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

Donor ABO Blood Type

Recipient ABO Blood Type

Pair 1
A
B

Pair 2
B
A

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American Society of Transplant Surgeons
Wait List Paired Donation

Incompatible Donor/Recipient Pair

Donor donates → DD wait list

Recipient → Increased wait list priority
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

**ASTS**
American Society of Transplant Surgeons
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

- Provided ethical and scientific foundations for clinical trials of paired donation

The New England Journal of Medicine 336,1752-1755 (June 12), 1997

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 recipient B, while Donor B provides a kidney to ABO incompatible recipient A (ABO matches make some donations unacceptable under current standards of care). Although several trials of renal transplantation between ABO incompatible donors and recipients have had good results, these trials were small, and such transplants are not routinely performed in the United States.

In 1986, Rapaport set forth the idea of paired kidney exchanges. He envisioned a process in which the two donor-recipient pairs would be treated at their separate transplantation centers, and the procedures would be performed simultaneously, with an immediate exchange of the two kidneys by special courier.

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 a recipient's 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 the recipient in exchange for another kidney for a donor with ABO compatible but clinically suitable recipient.

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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.

American Society of Transplant Surgeons
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 nonthreatening 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 recips (%)</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

ASTS
American Society of Transplant Surgeons
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

American Society of Transplant Surgeons
Korean Paired Donation Program

110 transplants performed (55 exchanges)

Graft survival
- 95% 1 year
- 82% 5 year

No difference in graft survival between HLA haploidentical controls

*Transplantation 67:336, 1991*
Paired Donation Network
Web-based Computer Matching
PDN Patient Education Brochure

Hospitals Participating in the Living Donor Kidney Exchange Program:
- Children's Hospital of Ohio, Columbus, Ohio
- The Ohio State University Medical Center, Columbus, Ohio
- Cleveland Clinic Foundation, Cleveland, Ohio
- Medical College of Ohio, Toledo, Ohio
- Miami Valley Hospital, Dayton, Ohio
- The Ohio State University Medical Center, Columbus, Ohio
- Solara Health System, Arizona, Arizona
- University of Cincinnati Hospitals, Cincinnati, Ohio
- University Hospitals of Cleveland, Cleveland, Ohio

If you have questions, talk to your transplant center or contact:
The Ohio State University Transplant Center
7100 North High Street, Suite 300
Columbus, Ohio 43211
Phone: 614-294-5600
www.osu.org

If you and your living donor don’t match, the Living Donor Kidney Exchange Program might be right for you.

Development of this brochure was supported and funded by Second Chance.

"You can't live it with us, but you can pass it on"
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
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
Rank Order Optimization

- 35 D/R pairs in match run

Matches

<table>
<thead>
<tr>
<th>Match</th>
<th>Pair 1: Pair 2</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Match 1</td>
<td>Pair 3: Pair 20</td>
<td>15</td>
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<tr>
<td>Match 2</td>
<td>Pair 4: Pair 21</td>
<td>13</td>
</tr>
<tr>
<td>Match 3</td>
<td>Pair 5: Pair 25</td>
<td>12</td>
</tr>
<tr>
<td>Match 4</td>
<td>Pair 6: Pair 26</td>
<td>9</td>
</tr>
<tr>
<td>Match 5</td>
<td>Pair 3: Pair 4</td>
<td>20</td>
</tr>
<tr>
<td>Match 6</td>
<td>Pair 5: Pair 6</td>
<td>18</td>
</tr>
</tbody>
</table>

- 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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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 transplantation.
First Accept v Optimized
Hopkins Model: Shortcomings

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)