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**DETECTION OF CYTOMEGALOVIRUS ANTIBODIES IN
PRE & POST RENAL TRANSPLANTATION**

THESIS

SUBMITTED IN PARTIAL FULFILMENT FOR

THE MASTER DEGREE

IN BIOCHEMISTRY

BY

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Mona Michel Zaki

**INTRODUCTION
AND
AIM OF THE WORK**

INTRODUCTION AND AIM OF THE THESIS

Cytomegalovirus belongs to the herpes virus group (herpes virus 5) and produces large intranuclear (10 to 15 nm) and inconspicuous cytoplasmic (2 to 4 nm) inclusions which occur in all types of normal and neoplastic tissues (Metseelaar and Simpson, 1982).

Cytomegalovirus resembles the viruses of this group morphologically in the ability to form intranuclear inclusions and in its propensity for subclinical infections.

It is characterized by its peculiar affinity for salivary glands hence it was formally named salivary gland virus (Ray, 1980).

The nature of the clinical response to infection appears to depend upon the age at which infection takes place and the route of infection.

Patients with recurrent infection as well as those with primary infection had IgM antibody to CMV that was detectable. There was no difference in distribution of peak levels of IgM antibody by Radio Immuno Assay, neutralizing antibody or other antibodies between viremic and non viremic patients or in relation to clinical severity of infection (Pass et al, 1983).

Detection of Immunoglobulin M(IgM) antibody to cytomegalovirus has been proposed as a rapid method of diagnosing primary infection with

this virus. Studies have shown that IgM antibody to CMV in pregnant women generally signifies recent primary infection (Chou et al, 1987).

In organ transplant population, CMV specific IgM antibody is observed in some persons with non primary CMV infections. Among previously CMV-seropositive renal transplant recipients, Betts and Schmidt observed that cytolytic IgM antibody to CMV occurred almost exclusively in those with seropositive kidney donor, suggesting that the antibody response may have reflected reinfection with a donor strain (Betts and Schmidt, 1981).

The aim of this work:

Is to study the incidence of IgM & IgG antibodies in pre and post renal transplant patients using the most specific technique namely enzyme linked Immuno Sorbent Assay technique (Smith, 1987);

The enzyme linked Immuno Sorbent assay technique has been shown to be effective in detecting and titrating CMV antibody (IgM & IgG) the result of this technique are much better than those of immunofluorescence test (Schmidt et al, 1977).

**REVIEW OF
LITERATURE**

REVIEW OF LITERATURE

Part I: MORPHOLOGY OF CMV

CYTOMEGALOVIRUS EFFECT:

The cytomegalovirus (CMV) is member of the herpes virus group, which includes Herpes simplex virus, varicella-zoster virus, Epstein barr virus and cytomegalovirus. The cytomegalovirus is widely distributed in many animal species including monkeys, pigs, rodents, horses, sheep, dogs and humans. Each virus is specific for its own host and can be isolated only in homologous fibroblast cell cultures producing large characteristic intranuclear inclusions with production of characteristic enlarged cells: hence the name cytomegalovirus antigenic heterogeneity exists among human CMV, yet there is no real evidence suggesting separate serological types (Tobin, 1987).

Cytomegalovirus (CMV), which was initially isolated from patient with congenital cytoplasmic inclusion disease, is now recognized as an important pathogen in all age groups, in addition to inducing severe birth defects. CMV causes a wide spectrum of disorders in older children and adults, ranging from an asymptomatic subclinical infection to a mononucleosis syndrome in healthy individuals to disseminated disease in the immunocompromised (Hirsch, 1987).

VIROLOGY:

CMV is a member of the herpes virus group and thus contains doubled stranded DNA, a protein capsid and a lipoprotein envelope. Like other members of the herpes virus group, CMV demonstrates icosohedral symmetry, replicates in the cell nucleus and can cause latent infection. CMV can be distinguished from other herpes viruses by certain biologic properties such as host range and the type of cytopathology induced (Hirsch, 1987).

As its name implies, cytomegalovirus disease is a condition in which one results of infection with the virus is the formation of giant cells in the host's 3 tissues.

These cells may measure between 20 and 40 um in diameter, and they are characterized by the presence of intranuclear and intracytoplasmic inclusion bodies. The intranuclear bodies are from 65 to 120 nm in diameter tend to be eosinophilic and have a dense central core with a single enveloping membrane. The intracytoplasmic bodies are smaller and numerous are basophilic and may have a double membrane. These features are seen both in naturally infected host cells and in tissue culture cells. The inclusion bodies are probably virus particles (Weller, 1965).

Cytomegaloviruses are very unstable, their half life at 37c being only 45 minutes, at 60c their infectivity may or may not be retained, but the

addition of 70% sorbitol to the material before freezing makes them more stable (Weller & Hanshaw, 1962).

The viruses are labile at pH 3.0 and are sensitive to ether (Weller, 1965).

GROWTH AND ANIMAL INOCULATION:

Cytomegalovirus derived from patients can be grown on tissue cultures of human fibroblast or myomaternal cells but will not grow readily on cells from other animals. Cytomegalovirus from other animals will not with rare exceptions, grow on human tissue culture cells, but only on homologous fibroblast cells cultures (Tobin, 1987).

This host specificity is a main characteristic of this group of viruses and is shown both in animal inoculation and tissue culture tests. As a result, antisera can not be prepared in animals against human cytomegalovirus. Growth on tissue culture may be very slow: in one series of tests, cytopathic changes were first noted between 16 and 49 days after inoculation (Dios et al, 1967).

However infected tissue such as lung may contain as much as 10 tissue cultures infected doses in 1g (Hedley & Craighead, 1965). An odd feature is that human cytomegalovirus grows very unwillingly, if at all in tissue culture of human epithelial cells, though in the body these are the cells most often affected (Hedley & Craighead, 1965).