CHAPTER 21

The National Kidney Registry: Transplant Chains – Beyond Paired Kidney Donation

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The advent of chain transplantation is one of the most exciting advancements to the field over the past 25 years. If transplant programs are able to make a paradigm shift and adopt new attitudes of cooperation rather than competition, this innovation has the potential to greatly expand the donor pool with high quality living donor organs.

Since facilitating its first transplants in 2008, the National Kidney Registry (NKR) has become the most productive paired exchange system in the world, with 62 transplants facilitated in 2009, over 100 transplants facilitated to date and 200 transplants forecasted for 2010. By working with leading transplant centers and leveraging cutting edge computer technology, the National Kidney Registry has broken through many of the barriers that have stalled preceding paired exchange efforts.

EVOLUTION OF CHAIN TRANSPLANTATION

Chain Transplantation is a byproduct of "nondirected living donation" and "paired kidney exchanges" which have independently evolved over time. Although living unrelated and nondirected donor transplants had been reported since the 1960's, it wasn't until the 1980's that the opportunity to expand the living donor pool was appreciated (1). Until that point, the perceived low patient and graft survival rates were felt to justify living donation only from genetically related individuals with at least one HLA haplotype in common. During the 1990's, kidney transplants between spouses and "emotionally related" individuals markedly increased. In 2001, the number of living donors exceeded the number of deceased donors for the first time. Today, nearly half of living kidney donors are not biologically related to the recipient. With improved media forms such as the internet, the relationship between donor and recipient has been stretched to include members of the same faith sanctuary, casual acquaintances or even unknown individuals. Kidneys from this latter group of "altruistic", "good Samaritan", or the preferred term "nondirected donors" (NDD), those without a specific patient to whom the kidney is donated, are increasingly being utilized to trigger multiple chain transplants (Fig. 1).

The emergence of kidney exchanges is somewhat vague. The idea that 2 living donor/recipient pairs could exchange kidneys to circumvent immunologic incompatibility may have been developed as early as 1970, however the first publication by Felix Rapaport appeared in 1986 (2). On October 3, 2000 the first recorded US paired exchange occurred at Rhode Island Hospital. The pairs

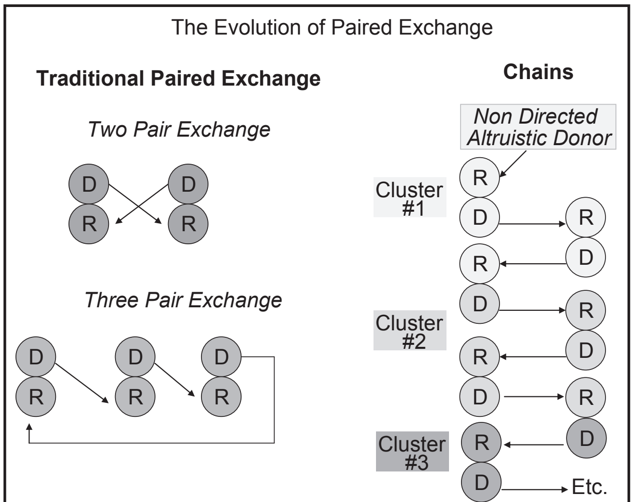

Figure 1. Variations on paired exchanges.

consisted of 2 offspring, each of whom wanted to donate to their corresponding mother but had blood type incompatibilities (reciprocal A/B and B/A). This historic exchange was performed in sequence by Dr. Paul Morrissey and Dr. Anthony Monaco with minimal media attention.

The first paired exchange program in the world was established in Korea in 1999. A year later, the first paired exchange program in the US was started by Lloyd Ratner at Johns Hopkins. The Paired Donation Consortium was established by Steve Woodle from the University of Cincinnati in 2002 and was the first system to organize exchanges between transplant programs in the United States. As other networks and paired exchange programs were initiated, new and more powerful matching strategies began to emerge.

In 2006, Montgomery, et al, proposed a variation on traditional paired donation called "domino paired kidney donation" where a nondirected donor was matched to a recipient who had a willing, but incompatible living donor, in turn the incompatible donor agreed to give their kidney to the first compatible patient on the deceased donor waiting list (3). This set the stage for Michael Rees to expand on the "Domino Chain" approach by utilizing the incompatible donor as a "bridge donor" who could donate to another incompatible pair and continue a chain indefinitely, at least in principle. Rees subsequently started the first "NEAD" (never ending altruistic donor) chain in 2007, facilitating 10 transplants over a period of about a year (4). In practical application, attempting to extend chains indefinitely was a suboptimal strategy as chains could quickly run out of compatible pairs. This lead to broken chains as bridge donors waited long periods of time to donate and continue the chain. In 2009 the National Kidney Registry began facilitating hybrid chains by dynamically applying Domino and NEAD approaches to specific segments within a chain thereby balancing chain capacity to pool size in real-time. This minimized the chance of broken chains and reduced or eliminated bridge donor wait times, allowing for more transplants. These additional transplants included some recipients on the deceased donor wait list who received living donor kidneys when chains were systematically terminated.

ADVANTAGES OF CHAINS OVER TRADITIONAL PAIRED DONATION

Reciprocity Limits the Options in Paired Donation

One of the greatest advantages of chains over traditional paired exchange is that chains do not rely on reciprocal matching. This enables each donor in the chain to be matched with the recipient that yields the longest or highest quality chain. This lack of reciprocity facilitates more transplants and drives superior matching performance. For example, the probability of finding a ABO match for a recipient using traditional paired exchange (requiring a reciprocal match) is approximately 21% compared to 46% for a recipient in a chain (Fig. 2).

Since there is no reliance on reciprocal matching, the software for chains can be programmed to find superior age and HLA matches among ABO compatible patients and donors. In an unpublished simulation study that utilized blood type and HLA data on 440 unrelated pairs from the UNOS Registry, the NKR chain matching program achieved a 50% zero HLA-A,-B,-DR antigen mismatch rate in the first 50 transplants (e.g. 25 of the 50 matches were HLA matched). This improved match quality will lead to prolonged graft survival. Figure 3 sug-

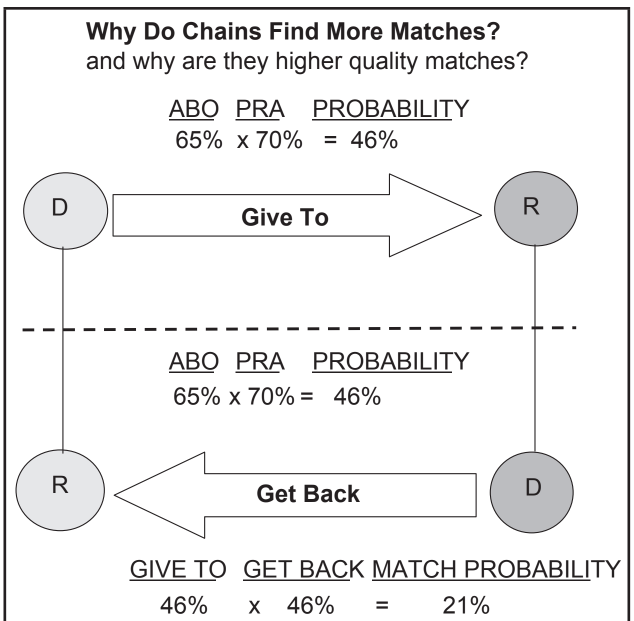

Figure 2. Probability of compatibility by reciprocal paired donation.

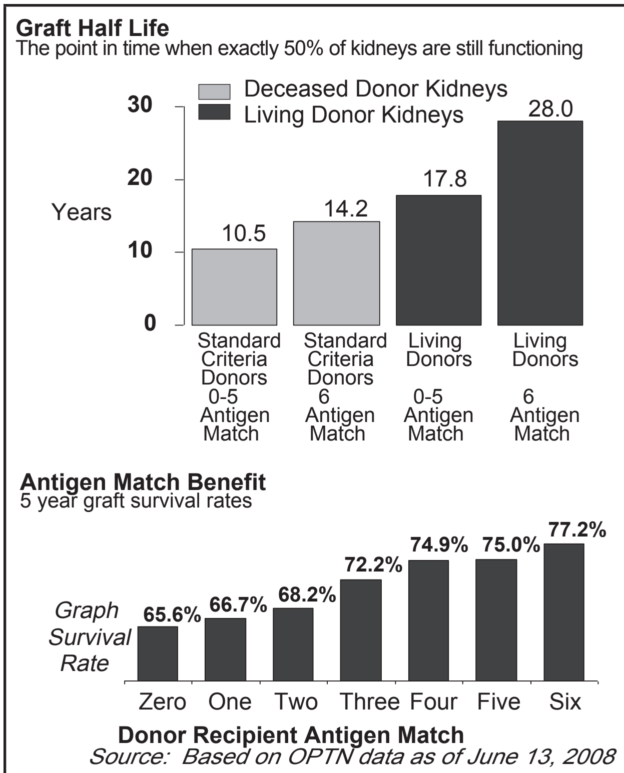

Figure 3. Benefits of better HLA matching.

gests that the expected half-life of an HLA-matched living donor kidney could be as high as 28 years compared to 18 years for one that is completely mismatched (5). Better matching will therefore reduce the competition for organs on the waiting list as many recipients currently return to the wait list after their first transplant fails. To underscore the significance of this, 19% of candidates on the deceased donor waiting list have already had one transplant (http://www.optn.org).

Chains Improve Transplant Logistics

Traditional paired exchange transplants are performed simultaneously to eliminate the possibility of donors withdrawing and creating a situation where a patient's donor donates a kidney to another pair and the patient does not get a kidney in return. Chain transplantation does not have such a risky downside. If a donor withdraws in a chain, the next recipient in the chain suffers no irreparable harm as they have not lost their original willing incompatible donor (Fig. 4). This allows the transplantations within a chain to be performed non-

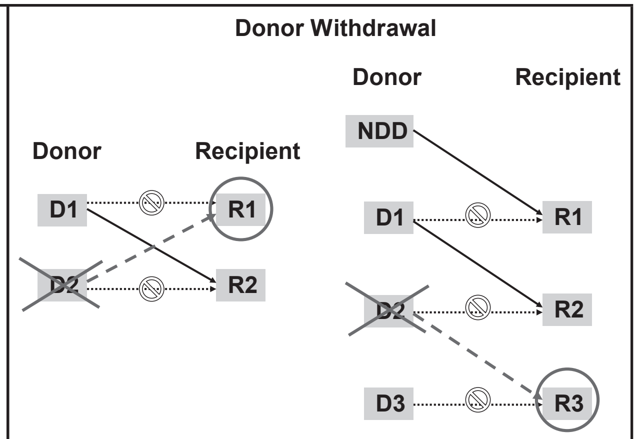

Figure 4. Impact of donor withdrawal on paired donation.

simulataneously. The fact that transplantations are performed simultaneously during paired exchanges places a tremendous burden on hospitals, operating rooms, surgeons, nurses, support staff and the patients. For example, a simultaneous 3-way paired exchange requires 3 donor surgeons (likely laparoscopically trained), 3 recipient surgeons and 6 operating rooms. Very few transplant programs in the country can field the surgeons and operating rooms to support this requirement. Conversely, a small center with one donor and recipient surgeon could complete a chain involving the same 6 patients quite easily. The altruistic donor could donate to the first recipient on one day, the recipient's original incompatible donor could then donate to the second recipient the following day (or following week, to help their "loved one" who just received a transplant recover) and so forth. The logistical simplicity of chains levels the playing field and does not advantage larger programs when organizing exchanges.

THE NKR APPROACH

During 2008, as the NKR was building a core of 10 transplant centers and establishing its approach to facilitating transplants, 21 transplants were completed (Fig. 5). During 2009, with more established protocols, 62 transplants were facilitated. As of March 11, 2010, the NKR was working with 44 centers and another 28 transplants had been performed, placing the registry on track to complete

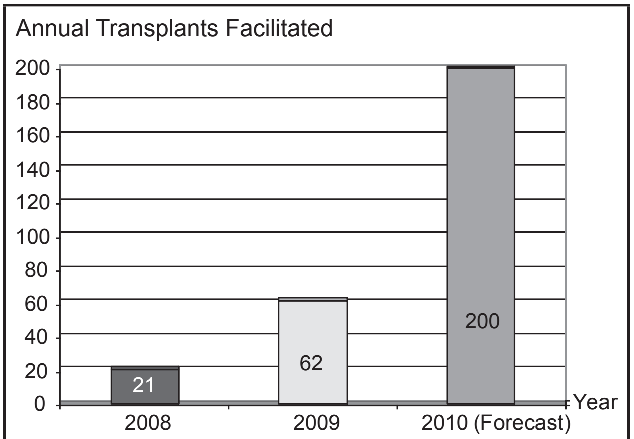

Figure 5. Annual and projected NKR transplants facilitated.

more than 250 transplants by the end of 2010. At the end of 2009, NKR had facilitated transplants for 40% of the recipients enrolled during the prior 2 years (Table 1). This number is expected to increase to 65% by the end of 2010 reducing the average wait time to 9 months. The long-term goal is to reduce average wait time to less than 6 months.

A Non-Transplant Approach to Facilitating Transplants

The National Kidney Registry was started and is personally managed by a complete transplant industry outsider – a dad who wanted to donate a kidney to his daughter, but could not because he was crossmatch incompatible. The challenges in his frustrating search for a compatible donor for his daughter led him to recognize that there are thousands of people who face these same challenges every year (www.nationalkidneyregistry.org). If all incompatible donors and recipients were simply listed in one common pool and modern computer technology was used to find matches, the problems related to incompatible donors would be a thing of the past. The National Kidney Registry was founded to solve this problem and help people facing kidney failure find a compatible donor.

NKR has benefited from a lack of physician bias in the core development team (no member of the core team has a medical background – most have business and technology backgrounds) allowing for rapid innovation. The team has been able to rely on the strong support and guidance from an experienced Medical Board made up of transplant industry veterans. As a result, many bold innovations have been implemented, which have accelerated matching success, including:

- Effective incorporation of out of sequence chain transplants
- Effective use of OPO infrastructure to ship kidneys eliminating donor travel
- Implementation of real-time geotracking technology for shipped kidneys
- Identification and listing of all relevant HLA antigens and antibodies
- Development of a pilot program to utilize deceased donor kidneys to start chains
- Inclusion of non-A1 donors to match acceptable O and B blood group patients
- Real-time matching software allowing for 12-way match offers
- Daily match runs supporting immediate match identification and chain repair
- Automated match offer tracking for organized and efficient operation
- Assessment of pair match probability for initiation of advanced match strategies
- Use of donor and recipient preferences to control the match process
- Elimination of personalized information avoiding HIPAA issues
- Web portal for easy pair enrollment and fast center startup

Table 1. Percentages of enrolled patients transplanted each year.

		2008	2009	2010
A	Ending Recipient Pool	80	127	150
B	Transplants	21	62	200
C	Cumulative Transplants	21	83	283
D	Cumulative Recipient Pool	101	210	433
E	Percent Transplanted (C/D)	20%	40%	65%
F	Average Wait Time (A/B)	3.8 Years	2.0 Years	9 Months

Shipping Living Donor Kidneys

Shipping living donor kidneys has been a disturbing prospect to many transplant professionals because of the perceived association between prolonged cold ischemic time and poorer graft function, which has often been considered the defining difference between living and deceased donor kidneys (6). Lacking a strong bias and with the flexibility in the start times of chain transplants, shipping living donor kidneys was a practical and expedient way to facilitate chains. The willingness to ship living donor kidneys expanded the options for pairs in the NKR as it broadened the geographic area from which compatible donors and recipients could participate.

Over the past 2 years, NKR centers have shipped many living donor kidneys from coast to coast for transplantation, some with cold-ischemia times approaching 14 hours (7). As Collins and Terasaki noted 40 years ago when they shipped living donor dog kidneys from Los Angeles to London, Tel Aviv and Sydney, the prolonged cold ischemia times do not appear to have deleterious affects on the allograft (8).

Currently, when chain participants express preferences supporting the shipment of kidneys, the kidney travels instead of the donor. This allows the donor to recover with their intended recipient (spouse, family member or friend), rather than traveling and recovering in an unfamiliar city and surroundings. These living donor organs are typically shipped unaccompanied on commercial airlines at a minimal cost. This is arranged by local organ procurement organizations (OPOs), who utilize the same policies and procedures that have become well established for the transportation of deceased donor organs. The existing OPO organ shipping capability is being enhanced with geo-tracking devices to provide real-time tracking of the organ to prevent lost or misrouted kidneys.

The United States has already established international exchanges for deceased donor organs, so it would not be much of a stretch to apply this to living donor organs. In fact, in the same time it takes for a kidney to travel across the United States a kidney could also travel across the Atlantic, between New York and London. This would obviously greatly expand the donor pool. More practically living donor kidneys could easily be shipped between the major centers of Canada and the United States, where health care standards are similar and flight times are often less than 3 hours.

Match Software

As the size of the donor/recipient pool increases, the number of transplants that can be facilitated by chains, increases remarkably. For example, in a 3-deep chain, a pool of 100 incompatible donor/recipient pairs will generate approximately 10 billion possible transplant combinations. If the pool is doubled, the numbers of possible transplant combinations increases to 320 billion. With 500 pairs in the pool, a staggering 31 trillion possibilities would be evaluated (Fig. 6). Optimizing ABO and HLA compatibility, age considerations, travel restrictions, addition of NDDs, addition of new pairs and other donor/recipient preferences requires sophisticated software for evaluating and selecting possible matches (Fig. 7).

Different registries have developed a variety of computerized systems to support multi-center traditional paired exchanges and chain matching. Most of the early systems were based on integer

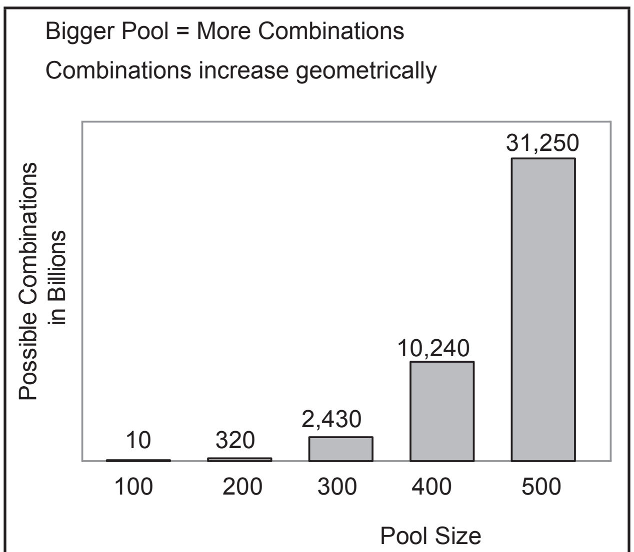

Figure 6. Potential combinations increase with pool size.

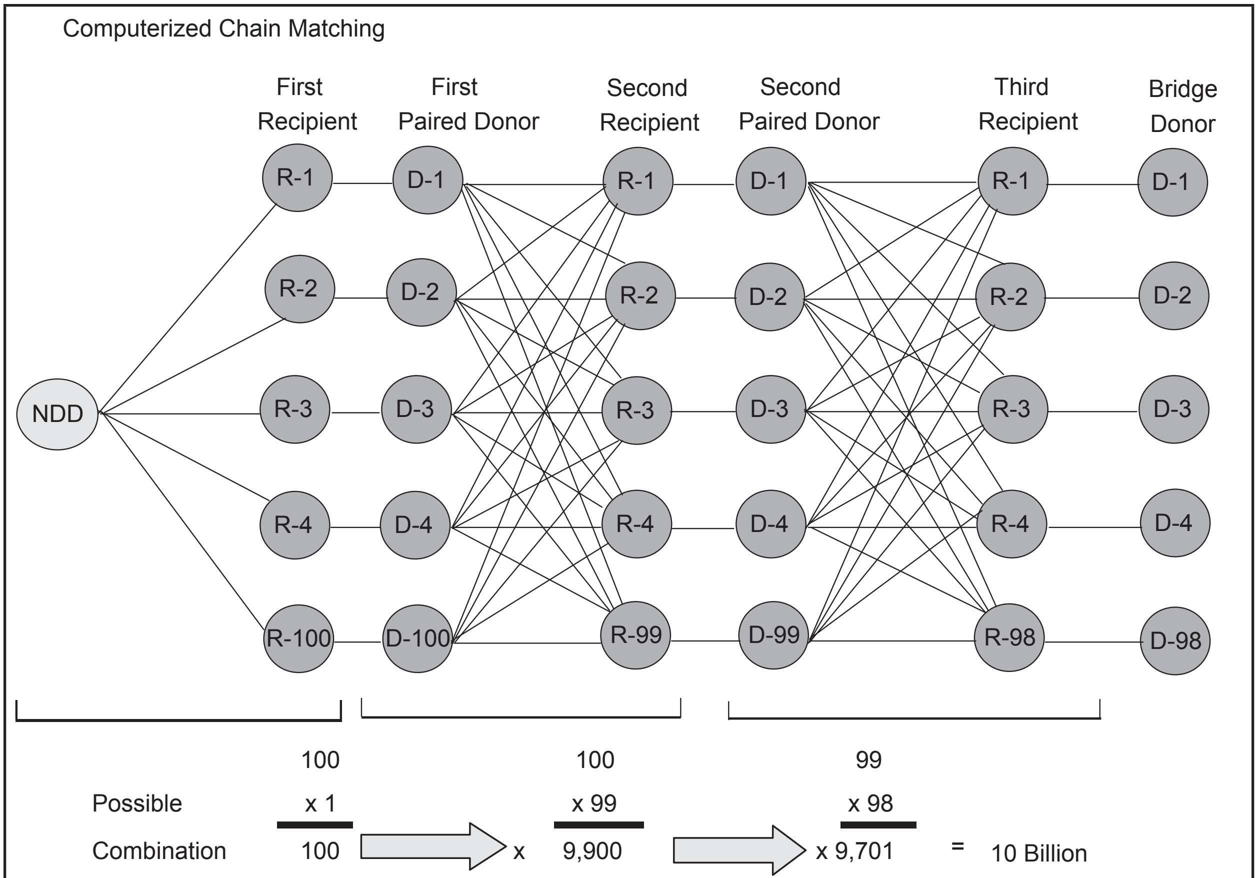

Figure 7. Complexities of multiparameter optimization.

Table 2. Time-to-match estimates based on blood types and recipient sensitization level.

Recipient Blood Type	Direct Donor Blood Type	Recipient PRA Score		
		< 50%	50%-95%	> 95%
AB - Easiest -	O	1 – 2 weeks	1 – 4 weeks	1 – 6 weeks
	B	1 – 3 weeks	1 – 6 weeks	unknown
	A	1 – 4 weeks	1 – 8 weeks	unknown
	AB	unknown	unknown	unknown
A	O	1 – 2 weeks	1 – 4 weeks	1 – 6 weeks
	B	1 – 3 weeks	1 – 6 weeks	unknown
	A	1 – 4 weeks	1 – 8 weeks	unknown
	AB	unknown	unknown	unknown
B	O	1 – 4 weeks	1 – 8 weeks	1 – 12 weeks
	B	1 – 6 weeks	1 – 12 weeks	unknown
	A	1 – 8 weeks	1 – 16 weeks	unknown
	AB	unknown	unknown	unknown
O - Hardest -	O	1 – 8 weeks	1 – 16 weeks	unknown
	B	unknown	unknown	unknown
	A	unknown	unknown	unknown
	AB	unknown	unknown	unknown

programming algorithms which were the best tools to solve the complex mathematical problem presented by the traditional paired exchange reciprocity requirement. With the advent of chains, these original integer programming solutions had to be modified to accommodate the radically different mathematical challenge presented by chains. The NKR system was created solely based on the chain model utilizing technology components employed by modern capital market exchange systems (e.g. New York Stock Exchange) and not dependant on any integer programming algorithms.

Innovations to Improve Effectiveness

The innovations pioneered by the National kidney Registry and its Medical Board have driven tangible results as measured by transplants facilitated, speed to match, percent of pool transplanted and average wait time.

The NKR estimates of time to match for patients and donor enrolled in the Registry are summarized in Table 2, and can be as short as 1-2 weeks for a mildly sensitized AB patient with an O donor. Wait times have not yet been determined for more difficult broadly sensitized, blood type O patients.

To provide the information that allows participating centers to leverage advanced matching strategies, the NKR automated the metrics for calculating adjusted PRA scores (A-PRA, which also reflects ABO incompatibility) as illustrated in Table 3. The

Table 3. Match Power Report (Generated Tuesday, 1/19/2010 7:52 AM).

Center	Recipient	A-PRA	R ABO	R Age	Days In NKR	R Match Power	Donor	D ABO	D Age	Donor Match Power	Pair Match Power
Allegheny	AGHCC	100%	O	42	83	0%	GUSTIN	A	43	0.0%	0
Allegheny	AGHLBK	100%	O	33	46	0%	AGHGA	O	43	25.6%	0
Columbia	R5408800	97%	O	36	241	3%	D2028069	O	54	26.7%	81
Cornell	BROD	100%	A	45	592	0%	MORE	B	53	2.3%	0
Sharp	SHARPVIDR	84%	A	56	69	16%	SHARPVIDD	A	55	0.0%	0
Stanford	SUR1040	100%	O	33	229	0%	SUD1041	O	55	25.6%	0
Stanford	SUR1050	77%	O	68	229	23%	SUD1051	A	38	0.0%	0
Stanford	SUR1080	60%	O	57	27	40%	SUD1081	A	58	0.0%	0
UCLA	RBG	60%	O	49	155	40%	DSG	A	47	0.0%	0
UCLA	RFD	60%	O	61	42	40%	DKD	A	61	0.0%	0
UCLA	RJH	94%	O	39	92	6%	DAL	O	32	26.7%	162
UCLA	RKR	60%	O	49	214	40%	DMT	A	51	0.0%	0
UCLA	RMH	100%	AB	51	290	0%	DKB	O	56	23.3%	0
UCLA	RPC	97%	O	58	483	3%	DJEC	O	35	23.3%	71
UCLA	RRG	96%	AB	37	290	4%	DMG	A	36	0.0%	0
UCSF	RCAMRILOM	100%	O	65	437	0%	DMALDM	O	34	25.6%	0
UCSF	RDELCLZDAD	63%	O	29	437	37%	DDELZC	A	30	1.2%	45
UCSF	RDRNNM	99%	A	58	39	1%	DVRLAJ	B	39	0.0%	0
UCSF	RGRCAL	99%	O	51	83	1%	DOLVRZL	O	33	26.7%	27
UCSF	RHVRM	100%	A	66	418	0%	DHVRK	O	30	26.7%	0
UCSF	RNKIB	60%	O	63	353	40%	DOWNSC	AB	31	0.0%	0
UCSF	RPLTOL	98%	O	71	377	2%	DQUONA	A	38	0.0%	0
UCSF	RPRYJ	99%	O	46	293	1%	DGRHMC	A	47	1.2%	1
UCSF	RRKTL	68%	O	30	280	32%	DHYWDS	B	30	0.0%	0
UCSF	RRVASS	100%	O	25	437	0%	DRIVASM	O	41	25.6%	0
UCSF	RVRSS	100%	O	49	340	0%	DANDJKAT	O	51	20.9%	0
UCSF	RWIRW	60%	O	51	437	40%	DWEIRA	A	36	0.0%	0
UTMC	R25UTMC	98%	O	53	208	2%	D25 DB25	A A	31 22	0.0% 0.0%	0 0
UTMC	R30UTMC	100%	A	46	77	0%	D30UTMC	O	51	27.9%	0
Washington	JH1949	100%	A	60	98	0%	KAJ1951	A	58	1.2%	0
Washington	MTN1952	93%	B	57	98	7%	LST1968	O	41	25.6%	181
Washington	RMC1975	63%	O	34	98	37%	MRC1976	A	33	0.0%	0
Washington	SSV1964	95%	AB	45	98	5%	SMT1965	A	44	0.0%	0
Washington	TLA1966	100%	O	43	98	0%	KEB1987 KF1964	A O	22 45	0.0% 27.9%	0 0

A-PRA score is then inverted to determine the probability of a recipient finding a match in the pool at any given time. The recipient's paired donor is also evaluated to determine how many recipients in the pool they match to determine the power of the donor. The recipient score and donor score are then multiplied against each other to determine the pair's exchange power score (far right column). Based on these metrics, participating centers can implement advanced matching strategies (e.g. add another donor, desensitization, relax preferences, etc.) that will improve the odds of a pair finding a match.

FUTURE DIRECTIONS

A National Kidney Paired Exchange Program

While Korean and Dutch government sponsored national kidney registries have enjoyed success (9,10), other government sponsored programs have lagged. In the United States, UNOS has been working on a national paired exchange program since 2004 with no transplants facilitated to date. Meanwhile, non-government efforts including the NKR have filled the void by facilitated numerous transplantations and demonstrating exceptional cooperation between transplant centers from coast to coast. The practical aspects of exchanges may be evolving too rapidly for a large governing body such as UNOS to keep up. Additionally, the paired exchange model being adopted by UNOS may include fatal flaws such as infrequent monthly match run cycles, requirements to start all donors simultaneously and restrictions on the use of chains. The process of monthly match runs is already obsolete as some systems are now executing daily match runs, allowing faulty chains to be repaired and patients to get a transplant in a shorter timeframe. The simultaneous surgery requirement, although mitigating some risk, requires capacity that only exists in the largest centers, and will exclude smaller transplant centers from participating. Any restrictions on the use of chains will render inferior quality and quantity of matches.

Donor Withdrawal and Broken Chains

There has been much debate about whether bridge donors can be trusted to "pass on" the generosity and donate to the next recipient in the chain after their intended recipient has already received a kidney transplant. Based on NKR observations of over 100 chain transplantations, only 3 bridge donors have withdrawn, all during 2008. In all cases, the downstream recipient had not been identified yet, and in all cases, no recipient suffered irreparable harm as their incompatible donor (family member, spouse or friend) had not donated. There were none in 2009 with 3 times as many transplants facilitated that year.

Actual clinical experience indicates that the vast majority of bridge donors are so grateful of their intended recipient's improved health that they look forward to "paying the gift forward" to the next recipient in the chain. Even if bridge donors have to wait months before donating, are required to lose weight or need to modify their lifestyle (i.e. reduce alcohol intake) they remain motivated and follow through with donation to the next complete stranger in the chain. In fact, several donors have donated their kidney to the next recipient in the chain 1 to 21 days BEFORE their intended recipient received a kidney (7). In these situations, the recipient lost their "bargaining chip" as their intended donor had already donated, but had faith that the upstream donor would honor their promise to donate.

An important factor in minimizing donor withdrawal resulting in broken chains has been the transplant center's judgment regarding the reliability of any given bridge donor. If a bridge donor is determined to be unreliable then the chain can be quickly ended (i.e. converted to a domino segment). Our experience suggests that approximately 75% of the time, the selected bridge donor is determined by the transplant center staff to be reliable.

Compatible Pairs

Many medical professionals and their patients are beginning to realize that compatible pairs can improve their donor recipient match by participating in a chain (11,12). These benefits are most pronounced for compatible pairs comprising an O donor and a non-O patient, since there are shortages of these blood types in all exchange programs. Improved matches are usually evaluated on 3 dimensions; donor age, HLA match and donor size. Although the improvements in patient outcomes are well documented related to donor age and HLA match, there is limited research to demonstrate donor size improves graft survival or half-life. In addition to achieving a better outcome, the compatible pair will typically facilitate many more transplantations by filling a missing gap in the chain and increasing the liquidity of the pool. This may be a strong yet underappreciated factor for patients and their prospective donors.

In some cases a compatible pair will have a low probability of improving their match by participating in a chain. For example, when the donor is an age compatible zero mismatch sibling or when a well matched offspring is donating to their father; the match quality for these compatible pairs may be difficult to improve upon.

Starting Chains with Deceased Donors

Chains could be triggered by deceased donor kidneys. In these cases, the last living donor of the chain could close the chain by donating to the deceased donor waiting list at the originating transplant center. The chain could be designed in many cases to provide a donor of the same blood type to the list to maintain balance. Thus, a predetermined chain might be set up with an unsensitized patient who would be given priority for the next appropriate deceased donor kidney and quickly return a living donor to the list to replace the one used to start the chain.

Combining Desensitization with Chains

Transplant teams specializing in desensitization often see the rapid growth of chain transplantations as a threat to their clinical workload. Likewise, proponents of exchanges often point out the added expense ($30,000/transplant) and immune-mediated injury associated with desensitization (13). However, these 2 approaches are not mutually exclusive and in actuality can be quite complementary. With access to desensitization and chain matching, a center can essentially "stack the deck" in favor of the patient. For example, a potential recipient who has multiple HLA antibodies, some of which are stronger and others that are weaker. When this pair is placed into a registry, the weaker antibodies that are removed through desensitization can be ignored in the matching process. In this case, the center would not list these weak antibodies for this patient and the patient could receive a transplant through a chain in combination with desensitization (e.g. single-dose IVIG).

Speed to Match

As more recipients learn of chain transplantation, the pool of pairs will increase in size allowing for more match combinations. As the pool increases in size and the transplant centers learn the new process of multi-center chain transplantation, the time from initial listing in a registry to finding a match will shorten. This is critically important in light of the fact that the longer a patient is on dialysis, the lower their graft survival rates.

Ethical Considerations

Living donor transplants have not been actively overseen by government agencies in the past and are not subject to universal regulations regarding their allocation. With the growth of living donor transplants and particularly chains where donors are allocated to patients they may not know, there is a need for the transplant community to establish some guidelines.

NDD Allocation and Coercion

Social concerns for NDDs include their motivation, possible hidden compensation and psychiatric history to name a few. Our experience indicates that only 2% of inquiring NDD candidates makes it all the way through the evaluation process to actual donation. In addition to appropriate medical and psychological screening, other ethical issues exist. Should the kidney be allocated to the center's deceased donor list, 6-antigen match national list, a child, or to start a chain? These questions can only be answered by the donor, so it is important that the donor know all the options before they decide.

Utility vs. Justice

Taken at face value, the concept of never ending chains described by Michael Rees sounds tremendous (4). A single nondirected donation can be theoretically expanded to facilitate hundreds of transplantations (utility). However, over time, this concept has been challenged. First, computer simulations and clinical experience indicate that chains do not go on indefinitely. Second, since the non-directed living donor organ allocated to trigger a chain is an organ not allocated to the deceased donor list, critics argue that such an arrangement disadvantages the candidates on the deceased donor wait list. One solution to this criticism might be to arrange for the last donor in a chain to donate to the next candidate on the deceased donor waiting list (justice). In fact, chain segments that have the greatest propagation power (those that end with a blood group O bridge donor) might be encouraged to continue while weaker chain segments (those ending with an AB bridge donor or any chain where there is difficulty placing a bridge donor) would be ended by donation to the deceased donor list.

It is important to realize that candidates on the deceased donor waiting list collectively benefit when non-directed living donor organs are allocated to initiate chains. Living donors are liberated throughout a chain, removing patients from the wait list. Without chains these living donors would never have been utilized due to incompatibility. This net gain of living donors reduces the competition for deceased donors for those candidates on the waiting list allowing other patients to move up the wait list and take the place of the recipients on the wait list that received a kidney from a living donor in a chain. The resulting multiplier effect is powerful. For example, if one donor starts a chain that is closed after 10 transplants, 9 recipients are removed from the wait list when they receive a living donor transplant and one recipient on the wait list receives a kidney directly from the last living donor in the chain.

CONCLUSION

If programs can cooperate with and be accepting of one another, then chains have the potential to revolutionize kidney transplantation. Not only will thousands of patients with incompatible living donors be able to receive a living donor transplant, but the quality of donor-recipient matching will improve as an increasing number of compatible pairs enter chains, leading to better patient outcomes and longer graft survival. By the end of the decade, the current practice of living donors giving their kidney to a friend or family member may be a relic of the past (except for well matched siblings) with most donors giving their kidney to a stranger in a chain so that their recipient can get a better matched, longer lasting kidney.

ACKNOWLEDGEMENTS

The National Kidney Registry is a non-profit 501C3 corporation. Since its inception it has received over $2 million in contributions. The primary focus of National Kidney Registry is to facilitate as many successful transplants as quickly as possible. NKR is not owned or controlled by any single hospital so it does not have any conflicts of interest. Over 40 transplant centers are now working with NKR including 75% of the largest living donor programs in the U.S. (based on 2008 UNOS reported LD transplants). Table 4 is a list of some of the participating centers.

Table 4. Participating Centers.		
Allegheny General Hospital	Pittsburgh	Pennsylvania
Barnes-Jewish Hospital	St. Louis, MO	Missouri
California Pacific Medical Center	San Francisco	California
Case Medical Center Cleveland	Cleveland	Ohio
Charleston Area Medical Center	Charleston	West Virginia
Children’s Hospital St. Louis	St. Louis	Missouri
Fletcher Allen Health Care	Burlington	Vermont
Hackensack University Medical Center	Hackensack	New Jersey
Intermountain Medical Center	Murray	Utah
Lankenau Hospital	Wynnewood	Pennsylvania
Loma Linda Medical Center	Loma Linda	California
Loyola University Medical Center	Maywood	Illinois
Mayo Clinic Hospital	Phoenix	Arizona
Methodist Hospital	Houston	Texas
Montefiore Medical Center	Bronx	New York
Mount Sinai Medical Center	New York	New York
Newark Beth Israel Medical Center	Newark	New Jersey
New-York Presbyterian Columbia	New York	New York
New-York Presbyterian Cornell	New York	New York
Northwestern Memorial Hospital	Chicago	Illinois
Ohio State University Medical Center	Columbus	Ohio
Our Lady of Lourdes	Camden	New Jersey
Pinnacle Health Systems	Harrisburg	Pennsylvania
Robert Woods Johnson	New Brunswick	New Jersey
Saint Barnabas Medical Center	Livingston	New Jersey
Sentara Norfolk General Hospital	Norfolk	Virginia
Sharp Memorial Hospital	San Diego	California
Stanford University Medical Center	Palo Alto	California
UC Davis Medical Center	Sacramento	California
UCLA Medical Center	Los Angeles	California
UCSF Medical Center	San Francisco	California
University Medical Center of Southern Nevada	Las Vegas	Nevada
University of Maryland Medical Center	Baltimore	Maryland
University of Minnesota Medical Center	Minneapolis	Minnesota
University of Mississippi Medical Center	Jackson	Mississippi
University of Pennsylvania Hospital	Philadelphia	Pennsylvania
University of Southern California	Los Angeles	California
University of Utah Medical Center	Salt Lake City	Utah
University of Virginia Medical Center	Charlottesville	Virginia
University of Washington Medical Center	Seattle	Washington
Virginia Transplant Center	Richmond	Virginia

SUMMARY

The National Kidney Registry (NKR) has facilitated more than 100 transplants at 24 centers in the past 2 years and the numbers are rapidly increasing. The NKR has inherent capability for rapid change as innovations are developed and incorporated in the approach to matching donors and recipients in transplant chains. Kidneys are shipped with geotracking devices utilizing existing OPO procedures whenever patients are willing to accept them. This reduces the need for donor travel and increases the geographic area where matches can be made. Out-of- sequence transplants can be performed to improve logistics. Matching software is designed to facilitate chain transplantation and incorporates metrics that help transplant centers develop strategies to improve the chances that their patients can be transplanted. Daily match runs and close attention to repairing broken chains have been critical to growing the number of transplants that can be facilitated. A number of new innovations are expected to increase the opportunities for patients and their potential living donors.

REFERENCES

1. Levey AS, Hou S, Bush HL. Kidney transplantation from unrelated living donors. Time to reclaim a discarded opportunity. N Engl J Med 1986; 314:914.

2. Rapaport FT. The case for a living emotionally related international kidney donor exchange registry. Transplant Proc 1986; 18:5.

3. Montgomery RA, Gentry SE, Marks WH, et al. Domino paired kidney donation: a strategy to make best use of live non-directed donation. Lancet 2006; 368(9533):419.

4. Rees MA, Kopke JE, Pelletier RP, et al. A nonsimultaneous, extended, altruistic-donor chain. N Engl J Med 2009; 360:1096.

5. Cecka JM. The OPTN/UNOS Renal Transplant Registry. In: JM Cecka and PI Terasaki, Eds. Clinical Transplants 2005. Los Angeles, UCLA Immunogenetics Center, 2006; 1.

6. Simpkins CE, Montgomery RA, Hawxby AM, et al. Cold ischemia time and allograft outcomes in live donor renal transplantation: Is live donor organ transport feasible? Am J Transplant 2007; 7:99

7. Butt FK, Gritsch HA, Schulam P, et al. Asynchronous, out-of-sequence, transcontinental chain kidney transplantation: a novel concept. Am J Transplant 2009; 9(9):2180.

8. Collins GM, Bravo-Shugarman M, Terasaki PI, Braf Z, Sheil AG, Williams G. Kidney preservation for transportation. IV. Eight-thousand-mile international air transport. Aust N Z J Surg. 1970; 40(2):195.

9. Roodnat JI, Kal-van Gestel JA, Zuidema W, et al. Successful expansion of the living donor pool by alternative living donation programs. Am J Transplant 2009; 9:2150.

10. Huh KH, Kim MS, Ju MK, et al. Exchange living donor kidney transplantation: merits and limitations. Transplantation 2008; 86:430.

11. Gentry SE, Segev DL, Simmerling M, Montgomery RA. Expanding kidney paired donation through participation by compatible pairs. Am J Transplant 2007; 7:2361.

12. Ratner LE, Rana A, Ratner ER, et al. The aaltruistic unbalanced paired kidney exchange: proof of concept and survey of potential donor and recipient attiitudes. Transplantation 2010; 89:15.

13. Montgomery RA. Renal transplantation across HLA and ABO antibody barriers: integrating paired donation into desensitization protocols. Am J Transplant 2010 (Epub ahead of print)