The mechanisms by which neutrophils kill micro-organisms are not clearly understood, but after ingestion the bacteria, they are acted upon by hydrolysing enzymes derived from lysosomes (Cline and Lehrer, 1968 and Stossel, 1974).

II- Specific or acquired immunity :

This type of immunity is dependent upon antibodies or the cell-mediated immunity mechanism. The macrophages are an important link between the innate and the acquired immune mechanisms, partly by passing antigens or their products to the lymphoid cells and partly retaining antigens to ensure that lymphoid cells are not overwhelmed by excess antigen (Greaves et al, 1973).

The autogenic maturation time of lymphoid system relative to birth differs from one species to another. As measured by the onset of immune responsiveness as well as by the appearance of peripheral T and B cells, mice and birds develop their immune system just before and after birth, whereas sheep and humans develop functional immune systems early in gestation, well before birth (Jerne, 1973).

However, in all species the immediate postnatal period is marked by dramatic differentiative changes in the immune system, reflecting the sudden exposure to a host of environ-