HAPTOGLOBIN IN EPILEPSY

Thesis

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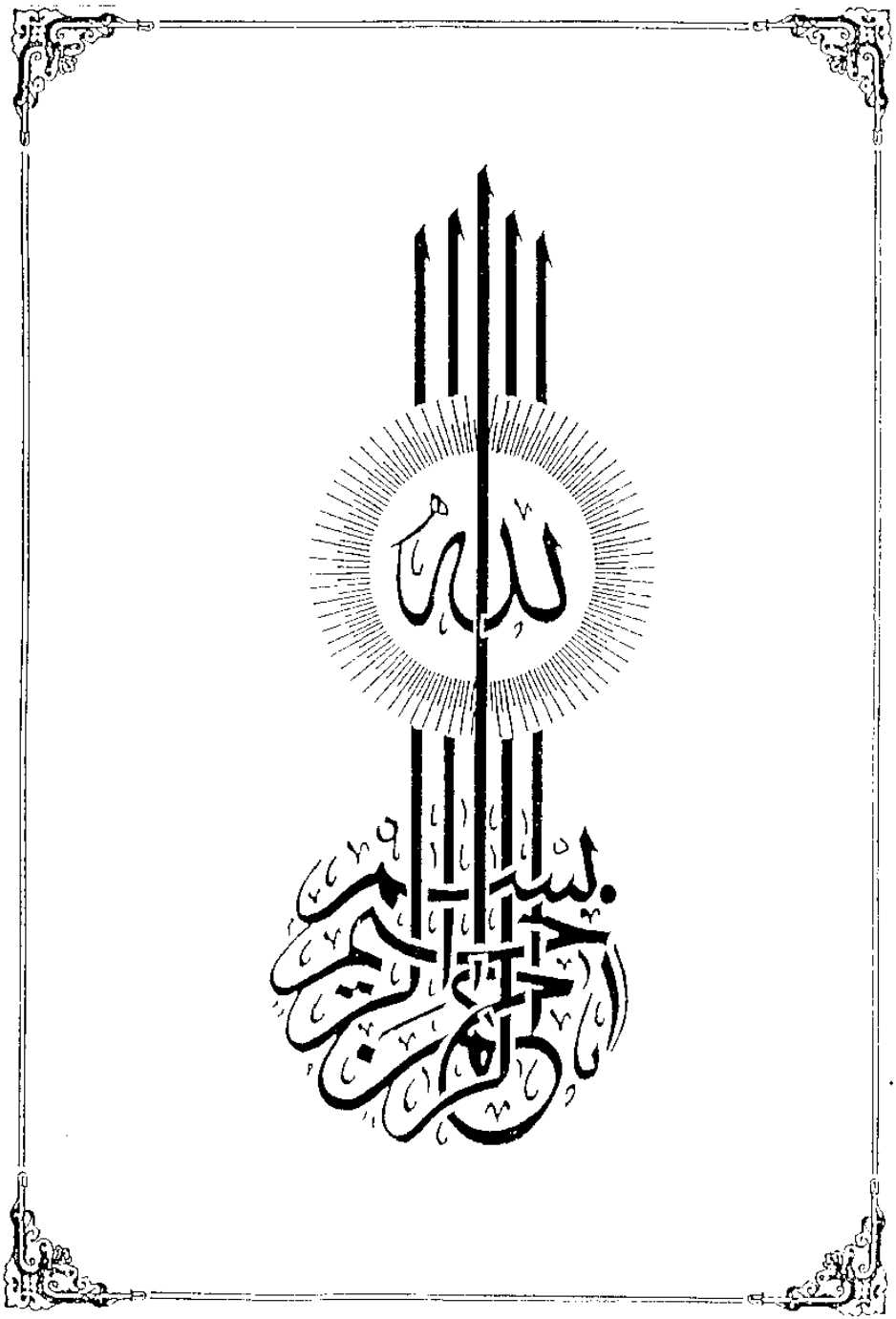

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List of Abbreviations

Hb - Haemoglobin

Hb Bc - Haemoglobin binding capacity

Hp = Haptoglobin

R.E.S - Reticuloendothelial system.

IgM = Immunoglobulin M

IgG = Immunoglobulin G

HPo - Ahaptoglobinaemia

P-HP - Haptoglobin concentration in plasma

PPD = Purified protein derivative

INTRODUCTION AND AIM OF WORK

INTRODUCTION

Haptoglobin is a plasma protein synthesized by the liver. Its electrophoretic mobility lies in the range of the alpha-2 protein of which it is quantitatively the most important part.

It has been known that the biological function of haptoglobin is associated withthe metabolic pathways of hemoglobin, as it immediately binds the hemoglobin which is liberated from RBCs and transports it to the reticuloendothelial system. Another important part of the biological function of haptoglobin seems to be associated with acute phase reaction caused by inflammation or some other cell destruction (Salmi, 1973).

The term epilepsy or recurrent convulsive disorder, designates a variable symptom complex characterized by recurrent, paroxysmal attacks of unconsciousness with a succession of tonic or clonic muscular spasms or other abnormal behavior. The exact etiology of what is called idiopathic or cryptogenic epilepsy is difficult to be reached, familial incidence is higher among this group (Baird, 1983).

Panter et al (1985) proposed that inefficient clearance of interstitial hemoglobin from the central nervous system may predispose to encephalic inflammation and the appearance of seizure disorders.

With this idea in mind, haptoglobin with its intimate relation to hemoglobin, if it is found decreased, either inherited or acquired via traumatic processes, may be the cause of ineficient clearance of hemoglobin from central nervous system engendering the peroxidation of brain lipids and disturbing brain metabolism.

AIM OF THE WORK

The aim of this work is to estimate the haptoglobin level in different types of childhood epilepsy to find out a possible relation of haptoglobin level to inherited or acquired epilepsy.

REVIEW OF LITERATURE

HAPTOGLOBIN

Haptoglobin is a serum protein that is present in all mammals and vertebrates. It represents about one-fourth of the normal α_2 globulin fraction (Putnam, 1975). Haptoglobin originally identified by Polonovski and Jayle (1939). Haptoglobin has the remarkable property that it forms a stable, effectively irreversible complex with hemoglobin that has been released from erythrocytes in the circulation (Wejman et al, 1984). This property is the basis of their discovery and of their denomination. (Greek Hapto = I attach myself to), (Jayle and Moretti, 1962). This complex is removed from the blood stream in the liver, digested there, and the iron recycled. Based upon this very strong binding, it has been suggested that haptoglobin is involved in recycling of hemoglobin iron, although Eaton et al (1982) have propsoed that it may function as a bacteriostat to deny heme iron to pathogenic bacteria.

Structure:

Haptoglobin is composed of two types of chains, a light (L) chain and a heavy (H) chain, which are now known to be synthesized as one polypeptide and

then processed to form the two chains (Haugen et al, 1981).

The H and L chains are connected by a disulfide bridge. In addition, the HL unit is joined to another HL via a disulfide bridge between the L chains to form the complete molecule which can be symbolized as H-L-L-H (Black & Dixon, 1968).

Haptoglobin is composed of four disulfide-linked polypeptide chains: two identical, invariant B-chains controlled by a single locus, Hp^B, and two variant α chains (Linke, 1984).

The α Chain:

The haptoglobin α chain is polymorphic with three common phenotypes; 1, 2, and 2-1. Further studies have revealed two common electrophoretic Hp α1-Subtypes, 1S (slow) and 1F (fast) (Teige et al, 1985). The two $Hp\alpha_1$ chains differ only by a single amino acid, the F variant with lysine and the S variant with glutamic acid at position 54. (Linke 1984).

The $Hp\alpha_2$-chain is assumed to be the result of an unequal crossing over and gene duplication of two $Hp\alpha_1$-genes (Smithies et al, 1962). In accordance

with this theory the Hpα_2-chain has been shown to exist in three different isoelectric forms; 2FS, 2FF, and 2SS with a molecular weight nearly twice that of the Hpα_1-chain (Connell et al, 1966).

In human this L chain has no carbohydrate and it contains a single cystine, one cysteine which binds to the H chain, and one cysteine that binds to another L chain (Wejman et al, 1984).

B chain:

Haptoglobin B chain is a glycoprotein exhibiting a high degree of isoelectric heterogenity (Teige et al, 1985). The B chain was found to play a special role in biological properties of haptoglobin molecule. Formation of the Hp complex showing peroxidase activity with hemoglobin was ascribed to the binding of one half molecule of hemoglobin for each B chain present in any haptoglobin phenotype (Dobryszycka and Guszynski, 1985). Most antigenic determinants are located on the B chain (Javid and Fuhrman, 1971).

Moreover, structural similarity of the B chain to the family of serine protease might suggest that this region has been preserved intact during evolution