FACULTY OF MEDICINE
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AIDS VIRUS IN β LIVER AFFECTIONS

THESIS

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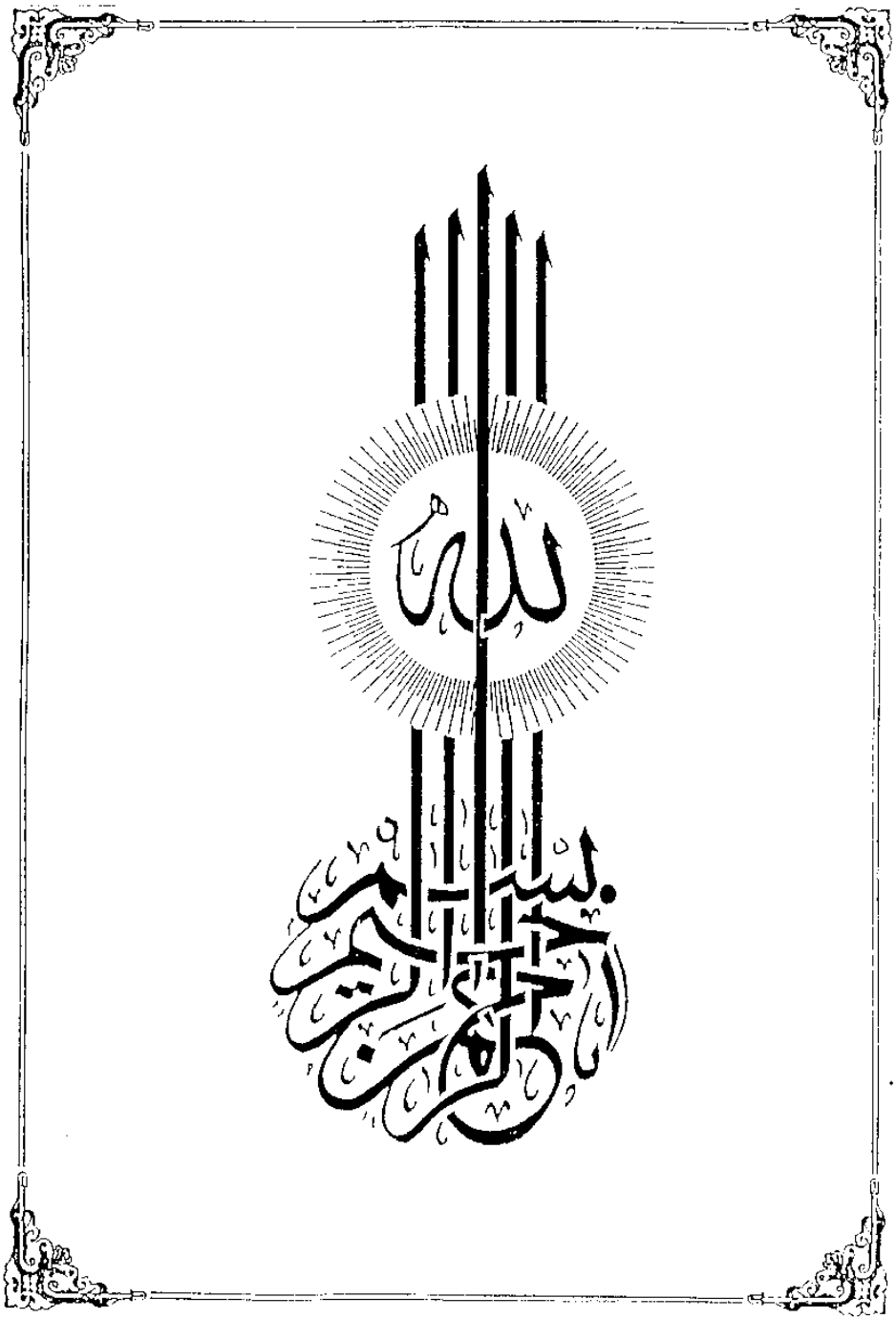
In the Name of Allah,

the Beneficent, Merciful



TO :

MY MOTHER & MY WIFE

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CONTENTS

INTRODUCTION & AIM OF THE WORK

Introduction and Aim of the work

Many mechanisms of immuno-suppression may be operating in schistosoma infected patients.

This may be in the form of inhibition of T or B cells or the appearance of T suppressor cells or it may be a non specific inhibation as there is preliminary evidence that schistosoma might release non specific factors to block effector mechanisms (WHO, 1974).

So in ₿ patients T cells are deficient qualitatively or quantitively (Contor, 1975).

Infections by organisms taking advantage of T cell defects were described in AIDS. Also there is observation of intercurrent infections by viruses, bacteria, fungi and parasites in AIDS.

₿ patients in our country are also subjected to injections and even transfusions which expose them to HTLV-III infection and many of them are already carriers of hepatitis B virus and their immunity is aleardy questioned therefore it is important to try to find out the possibility of HTLV-III infection or carrier state in these patients.

REVIEW OF LITERATURE

HISTORY AND IMMUNO VIROLOGY

Acquired immunodeficiency syndrome (AIDS) is a newly discovered viral disease in man. It is a major puplic health problem in the United States. As of early, 1987, about 30000 cases of acquired immunodeficiency syndrome (AIDS) were reported in the United States, and it is expected that another 250000 or more will be recorded by 1991 (Donald et al., 1987). Outside the United States, AIDS cases have been reported from more than 40 countries on five contints, but differences in reporting and surveillance criteria pose problems for comparison of the epidemic's course in different parts of the world (Peter, 1986).

Historical :

In June 1981 the Centers for Disease Control (CDC) first published reports of the unusual occurrence of five cases of pneumocystis carinii pneumonia among previously healthy male homosexuals in Los Angeles. Shortly after came equally surprising reports of an aggressive form of Kaposi's Sarcoma (Gottlieb et al., 1981 and Siegal et al., 1981). Additional cases were identified retrospectively as back as 1978 (Peter, 1986). Recently, the clinical definition of AIDS has been expanded to include groups of patients, even in the absence of Kaposi's Sarcoma or opportunitic infection (Frideman et al., 1986).

The initial appearance of AIDS among sexually active gay men prompted speculation that something about that life-style was causing derangements in the immune system and a resultant in-ability to combat infection (Peter,1986).

Eary theories pointed to coexisting chronic cytomegalo-virus which is sexually transmitted and intensive recreational drug-use as two possible etiologies for immunosuppression seen in AIDS (James, 1985).

By late 1981, however, AIDS had been reported in hetrosexual intravenous drug abusers (Fauci et al., 1984), and in mid-1982, the first cases among hemophilics were noted (Jason et al., 1986). Shortly afterward, tranfusion-associated AIDS was documented, as was transmission from male to female sexual partners (Peter, 1986). That sequence led to hypotheses about an infection etiology through a blood-borne, transmissible agent. These hypotheses were strengthened in 1983 and 1984 by the discovery and characterization of a pathogenic retrovirus new to man found in AIDS patients and termed, variously, human T-cell lymphotropic virus type III (HTLV-III) (Barre - sinoussi et al., 1983), lymphadenopathy associated virus (LAV) (Popovic et al., 1984) and AIDS-associated retrovirus (ARV) (Levy et al., 1984), for simplicity it will be called the AIDS virus. HTLV-III/LAV is currently accepted as the

infectious agent the causes AIDS, although other, still undeterminaed cofactors may also be necessary for the full expression of the disease (Peter, 1986).

Possible cofactors might be infections, genetic, behavioral, or environmental in origin (Broder SW, 1984).

It is now also clear that homosexuality, promiseuity and drug abuse can not cause AIDS without infection with the virus is potentially lethal to all men, women and children irrespective of life-style or sexual activity (Broder SW, 1984).

Risk groups

The majority of persons with AIDS fall into groups with identifiable risk charateristics : homosexual or bisexual men, intervenous drug users, blood transfusion recipients, hemophiliacs, and infants born to mothers suffering from HTLV-III/LAV infection (Scott et al., 1984).

There has also been an increasing number of persons with AIDS whose only risk factor has been heterosexual contact with a person known to have AIDS or a person at risk for AIDS (Handsfield H. et al., 1986).

Several reports from Africa, Haiti, and the United States suggest that significant female to male transmission

may also occur through contact with female prostitutes (Redfield RR et al., 1985). Though these data support the concept that heterosexual contact is a route of transmission for HTLV-III/LAV, the efficiency and risk factors or mechanisms associated with the heterosexual transmission of HTLV-III/LAV are still unknown.

Evidences that HTLV-III is the causative agents :

By 1983, increasing evidence began to suggest that AIDS might be caused by a transmissible agent (Gallo et al., 1984). On going epiolemiologic surveillance, and the occurrence of AIDS among transfusion recipients and hemophiliacs, pointed toward a possible viral agent transmitted through a blood-borne route. The suggestion of congenital infection in pediatric AIDS cases gave further support to such hypotheses, and implied an additional parallel between the emerging epidemiology of AIDS and hepatitis B. (James, 1985). Meanwhile, immunologic studies of AIDS patients were indicating that many of the immune defects seen in the disease could be traced to a specific subset of T lymphoeytes, the T_4 helper/inducer subset (Peter, 1986).

Characterisics study of the virus :

The AIDS virus is a rltrovirus of subfamily lentivirinae (Gonda et al., 1985) of which only three other species are known : the lentiviruses causing moedi-visna in sheep, infectious anaemia in horses and encephalitis - arthritis in goats. The retroviruses or RNA tumor viruses can cause transformation of many cells. They are found in almost all vertebrate species, and in animals they cause tumors primarily of connective tissues (sarcomas) or the hematopoietic system (Peter, 1986). They have also been implicated in certain carcinomas, such as those caused by mouse tumour virus. For many years the discovery that certain tumour viruses contain RNA rather DNA, it was not understood how cells transformed by an RNA tumour virus could produce silent virus for generation after generation. In 1964, Temin proposed that upon infection, the vival RNA genome was transcribed into DNA by reversal of the usual flow of information transfer (Laurence, 1985).

Later on some investigators began to consider wether AIDS might be caused by one of newly discovered family retroviruses known to attack T_4 lymphocytes called human T-lymphotropic viruses, (HTLVs) (Barre - sinoussi et al., 1983). The designation retrovirus indicates that these viruses carry their gentic material in RNA, rather than

associated virus (LAV) and believed it to be a new member of the HTLV group. The finding in some AIDS patients of antibodies to elements of the HTLV-I and the less common HTLV-II membrane proteins also suggested cross-reactivity with a possible new HTLV variant (L. Montagnier, 1985).

Efforts to characterize this virus and compare different isolates were happened, however, by the inability to culture the viuas on a large scale. Unlike HTLV-I and II, which can reproduce indefinitely on T-cell populations by transforming and immortalizing cells, this new agent did not show sustained growth in vitro (Weiss, 1985).

In fact, all the cell cultures infected with it seemed to die off soon after the virus was introduced, Gallo (1985) at the NCL experienced similar difficulties in trying to propagate a retro virus isolated from AIDS patients in United States. He suggested finally that the virus itself was killing the cells through a direct cytopathic effect (CPE) (Gallo, 1985). The discovery in his laboratory in early 1984 of a line of neoplastic T cells that promote growth of the virus and resist its CPE led directly to the large-scale production of virus which has allowed further characterization and definition of this new HTLV. The virus has been called HTLV-III and comparisons of this agent, the lymphadenopathy -