The Paired Donation Network

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Paired Donation: Definition

- In a paired donation, two living kidney donor/recipient pairs (both of whom cannot undergo transplantation because of ABO or crossmatch incompatibility) are paired so that the donated kidneys are transplanted into the matched recipients (not the original intended loved ones) thereby circumventing immunologic barriers and allowing both recipients to receive a living donor kidney transplant.
Paired Donation for ABO Incompatibility

<table>
<thead>
<tr>
<th>Donor ABO Blood Type</th>
<th>Pair 1</th>
<th>Recipient ABO Blood Type</th>
<th>Pair 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>B</td>
<td>A</td>
</tr>
</tbody>
</table>
Incompatible Donor/Recipient Pair

Donor donates $\rightarrow$ DD wait list

Recipient $\rightarrow$ Increased wait list priority
Wait List Paired Donation: Definition

- In a wait list paired donation, a living kidney donor (who cannot donate to his or her loved one because of ABO or crossmatch incompatibility) donates a kidney that is distributed to the deceased donor wait list, and in return, his or her loved one receives increased priority on the deceased donor wait list. In this scenario, a deceased donor kidney is received in return for the donated live donor kidney.
Primary ethical and medical problem is that a living donor kidney is donated and a deceased donor kidney (i.e., a kidney of comparatively lesser medical quality) is received in return.
Paired Donation: Historical Aspects

Transplant Proc 18: Supp 2: 5-9, 1986

- Rapaport - first published record suggesting living kidney donor exchanges
  - Two living donor/recipient pairs
  - Separate transplant centers
  - Simultaneous procedures
  - Exchange of kidneys by courier
Paired Donation: Historical Aspects

- Before paired donation could become a clinical reality, unrelated living donor transplantation had to become an accepted procedure in the transplant community.

- By the mid-1990’s, a significant number of unrelated living donor transplants were being performed in the transplant community.
First Full Length Publication on Paired Donation

Sounding Board

ETHICS OF A PAIRED-KIDNEY-EXCHANGE PROGRAM

ALTHOUGH transplantation is the best treatment for many people with end-stage renal disease, the gap between the number of organ donors and the number of potential recipients continues to widen. Patients are often treated with dialysis for years while awaiting transplants, and many die. At the University of Chicago, between 10 and 20 percent of patients with available living donors cannot receive transplants from them because of ABO incompatibility. We propose to increase the supply of organs by using kidneys from living donors who are ABO incompatible with the intended recipients but are ABO compatible with other recipients. Through an exchange arrangement between two donor-recipient pairs, Donor A provides a kidney to ABO compatible recipients and Donor B provides a kidney to ABO incompatible recipients.

A PROPOSAL FOR A PILOT STUDY

To increase the number of successful kidney transplantsations, we propose a pilot study of the clinical and ethical aspects of paired kidney exchanges, with all the procedures to be performed at a single hospital. The study will work as follows. If all recipients’ potential living donors are determined to be unsuitable, a potential donor rejected solely on the basis of ABO incompatibility will be offered the opportunity to provide a kidney to a recipient with an ABO compatible living donor. Donor A provides a kidney to an ABO compatible recipient, and Donor B provides a kidney to an ABO compatible recipient.

Provided ethical and scientific foundations for clinical trials of paired donation
Paired Donation Programs: Ethical Issues

- Coercion
- Right to withdraw consent
- Privacy and confidentiality
- Commercialization and exploitation
- Informed consent and the right to medical knowledge
- Altruism balance
Ethical Issues

- Coercion
  - In the absence of exchange programs, unwilling or ambivalent donors may be relieved that they are excluded by ABO or HLA incompatibility.
  
  - Exchange programs remove these medical exclusions, thereby creating the potential for increased coercion for the hesitant or unwilling donor.
Ethical Issues

- **Right to Withdraw Consent**
  - Potential donors must be reminded throughout the evaluation process that they may withdraw consent, and that withdrawal will be on the basis of medical, not psychological grounds.
  - Potential donors must be *specifically* asked throughout the process if they have doubts or reservations about the process. These conversations must be held in a nontthreatening environment.
Ethical Issues

- Privacy and Confidentiality
- Informed Consent and the Right to Medical Knowledge

- All patients have a right to privacy, and a right to confidentiality of their medical condition and medical records.

- Patients also have the right of informed consent and a right to medical knowledge.
Ethical Issues

- Medicolegal Protection
  - Untoward outcomes, or unexpected transmission of tumor or disease via the donor kidney, even when inadvertent and unpreventable, creates potential medical-legal liabilities.

- These issues must be covered in the informed consent process.
Ethical Issues

- Commercialization and Exploitation
  - In most western civilizations, it is illegal to purchase or sell organs or to participate in such commercial activities.
  - Despite these laws, and adoption of these principles by transplant programs, the possibility still exists that covert arrangements for such compensation may still occur.
Paired Donation for ABO Incompatibility

Problem: only represents 12% of combinations
# Predicted ABO Frequencies for Live Donor Recipients with ABO Incompatible Donors

<table>
<thead>
<tr>
<th>Race</th>
<th>O (%)</th>
<th>A</th>
<th>B</th>
<th>AB</th>
<th>ABOi O Recips (%)</th>
<th>ABOi A, B recipients (%)</th>
<th>ABO Compatible (% of pairs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cau</td>
<td>45</td>
<td>40</td>
<td>11</td>
<td>4</td>
<td>25%</td>
<td>12%</td>
<td>63%</td>
</tr>
<tr>
<td>AA</td>
<td>49</td>
<td>27</td>
<td>20</td>
<td>4</td>
<td>25%</td>
<td>14%</td>
<td>61%</td>
</tr>
</tbody>
</table>
The O blood group donor shortage problem exists for paired donation also.
Solving the O blood group shortage:

1) Include crossmatch positive D/R pairs
2) Educate donors/recipients about the need for O blood group donors to participate
3) Allow listing of each recipient with multiple donors
Living Unrelated Organ Donation: An Exchange Proposal

Francis L. Delmonico, Jeffrey S. Stoff, Edgar Milford, William E. Harmon and E. Steve Woodle

First US Consortium Based Paired Donation Program: 6 New England States
Hierarchical Paired Donation Programs: “Bailout” Phenomenon

Initial Consideration: Paired Donation

Not Possible

Secondary Consideration: Wait List Paired Donation

The overall ratio of paired donations: wait list paired donations that are performed is a function of how frequently paired donation matches are achieved.
Wait List Paired Donation: PDC Policy

- Wait list paired donation is a medically and ethically inferior option to paired donation.

- Waiting times for almost all groups appear to be shorter with paired donation than on the deceased donor wait list.

- Wait list paired donation should only be allowed when there is convincing evidence that it will provide a transplant more quickly than will paired donation.

- The negative effects of wait list paired donation on paired donation waiting times must be carefully weighed.
Korean Paired Donation Program

- Initiated by Dr. Kil Park in Seoul in 1991
- Experience first reported in 1999
- Not performed under rigid prospective protocol
- First used to circumvent crossmatch positive transplants
- First used living related donors
Korean Paired Donation Program

Transplantation 67:336, 1991

- 110 transplants performed (55 exchanges)
- Graft survival
  - 95% 1 year
  - 82% 5 year
- No difference in graft survival between HLA haploidentical controls
Paired Donation Network
Web-based Computer Matching
PDN Computer Matching

- Match run frequency can be variable
- Initial version: manual rank order determination
- Matching criteria: waiting time, distance, age, HLA matching, PRA, serologies
- Crossmatching performed after match run completed
- 2 pair and 3 pair matches currently considered

ASTS
American Society of Transplant Surgeons
8 of 43 (24%) registered recipients transplanted in first year

10 of 68 (15%) registered recipients transplanted to date

4 additional recipients have completed evaluations and have scheduled paired donation procedures
Optimization Approaches

- Scaled Optimization
  - Two pair donation
  - Three or four pair donation

- Rank Order Optimization
  - Manual v Computer-based v First Accept
  - Pre-Crossmatching v Post-Crossmatching
“First Accept” Approach

- 35 D/R pairs in match run
- Matches
  - Match 1) Pair 3: Pair 4 20
  - Match 2) Pair 5: Pair 6 18
  - Match 3) Pair 3: Pair 20 15
  - Match 4) Pair 4: Pair 21 13
  - Match 5) Pair 5: Pair 25 12
  - Match 6) Pair 6: Pair 26 9

- Transplanting first 2 matches excludes the next four matches and transplants four patients and 38 points

ASTS
American Society of Transplant Surgeons
Rank Order Optimization

- 35 D/R pairs in match run
- Matches
  - Match 1) Pair 3: Pair 20 15
  - Match 2) Pair 4: Pair 21 13
  - Match 3) Pair 5: Pair 25 12
  - Match 4) Pair 6: Pair 26 9
  - Match 5) Pair 3: Pair 4 20
  - Match 6) Pair 5: Pair 6 18

- Rank order optimization provides the greatest number of transplants (8 transplants) and the greatest number of points (49)
Kidney Paired Donation and Optimizing the Use of Live Donor Organs

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Sommer E. Gentry, MS
Daniel S. Warren, PhD
Brigitte Reeb, MFA
Robert A. Montgomery, MD, DPhil

Context  Blood type and crossmatch incompatibility will exclude at least one third of patients in need from receiving a live donor kidney transplant. Kidney paired donation (KPD) offers incompatible donor/recipient pairs the opportunity to match for compatible transplants. Despite its increasing popularity, very few transplants have resulted from KPD.

Objective  To determine the potential impact of improved matching schemes on the number and quality of transplants achievable with KPD.

Design, Setting, and Population  We developed a model that simulates pools of incompatible donor/recipient pairs. We designed a mathematically verifiable optimized matching algorithm and compared it with the scheme currently used in some centers and regions. Simulated patients from the general community with characteristics drawn from distributions describing end-stage renal disease patients eligible for

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First Accept v Optimized

Figure 2. Potential Matches Using Mathematical Optimization Compared With the Currently Used Practice of First-Accept Matching

- First-Accept Matching Scheme
- Optimized Matching Algorithm
Editorial

The Potential of Paired Donation Programs: Modeling and Reality

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Densely populated regions are inherently ideal for paired donation consortia, as geographic distances are limited and the number of potential donor/recipient pairs in a given consortium should be relatively high. More heavily populated regions of the United States (e.g. the east and west coasts) are advantageous. In contrast, the sparsely populated areas of the United States (e.g. Wyoming, Montana, Idaho, western Kansas and Nebraska) will suffer from the substantial geographic barriers to paired donation.
Several assumptions in the modeling approaches of the present study warrant consideration. First and foremost, the authors modeled a *national*-paired donation program, but in reality, the geographic barriers (i.e., large travel distances) in a nationalized program will present a substantial barrier. In the Paired Donation Consortium (PDC) (for-

The model also assumed that a relatively large number of donor/recipient candidates would be available for matching. To date, no paired donation program has yet to have substantially more than 20 donor/recipient pairs available for matching at any point of time. Although modeling of

The model used in this study assumed 100% referral rates of ABO- and cross-match-incompatible pairs to the national-paired donation program. Experience from the
Midwest PDC
Member Programs

Ohio
- Case Western Reserve
- Cleveland Clinic
- University Hospital – Cincinnati
- The Christ Hospital
- Medical College of Ohio
- Ohio State University
- Miami Valley Hospital
- Summa Health System, Akron
- Cincinnati Children’s Medical Center

Indiana
- Methodist Hospital, Indianapolis

Kentucky
- University of Kentucky

Illinois
- University of Illinois, Chicago

Maryland
- University of Maryland

Michigan
- University of Michigan
- Henry Ford Hospital, Detroit
- Harper University Hospital, Detroit
- St. John’s Hospital, Detroit
- Children’s Hospital of Michigan
- Hurley Medical Center, Flint
- St Mary’s Hospital, Grand Rapids
- William Beaumont Hospital, Royal Oak

West Virginia
- University of West Virginia
- Charleston Medical Center

Pennsylvania
- University of Pittsburgh
- Pittsburgh VA Medical Center
- Pittsburgh Children’s Hospital
- Allegheny Medical Center

Wisconsin
- St. Luke’s Medical Center

New York
- SUNY Buffalo
PDN: Regional Consortia Membership as of 12/1/05

- **Formed**
  - PDC (10 states, 30 programs)
  - New Jersey PDC (1 state, 6 programs)
  - Southeastern PDC (4 states, 18 programs)
  - Southwestern PDC (4 states, 19 programs)
  - Southern California PDC (1 state, 2 programs)

- **In process of formation**
  - Upper Midwest (three states)
  - Great Plains (four states)
  - Northern California (6 programs)
  - Eastern Seaboard (12 programs, six states)
  - Rocky Mountain (four states)
PDC Nationalization

- States with tx Programs that have agreed to join PDC
- States with test website(s)
- No kidney transplant programs
- Transplant Centers with test websites