IMMUNOLOGICAL FACTORS IN RENAL TRANSPLANTATION

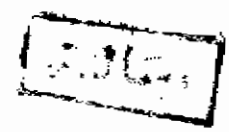
ESSAY

Submitted for the Partial Fulfilment of
The Master Degree in Urology

By

ALY M. EL BASSEL

M. B. B. Ch.



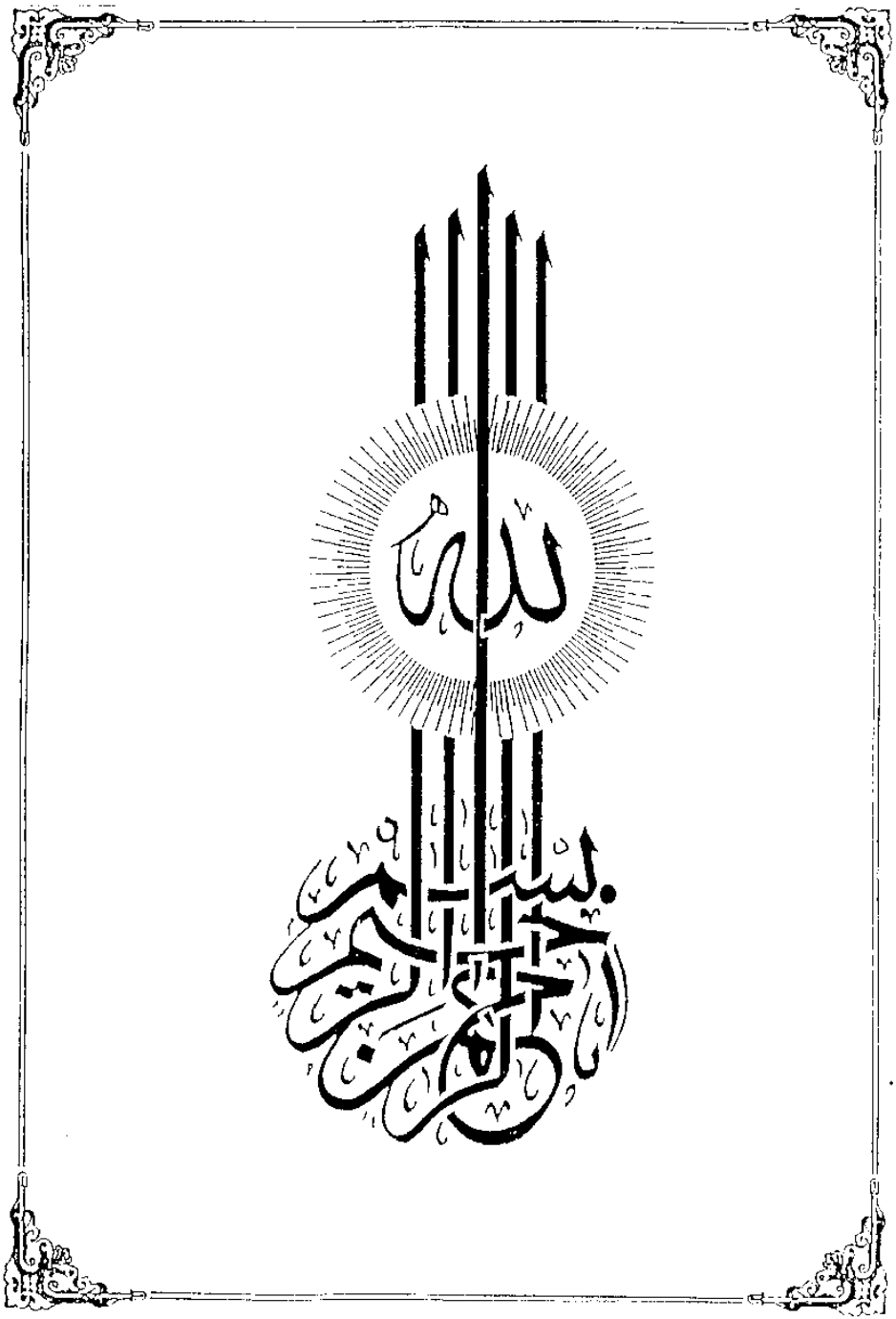
Under the Supervision of

Prof. Dr. HATEM EL BIALY

Professor of Urology

Faculty of Medicine
Ain Shams University
CAIRO

1983



Acknowledgement

I am deeply grateful to Dr. Hatem El Bialy professor of Urology, Ain Shams University, for his faithful supervision, guidance and encouragement.

Thanks to Dr. Amr Elwany the director of police hospital for his help and valuable advice.

I would like also to present my gratitude to all members of urology department, Ain Shams University for their assistance and kindness.

****

CONTENTS

CONTENTS

****

INTRODUCTION

Introduction

All higher animals are equipped to recognize allografts as foreign. Such an allograft sets in train an immunologic conflict leading to graft rejection. The protagonists in the confict are the antigenic structures of the graft and the immunologically competent cells of the host.

In humans as in all other mammals there is a chromosomal region containing genes of fundamental importance to immune responses. These genes include, among others, the HLA histocompatibility genes (Herbert, 1978).

The HLA gene products were first defined by reactions of antisera with leukocytes and the terminology was intended to represent H for human, L for leukocyte, and A for the first defined genetic region for human leukocyte antigens (Dausset and Snejaard, 1977).

The human major histocompatibility system is a cluster of genes on the VIth human chromosome that determine the structure of cell-surface glycoproteins found on all the cells of the body. These glycoproteins differ from individual to individual and form a complex set of antigenic determinants that constitute the strongest (major) antigenic barrier to tissue transplantation between genetically non-identical individuals (Sasazuki et al, 1977) .

Meanwhile the characteristic of the individual as a whole and their complexity is such that there are probably no two persons in the world with an absolutely identical antigenic structure, except of course, for identical twins.

It is generally held that the immune response to an allograft belongs to the class of immune reactions known as cell mediated, and thus related to delayed hypersensitivity reactions such as the tuberculin reaction. This cell-mediated response is distinguished from humoral responses (in which cells are in fact involved, but act by releasing circulating antibodies into the blood).

It will be seen later on that the role of circulating antibodies is in fact far from negligible in the process of rejection of homotransplanted organs. But there is no doubt that the cell-mediated immune response is the predominant factor in allograft rejection (Jean Hamburger et al, 1972).

The aim of this essay is to present a concise review of the role of the immunological factors in renal transplantation. The general principles of immunology in relation to renal transplantation is the first described. Then the importance of immunological monitoring in transplantation is outlined. The complications of renal transplantation is briefly discussed, that follows a brief account of the immunosuppression. Finally a summary concludes this essay.

****

GENERAL PRINCIPLES OF IMMUNOLOGY IN RELATION TO RENAL TRANSPLANTION

Terminology

The words graft and transplant are used synonmously it was formerly suggested that the term transplantation should be reserved for the connection of organs to the host vessels and that the word grafting should be used when tissue fragments were implanted without vascular suture. But usage, which is overriding in matters of terminology, has supported this distinction and many authorities talk now of grafting a heart or a kidney.

Autotransplantation or autograft

Signifies that the organ is reimplanted in the same body from which it has been removed. Donor and recipient are one and the same person. It may be necessary for example to carry out kidney autotransplantation to the iliac fossa when there is an irreparable vascular lesion in the part of the aorta which normally gives rise to the renal arteries, there are no immunologic proplems in autotransplantation.

Isotransplantation or isograft

Signifies that both donor and recipient have a similar antigenic structure, at least as far as we are concerned here. This is exemplified in man by transplantation between identical twins who as far as basic antigenic stucture concerned, are but two examples of the one individual. Like autografts, isografts in gneral pose no immunolgic proplem.

Homotransplantation or allografting

Is carried out between individuals of the same species,

for example from rat to rat or from man to man. This is the usual form of kidney transplantation, and it is with this that the present work is mainly concerned.

Heterotransplantation or xenografting

Signifies that donor and recipient belong to different animal species.

The first efforts at renal transplantation in man were heterotransplants. In 1906, Jaboulay tried to connect goat and pig kidneys to the arm vessels of uraemic patients. More recent attempts to transplant kidneys from monkeys to man also fall into this category of heterotransplantation, although some authors point out that this is a special case because both donor and recipient are primates, and as such undoubtedly have some immunologic features in common (Balner and Van Rood 1967).

****

The Sequence of events following a homotransplantation

Tissue cells carry cell-surface markers. If the markers on a grafted cell differ from those present in the host, they are rapidly recognized as foreign and a complex series of changes is initiated (Good and Fisher, 1971).

These processes lead, in most instances to the formation of antibodies and to the appearance of activated or killer lymphocytes. Antibody production is the function of certain specialized cells called B cells, and plasma cells derived from them, other reactive lymphocytes that are not producers of antibody are called T cells (Greaves et.al.,1973). The origin of both cell types appears to be in the yolk sac and later, in the bone marrow.Both are present in the spleen (Cerrottini et. al., 1971).

Stem cells leave the marrow and enter the thymus there they continue in a rapid state of cell division. In the mouse, where they have been most carefully studied, thymic lymphocytes can also be subdivided. The majority carry antigenic markers called theta and TL (Boyse et.al., 1970).

Thymocytes leaving the thymus migrate to lymph nodes and spleen and may then recycle through the blood stream and tissues (Brent and Holbrow, 1974).

Whether B cells pass through the thymus or pass directly to lymph nodes has not yet been clarified, they do not have a characteristic marker corresponding to TL, but in later development another antigen, PC does appear (Takahaski et. al., 1970). T-cells also known as thymus-dependent or thymus

derived cells, are responsible for delayed type responses (Mc Clusky and Cohen, 1974). It is believed that T cells carry immunoglobulin on their surfaces.Attempts, however, to demonstrate Ig on T cells have been disappointing with the exception reported by Binz and Wigzell (1975), who produced antibody to T rat lymphocytes in F1 hybird animals. The Binz-Wigzell antibody differs from most antiglobulins in being an anti-idiotype,i.e. reacting against the variable portion of the Ig molecule.

In contrast, B cells carry easily identified immunoglobulin heavy and light chains on their surface (Moller,1975).

While the majority of B lymphocytes bear Ig molecules on their surface and secrete the same Ig, there are exceptions. Some cells carry two surface Ig markers . But secrete only one class of Ig, while in certain pathologic states, abundant B cells may be present but fail to secrete significant amounts of Ig, giving rise to hypogamma globulinaemia (Smater,1976).

In the chicken, B cells develop in the bursa of Fabricius. Bursectomy at the time of hatching depletes most of the B cell population and the chick is unable to make antibody in the normal way (Elves 1972). The earlier the bursectomy is carried out, the more severe the depression . T cell reactivity remains relatively normal . These chicks will reject skin grafts. There is no known analogue of the bursa in mammals, the term B cell,however, can be equated with "bursal cell equivalant" (Yoffey,1967). Thymectomy in new born rodents or newly hatched chicks depletes the host of T cells and results