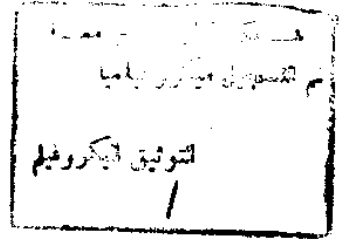


ORGAN TRANSPLANTATION: AN UPDATE

An Essay
Submitted for partial fulfilment of
Master Degree in General Surgery



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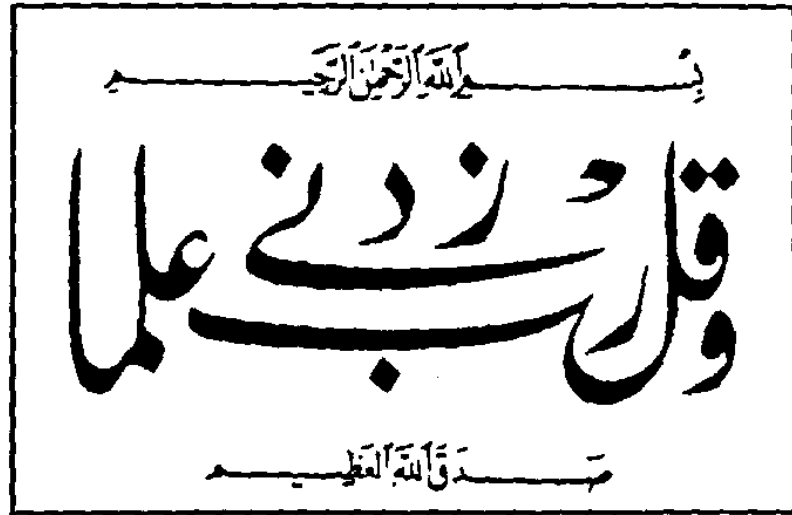
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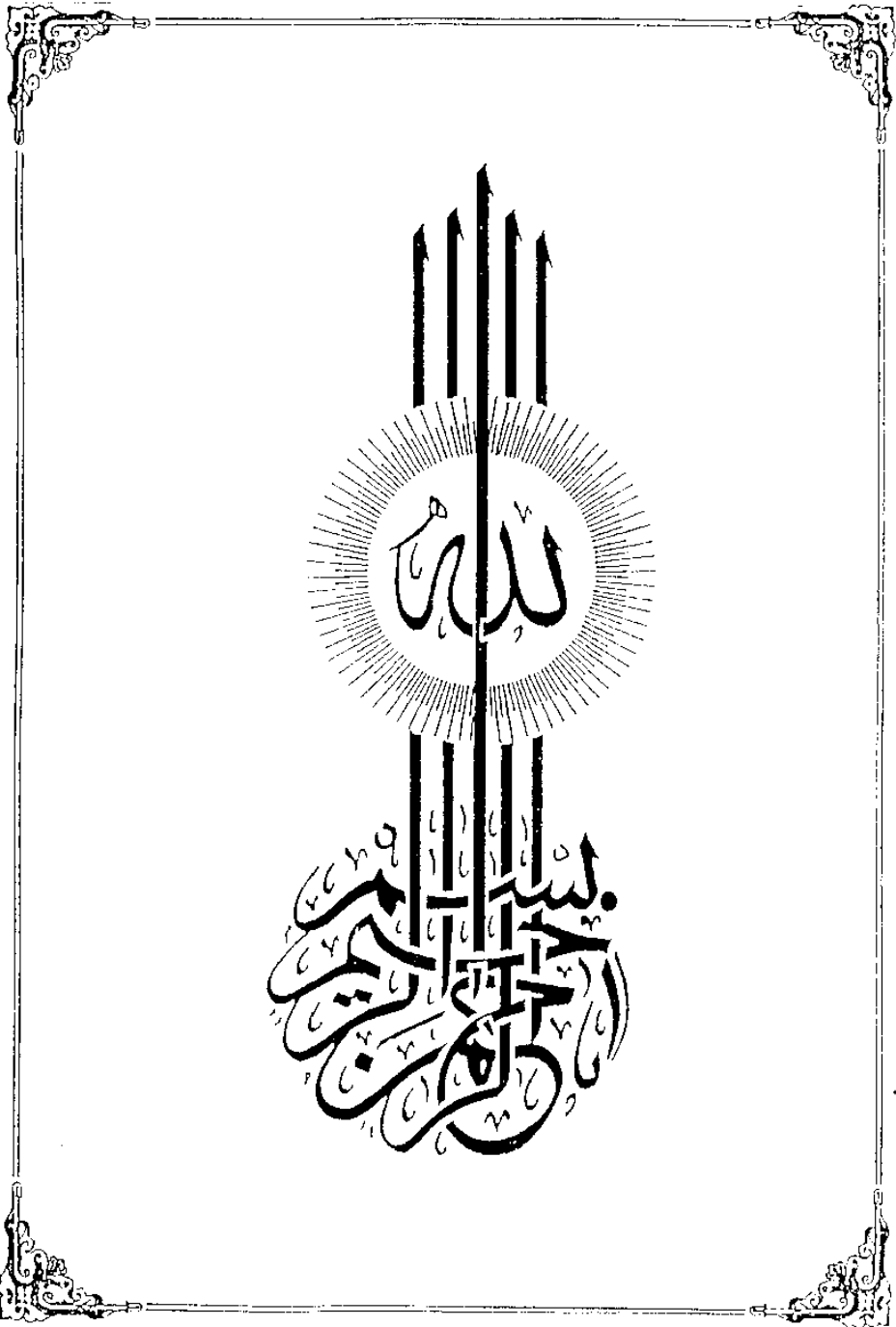
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Contents

	Page
Introduction	1
Tests of compatibility between donor and recipient	5
Renal transplantation	31
Liver transplantation	60
Pancreas Transplantation	100
Summary	157
References	161
Arabic summary	

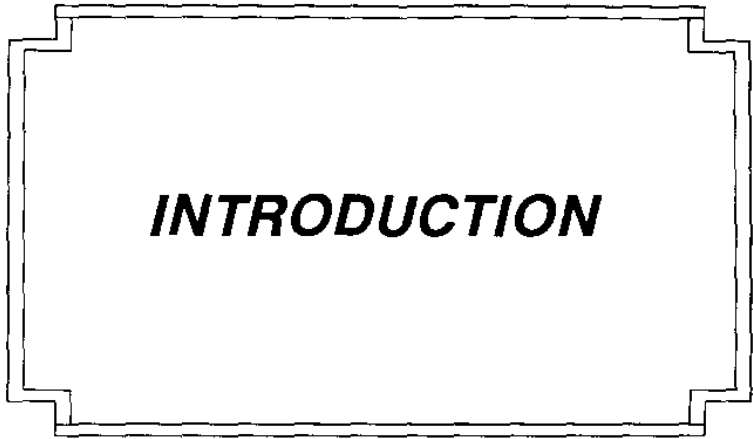
LIST OF TABLES

	Page
Table (1) : Present listing of HLA specificities	8
Table (2): Typing of unknown lymphocytes for HLA-D by means of mixed leucocyte culture.	25
Table (3): Indications for renal transplantation.	32
Table (4): Programmed evaluation of the potential transplant recipient.	35
Table (5): Indications for liver transplantation.	61
Table (6): Contraindications to liver transplantation.	70
Table (7): Liver transplantation: Results since 1986.	98
Table (8): Criteria for pancreas transplant patients at the University of Minnesota.	104
Table (9): Pre- and Post-pancreas transplant evaluation at the University of Minnesota.	107
Table (10): Criteria for selection of living-related pancreas donors.	111
Table (11): Pancreas preservation solution used at the University of Minnesota.	124
Table (12): Current immunosuppressive protocols for non- uremic, non-kidney transplant recipients of pancreas grafts at the University of Minnesota.	143

LIST OF FIGURES

		Page
Fig. (1):	Map of human chromosome 6.	7
Fig. (2):	Lymphocytotoxic test.	13
Fig. (3):	The effect of the number of HLA-DR antigen between recipient and donor on the outcome of first cadaver transplants.	17
Fig. (4):	Incision for adult and child transplantation	47
Fig. (5):	Renal transplantation (Recipient operation)	47
Fig. (6):	Diagram of veno-arterial bypass without systemic heparin.	81
Fig. (7):	Diagram of orthotopic liver transplant showing the anastomoses.	84
Fig. (8):	Orthotopic liver allograft showing biliary drainage into the Roux loop.	85
Fig. (9):	Biliary reconstruction	93
Fig. (10):	Pertinent pancreatic anatomy in segmental graft donor.	113
Fig. (11):	Mobilization of tail of pancreas from a cadaveric donor.	115
Fig. (12):	Pancreatic segment following removal from a non- liver donor.	115
Fig. (13):	Options for management of the blood vessels to the pancreas.	116

	Page
Fig. (14): Whole pancreas procurement in the non-liver donor.	119
Fig. (15): Isolated pancreaticoduodenal grafts from a cadaveric donor.	120
Fig. (16): Maneuvers for removal of a whole pancreas and a liver from a cadaveric donor.	123
Fig. (17): Technique for revascularization in the recipient of a segmental pancreatic graft from a cadaveric non-liver donor.	126
Fig. (18): Injection of a synthetic polymer into the duct of a segmental pancreas graft following revascularization.	129
Fig. (19): Enteric drainage of a segmental pancreas graft to a Roux-en-Y limb of the recipient jejunum.	130
Fig. (20): Enteric drainage of a pancreaticoduodenal or whole- pancreas graft with a duodenal patch.	133
Fig. (21): Whole pancreas transplantation with bladder drainage.	135
Fig. (22): Pancreaticoduodenal transplantation with bladder drainage.	137
Fig. (23): Results of oral and intravenous glucose tolerance tests before and one year after a segmental pancreas transplant.	151
Fig. (24): Insulin independent rates and patient survival rates for all pancreas transplant cases reported to the Registry by era for 1966-1977, 1978-1982, and 1983-1986).	153



INTRODUCTION

INTRODUCTION

The substitution of a healthy organ for a non-functioning one is an old medical dream. Today, this dream is becoming a reality for an increasing number of patients.

Skin transplantation dates back to about 1500BC. , corneal and bone transplantation developed in the second half of the nineteenth Century, and whole organ transplantation was pioneered by Alexis Carrel 60 years ago, who designed the surgical techniques of vascular anastomosis.

Only with the advent of immunosuppressive drugs to prevent rejection in the early 1960s did successful kidney and other organ transplantation become a clinical reality. Orthotopic cardiac allografting was made possible with the use of the extracorporeal circulation in 1960 by Lower and Shumway in their laboratories. Successful liver transplantation was initiated by Starzl in 1963; Pancreas was transplanted in 1966 and small bowel in 1967 by Lillehei.

The first clinical allograft rejection occurred in 1952 in Paris a few days after a young boy received his mother's kidney. To prove the immunologic incompatibility between recipient and allograft, Merrill (1956) in Boston performed the first kidney transplantation between identical twins. The absence of rejection between these two genetically histocompatible tissues was indirect proof of the role played by the immunologic defenses of the recipient against the foreign tissue that allowed the rejection to occur. The role of the lymphocytes as key factors during the rejection process was defined by Hamburger and Merrill (1962) using antileukemic treatments (corticosteroids and total body radiation). Schwartz, using azathioprine, and Woodruff, introducing the antilymphocyte globulin, completed the therapeutic tools in clinical transplantation between 1960 and 1980.

Without clear and legal definition of clinical death, the efficient use of a single vital and viable organ was impossible. Following several years of interim discussions, the concept of "brain death" was finally accepted, opening the door to a new era in transplantation.

Since the introduction of cyclosporine in 1980, the survival rate

worldwide for cardiac recipients is now reaching 60 percent at five years. Following the leadership of Starzl (1980) in the United States, Calne (1982) in England, and Bismuth (1986) in France, the 1-year survival rate for liver transplantation is now reaching 70 percent.

There are two main factors which limit organ transplantation as a successful treatment. They are (1) Immunological - the problem of rejection, and (2) "Supply and demand" - the supply of organs continually falls behind the demand of increasing numbers of patients with end-stage organ disease [Mee, 1992].

Cost containment is currently the principal focus of any decision regarding policies and planning. If the number of organs available for transplantation remains limited, the financial impact may well be kept under "control", and any debate regarding ethical and economic issues will remain secondary. If transplantation becomes commonplace, issues of cost rather than long-term effectiveness will more likely influence the conduct of policy makers governing our budgeted resources. The goal to balance limited resources and the cost of saving one life should be considered in respect to the law of humanity as well as the law of diminishing

returns when making comparisons as to the efficacy of other more wide-reaching, life-preserving, medical strategies for larger populations, [Cabrol and Painvine, 1986].

***TESTS OF
COMPATIBILITY
BETWEEN DONOR
AND RECIPIENT***

TESTS OF COMPATIBILITY BETWEEN DONOR AND RECIPIENT

The replacement of diseased organs by transplants of healthy tissues has long been an objective in medicine but has been complicated by the attempt of the body to reject grafts from other individuals. The antigens which provoke this rejection are the histocompatibility (H) molecules of which two groups exist, major and minor. The major H molecules induce acute rejection of allogenic (genetically dissimilar) tissue, in contrast to the allogenic minor H molecules, which normally induce chronic graft rejection.

In man, there are three classes of major histocompatibility locus antigens (HLA) which are involved in graft rejection, class I, class II, and class III. The genes for these are on chromosome 6, in a cluster called the major histocompatibility complex (MHC). The class I Molecules are encoded by three different loci, HLA-A, B, and C, the class II by another three loci, HLA-DP, DQ and DR, and the class III by c2, c4 and Bf, (Fig. 1 & Table I).

HLA antigens are glyco-proteins floating in the plasma mem-
