MIXED LYMPHOCYTE CULTURE TEST AND BLOOD CULTURE FOR RENAL TRANSPLANT PATIENTS

THESIS

SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MASTER OF BACTERIOLOGY

by

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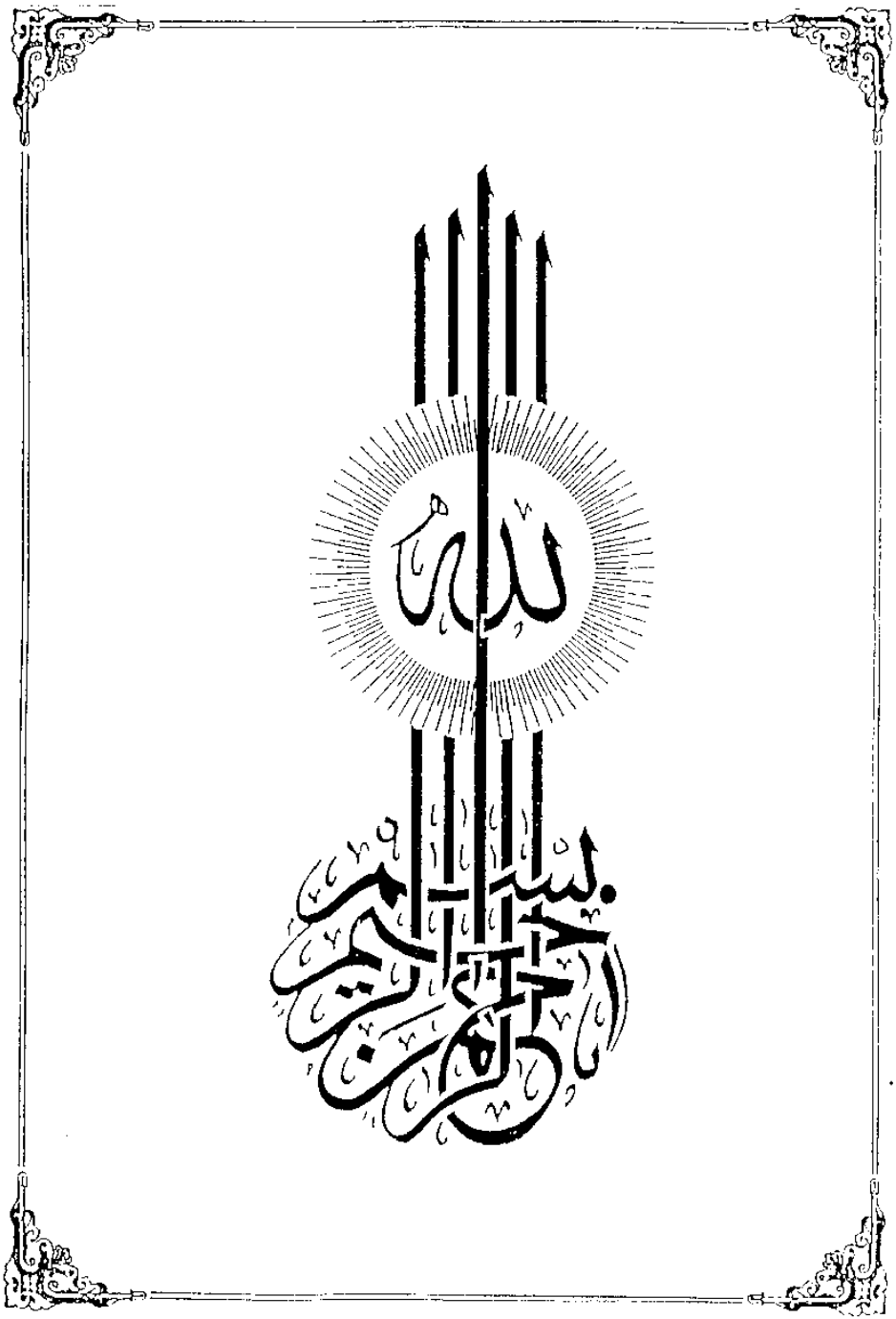
1990

ACKNOWLEDGEMENT

I would like to thank Professor Dr. Tahani Abd El-Hamid Mohamed, professor of Microbiology and Immunology, Ain Shams University, for her helpful collaboration and valuable suggestions, which were of utmost importance to perform this work.

My sincerest thanks are also due to Professor Dr. Rasha Youssef Khalil, professor of Microbiology and Immunology, Ain Shams University. I am most grateful to her for encouraging me to proceed with this work and for the interest she has taken in planning and supervising the contents of this work.

Finally, I wish to convey my utmost thanks to all those who offered me facilities for my filed work and to all the colleagues who helped in the preparation of this work.



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INTRODUCTION
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Kidney transplantation is now widely available for the treatment of end stage renal failure.

There are several techniques which are used in order to select the proper donor of the recipient patients. All of them are based on testing the degree of compatibility at the M.H.C. genes.

The HLA-D locus which was first detected by "Mixed Lymphocyte Culture" test (MLC) is based on the fact that when lymphocytes of two genetically different ie allogeneic individuals are cultured together, each individual's T cells recognize the histocompatibility antigens of the other as foreign, and respond by transforming and dividing.

Infection has been a major cause of death among renal transplant recipients even before renal transplantation. This is due to altered defense mechanism secondary to immunosuppressive agents, frequent admission to hospitals with the risk of exposure to antibiotic

resistant organisms and the maintenance hemodialysis for patients waiting kidney transplant.

Septicemia is the most common type of infection in these patients so that diagnosis and treatment of such infections are essential in developing optimal conditions for renal transplant.

The aim of this work is to find the relationship between the degree of stimulation using the MLC test and the degree of matching of the DR locus in order to select the proper donor of the recipient patients. It aims also at detecting the possible occurrence of bacteremia in renal transplant patients, as well as to isolate and identify the organisms which may cause bacteremia for proper treatment so that optimal conditions are developed for renal transplant.

REVIEW OF LITERATURE

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RENAL TRANSPLANTATION

Interest in the possibility of replacement of diseased or amputated parts of the body probably dates from ancient times, but it was not until the twentieth century that immunologic processes were identified as the mechanism responsible for rejection of tissue grafts while the goal of achieving donor-specific tolerance to grafted tissues without resorting to broadly immunosuppressive treatments has not been achieved in clinical circumstances, transplantation of tissues between genetically distinct donors and recipients (allografts) has proved useful in several clinical circumstances. Kidney transplantation is now widely available for the treatment of patients with end stage renal failure. Although chronic haemodialysis offers prolonged survival for individuals with end stage renal failure, the technique is inconvenient and time consuming. Dialysis therapy does not produce full rehabilitation, whereas recipients with successful kidney allografts often achieve remarkable rehabilitation (Strom et al., 1981).

Tissue typing and clinical immunogenetics

The two most important histocompatibility systems in man are the ABO blood group system and the HLA system The rule governing transplantation with regard to the ABO system is the same as that for blood transfusion ie the donor must be compatible with the recipient.

Evidence that HLA system is the major histocompatibility system (MHS) in man is derived from the observed superior success rate in living related donor renal and bone marrow transplantation using HLA identical sibling donor and recipient pairs (Strom et al., 1981).

Major histocompatibility system

The HLA system is localized on the short arm of chromosome 6 and at the present time the system is known to comprise several loci: five of the loci (A, B, C, DR and DC) code for serologically detected cell surface antigens, HLA-D codes for determinants detected by the "Mixed lymphocyte culture" (MLC) test (Perkins, 1978).

a) Class I antigens

These antigens are coded for the A, B and C loci and were the first series of HLA antigens detected, the A and B in 1968 and the C in 1970. In the caucasian population, all or nearly all of the A and B antigens have been discovered, although variants of existing antigens are still being found.

Not all of the C locus antigens have been defined. Class I antigens have been detected on all cells of the transplantable organs, such as kidney, heart, liver and pancreas.

Indeed, the antigens are expressed on virtually all cells except mature erythrocytes in man (Hart et al., 1981).

In the kidney, by the use of monocloncal antibodies antigens have been shown to be expressed on the endothelium of all blood vessels, on the tubules, on the mesangium and dendritic cells (Braun, 1983).

The HLA-B molecule carries at least two different types of HLA antigens. One is the subtypic (private) antigen such as Bw51, Bw52. At least 40 alleles are

known. The other is a public antigen which is either Bw4 or Bw6. Other antigens, also referred to as public or supertypic antigens, have been described and do not correlate with known HLA antigens.

At least one of these antigens is present on the HLA-A as well as the HLA-B molecule (Amos et al., 1975).

Class II antigens

These antigens are coded for by DC and DR loci. In the early 1960s, it was shown that when lymphocytes from two unrelated individuals were cultured together in vitro, each set would undergo blast cell transformation and mitosis. It was postulated that this mixed lymphocyte reaction (MLR) might represent the in vitro homologue of the vivo immune response to an allograft (Dick and Crichton, 1972).

In the early 1970s, the determinants (HLA-D) responsible for the initiation of MLC response were identified. These determinants found on B but not T lymphocytes will stimulate cells from individuals who do not possess the same determinant.

Typing for the D determinants is based on stimulation of a responding cell population by homozygous typing cells (HTC) which are homozygous for a single D determinant (Perkins, 1978).

In culture, cells that do not respond to a particular HTC will lack the determinant (Ting, 1984).

The invitro technique which detects HLA-D differences is known as "mixed lymphocyte reaction" or MLR.

In this test, the cells of two individuals are grown together in mixed culture and the amount of MLR cross-match can be determined.

The DR (*D-related*) antigens are newly recognized series. They are expressed on B lymphocytes and on other lymphoid cells such as Macrophages, Langerhans cells of the skin, monocytes, ... but not T lymphocytes nor platelets (Bodmer et al., 1978).

DR antigens, while physically unlike HLA-A, B and C share the characteristics of great polymorphism and cross reactivity between alleles.

The HLA-DR antigens appear to be analogous to the (Ia antigen) in mouse as regard the physical properties and the distribution. Ia antigens are the products of genes in the immune response region (Klein, 1975).

DR antigens were serologically detected first in 1973 and organized into a system of allelic antigens in 1977 (Shaw et al., 1980).

The incomplete correspondence between HLA-D and HLD-DR is now becoming certain. Some of the antigens are relatively easy to define such as DR1, 2, 3, 4, 5 and 7. Others are difficult to accurately define, particularly DRw6 for which there are no monospecific antisera. Nevertheless, it has been possible to define three variants of this antigen.

The DC system of antigens was recognized in 1979 and comprises only three alleles (Ting, 1984).

Immunochemical studies have shown that these antigens reside on a molecule distinct from that carrying the DR antigens (Shaw et al., 1980).

In the kidney, the antigens of class II MHC are expressed on glomerular endothelium, the intertubular