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# Donor Kidney Exchanges

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**Kidney transplantation from live donors achieves an excellent outcome regardless of human leukocyte antigen (HLA) mismatch. This development has expanded the opportunity of kidney transplantation from unrelated live donors. Nevertheless, the hazard of hyperacute rejection has usually precluded the transplantation of a kidney from a live donor to a potential recipient who is incompatible by ABO blood type or HLA antibody crossmatch reactivity. Region 1 of the United Network for Organ Sharing (UNOS) has devised an alternative system of kidney transplantation that would enable either a simultaneous exchange between live donors (a paired exchange), or a live donor/deceased donor exchange to incompatible recipients who are waiting on the list (a live donor/list exchange). This Regional system of exchange has derived the benefit of live donation, avoided the risk of ABO or crossmatch incompatibility, and yielded an additional donor source for patients awaiting a deceased donor kidney. Despite the initial disadvantage to the list of patients awaiting an O blood type kidney, as every paired exchange transplant removes a patient from the waiting list, it also avoids the incompatible recipient from eventually having to go on the list. Thus, this approach also increases access to deceased donor kidneys for the remaining candidates on the list.**

**Key words:** Donor, exchanges, kidney

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## Introduction

Kidney transplantation from live donors has become the predominant experience for most transplant centers in

the United States (1). The excellent outcome achieved by live kidney donation has made this practice so widely accepted that pre-emptive transplantation of a kidney to a patient prior to initiating dialysis is now a routine. Moreover, the opportunity for transplantation from live donors is no longer restricted by the degree of human leukocyte antigen (HLA) match (2). Successful kidney transplantation can be achieved even if the donor is completely HLA mismatched to the recipient. The outcome of kidney transplant from a spouse or friend HLA mismatched with the recipient is not significantly different than the outcome obtained from a haploidentical parent or sibling (3).

Despite these advances, the hazard of hyperacute rejection has precluded the transplantation of a kidney from an ABO blood type donor incompatible with a potential recipient. The same limitation has applied to the transplantation of a kidney to a recipient who has preformed HLA antibody reactive to the donor. Nevertheless, with the expansion of unrelated live donor kidney transplantation, protocols that remove isoagglutinin and HLA antibodies by plasma exchange and other approaches have recently been developed to overcome these biologic barriers (4,5). Currently, however, these plasma exchange protocols that include the administration of intravenous immune globulin (IVIG) are technically demanding and expensive – in some instances not yet approved by third party payers. Furthermore, an unpredictable rate of accelerated rejection and allograft loss occurs with the plasma exchange/IVIG approach. An alternative program of kidney exchange between live and deceased donors that derives the benefit of live donation and avoids the risk of incompatibility has been undertaken in New England.

## Methods

Region 1 of the United Network for Organ Sharing (UNOS) has devised a system of kidney transplantation that would enable either a simultaneous exchange between live donors at the same or two different centers (a paired exchange), or a live donor/deceased donor exchange to incompatible recipients who are waiting on the list (a live donor/list exchange). UNOS Region 1 consists of 14 New England transplant centers and two Organ Procurement Organizations (OPO): New England Organ Bank (NEOB) and LifeChoice Donor Services (LDS). All of the Region 1 transplant centers and both OPOs endorsed the exchange proposal prior to its submission to UNOS. The proposal was also reviewed by the medical board of the End Stage Renal Disease (ESRD) Network of New England. The Region 1 program was also discussed at New England 'town' meetings conducted by the ESRD Network, so that dialysis patients waiting on the list could have

an important input to the plan. The plan was approved by the UNOS Board of Trustees in the fall, 2000, and initiated in New England in February, 2001.

### Candidacy for the list exchange

As a result of these deliberations, stipulations regarding recipient candidacy for the list exchange process were developed (Table 1). These included the following provisions: the list exchange recipient should be undergoing a first kidney transplant (simultaneous heart, liver, or pancreas transplant excluded), on dialysis, unsensitized (reactivity to a panel of HLA not greater than 10%), and be on the list of New England candidates awaiting a kidney transplant (with an established care relationship with a UNOS Region 1 center). No patients residing outside New England have been accepted for the list exchange program. Each of the donor recipient incompatible pairs was reviewed by a Renal Transplant Oversight Committee (RTOC) of the Region.

### Candidacy for the live donor exchange

None of the provisions regarding the list exchange recipient was applicable to the live donor exchange candidate. Live donor transplantation, pre-emptive of the initiation of dialysis has become the preferred approach, and the sensitization status of the recipient was only relevant to identify a crossmatch-compatible donor. Thus, the provisions of the live donor exchange program were fundamentally different from those of the list exchange program. Since there was no participation of those on the deceased donor waiting list, there was no prohibition to the use of preemptive transplantation, especially with its multiple advantages. The sensitization status of either of the intended exchange recipients was relevant only in terms of identifying a crossmatch-negative living donor.

Since the live donor exchange patient would be undergoing a kidney transplant from a live donor, recipient suitability was determined by the transplant centers involved.

### Region 1 policy

If an incompatible donor recipient pair is identified by ABO blood type or T-cell crossmatch incompatibility, the transplant center contacts the Medical Director of either LDS or the NEOB after it is determined that the donor is an acceptable candidate. Prior to this referral, the center establishes that the donor wishes to provide a kidney to an unknown recipient by an exchange. The charges for donor evaluation are covered by the cost center of the transplant unit of the incompatible recipient. The submission of a suitable donor to the Region also assumes that the potential donor has undergone psychiatric/psychological evaluation.

If there is an opportunity for living donor exchange between two incompatible pairs from two transplant centers, the Medical Director of the OPO contacts each transplant center to inquire whether such an exchange would be feasible. The final interaction is determined by the transplant centers involved in a donor exchange. If more than one incompatible pair is temporally identified for a live donor exchange, priority is given by the precise date of notice to the Medical Director.

**Table 1:** Recipient requirements for live donor list exchange program

- Candidate for a first deceased donor kidney
- On dialysis
- Unsensitized (<10%)
- On the New England Region 1 waiting list
- An established care relationship with a UNOS Region 1 center

If there is no opportunity for living donor paired exchange, then an opportunity arises for a live donor list exchange. By that procedure, the incompatible living donor provides a kidney to a patient on the transplant center's deceased donor waiting list, in exchange for a kidney allocated from the Region's deceased donor pool to the incompatible recipient of the live donor. The allocation of this Region deceased donor kidney is awarded by a priority in relation to the standard waitlist; however, this priority does not supercede the compulsory allocation rules of UNOS (Table 2). Thus, emergency kidney allocation alone or kidney allocation with liver or heart transplants, 0 mm sharing precede allocation to the exchange recipient. Each proposed exchange is reviewed by an executive group of the RTOC of Region 1, before a list recipient is identified (Table 3).

The duration that the RTOC will wait for a live donor exchange pair to come forward from another center has not been regulated, although the general practice has been to ask such pairs to wait a minimum of one month, in order to avoid flooding the system with 'unnecessary' list exchanges. If no such pair is identified, the center can proceed with the live donor list exchange process. The opportunity for a live donor exchange is clearly influenced by the donor recipient characteristics, for example the O blood type donor with a crossmatch-incompatible recipient or an A blood type/B blood type incompatibility has a better chance of finding another donor recipient pair.

### Selection of the list recipient

The transplant center notifies the OPO tissue-typing laboratory to perform a UNOS match run of the prospective donor to the transplant center list in which the donor was evaluated. The transplant of the living donor kidney to the list recipient is performed at the transplant center that evaluated the living donor. The recipient (unknown to the living donor) is identified from the match run that uses the Region 1 standard allocation system to identify

**Table 2:** The Region 1 allocation plan

1. Region 1 kidney + life saving extrarenal
2. Region 1 emergency kidney
3. Region 1 0 mm kidney/pancreas
4. UNOS 0 mm kidney/pancreas
5. Region 1 kidney/pancreas (offer to the top 12 of the unsensitized UNOS match run)
6. UNOS 0 mm mandatory share
7. Region 1 list to incompatible recipient\*
8. Region 1 two-for-one protocol and/or marginal donor
9. Payback kidneys to outside Region 1
10. Region 1 kidney allocation by policy approved October, 1997.

\*The allocation priority occurs after compulsory UNOS allocation for matching and medical urgency.

**Table 3:** Procedural steps of the Region 1 plan

1. Live donor exchange is preferable for identified incompatible donor/recipient pairs.
2. If no live donor exchange is feasible, a live donor list exchange is considered by Oversight Board.
3. The recipient (unknown to the living donor) is identified from the match run using the center list and ABO blood type (identical).
4. Following transplant of the kidney from the living donor to the highest ranking appropriate individual identified by the transplant center's list, the incompatible recipient for whom the donor kidney was originally intended receives the right of first refusal for the next ABO identical (crossmatch negative) deceased donor kidney available within the Region.

recipients for deceased donor kidneys. These include ABO blood type (identical), and time waiting as the principle ingredients. However, HLA matching (OMM only), pediatric, and sensitization points are also awarded. The recipient selection may be affected by the sensitization status of prospective candidates on the list; some of the longest waiting excluded because of crossmatch reactivity with the prospective donor. However, distinctions analogous to those employed in selecting candidates for nondirected live donors (6) or extended criteria donor deceased donors (7) have been made between crossmatch-compatible recipients. Thus, not all of the recipients were No. 1 on the match run; in some instances (see below) the patient at the top of the match run was either sensitized to donor antigens or had developed a medical contraindication since the time of listing that precluded transplantation. The executive group of the RTOC reviewed and authorized the selection of each list recipient.

#### **The list exchange transplant procedure**

Following the transplantation of the kidney from the living donor to the highest ranking appropriate individual identified by the center list, the incompatible recipient for whom the donor kidney was originally intended receives the right of first refusal for the next ABO identical (T-cell crossmatch negative) deceased donor kidney available within the Region. This offer is made to the transplant physician on call for the center caring for the incompatible recipient of the live donor. This patient continually receives that right of refusal until transplantation. The UNOS match run reveals the name of the candidate at the top of the list stratified by compatible ABO blood type and time waiting. It is conceivable that following the live donor transplantation to the list, the recipient could develop a contraindication for transplantation or die while waiting for a deceased donor kidney offer. That untoward development has not occurred in our experience; but that possibility should be considered in the candidacy of the recipient for the exchange. Such a possibility also influences the consideration of the patient's candidacy for the list exchange. If there are medical co-morbidities that could affect the patient's survival in waiting a relatively brief period of weeks to months for the transplant, then the overall medical condition of the patient becomes an important factor in deciding whether to accept the patient for a list exchange. Once a donor/recipient pair assumes the No. 1 slot in the queue, they both need to be reassessed at the center's discretion to determine that no intervening events rendered either unsuitable to proceed.

## **Results**

Four live donor paired exchanges and 17 live donor list exchange kidney transplants have been performed as of December 31, 2003. Nine of the 14 Region 1 transplant centers have participated in the program.

#### **Live donor paired exchange kidney transplants**

Simultaneous paired exchanges occurred via transplant procedures performed at the following centers: Rhode Island Hospital, New England Medical Center, Children's Hospital Boston, Dartmouth Hitchcock Medical Center and the Massachusetts General Hospital. Two of the exchanges were done at single center with the incompatible pairs identified within these centers (RIH and MGH). Otherwise the donors traveled to the recipient center with exchange transplants performed simultaneously. One of these transplants failed within weeks of the procedure, and one recipient died accidentally with a functioning allograft. The other six patients were alive with excellent renal function. There was no live donor complication.

#### **List recipient transplants**

All of the list recipients of the living donor were blood type identical (Table 3); eight of the 17 candidates selected from the list were the longest waiting crossmatch-compatible recipients on the transplant center list (as displayed on the match run). The duration of time that the 17 list recipients had been waitlisted for a kidney ranged from 121 days to more than 2000 days (Table 4).

However, there were seven list transplants in which the highest ranking candidates had active medical conditions that contraindicated transplantation and necessitated their being bypassed. There are patients whose medical

**Table 4:** Region 1 live kidney donor to the center list transplants

Live donor, relationship	Live donor, age	Center list recipient, age	List recipient, ABO blood type	List recipient, PRA	List recipient wait, days
Mother	43	37	O	0%	725
Wife	51	30	A	0%	812
Wife	50	54	A	2%	410
Neighbor	69	63	A	0%	501
Wife	62	53	A	0%	396
Brother	39	38	A	5%	716
Mother	56	31	B	0%	2126
Friend	51	37	AB	0%	458
Fiancé	46	51	A	0%	901
Husband	34	58	B	0%	1086
Friend	33	39	B	0%	942
Husband	66	47	AB	14%	121
Friend	47	54	A	2%	577
Sister	55	54	B	0%	1547
Wife	44	37	A	0%	199
Sister	36	55	A	0%	609
Wife	50	50	A	0%	708

contraindications to transplantation become apparent when they are offered a kidney (having risen to the top of the list). There are also instances when there may be candidates for a deceased donor kidney who may not be acceptable at some centers for live donor transplantation. The center presents the reasons of passing over any higher ranking recipients to the RTOC.

### Deceased donor transplants

All of the deceased donor recipients had established care relationships with Region transplant centers, were unsensitized, on dialysis, and underwent their first deceased donor kidney transplant (Table 1). All of the deceased donor recipients were O blood type except for one recipient (Table 5). One of the patients (Table 5) had undergone a lung transplant previously. Two of the list recipients underwent a repeat transplant (Table 5) because the initial transplant failed due to a renal vein thrombosis within days following transplantation. One of these patients, although initially unsensitized, developed a panel reactive antibody level of 29%. This sensitization level did not, however, prevent the patient from eventually undergoing a second successful transplant.

The characteristics of the deceased donors who provided region pool kidneys to the incompatible recipients are provided in Table 5. The donor age ranged from 12 to 56 years. The cause of death was usually trauma; however, there were six donors whose cause of death was a cerebrovascular accident. The interval between the live donor and the deceased donor transplants ranged from 5 days to more than 3 months (Table 5). There was a period of 4 months in

2003, in which there were three candidates waiting for a deceased donor kidney following the live donor transplant to the list. During this time, the RTOC decided to defer further kidney exchanges between live and deceased donors until the list of candidates was shortened. The Region has subsequently agreed that not more than two candidates would be listed simultaneously to avoid an unpredictable period of waiting on the list.

### Discussion

The approach of kidney donor exchanges has been developed to increase the number of live donor transplants. Such kidney exchanges are now accomplished in various parts of the world, in Baltimore, Washington D.C, the Middle East and Asia (8,9). The ethical propriety of this practice is supported by the success of unrelated live donor kidney transplantation (2). In New England, the UNOS Region 1 program of paired exchange has been designed to prioritize simultaneous live donor transplantation before a list exchange, so that donor equipoise is achieved and the deceased organ donor pool is preferentially retained for list candidates (10). The incompatible blood type A → B and B → A phenomena should be paired-up as often as possible, since live donor transplantation (even though HLA mismatched) provides the best result for both recipients. In the development of the New England program, Region 1 recognized that the opportunity to achieve such a match would be increased with a larger geographical size of the sharing area. Further, we anticipated that a search time would be necessary to enhance the identification live donor pairs before moving to the list exchange process. However, when

**Table 5:** Deceased donor transplants to the (live donor incompatible) recipients following live donation to the list

Deceased donor, age	Deceased donor, cause of death	Recipient, ABO	Recipient, age	Recipient, PRA	Waiting on list, days	Kidney Tx No.	ESRD	Transplant, time between live donor and deceased donor
32	Head trauma/MVA	O	12	0%	137	1	Solitary small kidney	17 days
17	Head injury/MVA	O	40	2%	290	1	Diabetic	56 days
27	CHA/MVA	O	53	0%	69	1	HTN	10 days
47	SIGSWTH	O	30	0%	932	1	Reflux nephropathy	15 days
31	ICH/CVA	O	65	3%	382	1	PKD	22 days
22	SIGSWTH	O	40	2%	406	1	Diabetic	29 days
56	ICH/CVA	O	37	2%	131	1	Diabetic	5 days
16	MVA	O	36	0%	151	1*	Calcineur inhib nftx	5 days
41	ICH/CVA	O	41	0%	85	1	Diabetic	27 days
21	GSWTH	O	36	0%	125	1	Lupus nephritis	7 days
16	ICH/MVA	A	35	0%	230	1	Reflux nephropathy	6 days
13	ICH/MVA	A	35	0%	198	2**	Failed transplant	198 more days
21	GSWTH	O	59	2%	277	1	HTN	12 days
23	Head trauma/MVA	O	47	0%	194	1	PCKD	15 days
12	AVM	O	47	29%	137	2**	Failed transplant	137 more days
48	CVA	O	46	6%	196	1	Diabetic	67 days
35	ICH	O	37	0%	303	1		94 days
48	CVA	O	43	0%	73	1	Diabetic	37 days
44	ICH/SAH	O	55	0%	940	1	PCKD	10 days

\*This patient was a recipient of a kidney transplant following lung transplantation.

\*\*These patients underwent a second kidney transplant following failure of the primary (see text). Calcineur inhib nftx, calcineurin inhibitor nephrotoxicity.

it becomes evident that a live donor exchange is not possible, the transplant center counsels the incompatible pair of the list exchange opportunity. Before the incompatible living donor given to the list (with the expectation that the deceased donor pool will furnish a kidney to the incompatible recipient), a thorough discussion must take place between the transplant center physician and the incompatible pair. There must be appropriate disclosure of the difference in outcome that can be achieved by live versus deceased donor transplantation.

However, the list exchange program offers an opportunity to undergo transplantation to the alternative of remaining on dialysis. The comparative rate of mortality that is associated with dialysis versus transplantation is substantial at every age group; and thus, the impetus to foster transplantation is evident even though equipoise is not achieved by the live donor/deceased donor exchange (11).

### **Ethical considerations of the candidacy for the list exchange**

The stipulations regarding recipient candidacy for the list exchange process were necessary to avoid an additional burden to those waiting on the ABO blood type O list for a deceased donor kidney (see below). The provisions (Table 1) included the following: that the list exchange recipient should be on dialysis and undergoing a first kidney transplant. The stipulations of dialysis dependency and candidacy for first transplant had two ethical considerations:

- 1 More than 98% of the Region 1 listed population is on dialysis as evidence of their ESRD condition; thus, there could be an understandable objection to someone getting a first transplant (if they had not reached dialysis yet) ahead of an O listed patient on dialysis. Region 1 has a long standing sensitivity to those on dialysis; our current kidney sharing plan precludes the accumulation of waiting time points until the candidate is on dialysis.
- 2 Patients could understandably feel disadvantaged if list exchange patients were capturing a second transplant from the deceased donor pool when most had not received an opportunity to undergo their first transplant.

The reason for the unsensitized stipulation was to make certain that a high PRA would not prevent the exchange process from being completed, nor for the patient to have an expectation to receive a kidney from the deceased donor pool that could not be readily accomplished.

Only patients listed in New England and primarily affiliated with a transplant program in Region 1 were eligible to participate. As the program gained media exposure, many patients from outside the Region inquired about participation. However, so as not to penalize waitlisted patients, partic-

ularly those with ABO blood type O, patients outside the Region were uniformly excluded.

### **The O list**

This exchange program has a clear utilitarian goal: to have more recipients undergo successful transplantation by expanding the pool of compatible live donors. However, as noted in the Table 4, only one of the live donors was an O blood type, the remainder were either A, B, or AB blood type. The biological reality is that an O blood type live donor is rarely available unless the recipient is crossmatch incompatible with the donor. Thus, deceased donor kidneys of the O blood type become the major source of the donor pool provided for the exchange recipient.

Affording the exchange recipient an allocation priority for an O blood type kidney has been criticized as a disadvantage for the O list of candidates awaiting a deceased donor kidney (12,13). We concur that there is a temporary disadvantage for the longest-waiting O candidates on the list at the time an exchange program is implemented. However, in our Region 1 experience, most candidates (one exception became inactivated because of a peritoneal dialysis infection) who were bypassed on the day that the allocation priority was awarded to the exchange recipient, waited only several weeks to months longer than they would have without the exchange process—a small incremental fraction of time compared to the 4–5 years total time that they wait in our Region. Moreover, it is important to note that this bypass effect on the entire list is transient. The deceased donor recipient in an exchange represents an O blood type patient not placed on the ‘bottom’ of the O list, and therefore will not ascend to the ‘top’ of the list, 4–5 years later. Their absence from the top of the list at this later time constitutes a mitigating ‘advantage’ for the next candidate with the same wait time magnitude—several weeks to months. In other words, the small initial disadvantage to the O list disappears completely once an exchange program in any given area has been in place for a period equaling the wait time threshold for unsensitized O patients in that area. In our view, this ‘investment’ is well worth the incremental increase in flexibility in discussion and planning for ESRD patients, and the resulting increase in live kidney donation.

The benefits of pre-emptive renal transplantation although recognized since the institution of the program, have become more obvious (11). Again with the approval of the ESRD Network of New England, the Oversight Board is now considering a revision of the policy to allow for pre-dialysis deceased renal transplantation after completion of the live donor transplant portion of the exchange.

### **Legal status as a gift**

Section 301 of the National Organ Transplant Act of 1984 (NOTA), 42 U.S.C. 274e states: ‘It shall be unlawful for any person to knowingly acquire, receive, or otherwise



transfer any human organ for valuable consideration for use in human transplantation...'. As the program was promulgated, the UNOS Region 1 program came under scrutiny as to whether the exchange of kidneys between live donors and from a live donor to a list recipient constitutes a 'transfer...for valuable consideration'; and thus, violates section 301 of NOTA. Valuable consideration under NOTA § 301 has traditionally been considered to be monetary transfer or a transfer of valuable property between donor, recipient and/or organ broker in a sale transaction. Thus, the Region formally approached UNOS for a legal review and the General Counsel to UNOS; Malcolm E. Ritsch, Jr., provided the following position statement: dated March 7, 2003<sup>1</sup>: *'The donation of an organ is properly considered to be a legal gift, rather than a contractual undertaking. By definition, there is no "consideration" at all in a gift transaction. Like all gifts, organ donations may be made for specific purposes'. There is no "valuable consideration" under NOTA § 301 in any of these living donation arrangements. In fact, there is no "consideration" present at all. The donor receives none, the recipient gives none and none is transferred to a broker'.* With this analysis from UNOS, the Region has continued its program.

### Unable to guarantee outcome

Renal vein thrombosis complicated two of the exchange cadaver renal transplants. Since no provision existed to address immediate failure was formally considered in the original program, it was elected to provide these individuals a second opportunity to successfully complete the deceased donor component of the exchange (Table 5). This approach was given with the UNOS precedent established by its Kidney Pancreas Committee to restore wait times to individuals who lose their kidney in the immediate period following transplantation. However, the RTOC subsequently agreed that any future exchange could only offer the opportunity for a single cadaver renal transplantation with this special allocation priority. Having accomplished that transplant procedure, the patient would then assume their previous UNOS wait time status, regardless of the outcome. Patients participating in the exchange program are now informed of this inability to guarantee outcome at the time of consent.

Finally, attention to the queue of patients awaiting completion of the live donor exchange required some internal regulation. Due to a limited number of suitable ABO blood type O donors, the RTOC has been obliged to limit those waiting, to two exchange patients. This Region rule avoids a prolonged interval for completion of the exchange—a period the recipient may be vulnerable to illness, sensitization or other medical mishaps that may prolong the wait

time or even eliminate the potential to proceed with kidney transplantation.

## Conclusion

The New England experience of kidney donor exchange represents an alternative plan to increase the number of organs from living donors, when ABO incompatibility or a positive crossmatch precludes transplantation between a live donor and their intended incompatible recipient. A paired exchange of kidneys from live donors is an uncommon but useful approach to providing a simultaneous transplant. A Regional system of exchange can also yield an additional donor source for patients awaiting a deceased donor kidney. As every paired exchange transplant removes a patient from the waiting list, it also precludes the incompatible recipient from having to go on the waiting list. This approach also increases access to donor kidneys for the remaining transplant candidates on the list. A consensus procedure developed by the Region prospectively and maintained by an oversight committee representative of the Region, is vital to its continuing success.

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