CYTOMEGALOVIRUS INFECTION AFTER OPEN HEART SURGERY

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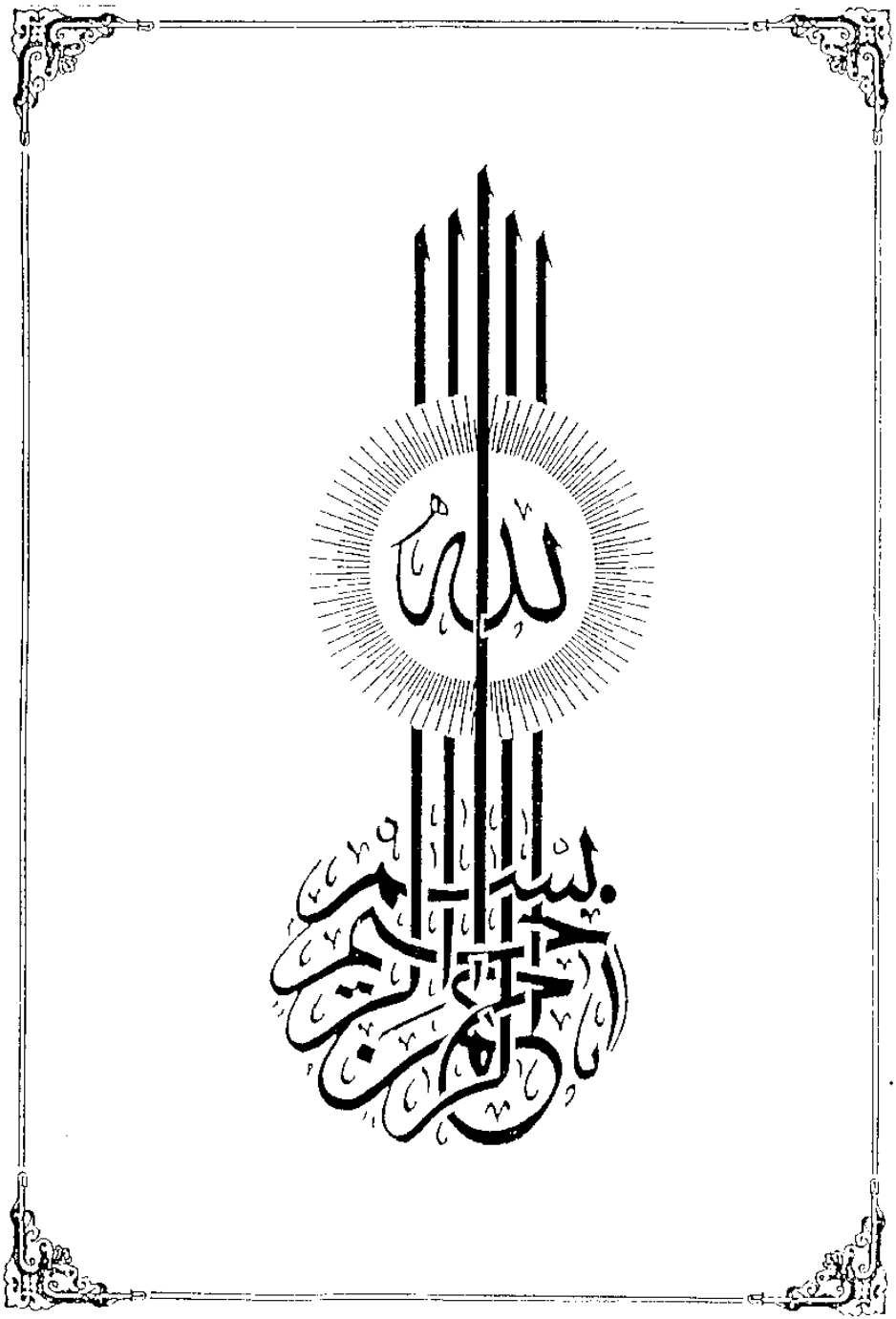
TO
MY BELOVED
HUSBAND

DR. M. M. EL-FIKY



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CONTENTS

INTRODUCTION

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The cytomegalovirus (CMV) is classified as one of the members of Herpes virus group. It acquires its name from the swollen appearance of the infected cells which may reach 40nm in diameter. (Pagano & Lemon, 1981).

Cytomegalovirus may cause either congenital infection known as cytomegalic inclusion disease (C.I.D.) or acquired infection occuring mainly in crowded areas of low socio-economic status, in patients under steroid therapy, in patients receiving multiple blood transfusions and in transplant recepients. (Garnett, 1981).

A syndrome called as post-perfusion syndrome following whole fresh blood transfusion by few weeks was noticed mainly after open-heart surgery which required multiple transfusions. (Caul, et al, 1971).

It is thought that this syndrome can result from primary or reactivated infection and it can occur in children as well as in adults. (Embil, et al, 1968; Beneke, et al, 1984).

The syndrome is generally self-limited condition that does not need treatment, but sometimes certain complications could occur as icteric hepatitis, myocarditis, polyneuritis,

normocytic normochromic anaemia, autoimmune haemolytic anaemia and certain immunological abnormalities as antinuclear antibodies and cryoglobulins. (Wisch, et al, 1973).

Sero-epidemiological studies have shown CMV infection highest antibody prevalences detected in the third world countries, antibody prevalence varies directly with age and inversely with the socio-economic status. (Tegtmeier, 1986).

Aim of the work

Our aim is to detect the incidence of sero-conversion to CMV complement fixing antibodies among patients who have received multiple units of fresh blood after open-heart surgery in the cardiothoracic surgery department of Ain Shams University.

REVIEW OF LITERATURE

THE NATURE OF CYTOMEGALOVIRUS

This virus is considered as one of the members of the herpes virus group. Although over 70 viruses of the herpes group are known to infect different animal species, there are only five distinct herpes viruses that commonly infect humans; herpes simplex virus (HSV) type 1&2, varicella zoster virus (VZV), cytomegalovirus (CMV), and Epstein-Barr (E-B) virus.

All these herpes-viruses resemble each other structurally and have the same biological properties. (Pagano & Lemon, 1981).

DESCRIPTION OF THE VIRUS:

The CMV is considered as the largest member of the human herpes virus family. It is approximately 200 nm in diameter. (Alford & Britt,1985).

The virus consists of 64 nm core containing the viral DNA enclosed by a 110 nm icosahedral capsid made up of 162 capsomeres. (Smith et al,1973.). The complete particle is enclosed by an envelope consisting of at least 25 to 30 virion-encoded proteins and glycoproteins. (Sarov et al,1975; Alford & Britt,1985).

The Core:

The linear double-stranded DNA of CMV (genome) is approximately 240 Kb in size (150X10 Daltons). It has a long and a short sequence bounded together in such a way that it can assume 4 isomeric forms (Fig. 1). (DeMarchi et al,1978; Geelen et al,1978).

The massive size of CMV genome would suggest that the virus can encode a myriad (i.e. countless number) of proteins. Approximately 33 structural proteins and an unknown number of infected-cell proteins are encoded by CMV.(Sarov et al,1975).

The Capsid:

It is an icosahedral structure surrounding the virion core (Fig. 2). It contains two structural proteins, the major and minor capsid proteins with molecular weight of 150K and 34K, respectively. (Sarov et al,1975).

Outside the virion capsid, two matrix proteins of 68K and 72K form a bridge between the capsid and the virion envelope. The 68K matrix protein represents the most abundant protein in the virion. An additional 200K protein is also proposed to be located between the virion capsid and envelope. (Gibson,1983).

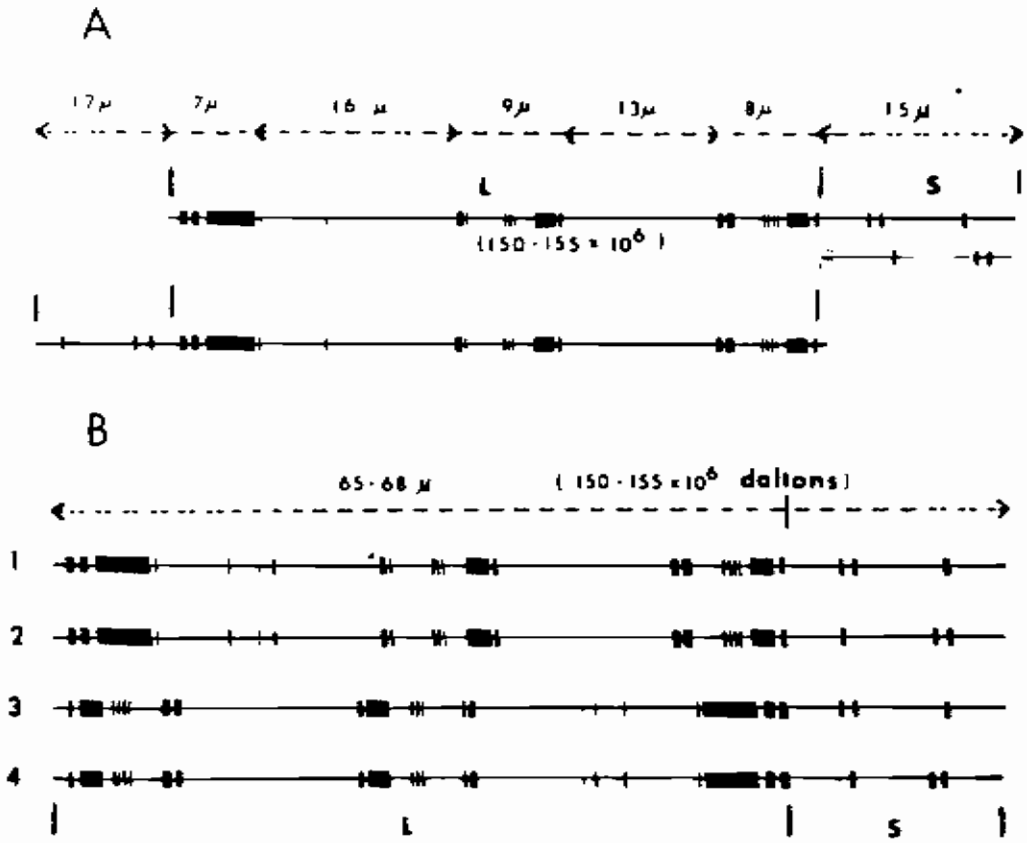

FIG. 1. Molecular arrangement of human cytomegalovirus DNA. Dark bars represent denatured regions. A: Summary of observed features and length obtained from study of partial denaturation of viral DNA. B: Four possible orientations of HCMV DNA. L, long segment; S, short segment. (Huang et al, 1980)

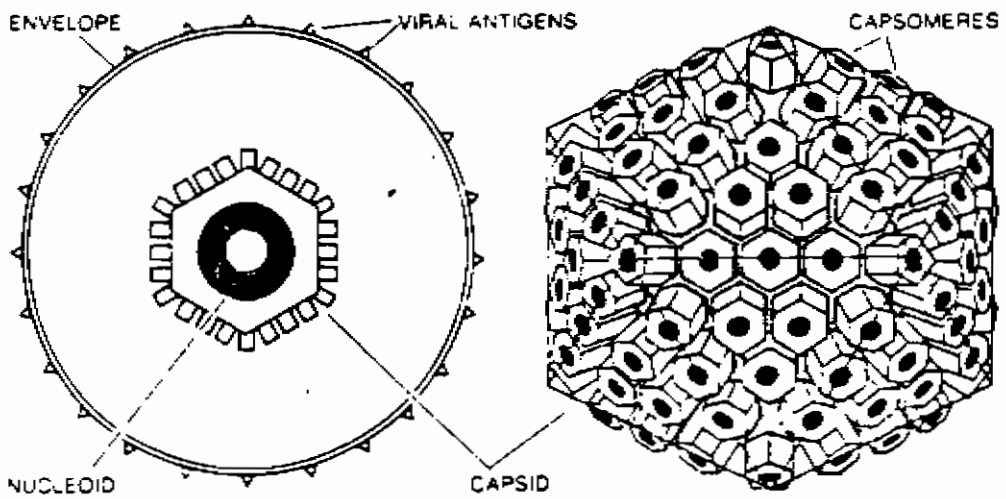

Figure (2): Structure of herpes group viruses. The virion consists of a central core, or nucleoid, which contains the viral DNA; a capsid, which is icosahedral in shape and made of tubular protein subunits called capsomeres; and an envelope derived from cellular membranes. The envelope contains viral proteins or antigens. (Henle, et al, 1979)

The Envelope:

The CMV envelope is a complex structure and consists of at least 6 glycoproteins, 3 of which are found in abundance. The glycoproteins with apparent molecular weight of 140K, 62K and 57K are the major protein constituents of the envelope. The other proteins are of lesser structural and functional role.

It is believed that the glycoproteins express antigenic sites for neutralizing antibodies. (Stinski,1976).

REACTION TO CHEMICAL AND PHYSICAL AGENTS:

Human CMV is completely inactivated by exposure to 20% ether for 2 hours, to pH less than 5, to 65°C for 30 minutes, or to UV light for 5 minutes. When we add 5-10% serum to the diluent, the virus is stabilized at 37°C but not at 4°C.

CMV does not withstand freezing and thawing or storage at -20° to -50°C without stabilizers. The infectivity of cell-free virus is best preserved by storage in $NaHCO_3$ free diluent at -80°C in the presence of 35% sorbitol. Virus infected cells suspended in Eagle's minimal essential medium (MEM) with 10-20% serum and 10% dimethylsulfoxide (DMSO) can

be stored with minimal loss of infectivity indefinitely in liquid nitrogen (-190° C). (Reynolds, et al, 1979).

ANTIGENIC CHARACTERISTICS:

Following infection, antibodies of IgG, IgM, and IgA classes can be detected using a variety of serologic tests. Antigens responsible for the various antibodies have not been precisely defined.

However, 2 complement fixing antigens have been described, a soluble and a viral associated antigen. The soluble antigen contains at least 2 polypeptides with molecular weights of 66,000 and 140,000 daltons. The smaller moiety is glycosylated and hyperimmune animal serum prepared against it does not neutralize the homologous virus. The virus-associated antigen, extracted by glycine buffer treatment of infected cells, appears to drive its antigenicity primarily from nucleocapsids. Both antigens develop primarily after viral DNA replication and are mostly cell associated. Supernatent fluid from infected cell cultures contains minimal amounts of complement fixing antigens. (Waner et al, 1973.).