IMMUNOGLOBULINS AND SERUM COMPLEMENT BEFORE AND AFTER SPLENECTOMY IN CIRRHOTIC PATIENTS

THESIS

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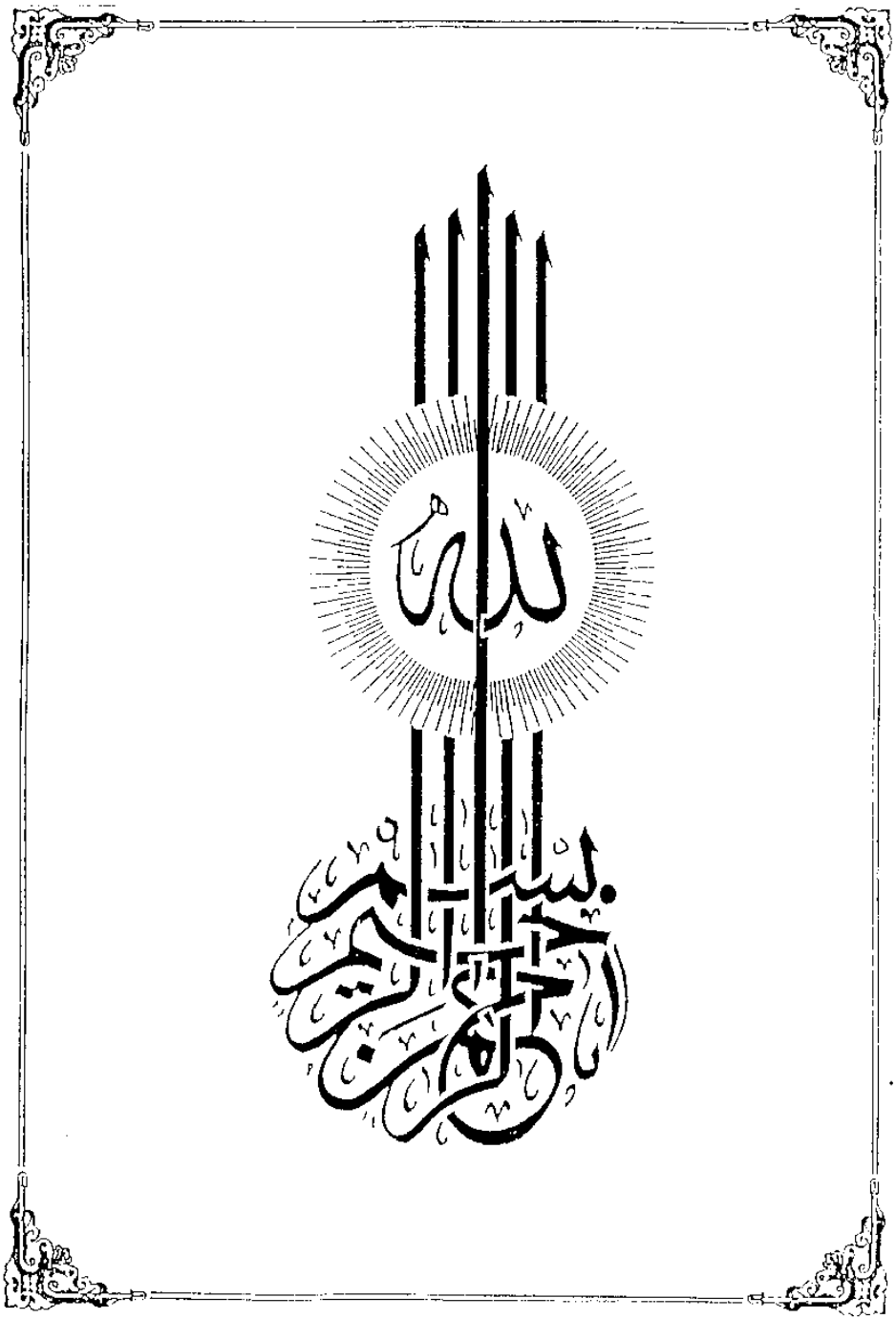

CONTENTS

Introduction
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The spleen acting as a filter to the blood stream, plays an important role in immunity; both humoral and cell mediated. It represents the meeting point between antigenic informations transported by the blood stream and the immune apparatus responsible for mounting the host response (Lockwood, 1983).

Splenectomy in cirrhotic patients with portal hypertension and splenomegaly is a common procedure in Egypt especially in those patients affected with schistosomiasis.

Increased serum IgG and decreased serum IgM were noted after splenectomy (Drew et al., 1984), other authors reported no change in serum IgG and IgM following splenectomy (Koren et al., 1984 and Chelazzi et al., 1985). The antibody response to pneumococcal vaccine showed no change in splenectomized patients (Sullivan et al., 1978).

Other reports indicated an impaired response (Hosea et al., 1981b & DiPadova et al., 1985). So the post splenectomy immunological changes are still controversial.

The aim of the present work is to investigate serum immunoglobulins and serum complement before and after splenectomy in cirrhotic patients.

Review of Literature

REVIEW OF LITERATURE

Immunity

Immune is a term derived from Latin word immunis which originally means exemption from military service or paying taxes. Immunity includes the mechanisms dealing with the adaptive response of an individual to infective agents, and it is divided into two main types:

I. Non specific or innate immunity

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

II. Specific or acquired immunity:

This type of immunity depends upon exposure to a foreign configuration with the subsequent recognition and reaction to it. It may be active or passive (Weir, 1981 & Hood et al., 1978).

Passive immunity is produced by giving the individual already formed antibodies or immunocompetent cells. This may be natural which the mother gives to her fetus through antibodies transferred by the placenta

or via colostrum during lactation. It may also be artificial in the form of artificial injection of gamma-globulins that were obtained from animals or other humans and injection of antitoxic sera.

Active immunity in which the body builds its own immunity following exposure to antigens.

Mechanism of immune response:

There are two types of effector mechanisms responsible for the specific immune responses: humoral and cell-mediated (Pierce & Benacerraf, 1975). Humoral immune response mediated mainly by antibodies, and cell mediated immune response mediated by specifically sensitised lymphocytes.

Physiology of immune responses :

Both cellular and humoral immune responses have been arbitrarily divided into three physiological limbs:

1. **Afferent limb:**

This comprises all processes involved in the transport of antigen to the immunity system.

2. **The central limb:**

This includes all processes culminating in production of the effectors of immunity (i.e. sensitized cells or humoral antibodies).

3. **The effector limb:**

Comprises all processes occuring between the release of effectors and their ultimate action upon the initiating antigen. (Gowans et al., 1962).

Cell-mediated immune response:

Cell mediated immune responses are the domain of the thymus-derived lymphocytes (T-cells) which recognize antigen by membrane receptors specific for that antigen (Warner, 1974). On exposure to an antigen small lymphocytes differentiate into large cells and divide to give rise to daughter small lymphocytes referred to as activated T-lymphocytes (Sprent & Miller, 1971).

After activation, T-lymphocytes are differentiated into cytotoxic killer cells, helper cells facilitating antibody response by B-lymphocytes and suppressor cells capable of inhibiting antibody production (Gershon, 1974). Activated T-lymphocytes produce lymphokines which

are non specific effectors of cellular immunity. Lymphokines are responsible for various effects on macrophages, monocytes, polymorphonuclear leucocytes and lymphocytes (Lawrence & Landy, 1969).

Humoral immune response:

The humoral immune response is dependent upon B-lymphocytes. B-lymphocytes arise in the bone marrow as stem cells which undergo a process of division and functional maturation into B-lymphocytes in the mammalian equivalent of the bursa of fabricious of chicken. (Cooper and Lawton, 1974). B-lymphocytes upon interaction with the antigen are transformed to plasma cells which synthesize and secrete a large amount of antibodies (Moller, 1975).

IMMUNOGLOBULINS

Gamma globulins were first recognised and designated as a distinct group of serum proteins by Tiselius (1937) and he termed these proteins gammaglobulins because they migrated more slowly in an electric field than globulins of two other groups called alpha and beta.

The term immunoglobulin is commonly used to describe serum proteins with antibody characteristics (Heremans et al., 1959). This includes the gamma globulins and also extends to include beta globulins (Chodirker & Tomasi, 1963).

Evans (1984) described immunoglobulins as being globular proteins containing carbohydrates and by definition are glycoproteins. Immunoglobulins occur as monomers and polymers and are divided into several classes and subclasses based on antigenic differences in various constituent polypeptides. Biochemical studies have revealed striking similarities in the structue of these immunoglobulins despite of many dissimilarities detected by physical and immunologic studies. In humans there are five molecular classes of immunoglobulins. These are designated as IgG, IgM, IgA, IgD and IgE.

The basic structure of immunoglobulins is composed of two pairs of polypeptide chains, two light chains of molecular weight 20.000 and two heavy chains with molecular weight of about 50.000 linked together by covalent disulphide bonds as well as noncovalent hydrophobic bonds (Weir, 1983).

Heavy chains of IgG, IgA, IgM, IgD and IgE are termed gamma (γ), alpha (α), mu (μ), delta (δ) and epsilon (ϵ) respectively. The heavy chains are specific for each immunoglobulin and they provide the basis for their individual specificity (Ritzman & Levin, 1967)

Light chains are common to all immunoglobulins, two types of light chains are known, kappa (k) and lambda (λ). Individual immunoglobulin molecules possess either K or λ light chains but not both (Mckelvey & Fahey, 1965).

Plasma cells are the antibody producing cells which according to the clonal selection theory of Burnett (1957) are formed by proliferation of small lymphocytes (B-lymphocytes) when antigen attaches to its specific receptors on surface of B-lymphocytes.

The effect of contact of antigen with these specific receptors is to stimulate the growth and proliferation of these cells into plasma cells. In this way body of cells or clone develops and as its size increases so does antibodies production appear (Walter, 1979).

Types of immunoglobulins :

I. **Immunoglobulin G (IgG):**

This constitutes approximately 75-80% of immunoglobulins, the normal serum concentration is 900-1800 mg/100 ml, its molecular weight is 150.000 and its carbohydrate content is 2.5% (Max Samter, 1971).

Being of low molecular weight it is equally distributed in the different fluid compartments. It is the only immunoglobulin which can be transferred across the placenta to the foetus supplying it with natural immunity. It has the longest half life of immunoglobulins which is about 6-23 days (Walter,1979).

The majority of acquired antibacterial and antiviral antibodies fall in this class. It is responsible for the major part of antibodies of secondary response. It appears late in infection but remains for a long time. It is an effective opsonin i.e. promoting phagocytosis. The reaction between IgG and antigen activate