STUDY OF ANTIHEPATITIS A IMMUNOGLOBULIN G IN BILHARZIAL LIVER FIBROSIS AND NON BILHARZIAL SUBJECTS

Thesis

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BY

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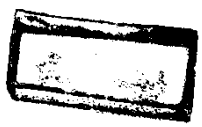

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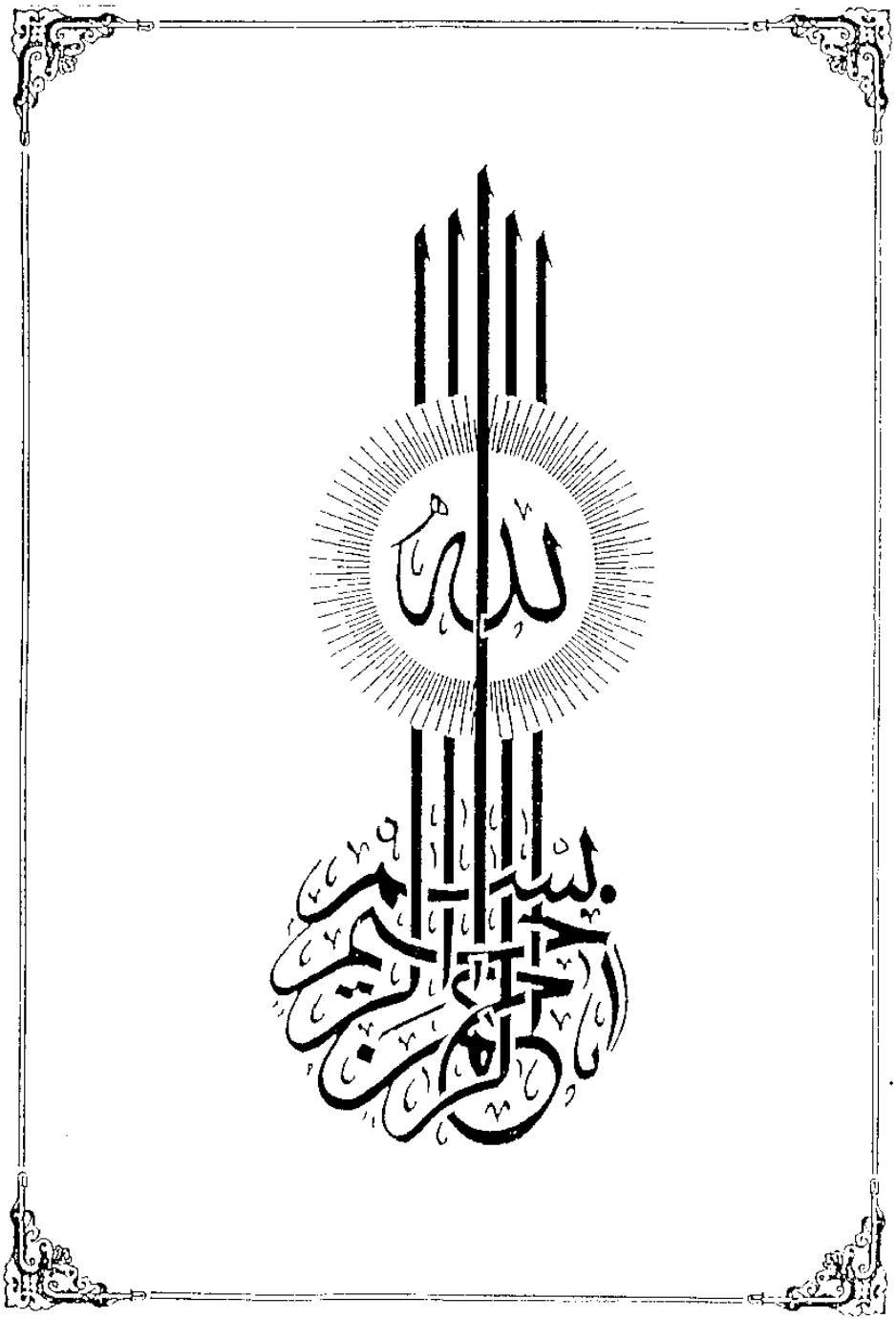

TO MY DAUGHTER :

S A R A H

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INTRODUCTION

Virus A hepatitis is considered one of major infectious diseases in Egypt. It is easily transmitted by feacal oral route and infection is common where standards of hygiene and sanitation are poor. Virus A hepatitis can be divided typically into inapparent, anicteric infection and icteric hepatitis.

Serological diagnosis of hepatitis A depends on the appearance of immunoglobulins. The first to appear is IgM which is detected during acute phase and reaches peak level at about 6 weeks after the onset of infection and decline thereafter.

The second immunoglobulin is IgG antihepatitis A which starts to appear 3 - 4 weeks after the onset and reaches peak level within 3 - 11 months. Identification of this antibody appears to be the most appropriate technique for the serological diagnosis of hepatitis A in the late convalescence or in serological studies of hepatitis A prevalence since it appears to be a persistent antibody.

Hepatitis A is characterised by absence of chronic hepatitis, no long term carrier states, and no reco-

gnized association with either cirrhosis or hepatocellular carcinoma.

Yet Bilharzial liver fibrosis is known to predispose to chronicity of virus B infection and its effect on virus A infection is therefore worth studying.

Our work is aiming to measure the prevalence of hepatitis A infection in middle aged persons who are expected to be exposed to virus A at a previous period of their life.

Also we aim to measure the prevalence of hepatitis A infection in patients with bilharzial liver fibrosis in comparison to normal individuals.

REVIEW

of

LITERATURE

IMMUNOGLOBULINS

IMMUNOGLOBULINS

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

Tiselius and Kabat next demonstrated that the antibodies of serum are restricted to the gamma globulins. Many years elapsed before the Nobel Prize ; winning works of Porter and of Edelman and their associates revealed much of the fine structure of antibody moleculer and stimulated a wave of research rarely equaled in any science (Evans, 1984).

Since antibodies are gammaglobulins they are referred to as immunoglobulins.

In the same article Evans described immunoglobulins as being globular proteins containing carbohydrate 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 structure 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, IgA, IgM, IgD and IgE. In each Ig refers to immunoglobulin and the third letter to some distinctive property of that immunoglobulin (Barrett,1978).

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 (Weir, 1983).

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 in surface of B lymphocytes (now thought to be antibodies equivalent in specificity to antibodies they will later secrete (Cremer, 1979).

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 :

IMMUNOGLOBULIN G (IgG)

This constitutes approximately 75 - 80 % of immunoglobulins, the normal serum concentration is 0.8 to 1.5 gm / 100 CC, molecular weight of this globulin 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 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 second response. It appears late in infection but remains for a longtime. It is an effective opsonin i.e. promoting phogocytosis. The reaction between IgG and antigen activate a complement system leading to release of several chemical

mediators including factors causing immune adherence as well as anaphylatoxins and permeability factors which initiate inflammation and hypersensitivity reaction (Weir, 1981).

Immunoglobulin G of virus A hepatitis starts to appear 3 - 4 weeks after the onset of infection and reaches peak level within 3 - 11 months. It appears to be a persistent antibody (Bouchier, 1980).

IMMUNOGLOBULIN M (IgM)

It is called macroglobulin because of its high molecular weight 900,000. Its carbohydrate content is 10 - 12 %. Its normal serum concentration is 0.039 to 0.117 gm% and it constitutes 5 - 10 % of electrophoretically isolated gammaglobulins (Max Samter, 1971).

It is essentially limited to blood stream and cannot cross the placenta (Walter, 1979).

It is the earliest response to antigenic stimulation but it is short lived, its presence indicates recent infection (Weir, 1983).

This globulin includes isohaaemagglutinin, Rh anti-

bodies, coldagglutinins, many of heterophilic antibodies and the rheumatoid factor (Max Samter 1971).

The high valency of IgM makes it more efficient in agglutination and complement fixation and it performs opsonization particularly efficiently (Weir, 1981).

IgM of hepatitis A virus is detected during the early acute phase of hepatitis A and reaches peak level at about 6 weeks after the onset of symptoms and declines thereafter (Stollerman et al.,1978).

IMMUNOGLOBULIN E (IgE)

This immunoglobulin is found in serum in trace amounts about 0.2 Ug/ml and appears to be increased in about 50 % of patients with parasitic and helminthic infections. Its molecular weight is 200,000, not crossing the placenta (Max Samter , 1975).

It has a tendency to attach to tissue cells. It is fixed to basophils and most cells and upon reaction with a corresponding antigen leads to injury of the most cells with release of histamine, serotonin, brodykinin, as well as slow reacting substance. This is responsible in humans for various forms of hypersensitivity reaction. It has been postulated that IgE plays a major role