REJECTION IN KIDNEY TRANSPLANTATION

ESSAY

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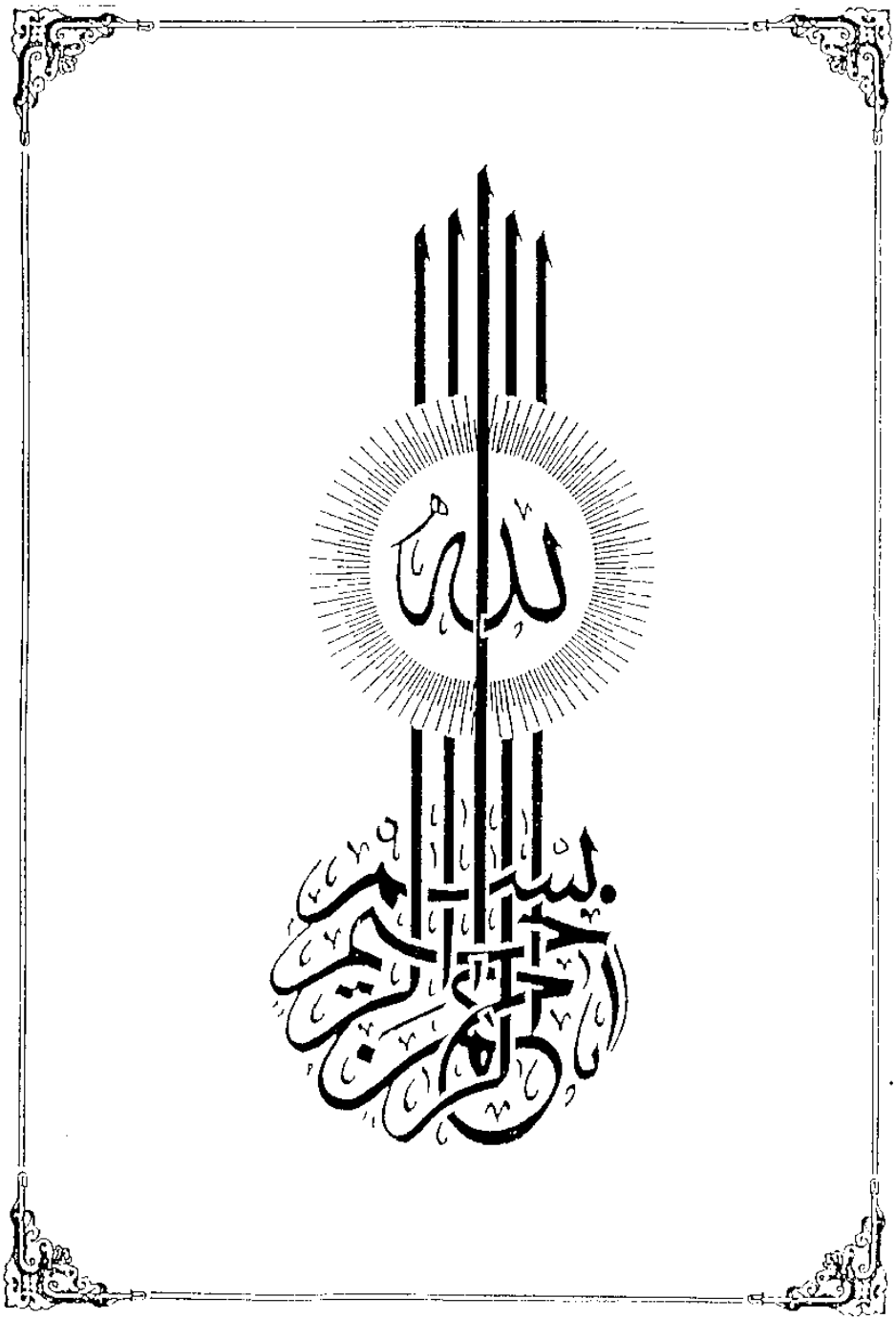
INTRODUCTION



INTRODUCTION

Grafts are classified according to the species of origin into:

1. An autograft:

is a transplant made from one site to another site in the same individual.

2. Allograft or Homograft:

is a transplant made from one individual to another of the same species. If the two individuals are isogenic i.e. of identical or nearly identical genetic structure, then the term isograft is used. Allograft is the common type used in kidney transplantation

3. Axenograft, or hetrograft is a transplant from one animal to another of different species.

Rejection is the most serious complication in kidney transplantation.

Review of the results of kidney transplantation shows that by two years after operation approximately 60% of grafts have failed, the majority due to rejection.

Rejection of homograft is an immune response which depends on an antigen anti body reaction.

In successful cases rejection and immunosuppression are balanced, and withdrawal of immunosuppression will result in rejection.

In this essay there is a review on rejection.

HISTORICAL REVIEW

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Transplantation of the human kidney is now a justified procedure for the treatment of advanced chronic renal failure. When it is successful, it has allowed many patients resume normal lives, when unsuccessful some are made worse and others die. Unfortunately excellent long term transplantation function is not routinely obtained except in the best matched, related donor and recipient combinations. Rejection causes the majority of failures. The results with probably matched familial donor are superior to those obtained with organs from cadaveric donor with 75-80% compared with 45-50% graft survival rates at one year. Grafts functioning at one year are subjected to a constant albict diminished incidence of failure over the subsequent years, primarily due to chronic rejection. (Charles W. Parker, 1980).

The problem of rejection was first appreciated by Carrel (1908). In the early 1950's sporadic attempts of human transplantation were successful at several centers, but unfortunately all recipients eventually died, as the immunosuppressive effects of ureamia in them (Hume et al., 1955) were not sufficient. Total body irradiation was first used as immunosuppressive agent at Peter Bent Brigham Hospital in January 1959. Infection and severe

marrow depression (Merill 1961, Murry et al. 1962) are its complications and lethal to the patients. Because of disappointing results from the use of total body irradiation chemical immuno-suppression in 1960 was tried and proved to be a more successful procedure and less injurous one.

ANTIGENICITY OF REJECTION

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Rejection of homograft is an immune response which depends on an antigen (Transplantation antigen) which excites the development of both humoral and cellular factors.

ANTIGENS IN KIDNEY TRANSPLANTATION

THE HISTOCOMPATIBILITY ANTIGENS

(TRANSPLANTATION ANTIGENS)

The strongest stimulation for rejection of any tissue incompatibility is the major histocompatibility complex (MHC). The human (MHC) is known as the (HLA) system (Human Leuccocyte Antigen). HLA occupies part of the short arm of the chromosome "6" and this segment of the chromosome is also called the HLA haplo type. (Bernard Amos et al. 1981).

The HLA system comprises a complex group of antigens which are present on the cell membranes, of all tissue cells other than erythrocytes. From 1960 onwards it was recognized that antigens present on human leucocytes might provide part of the explanation of allograft rejection (Walter & Isreal 1979).

Structure of HLA antigens:

HLA antigens are glyco proteins in nature. The molecular weight of antigens HLA-A, HLA-B & HLA-C is about 55,000 daltons.

The newly defined HLA-DRW antigens comprise one each of 2 glycosylated polypeptides of molecular weights, 33,000 and 28,000 daltons that are not convolently linked.

Inheritance of HLA:

The HLA system is a highly polymorphic one, and five major gene loci are at present recognized (on the short arm of chromosome '6'). They are called HLA-A, HLA-B, HLA-C, HLA-D, and the recently described HLA-DR which is closely related to the HLA-D locus. Each of these loci contains a considerable number of alleles.

Every individual inhirits one antigen from each series from each parent.

The C and D loci are closely linked to the A and B loci, and the probable order of these four loci on the chromosome is D, B, C, and A from the centromere pripher-ally.

Another completely different system involved with the immune response of other agents is closely associated with the HLA-D antigens. This system, the Ia (immune associated antigen system), also called the B-cell antigen system, because the antigens are found predominantly on B lymphocyte. The genetic region controlling this human Ia antigen system is very closely related to the D locus on

cromosome '6' and is called the HLA-DR locus, the antigens associated with this locus are now called HLA-DRw antigens.

Locus A	*Locus B*	*Locus C*	*Locus D*	*Locus DR*
HLA-A1	HLA-B5	HLA-Cw1	HLA-Dw1	HLA-DRw1
HLA-A2	HLA-B7	HLA-Cw2	HLA-Dw2	HLA-DRw2
HLA-A3	HLA-B8	HLA-Cw3	HLA-Dw3	HLA-DRw3
HLA-A9	HLA-B12	HLA-Cw4	HLA-Dw4	HLA-DRw4
HLA-A10	HLA-B13	HLA-Cw5	HLA-Dw5	HLA-DRw5
HLA-A11	HLA-B14	HLA-Cw6	HLA-Dw6	HLA-DRw6
HLA-Aw19	HLA-B15		HLA-Dw7	HLA-DRw7
HLA-Aw23	HLA-Bw16		HLA-Dw8	
HLA-Aw24	HLA-B17		HLA-Dw9	
HLA-A25	HLA-B18		HLA-Dw10	
HLA-A26	HLA-Bw21		HLA-Dw11	
HLA-A28	HLA-Bw22			
HLA-A29	HLA-B27			
HLA-Aw30	HLA-Bw35			
HLA-Aw31	HLA-B37			
HLA-Aw32	HLA-Bw38			
HLA-Aw33	HLA-Bw39			
HLA-Aw34	HLA-B40			
HLA-Aw36*	HLA-Bw41			
HLA-Aw43*	HLA-Bw42*			
	HLA-Bw44			
	HLA-Bw45			
	HLA-Bw46†			
	HLA-Bw47			
	HLA-Bw48			
	HLA-Bw49			
	HLA-Bw50			
	HLA-Bw51			
	HLA-Bw52			
	HLA-Bw53			
	HLA-Bw54†			
	HLA-Bw4			
	HLA-Bw6			

*Found so far only in Black populations.
†Found so far only in Mongoloid populations.

The nomenclature of HLA system
(Walter and Isreal 1979)

THE ANTIBODIES IN KIDNEY TRANSPLANTATION

The antibodies in Kidney Transplantation

The precursors of stem cells for the antigen-reactive cells, originate in the haemopoietic tissue. In the embryo, they are present in the primitive blood islands, in the foetus, they are present in the liver, and as the individual matures, they appear in the primary lymphoid tissues in the bone marrow. These precursors or stem cells, differentiate into antigen-reactive lymphocytes in the lymphoid tissue in two directions:

1. Cellular antibodies:

Lymphocytes migrate from the bone marrow to the cortex of the thymus gland to differentiate under thymus epithelial cells and are called T lymphocytes or T cells. Then they leave the thymus to settle in the lymph nodes (in the para-cortical area) and in the spleen (in the periarteriolar lymphoid sheaths), and these areas are called "Thymus dependent areas".

- T lymphocytes differentiated in the thymus dependent areas, become responsible for cellular immune response, when stimulated by specific antigen.
- T lymphocytes or T cells form a large proportion of the small lymphocytes, which circulate in the blood in a search for antigen, and they can live for months and even over a year.

- T lymphocytes or T cells, don't secrete antibodies, but release several mediators which play a role in starting the inflammatory response and allograft reactions. Among the important mediators produced by T lymphocytes are the chemotactic substances for polymorphonuclear leucocytes and monocytes and the factors which increase the capacity to destroy intracellular parasites.

2. Humoral antibodies:

Lymphocytes migrate from the bone marrow to differentiate in the lymphoid tissue of the appendix and Peyer's patches, and are called B lymphocytes or B cells (because they were first noticed in the lymphoid tissue of the Bursa of Fabricius in birds). Then, they leave the lymphoid tissue of the gut, to settle in the lymph nodes (in cortical and medullary cords), and in the spleen (in the white pulp and red pulp cords).

- The number of B lymphocytes or B cells in the blood is small and their life span is short and is measured in days.
- When B lymphocytes are stimulated by specific antigen and under the stimulation of T lymphocytes, they proliferate and differentiate into plasma cells, which synthesise and secrete antibodies i.e. immunogloculins, specific for the stimulating antigen with which they can combine (Hamburger et al. 1973).