IMMUNE COMPLEXES IN SCHISTOSOMIASIS

Thesis

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(Tropial Medicine)

By

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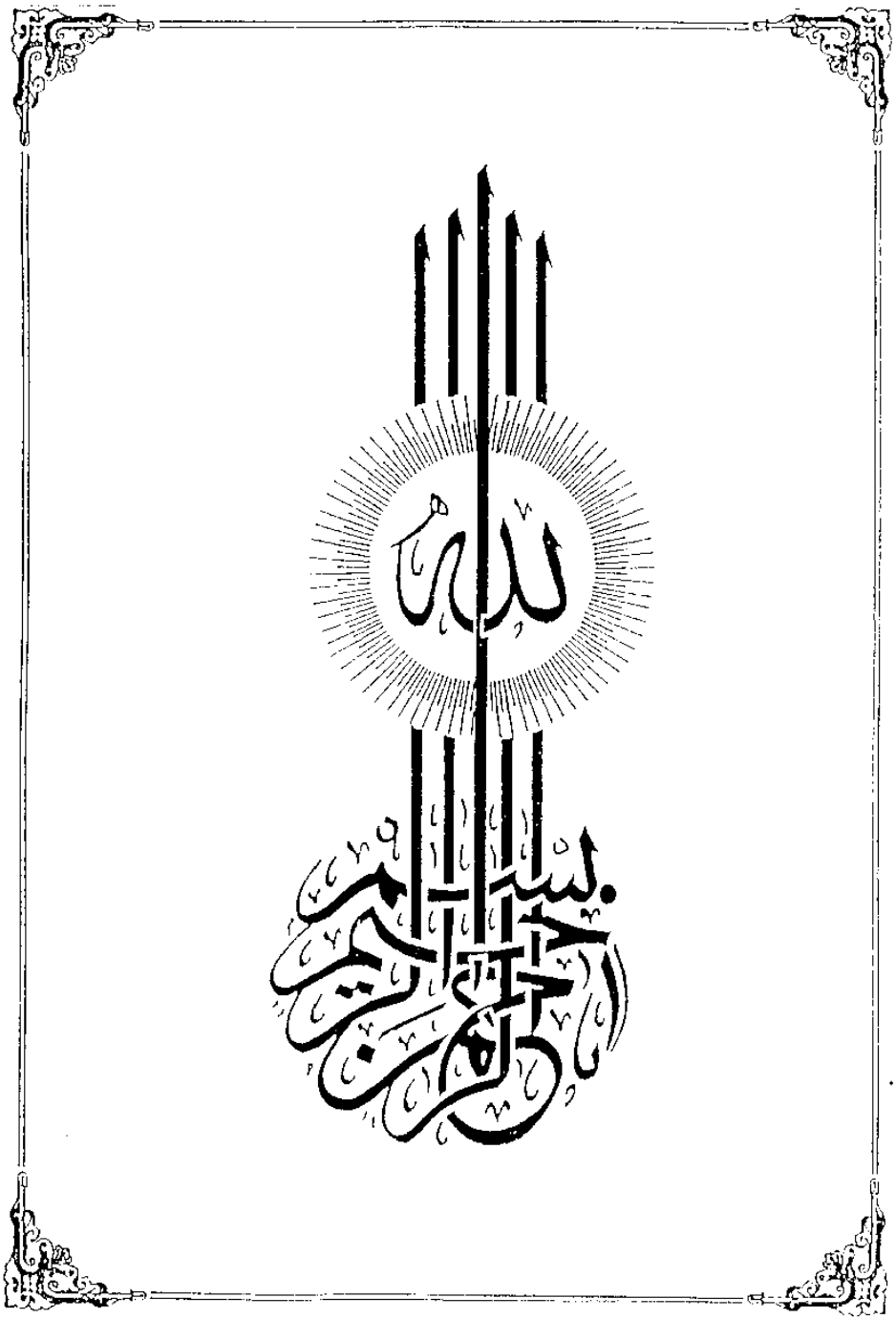

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Introduction

INTRODUCTION AND AIM OF THE WORK

Schistosomiasis is one of the major health problems of increasing importance in different part of the world as regard its prevalence, severity and related complications; as it attack many organs in the human which are considered as life threatening as hepatosplenomegaly, portal hypertension, nephropathies and anaemia.

Circulating schistosome antigens have been found in a variety of animals (Berggren and Weller, 1967; Carlier, Bout and Capron, 1978) and in man infected with S. mansoni (Madwar and Voller, 1975; Santoro et al, 1978). These antigens stimulate the formation of antibodies to form antigen-antibody complexes.

These antigen-antibody complexes have been suggested to be associated with the renal injury observed particularly in the hepatosplenic form of the disease (Rocha et al, 1976). In addition demonstration of glomerular capillary deposits of immunoglobulins, C_3 component of complement and schistosomal antigens (Falcao and

Gould, 1975) associated with elution of renal antischistosome antibodies in patients infected with S. mansoni (Moriearty and Brito, 1977) suggested an immune complex mechanism which probably requires activation of complement.

The aim of the work is to study the level of complement component, C_3 in schistosomal patients sera as an indirect method detecting the presence of circulating antigen-antibody complexes. To correlate this level with the degree of antigenemia of the patients and the function activities of the liver, as it is the major site of synthesis of this complement component.

Review of Literature

General aspect of immune response:

The term immunity has denoted resistance to possible attack by an infectious agent (Funderberg et al, 1978).

The response of the body to foreign elements involve both non specific and specific mechanism of defense. The non specific mechanism include the skin barrier and mucosa, antisepsis of mucosal secretions and simple phagocytosis by polymorphonuclear leucocytes and macrophages. Specific mechanism are those elaborated by the immune response.

There are two categories of immune response; the cell mediated response, produced by locally active lymphocytes present at the same time and place as specific antigen and the humoral response, which are wide spread distributed throughout the body (Widmann, 1979).

The major humoral elements, although ultimately derived from cells, include circulating factors such as immunoglobulins (especially IgG, IgM and IgA) and

complement. B lysins and lyzozyme may be also important elements in the humoral response.

Cell mediated response follow stimulation of thymic-dependent lymphocyte (T lymphocyte) with specific antigens allowing them later to release bioactive lymphokines, some of which interact with certain cells (macrophages) to enhance their capacity for phagocytosis and intra-cellular microbial activities against certain microbes. (Mc Call and Johson, 1979).

Both cellular and humoral immune responses to antigens can occur and in many infections one or the other predominates. The factors determining whether cellular or humoral response predominates in any infection are not fully understood. The chemical and physical nature of the antigens are important. Host factors are also important to determine the type of immune response (Page Faulk and Greenwood, 1977).

THE COMPLEMENT SYSTEM

Introduction:

The complement system consist of at least 18 chemically and immunologically distinct serum proteins which are mainly activated by antigen-antibody complex to interact with each other and with cell membranes.

The interaction lead to generation of biological activities, the biological sequalae of activation of this system range from lysis of spectrum of different kinds of cells, bacteria and viruses to direct mediation of inflammatory processes (Fearon, 1981).

Activation of complement initiate a cascade of specific proteolytic reactions in a manner analogues to the coagulation system. These reactions lead to either lesions in cellular membranes, cell cytolysis or the appearance of products which are biologically active in the process of inflammation, increasing immune adherence and attracting polymorphs and mononuclear leucocytes (Muller - Eberhard 1975, Widmann 1979).

Complement may damage host tissues and causes diseases rarely due to defects in the complement system (Cooper 1978, Fearon 1981).

Nomenclature: (according to WHO reports, 1968).

The classic complement (C) system in humans include nine components. In order of their reaction, the complement components are designated numerically from C_1-C_9. C_1 is a trimolecular complex of C_{1q}, C_{1r} and C_{1s} held together by ionic calcium. C_{1t} has recently been described as a further subunit of C_1, its function and significance are not yet clarified (Assimethand Painter 1975).

Proteins of complement system:

The individual proteins of this system are normally present in the circulation as functionally inactive precursor molecules, together they comprise about 4-5% of the total serum protein and 15% of the plasma globulin i.e. approximately 300 mg/dl. Quantitavely C_3 and C_4 comprise approximately two thirds of the complement system (Cooper, 1978 and Miller etal, 1980). They differ in their physical properties and their serum concentrations, but all are glycopoteins in nature (Muller and Eberhard, 1975).

The different protein components of the complement system, its regulators, its nature, molecular weight and concentration were summarised in the following tables (1, 2 and 3).

Table (1): Characteristics of complement components as classical pathway.

Name	Synonyms	Molecular weight	Electrophoretic mobility	Approximate serum concentration(ug/ml)
C_{1q}	CO_1, 115 protein	400,000	γ 3	190
C_{1r}	.....	168,000	B	
C_{1s}	C_1esterase	79,000	α_2	120
C_4	B_1E	240,000	B_1	430
C_2	...	117,000	B_2	30
Membrane - attack system				
C_3	B_{1c}	185,000	B_1	1300
C_5	B_{1f}	185,000	B_1	75
C_6	...	125,000	B_2	60
C_7	...	120,000	B_2	60
C_8	...	150,000	γ 1	Trace
C_9	...	79,000	α	Trace

Adopted from W.H.O. 1968 and Fearon 1981.