MATERNAL CYTOMEGALOVIRUS INFECTION AND INTRAUTERINE TRANSMISSION IN EGYPT

Thesis

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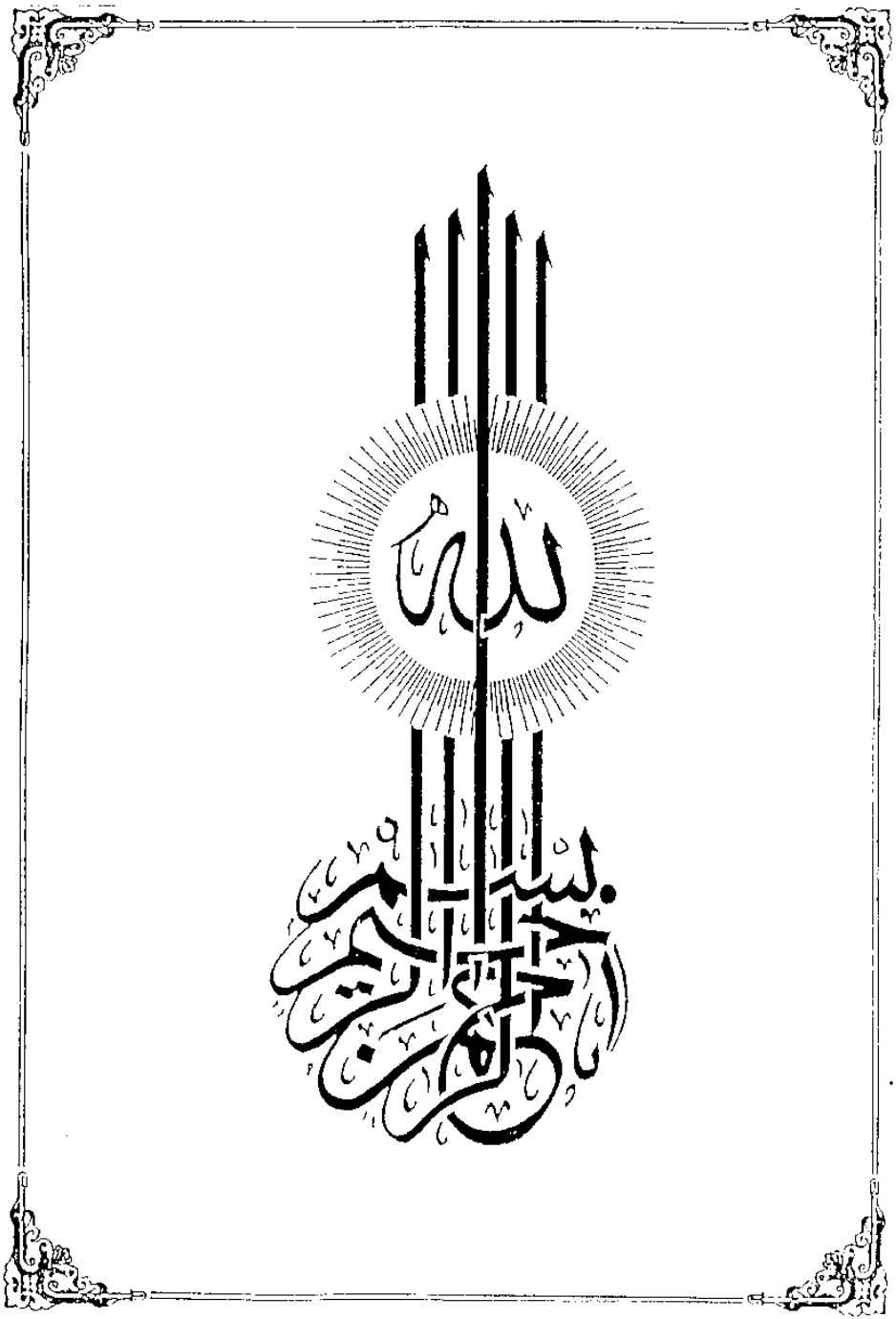

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List of Abbreviations

β_2m	β_2 microglobulin
CFT	Complement Fixation Test
CH_{50}	Minimum Hemolytic dose of complement
CID	Cytomegalic Inclusion disease
CMV	Cytomegalovirus
ED_{50}	50 % of Effective dose
EIA	Enzyme Immunoassay
ELISA	Enzyme Linked Immunosorbent Assay
HCMV	Human Cytomegalovirus
IFAT	Indirect Fluorescent Antibody Test
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IHAT	Indirect Hemagglutination Test
LA	Late Antigen
LBCF	Laboratory Branch Complement Fixation
MCMV	Murine Cytomegalovirus
OD	Optical Density
PFU	Plaque forming units
RF	Rheumatoid factor
SPA	Staphylococcal protein A
STD	Sexually Transmitted Disease
VDC	Veneral disease clinic

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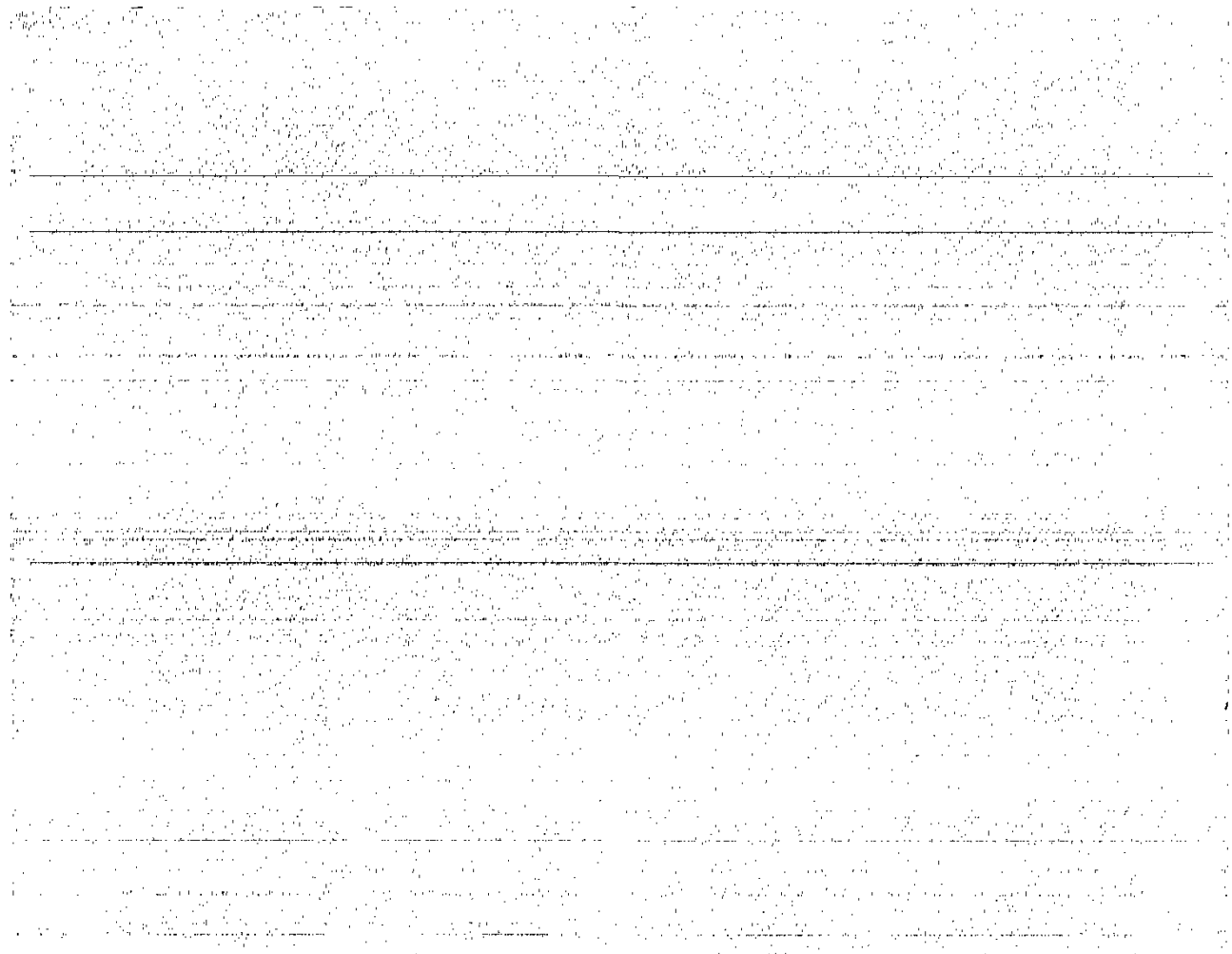
INTRODUCTION



INTRODUCTION

The obstetrical interest in cytomegalovirus (CMV) derives from the medical impact and long-term public health significance of the congenital form of this infection. Public awareness of the devastating effects of congenital CMV infection has increased considerably in recent years. Congenital CMV infection is unquestionably the most common intrauterine infection with a prevalence ranging from 0.4 to 2.3 % of all live births *(Stagno et al., 1981).*

CMV, a member of the herpes virus family, has been found in all populations thus far tested *(Gold and Nankervis, 1976).* Few individuals escape infection during their life time, however, the age at acquisition differs in various geographic and socioeconomic settings. CMV maintains a delicately balanced parasitic relationship with the human body that is probably the result of long standing coevolution. As in other herpes viruses, despite the development of a virogous immune response, viral shedding after a primary infection normally persists for months, even years, until the infection eventually becomes latent *(MacDonald and Tobin, 1978).* Thereafter, the latent state may be interrupted by periodic bouts of reactivations. In the vast majority of cases, CMV infections are subclinical, including those acquired in utero and at or shortly after delivery, so that infected individuals remain active and continue to expose other susceptible people. In addition to horizontal transmission, CMV has the ability to disseminate through the placenta *(Andersen et al., 1979).*

Congenital CMV infection is present in approximately 1 % of all newborn infants. However, the incidence of prenatal involvement is quite variable among different populations. In fact, contrary to what might have been

expected, there is a direct relationship between the incidence of congenital CMV infection and the rate of maternal seropositivity *(Embil et al., 1975).* This phenomenon is caused by the fact that virus can be transmitted to the fetus after reactivation of latent infection as well as after primary maternal CMV infections *(Stagno et al., 1977).*

During the first year of life an additional large number of infants become infected as a result of maternal-infant transmission. This occurs either at delivery from contact with an infected maternal genital tract (natal CMV infection) or by ingestion of infected breast milk *(Reynolds et al., 1973; Stagno et al., 1980).* By the end of the first year of life between 10 and perhaps 40 % of infants are excreting virus into the urine *(Stagno et al., 1980).* The rate of acquisition of CMV during the first year of life is influenced by the rate of seropositivity of the mothers and the prevalence of breast feeding. Probably other factors such as race and socioeconomic background may also operate. In premature infants who require prolonged and intensive medical care, blood transfusions are an important iatrogenic cause of CMV infection.

Acquisition of CMV infection beyond early infancy is gradual. Seroepidemiologic studies indicate that the incidence of infection is inversely related to socioeconomic status *(Gold and Nankervis, 1976; Alford et al., 1980).* A unique feature of CMV infection is persistent or intermittent excretion of virus in urine, milk, saliva, semen, cervical secretions, stools and tears. Children with congenitally, natally or postnatally acquired infections may shed virus into urine and saliva for years *(Stagno et al., 1975).* Close contact between these infected young children and uninfected playmates, that may occur in day care centers and boarding schools, is probably the most important factor responsible for the earlier and the more rapid acquisition of infection *(Hanshaw, 1983).*

In general, in developing countries the majority of the population has acquired CMV before reaching puberty, while in developed countries the infection is acquired at a lower rate *(Alford et al., 1980)*. In adolescents and young adults, the presence and persistence of CMV in saliva, the cervix, and semen indicates that the infection may be spread by droplet and by sexual contact *(Lang and Kummer, 1972)*. Evidence exists for the direct transmission of virus with blood products and transplant of organs. With blood transfusion, the risk of infection is directly related to the number of blood donors and the amount of blood transfused *(Gold and Nankervis, 1976)*.

Regardless of age and sex, the majority of postnatal primary CMV infections are clinically asymptomatic and pregnant women are no exception *(Gold and Nankervis, 1976; Alford et al., 1980)*. However, a small proportion of patients (1 to 5 %) may have a variety of clinical syndromes *(Klemola et al., 1969; Kumar and Nankervis, 1979)*. These include an infectious mononucleosis like illness, mild hepatitis, interstitial pneumonia, hemolytic anaemia, thrombocytopenia, and occasional signs of gastrointestinal and central nervous system disease.

In patients with immunodeficiencies, or malignant diseases, and in those receiving blood transfusions or transplanted organs, the probability of illness is greater *(Klemola et al., 1969)*. The mononucleosis-like syndrome associated with CMV, much like infections with Epstein Barr virus and toxoplasma gondii, is characterized by the appearance of fever, malaise, myalgia, sore throat, lymphocytosis with an excess of atypical cells, lymph node enlargement, and pharyngeal reaction. The acute stage lasts from 1 to 2 weeks to 2 months and is characterized by a slow subsidance of the lymphadenopathy, lymphocytosis and hepatic involvement *(Kumar and Nankervis, 1979)*.