YEAR BOOK®

YEAR BOOK OF TRANSPLANTATION 1992

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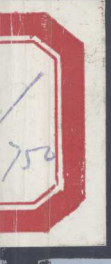

1992

The Year Book of TRANSPLANTATION

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Journals Represented

Mosby–Year Book subscribes to and surveys nearly 900 U.S. and foreign medical and allied health journals. From these journals, the Editors select the articles to be abstracted. Journals represented in this YEAR BOOK are listed below.

American Journal of Cardiology
American Journal of Diseases of Children
American Journal of Gastroenterology
American Journal of Kidney Diseases
American Journal of Medicine
American Journal of Roentgenology
American Journal of Surgical Pathology
Annals of Internal Medicine
Annals of Surgery
Blood
Bone Marrow Transplantation
British Journal of Surgery
British Medical Journal
Canadian Journal of Surgery
Chest
Clinical Genetics
Clinical Nephrology
Clinical Transplantation
Clinical and Experimental Immunology
Diabetes
Diabetologia
European Heart Journal
European Journal of Surgery
Gastroenterology
Hepatology
Journal of Clinical Microbiology
Journal of Clinical Pathology
Journal of Experimental Medicine
Journal of Heart Transplantation
Journal of Heart and Lung Transplantation
Journal of Immunology
Journal of Pediatric Surgery
Journal of Pediatrics
Journal of Thoracic and Cardiovascular Surgery
Journal of Urology
Journal of the American Medical Association
Journal of the American Society of Nephrology
Kidney International
Lancet
Lung
Medical Journal of Australia
Medicine
Metabolism
Microsurgery
Nephrology, Dialysis, Transplantation
Nephron
New England Journal of Medicine
New York State Journal of Medicine

Proceedings of the National Academy of Sciences
Quarterly Journal of Medicine
Radiology
Reviews of Infectious Diseases
Scandinavian Journal of Immunology
Science
Seminars in Hematology
Surgery
Surgery, Gynecology and Obstetrics
Therapeutic Drug Monitoring
Transplantation
Transplantation Proceedings
Virchows Archiv A: Pathological Anatomy and Histopathology

Standard Abbreviations

The following terms are abbreviated in this edition: acquired immunodeficiency syndrome (AIDS), central nervous system (CNS), cerebrospinal fluid (CSF), computed tomography (CT), electrocardiography (ECG), human immunodeficiency virus (HIV), and magnetic resonance (MR) imaging (MRI).

Publisher's Preface

We are pleased to present the premier volume of the YEAR BOOK OF TRANSPLANTATION. We are grateful to Dr. Nancy Ascher and her editorial colleagues Dr. John Hansen and Dr. Terry Strom for their belief in the need for this new series; for the hard conceptual work that went into defining the scope, structure, and limits of the content; and of course for the week-to-week work of developing the content for our readers.

Mosby-Year Book, Inc., started this series because organ transplantation has become a large, diverse clinical reality supported by an extraordinary range of scientific disciplines. We believe that all who are engaged in organ transplantation can benefit from "the YEAR BOOK service" — *surveillance* of the world medical literature, *selection* by experts of the most significant articles, *condensation* of those articles by skilled medical writers, and *commentary* from the experts who selected the articles.

We sincerely hope that this new publication will be of real value to its intended audience, and we invite your comments.

As Publishers, we feel challenged to seek ways of presenting complex information in a clear and readable manner. To this end, the 1992 YEAR BOOK OF TRANSPLANTATION provides structured abstracts in which the various components of a study can easily be identified through headings. These headings are not the same in all abstracts, but, rather are those that most accurately designate the content of each particular journal article. We are confident that our readers will find the information contained in our abstracts to be clear, concise, and easily accessible.

Table of Contents

1 Kidney Transplantation

Role of HLA Matching in Renal Transplantation

▶ ↓ As the transplant community moves sluggishly to expand the role of HLA matching in kidney grafts, the evidence continues to mount that the rate of engraftment—especially long-term—improves with the quality of the match. It has been long known that the quality of serologic matching for HLA class II molecules (DR, etc.) is inferior to the accuracy of matching for HLA class I molecules (A,B,C). Molecular genetic techniques are now shown to be more accurate than serologic analysis (1) for class II typing. Can these techniques be used within the time restraints imposed by current organ preservation techniques? Probably!—Terry Strom, M.D.

Reference

1. Mytilineous J, et al: *Transplantation* 50:870, 1990.

National Allocation of Cadaveric Kidneys by HLA Matching: Projected Effect on Outcome and Costs

Gjertson DW, Terasaki PI, Takemoto S, Mickey MR (UCLA Tissue Typing Laboratory, Los Angeles)

N Engl J Med 324:1032–1036, 1991 1–1

Introduction.—Transplantation of a cadaveric kidney matched at the HLA-A, B, and DR loci enhances graft survival in cyclosporine-treated patients. The value of a national system of kidney allocation based on HLA matching remains controversial. The costs of such a system may be unjustified. The effect of HLA matching on graft survival for all allocations of cadaveric kidneys in the United States was estimated.

Methods.—Data on 22,190 first-time cadaveric kidney recipients were partitioned to estimate the graft-survival rates in 5 mutually exclusive groups of transplants with increasing numbers of HLA mismatches. Overall graft survival was projected as a weighted average, using percentages of transplants in the hierarchical groups in recipient waiting pools of various sizes. The costs and benefits of HLA matching in a national system were compared with those of cyclosporine introduction, which was estimated to enhance graft survival by 7% of 10 years.

Results.—Sharing kidneys nationally based on hierarchical HLA matching enhanced graft survival by an estimated 5% at 10 years. The anticipated 5-year cost of this national system for 7,000 recipients would be $6.5 million less than the cost of using cyclosporine alone. This estimated cost included costs of graft removal and dialysis after transplant rejection (Fig 1–1).

Conclusions.—A national HLA allocation system will not add to the

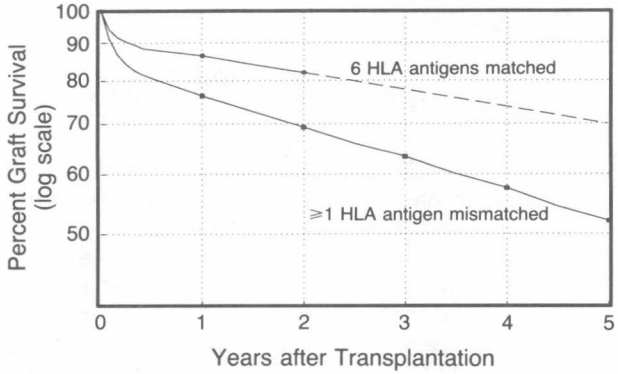

Fig 1–1.—Actuarial 5-year graft-survival curves *(solid lines)* and projections *(dashed line)* for 365 first-time recipients of cadaver kidneys matched for 6 HLA antigens and 21,621 recipients of transplants with at least 1 HLA-antigen mismatch. The differences between groups after 3, 6, 12, and 24 months were all significant ($P < .001$). (Courtesy of Gjertson DW, Terasaki PI, Takemoto S, et al: *N Engl J Med* 324:1032–1036, 1991.)

cost of renal transplantation. It will improve the long-term results by 5%, similar to that of cyclosporine. The initiation of a national kidney-sharing system based on hierarchical levels of HLA matches is proposed.

▶ What increases long-term kidney transplant engraftment, does not have serious side effects, is cost efficient and is hardly ever used in practice? You got it! The correct answer is HLA typing. I still don't understand why we don't use this powerful tool more effectively.—T. Strom, M.D.

A Report of 504 Six Antigen-Matched Transplants

Takemoto S, Carnahan E, Terasaki PI (UCLA Tissue Typing Laboratory, Los Angeles)

Transplant Proc 23:1318–1320, 1991 1–2

Background.—Since 1987, more than 500 transplants have been performed in recipients matched for 6 antigens (6Ag). Two-year survival rates were calculated using data from those cases.

Methods and Results.—The results in 6Ag, homozygous, and nonshipped kidneys from the University of California, Los Angeles Transplant Registry having more than zero mismatches transplanted in the same period were compared. The 6Ag results were significant from 3 months to 2 years for first cadavers. Second graft results were significantly better for up to 1 year. The matching effect disappeared for subsequent transplants. The poor results in 6Ag-matched recipients with multiple regrafts may have been a result of mismatches at other histocompatibility loci. Sixty-three percent of the first 6Ag grafts had a cold ischemia time (CIT) of less than 24 hours, whereas longer CITs did not adversely

Effect of High Plasma Renin Activity Percent in 6-Antigen Transplants

	No. of Cases	3 mos	6 mos	1 yr	2 yr
First Graft					
0%-10%	194	93.1	88.7	88.7	85.3
11%-50%	51	93.8	87.3	87.3	81.7
51%-80%	23	90.9	90.9	90.0	
>80%	46	88.9	88.9	83.3	83.3
>First Graft					
0%-10%	28	96.2	88.2	74.9	74.9
11%-50%	29	86.0	75.0	70.2	70.2
51%-80%	18	88.2	75.6	62.1	62.1
>80%	49	93.7	79.9	74.5	

(Courtesy of Takemoto S, Carnahan E, Terasaki PI: *Transplant Proc* 23:1318–1320, 1991.)

affect graft survival. No detrimental effect for high plasma renin activity was found for first or regraft 6Ag transplants (table). Forty percent of the regrafts had a plasma renin activity greater than 80%.

Conclusions.—The Six-Antigen Match Program, started in 1987, has been successful. One-year graft survival was 87%, compared with 79% for transplant Registry controls and 76% for contralateral controls. Hospital stays were shorter and serum creatinine levels were lower for 6Hg-matched recipients. Despite the fact that a higher than expected number of patients with 6Hg-matched transplants had diabetes, their 1-year graft survival rate was 89%.

▶ The reports from Teraski and Opelz' laboratories consistently demonstrate a salutary effect of HLA typing upon renal engraftment. This report joins a list of publications making this important point (see Table 1 in the original article). Perhaps the most profound impact of matching is noted in highly presensitized patients (table). This group fares miserably with HLA mismatched transplants but excellent engraftment can be achieved with HLA matched grafts. This study, which uses conventional serologic DR typing methods almost certainly underestimates the benefits of HLA typing because DNA-based methodologies will provide additional benefits because of their heightened accuracy.—T. Strom, M.D.

HLA Matching Enhances Long-Term Renal Graft Survival But Does Not Relate to Acute Rejection

Baltzan MA, Baltzan RB, Baltzan BL, Cunningham TC, Pylypchuk GB, Dyck RF, West ML (University of Saskatchewan, Saskatoon, Canada)

Medicine 69:227–231, 1990 1–3

Background.—The HLA system's effect on graft survival would be manifested in the rejection process. Forty living donor kidney grafts of patients with more than 1 but less than 2 haplotype matches were examined.

Patients.—The patients, average age 32 years, were treated during a 25-year period. The most common cause of renal failure was chronic glomerulonephritis. Thirty-one patients had 2 haplotype matches, and 9 had more than 1 but less than 2. There were 33 primary oper-ations. Prophylactic corticosteroids were used in all patients. Azathioprine was used in 34 patients and cyclosporine was used in 6.

Findings.—Among patients who were not treated with cyclosporine and who had 5 or fewer units of blood preoperatively, 65% had acute rejection. However, in those who had more than 5 units, only 18% had acute rejection. All such patients had successful reversal with high-dose steroids. There were 2 patients with chronic rejection, but no patient undergoing a second graft had irreversible rejection. One patient had chronic glomerulonephritis, perhaps because of recurrent disease. Technical and immunosuppressive complications resulted in the loss of 1 graft each, whereas 3 more patients died incidentally. As a whole, the group had a 1-year actuarial graft survival rate of 95% and a 10-year survival rate of 84%. Survivors were leading normal lives with no significant restrictions and minimal medications.

Conclusions.—In kidney transplantation, chronic rejection appears to be dependent on HLA factors and is largely preventable by close HLA matching. Acute cellular rejection appears to be independent of HLA. There may be a relationship between hyperacute and chronic rejection that represents parts of a spectrum of humoral immunity.

▶ OK, I picked this article because I believe the conclusions are correct (even if the sample size is too small to draw any firm conclusions). The large registries headed by Opelz and Terasaki show that the salubrious influence of HLA matching on successful engraftment grow with time. Whereas differences are modest at 1–2 years posttransplantation between well and poorly matched transplants, the typing effect is quite powerful at 5–10 years postransplant. Shouldn't we aim for more transplant "keepers?" So what if surgeons hate the notion of allocating kidneys on the basis of histocompatibility.—T. Strom, M.D.

The Effect of Individual HLA-A and -B Mismatches on the Generation of Cytotoxic T Lymphocyte Precursors

Zhang L, van Bree S, van Rood JJ, Claas FHJ (University Hospital, Leiden, The Netherlands)

Transplantation 50:1008–1010, 1990 1–4

Background.—Both the HLA system and cytotoxic T cells are known to play important roles in graft rejection, but there has been little study of the interrelationship between these factors. A limiting dilution analysis was used to study the correlation between HLA mismatching and cytotoxic T lymphocyte (CTL) precursor frequency.

Methods.—The subjects were 21 highly sensitized patients waiting for renal transplantation. The limiting dilution culture technique was used to ascertain CTL precursor frequencies against the patients' individual mismatched HLA-A and HLA-B alloantigens. A total of 33 HLA-A alloantigens and 55 HLA-B antigens was tested.

Results.—Cytotoxic T lymphocyte precursor frequencies against HLA-A antigens were significantly lower on the average than those against HLA-B antigens (Fig 1–2). High CTL precursor frequencies were induced by 44% of HLA-B antigens compared with only 15% of the HLA-A antigens. Frequencies were unaffected by the number of DR mismatches or the age and sex of the patients.

Conclusions.—Cytotoxic T lymphocyte precursor frequencies are higher

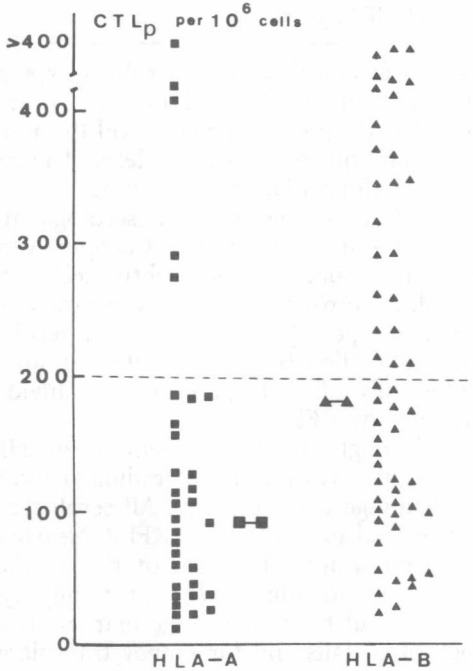

Fig 1–2.—Cytotoxic T lymphocyte precursor (CTLp) frequencies against individually mismatched HLA-A *(filled square)* and HLA-B *(filled triangle)* antigens in 21 patients. *Filled squares connected by a line* and *filled triangles connected by a line* represent the medians of CTLp frequencies against 33 HLA-A antigens and 55 HLA-B antigens, respectively. Mismatched HLA-B antigens showed significantly higher CTLp frequencies compared with those generated by mismatches of HLA-A locus antigens. ($P < .002$). (Courtesy of Zhang L, van Bree S, van Rood JJ, et al: *Transplantation* 50:1008–1010, 1990.)