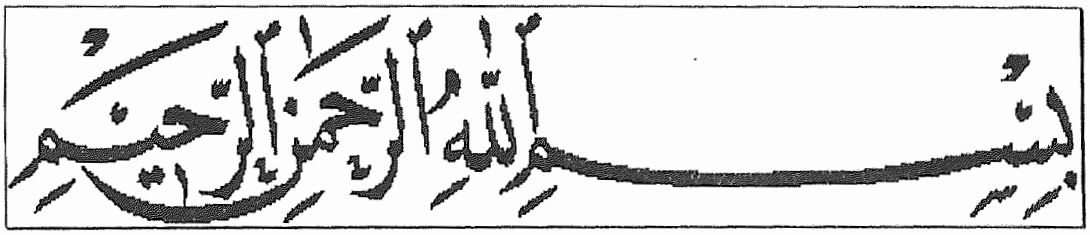

بسم الله الرحمن الرحيم

PREVALENCE OF HERPES SIMPLEX VIRUS II ANTIBODIES IN HABITUAL ABORTION

Ms. . Thesis Submitted in Partial Fulfillment of Master Degree of Clinical & Chemical Pathology

by

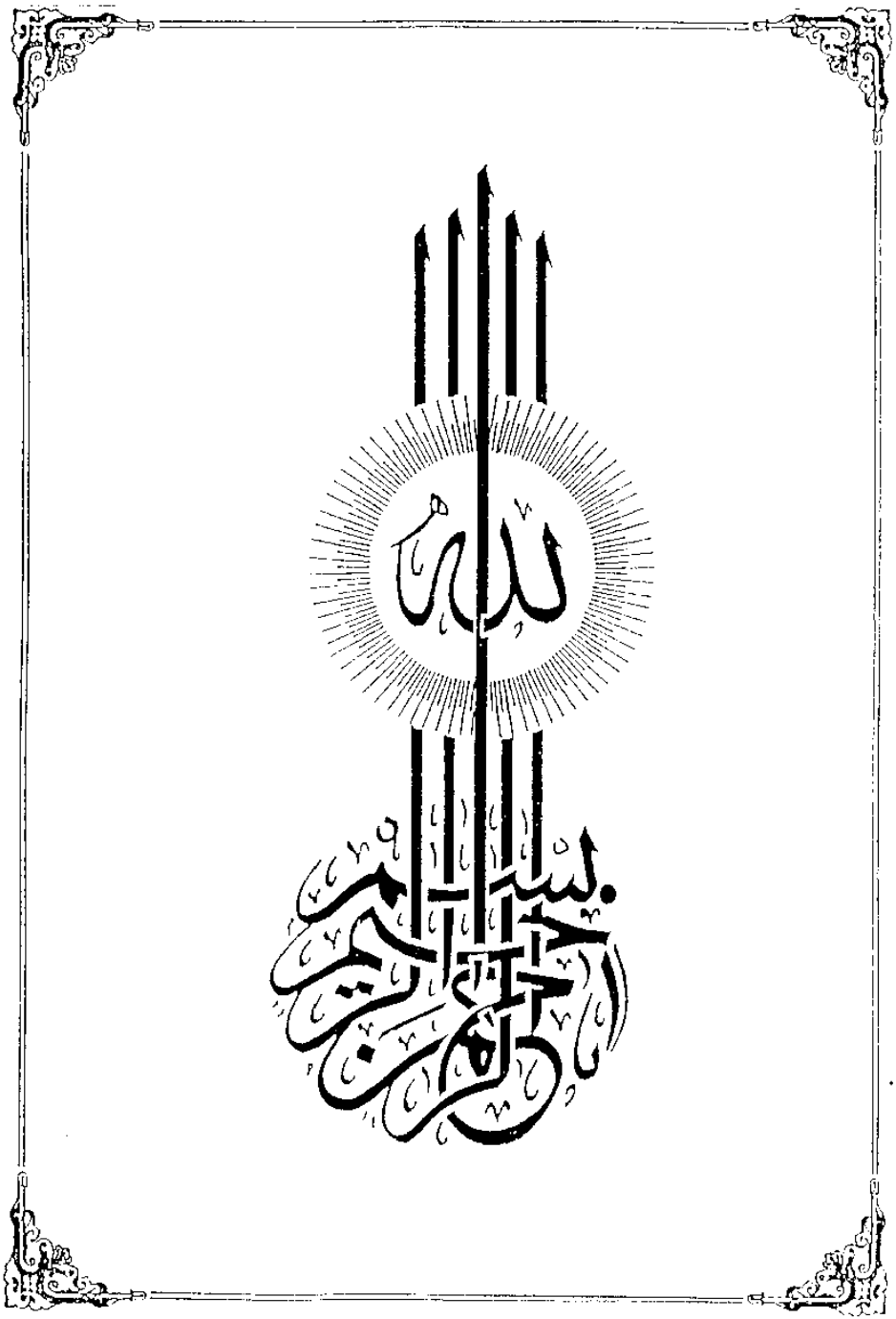
AMAL MOHAMED SALAH EL DIN HASSAN
M. B.B. Ch.

Supervisors

Professor Dr. **IBRAHIM KHALIL ALI**
Professor of clinical pathology
Faculty of medicine Ain Shams University

Dr. **MAGDA SALAH EL DIN GABR**
Lecturer of clinical pathology
Faculty of medicine Ain Shams University

Faculty of Medicine
AIN Shams University
1995



INDEX

ACKNOWLEDGMENT

I would like to express my great appreciation to **PROF. DR IBRAHIM KHALIL ALI** for offering me all the facilities to do this work, his encouragement , meticulous supervision and patience with me to finish my thesis

I am greatly thankful to **DR MAGDA SALAH EL DIN GABR** for her valuable time expended with me , continuous advise , constructive criticism , and helping me in all my work steps.

Also my gratitude to **DR. MALAKA ZAKARIA** for her precious advises and time for help. Actually I am greatly thankful to all staff of clinical pathology department AIN SHAMS UNIVERSITY.

INTRODUCTION

INTRODUCTION

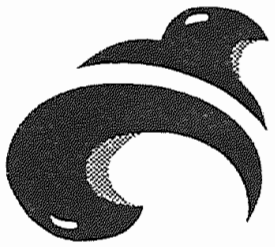
Habitual abortion is a common problem. Maternal infection with many etiologic agents especially in the first trimester of pregnancy may lead to abortion. Among these agents are: syphilis, toxoplasmosis, rubellavirus, cytomegalovirus, herpes simplex virus type II and listerioris.

Although these maternal infections with its subsequent vertical transmission may have an outcome of congenital malformed fetus, however this is not the case with herpes simplex virus II infection[HSV-II]. It follows that HSV-II has a single outcome which is abortion especially with the occurrence of vireamia in the first trimester of pregnancy.[Bolognese et al ; 1976].

As infection with HSV-II may be asymptomatic , symptomatic or the patient may be unaware of previous exposure to infection ,Langenberget and ass. In 1989 screened women for HSV-II and found many to be positive despite for lack of symptoms of infection.

Also Suarez et al in 1991 detected 21% of the population having inapparent genital herpes virus infection .

We aim in this work to carry out serological study for detection of HSV-II antibodies in Egyptian females complaining of habitual abortion.



REVIEW OF LITERATURE

REVIEW OF LITERATURE

STRUCTURE AND REPLICATIONS

Herpes simplex virus is a member of the family :Herpetoviridae and genus:Herpes virus which includes Herpes Simplex virus {HSV} , Varicella Zoster, Cytomegalovirus, Epstein-Barr virus, Human B cell lymphotropic virus and RK virus[*Fenner,1976;Grossman,1982*].

1-MORPHOLOGY

Herpes simplex virus particles are approximately 180-200 nm in diameter and consist of :-

-A cylindrical core structure around which the viral DNA is wounded and it is presented within the capsid .

-An icosahedral capsid approximately 85 -110 nm in diameter

-A granular zone or tagument which surrounds the capsid and contains several proteins . It is formed of 162 capsomers shaped like a long hallow prism . Twelve of the capsomers are pentagonal ,while 150 are hexagonal in shape .Each of them measures 9.5 x 12.5 nm and has a central hole which is approximately 4 nm in diameter.

-An envelope which is derived from the host cell as the particles bud from the nuclear membrane .Its membrane appears by the E/M as a three layered

structure analogous to membranes . The envelope is obtained by the virus during the process of budding through the inner lamellae of the nuclear membrane into the perinuclear cysternae . The outermost layer of the envelope contains projections or spikes , 8 -10 nm in length , which represent at least five viral - specified glycoproteins gA/B ,gC ,gD ,gE ,and gF . These proteins have an important role in attachment, and thus its importance for infectivity,[Wenger,1984 and Reichman, 1984]. HSV type-II gF may also be type specific [Balachandran et al., 1982],although there is evidence which suggests that type I gC and type II gC have related antigenic determinants [Zweig, 1983]. (fig 1) .

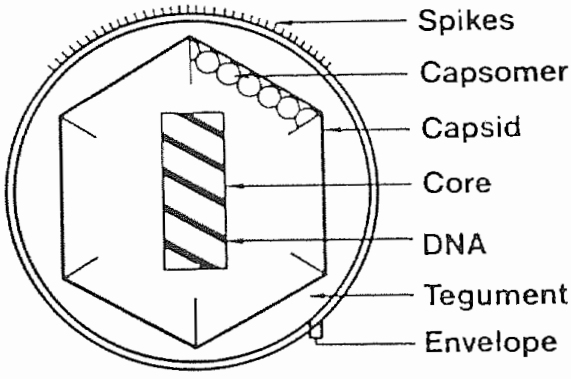


FIG.1: Model of herpes simplex virus showing the morphological substructures : envelop ,capsid, and core

2-STRUCTURE OF HERPES VIRUS GENOME.

The genome of HSV is a double - stranded DNA of a molecular weight of 100x10 daltons, wounded around a centrally located ,spool -shaped core. About 60 -70 proteins can be encoded by the genome, but only 50 proteins have been identified in infected cells.

The molecule consists of a long "L"and a short "S" components which comprise 82% and 18% of the genome respectively. Each of the components contains unique sequences, unique large [UL] and unique small [US] . The nucleotide sequences bracketing each unique region consist of inverted repeats; the "L"component bracketing sequences are designated ab and b"a", while those bracketing the 'S" components are designated a'c' and ca . because of this arrangement , the "L " and "S" regions can invert relative to each other , giving rise to four possible genome populations which differ only in the orientation of these regions. These components are not only important in viral DNA synthesis, but also for the establishment of latent infection [Wadsworth et al ;1975 and Lycke, 1990]. {fig 2}.

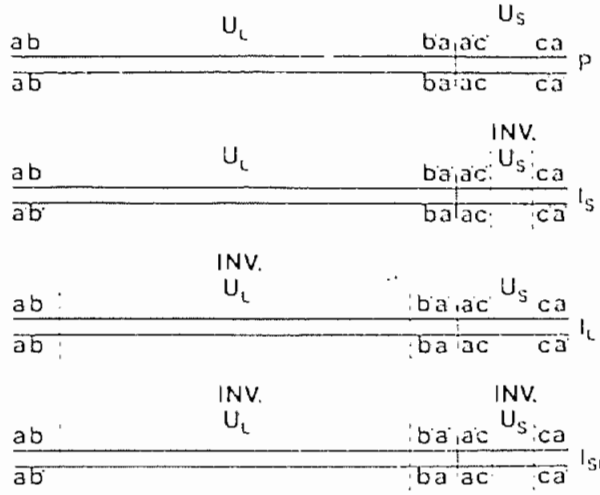


Figure 2 Four isomers of herpes simplex virus DNA. Two regions of unique DNA sequences, unique large (U_L) and unique small (U_S) are present in each isomer. Flanking each unique region are inverted repeats:

$$\begin{array}{ccccccccc} a & b & & b' & a' & & a' & c' & & c & a \\ | & | & \text{and} & | & | & \text{flank } U_L \text{ and} & | & | & \text{and} & | & | \\ a' & b' & & b & a & & a & c & & c' & a' \end{array}$$

flank U_S, respectively. The top isomer represents a prototype (P) with respect to the orientation of the U_L and U_S. The other three isomers, I_S, I_L, and I_{SL}, have inverted U_S (INV U_S), inverted U_L (INV U_L), and inverted U_L and U_S, respectively. Dashed vertical lines represent boundaries of the inverted unique sequences.

3-REPLICATION

An essential but not the sole attribute for virus pathogenicity is its ability to replicate in the environment of host tissue.

The replication cycles utilize host cell macromolecules and enzymes for viral genome replication ,transcription , and translation events, these include; B proteins, DNA polymerase having 3' -5' exonuclease activity , thymidine kinase ,deoxycytidine deaminase and ribonucleotide reductase.

For complete viral replication to oceur , virus particles must attach to receptors on plasma membranes of cells , this is followed by penetration, uncoating ,eclipse phase, assembly and release.

A;- Attachment : of virus particles to receptors on cell surface probably mediated by the envelope glycoprotien gD [Cohen GH, et al, 1983 | .

B;- Penetration : in which glycoprotein gB plays a critical role as penetration occurs by viropexis [pinocytosis] or fusion of the viral envelope with the cellular plasma membrane. This results in the release of nucleocapsids into the cytoplasm [Sarmiento et al ., 1979]

C;- Uncoating : Uncoating of the capsid occurs, and the viral DNA enters the nucleus by a poorly defined mechanism and can serve two purposes;

1- act directly as m-RNA or as a template for transcription of m-RNA.

2-to direct the synthesis of progeny nucleic acid

D- Eclipse phase:

In this stage the nucleic acid has been released, becomes unidentifiable for hours ,during this time transcription, translation and the formation of new nucleic acids are formed.

Transcription: The double stranded DNA is transcribed by DNA- dependent RNA polymerase 11 into a primary transcript which is then capped at its 5' end and polyadenylated at the 3' end [Honess RW,1974]. Splicing occur in which the length of the primary transcript is shortened by removal of one or more internal segments of RNA [introns] and rejoining conserved RNA segments [exons] to form the messenger RNA [m -RNA].The reading frame of m-RNA is the same as that of the primary transcript .,If the number of nucleotides in the intron is a multiple of three, on the other hand ,an altered reading frame is obtained if the intron consists of one or two nucleotides in excess of multiple triplets [Jones, et al ,1879 and Hones et al , 1979].

The linear double stranded DNA is converted to a circular form through the action of exonuclease , which causes complementary sequences "a " and " a' " at the termini [Knopfk , 1979]. This circular DNA serves as a template for replication in a rolling mechanism .Endonucleolytic cleavage of this circular pattern occur which results in a linear DNAs missing only the terminal sequences which are regenerated from the template strand to yield full size DNA [Ladin, et al ,1980 and Smily , et al ,1981].