TISSUE AND ORGAN TRANSPLANTATION

A THESIS

Submitted in Partial Fulfilment
For the Requirement of the
M. Sc. Degree (Medicine)

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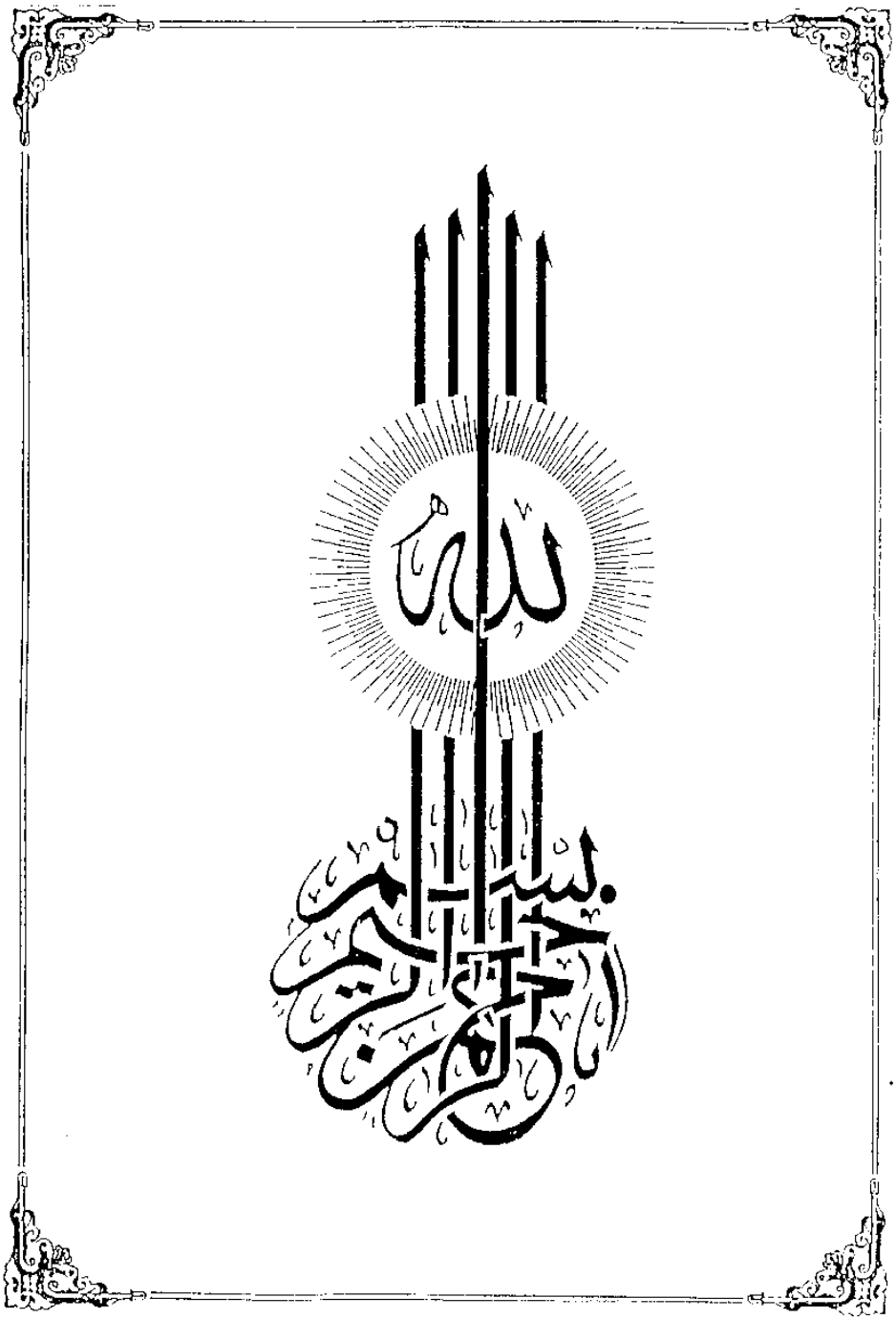
1980

TO MY PARENT , MY WIFE

AND MY SON



ACKNOWLEDGEMENT

I wish to express my sincere gratitude and my deep appreciation to my Professor Dr. M. Moneer El-Mehairy, Professor of Medicine, Ain Shams University for his generous, authoritative advice on various difficulties under whose supervision I had the honour to proceed with this subject. Professor Dr. Abo El-Magti Nabih Professor of Medicine Ain Shams University has given me much helpful counsel, advice, and encourgement, to whom my sincere thanks and gratefullness are due.

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INTRODUCTION

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For many years surgeons have attempted to graft normal tissue or organ from one animal to another. In the case of particular tissues successful transplants have been recorded for a long time. The first cornealgraft was made in 1852. Nevertheless for most tissues of higher animals there has been a record of repeated failures until lines of mice were bred (By careful brother - sister mating and selection, whose genetical constitution was Identical, or very nearly Identical).

In all members, such pure lines were known as Isogenic. When skin grafts are exchanged between Isogenic Individuals they become vascularized and persist and function indifinitely. The general difficulties experienced in the transplanatation of tissues are therefore not due to transplantation technique. They are in fact immunological, and derive from the fact that in oridinary populations every individual is likely to differ genetically from every other except in the case of uniovular (identical) twins. Indeed a small number of indentical

twins suffering from loss of skin through burning or from severe renal disease, have been able to benefit from grafts donated by their opposite numbers. Genetic differences are expressed ultimately by the synthesis of chemically different materials, whether these be required for the structure or the function of the cells, and individuals with different genetic constitution termed heterogeneic-are likely to differ in their chemical make up at least in some respects only certain of such differences. i e namely those involving lipoproteins or lipoglycopeptides associated with the surface membranes of most of but not all of the nucleated cells of the body and termed transplantation antigens, are important in determining the fate of the graft. The problem of grafting apart from the surgical technique is the problem of the immunological response of the recipient against the transplantation antigens of the graft, and sometimes, by cells, in the graft against the transplantation antigens of the host.

Clinical organ grafting is a surgical procedure, the objectives of which are straight forward, namely the replacement of the function of a diseased damaged or lost organ, by an organ transplante from another

individual. Most organ grafts have been used to replace vital function that cannot adequately be supplied by other means, for example, the kidney, heart, liver and lung. Loss of the secretions of other organs, such as these of the pancreas, thyroid, and adrenals can be made good by medication, which is usually safer than the immuno-suppressive regimes required to prevent graft rejection.

Graft rejection and shortage of donor organs for transplantation are the two central stumbling blocks to progress in clinical organ grafting. The surgical techniques and short term organ storage are well established, so that safe and predictable control of rejection and an adequate provision of donor organs would revolutionize the practice of surgery-grafts of bowel, endocrine glands and possibly limbs could become commonplace.

It would be helpful to define the terms used for transplants between individuals and species.

Auto-graft : Tissue grafted back on to the original donor.

Iso graft : Graft between syngencic individuals (i.e of identical genetic constitution, such as identical twins or mice of the same pure - line strain)

Allograft : (Homograft) - graft between allogencic individuals. (i.e. members of the same species but different genetic constitution) e.g man to man and one mouse strain to another.

Xerograft: (Heterograft)- Graft between xerogencic individuals (i.e. of different species) e.g. pig to man.

Allostatic : Grafts which are intended to serve a temporary or mechanical function after transplantation so that continued viability of the tissue is not required.

Allovital.: Grafts which are intended to perform continued full normal, metabolic function after transplantation.

Orthotopic : The placement of a graft in the anatomic position normally occupied by such tissue.

Heterotopic : The placement of a graft in an anatomic location not normally occupied by such tissue.

Adoptive Immunity : Specific permanent immunity conferred upon apreviously unsensitized individual by the administration of immunologically competent and committed cells from a previously sensitized donor.

First Set Phenomenon : The chronology and events leading to graft rejection following initial exposure of a recipient to the tissue of a donor.

Second Set Phenomena : The chronology and events leading to graft rejection following subsequent exposure of the recipient to tissue of the same donor.

It is with the allograft reaction that we have been most concerned although it should one day possible to use grafts from other species. The most common allografting procedure is probably blood transfusion where the unfortunate consequence of mismatching are well known. Considerable attention has been paid to the rejection of solid grafts such as skin and the sequence of events is worth describing. In mice for example, the skin homograft

settles down and becomes vascularized within a few days, between three and nine days the circulation gradually diminishe and there is increasing infiltration of the graft bed with lymphocytes and monocytes but very few plasma cells, necrosis begins to be visible macroscopically and within a day or so the graft is sloughed completely.

IMMUNOLOGICAL BACK GROUND OF ORGAN GRAFTING

IMMUNOLOGICAL BACK GROUND OF TISSUE TRANSPLANTATION

"Evidence that rejection is immunological":

(1) First and Second Set reaction:

It would be expected if the reaction has an immunological basis, that the second contact with antigen would represent a more explosive event than the first, and indeed the rejection of a second graft from the same donor is much acelerated. The initial vascularization is poor and may not occur at all. There is a very rapid invasion by polymorphonuclear leukocytes and lymphoid cells including plasma cells. Thrombosis and acute cell destruction can be seen by three to four days.

(2) "Specificity":

Second Set rejection is not the fate of all subsequent allografts but only of those derived from the original donor or elated strain. Grafts from unrelated donors are rejected as first set reactions.