DENDRITIC AFFECTION OF THE CORNEA

Thesis

Submitted in Partial Fulfilment for the

degree of M.S. in Ophthalmology

By

Fikry Mohamed Fathi Zaher

M.B.B.Ch

Faculty of Medicine

Ain Shams University

Supervised by

Prof. Dr. SALAH EL-DIN IBRAHIM ABDALLA

Prof. of Ophthalmology

Faculty of Medicine

Ain Shams University

Dr. SHAKER AHMED KHEDR

Ass. Prof. of Ophthalmology

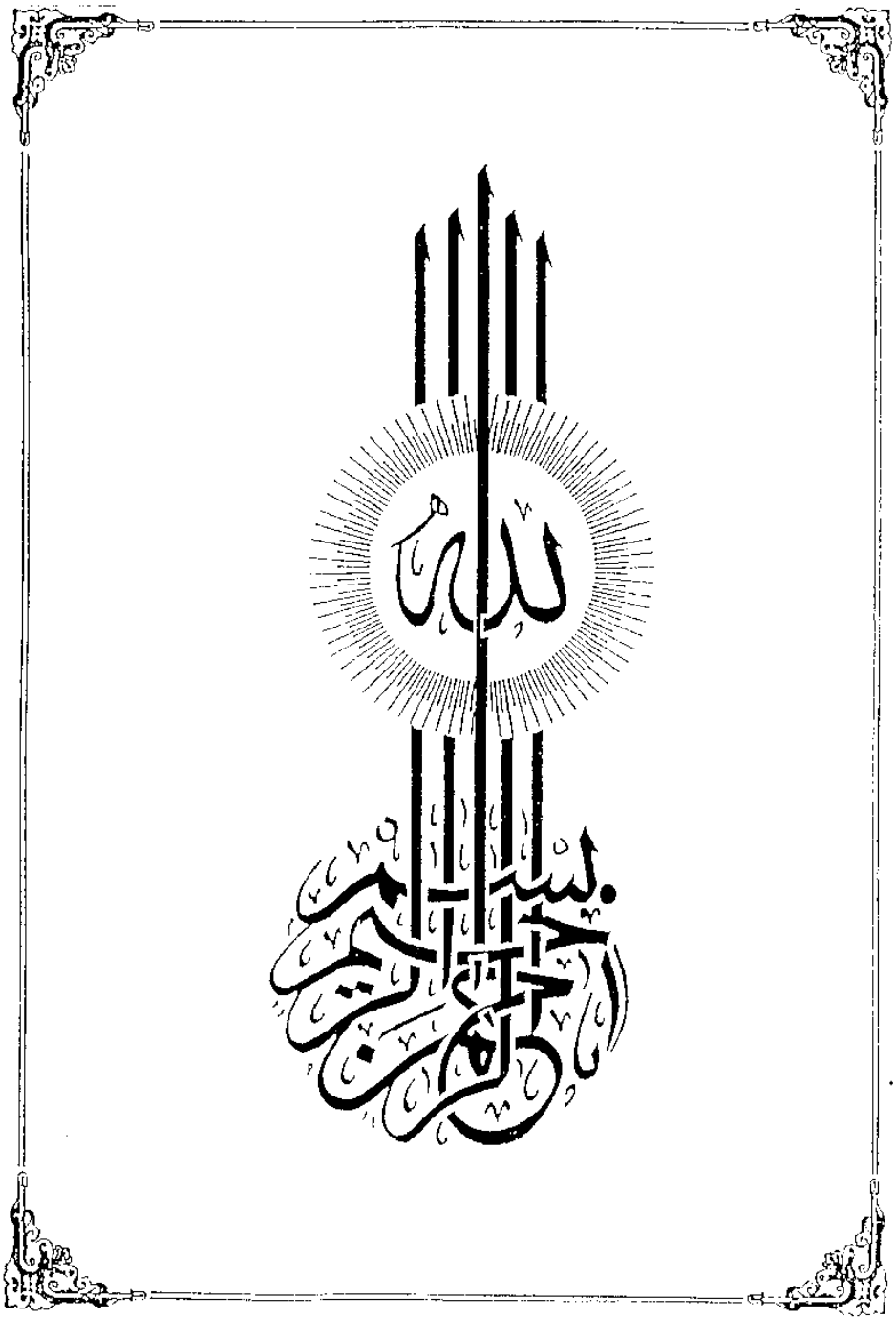
Faculty of Medicine

Ain Shams University

Cairo

1986

TO THE MEMORY OF PROF. DR. MOHI EL-DIN EL-ARABY



ACKNOWLEDGEMENT

*It is a pleasure and honour to work under the supervision of Prof. Dr. **SALAH EL-DIN IBRAHIM ABDALLA**, whose help and guidance to this thesis was great; offering all the facilities to serve this study.*

*I would like to express my deepest gratitude to Prof. Dr. **MAHMOUD HAMDI IBRAHIM** Prof. of Ophthalmology, Ain Shams University, for his kind guidance sincere help, encouragement and supervision.*

*I wish to extend my thanks to Dr. **SHAKER AHMED KHEDR**, Ass. Prof. of Ophthalmology, Ain Shams University, for his encouragement, enthusiasm and help throughout the course of this work.*

*All my thanks to Prof. Dr. **WAFIK HEFNY**, Head of Ophthalmology department, Ain Shams University and towards all professors and staff members of Ophthalmology department, Ain Shams University for their encouragement, fruitfull help and continuous cooperation.*

CONTENTS

INTRODUCTION AND AIM OF THE STUDY

Dendritic affection of the cornea caused by herpes simplex virus is a challenging disease to most ophthalmologists in practice due to its recurrent nature and possibility of stromal invasion and destruction ending in a bad prognosis concerning the visual outcome.

The aim of this study is to review the literature concerning herpes simplex virus affection of the cornea as regards its pathogenesis and diagnosis with special emphasis on the most recent lines of medical and surgical methods of treatment.

MICROBIOLOGY

I- MICROBIOLOGY

(a) Basic properties of viruses:

Viruses are the smallest infectious agents (20 - 300 nanometers in diameter) (Fig. 1), containing one kind of nucleic acid either ribonucleic acid (RNA) or deoxy ribonucleic acid (DNA) as their genome, usually as a single molecule. The nucleic acid is encased in a protein shell (Fig. 2) and the entire infectious unit is termed a virion (Jawetz et al., 1984).

Viruses differ from bacteria in a number of important ways:

(1) They are much smaller than most bacteria.

(2) They are obligate intracellular parasites, so can only survive inside a host cell.

(3) Their metabolism relies on enzymes provided by the host cell.

(4) They can carry their genetic information on RNA as well as DNA and are the only "life form" known to use R.N.A. in this way.

(5) They are not sensitive to the action of conventional antibiotics.

(6) They do not divide by binary fission but increase their numbers by a process known as replication (Corbitt et al., 1983).

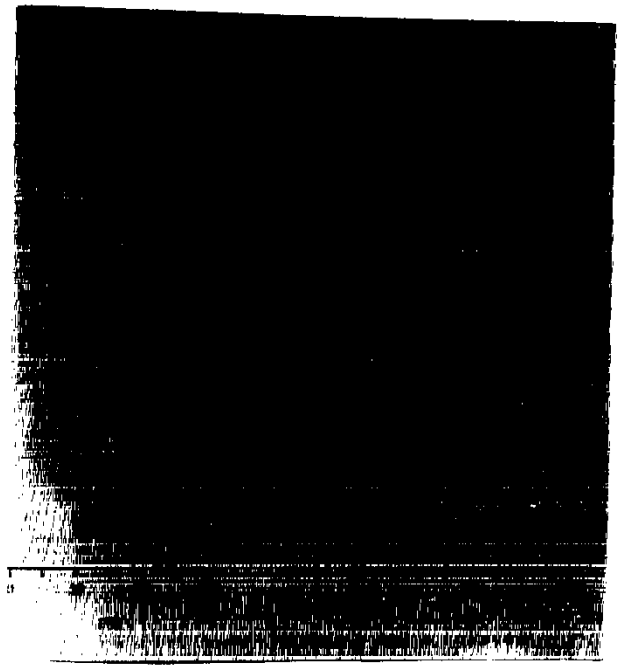


Fig. (1): Sizes of various micro-organisms.
(From Corbitt et al., 1968).

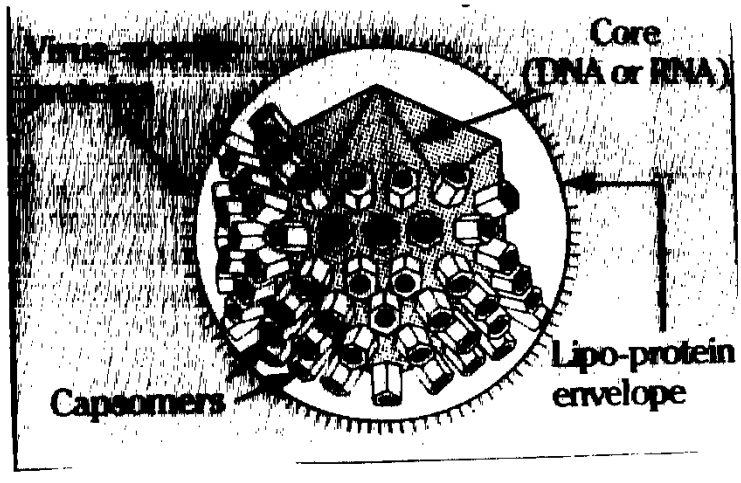


Fig. [illegible]

The Replication Process Fg. (3):

To gain entery to a cell, a virus must first form an attachment to its plasma membrane. Such attachment occurs through specific receptors on the cell surface but the initial encounter or collision is purely random.

Human viruses enter the cell by a process akin to phagocytosis known as viropexis. The virus particle is taken into an intracytoplasmic vacuole where, in a process known as uncoating, cellular proteases dissolve the protein capsid releasing the internal nucleic acid. Once within the cell, the viral nucleic acid either superimposes its own effect upon the metabolic processes of the cell or completely controls them. In either case, the infected cell is directed to produce many new copies of the viral nucleic acid, together with large numbers of virus-specific proteins ('Fig. 4). Some of these will eventually be incorporated into complete virus particles but many others, such as virus-specific enzymes, will remain free. At this stage in replication cycle it is not possible to detect infectious virus and accordingly this has been termed the eclipse phase.

Eventually, nucleic acid and structural proteins come together and spontaneously assemble to produce complete capsids. These are then released by one of two mechanisms: either by lysis of the cell (e.g. polio virus) or extrusion via the plasma membrane of the cell. During extrusion a virus may acquire an external envelope (e.g. influenza, herpes viruses). Viruses are

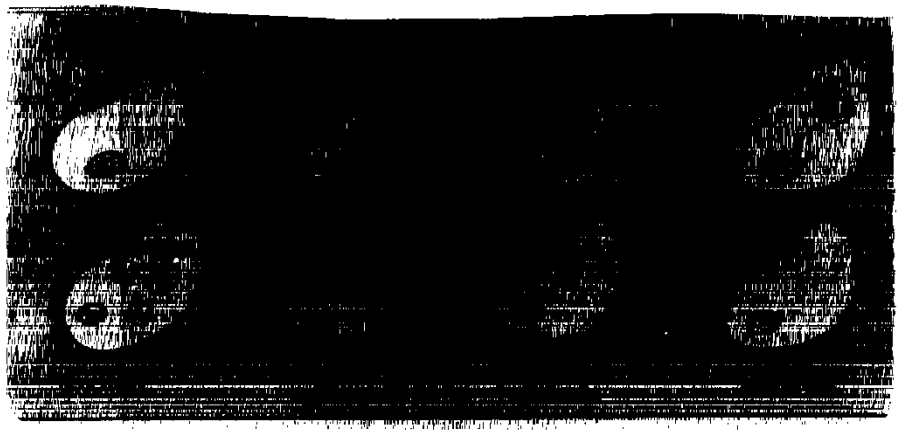
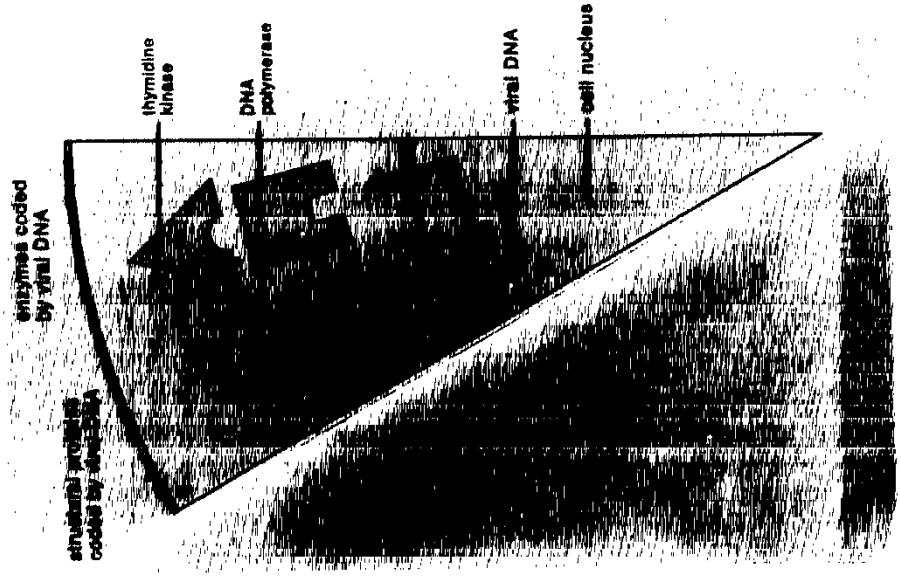


Fig. (3): The virus replication cycle.
(From Corbitt et al., 1963).



[illegible] thymidine
[illegible] viral DNA
[illegible].

then released into the extracellular environment, such as cell culture fluids or body secretions, and are then free to infect new cells or individuals. The replication cycle takes, in most cases, some twenty-four hours to complete (Corbitt et al., 1983).

In the course of virus multiplication within the cells, virus-specific structures called inclusion bodies may be produced (Jawetz et al., 1984).

These represent sites where virus protein synthesis occurs and can often be seen in biopsy and post-mortem material (Corbitt et al., 1983). They become larger than the individual virus particle and often have an affinity for acid dyes (e.g. eosin). They may be situated in the nucleus (herpes virus), in the cytoplasm (pox virus), or in both (measles virus). In many viral infections, the inclusion bodies are the site of development of the virions (the virus factories).

Variations in the appearance of inclusion material depend largely upon the tissue fixative used. Their presence may be of considerable diagnostic aid (Jawetz et al., 1984).

(b) Characteristics of the herpes virus family:

All herpes viruses are now grouped together in the family herpetoviridae but the individual members comprise a heterologous

group united primarily by their basic structure. At present about sixty viruses are placed in the family, but only four have man as their natural host (Corbitt et al., 1983).

Of the four herpes viruses which affect humans, two are well-known-herpes simplex (HSV) type I and type II, the cause of cold sores and genital herpes, and varicella zoster (VZV), the virus of chicken pox and shingles. The other two, cytomegalovirus (CMV) and Epstein Ban virus are not so well recoquised because clinical disease is less frequent. Together, they are the commonest agents to damage the foetus, the commonest cause of congenital mental illness and the commonest cause of blindness resulting from a virus infection (McKendrick and Sutherland, 1983).

They have often been called "opportunistic viruses" because infection is often not apparent and the clinical lesions commonly develop only after fever, shock, immunosuppression, ultraviolet light burns, or other trigger mechanisms (Grayson, 1983). They have a propensity for subclinical infection, latency following the primary infection, and reactivation thereafter (Jawetz et al., 1984).

Herpes viruses are morphologically (Fig. 5) indistinguishable from each other. They consist of four basic components. Firstly, there is an inner core of double stranded DNA, with associated DNA-binding proteins. Enclosing the DNA is a viral capsid formed from one hundred and sixty-two capsomeres,

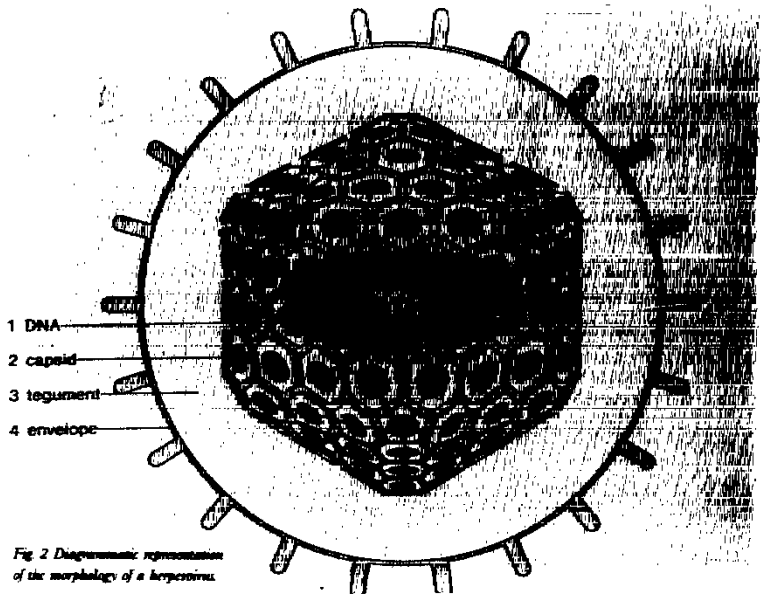


Fig. 2 Diagrammatic representation of the morphology of a herpesvirus.

Fig. (5): Morphology of a herpes virus.
(From Mc Kendrick and Sutherland, 1968).

each an elongated hexagonal protein prism with a central hole, which together give the capsid icosahedral symmetry. The capsid has a diameter of approximately 100 nm and is surrounded by a granular zone - the tegument, which varies in size in different herpes viruses. The nucleocapsid and tegument are enclosed in a loose lipid-containing envelope which is covered by short spikes. These may be involved in infectivity by adsorbing to cell membranes (McKendrick and Sutherland, 1983).

Replication takes place in the nucleus of the cell and Cowdry's type A eosinophilic intra-nuclear inclusion body is the remnant left after the virus has passed into the cytoplasm (Grayson, 1983).

All members of the family share this common morphology and cannot therefore be distinguished by electron microscopy (Corbitt et al., 1983).

However they do differ in a number of ways. While they all have linear double stranded DNA, the molecular weight of the DNA varies from 96×10^6 to 150×10^6 daltons and they differ in the number and disposition of unique and repeat sequences (McKendrick and Sutherland, 1983).

(c) **The herpes simplex virus:**

Herpes simplex virus is probably one the most common infectious agents of man. It produces a variety of clinical