

OPTN/UNOS Kidney Transplantation Committee
Report to the Board of Directors
November 16-17, 2009
Orlando, Florida

Summary

I. Action Items for Board Consideration

- None

II. Other Significant Items

- *Progress in Development of a New National Kidney Allocation System*
The Committee discussed aspects of a new system with representatives from the Pediatric Transplantation, Pancreas Transplantation, and Histocompatibility Committees. The Committee also reviewed results from the latest round of simulation modeling and discussed a path forward to simulate a system that improves matching of donors and recipients through two different mechanisms. (Item 1, Page 3)
- *Kidney Paired Donation*
The Committee voted to make several modifications to the operational guidelines for the KPD Pilot Program. Of these, the Committee agreed that match cycles would be eliminated for the interim implementation; that pairs would accrue 2 points per match run; and 3-way exchange would receive 290 points. Additionally, the Committee agreed to replace the terms “low stringency antigens” and “high stringency antigens” with the terms “unacceptable antigens” and “all other antibody specificities” respectively to improve clarity. Finally, the Committee agreed that that (-5) points be assigned for a match between a candidate and a donor with the candidate’s other antibody specificities in the KPD Pilot Program. (Item 2, Page 8)
- *Simultaneous Liver Kidney (SLK) Transplantation Policy*
The Committee discussed ways to simplify the SLK policy proposal to better utilize programming resources. (Item 3, Page 10)

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OPTN/UNOS Kidney Transplantation Committee Meeting

August 24, 2009

Ken Andreoni, MD, Chair

John Friedewald MD, Chair

1. Progress in Development of a New National Kidney Allocation System

As part of its efforts to develop a new national kidney allocation system, the Kidney Transplantation Committee received updates from the Histocompatibility, Pediatric, and Pancreas Transplantation Committees during its meeting on August 24, 2009. Additionally, the Committee reviewed results from the latest round of simulation modeling and discussed a path forward for the development of this system.

Histocompatibility Committee Update

Michael Cecka, PhD, Chair of the Histocompatibility Committee, presented the calculated panel reactive antibody (CPRA) project, which was approved by the Board in December 2007 (Exhibit A). The percent CPRA indicates how many donors will be incompatible with a particular candidate. The use of CPRA is a paradigm shift in organ allocation because it holds transplant centers accountable for the antigens that they list by awarding sensitization priority only when the candidate has enough unacceptable antigens to be sensitized to 80% of donors.

For programs that are using desensitization protocols, implementation of CPRA may cause some challenges. Once the candidate starts to get organ offers, the centers inactivate the candidate and begin desensitization. They reactivate the candidate once he or she is desensitized. Under the CPRA policy, these candidates will not be able to retain their sensitization points and receive offers because under CPRA, once the unacceptable antigens are removed, so are the sensitization points. Dr. Cecka assured the Kidney Transplantation Committee that the Histocompatibility Committee is looking at solutions to remedy this problem for a growing number of centers that are attempting desensitization for candidates on the deceased donor waiting list. One possible solution would be to create a committee-sponsored alternative allocation system for programs in this situation. An alternative system would keep the sensitization points in place for a time period (e.g., 6 months) even though the candidates are technically not sensitized during this time period. The Histocompatibility Committee is also looking into ways to make an alternative system fair. Dr. Cecka remarked that the Histocompatibility Committee would like to partner with the Kidney Transplantation Committee for this project.

Dr. Cecka also discussed the priority awarded to sensitized candidates. The Histocompatibility Committee is looking at mathematical functions to represent the degree of difficulty a candidate has in finding a compatible donor. Currently, at 79% CPRA, the candidate receives no priority and at 80%, the candidate receives 4 points. The Histocompatibility Committee does not believe that the function used to estimate histological barriers to matching are completely linear and is working with the SRTR to devise a better function that would improve efficiency for offers and placement of kidneys for highly sensitized candidates.

CPRA is improving the ability of clinicians to predict crossmatches and decide what kinds of donors ought to be offered to sensitized patients. A way to improve this clinical decision making is to improve donor typing. The Histocompatibility Committee has been investigating the quality of donor typing in the 120 active labs around the United States. They found that 50 labs had 90 discrepancies between the histological information listed on the match run and the donor histocompatibility form. Of these, a few labs are repeatedly entering discrepant data. The Histocompatibility Committee found that labs that are not using the most current tissue typing technology are more likely to enter discrepant data. Of the six percent of donors with incorrect histological information entered, about 24% were typed by serology and 75% were typed with DNA typing (the newer technology). The Histocompatibility Committee plans to propose that donor typing must take place through DNA methods (to include CW, DP, and DQ). The Committee believes that technology will help streamline allocation and reduce the expense because this one test can determine compatibility between the donor and the candidate. Dr. Cecka explained that the Committee is working with ASHI to generate consensus around these concepts.

Dr. Andreoni thanked Dr. Cecka and asked the he continue to keep the Kidney Transplantation Committee up to date on the progress of these projects.

Pediatric Transplantation Committee Consideration of Donor Profile Index (DPI)

Dr. Eileen Brewer described the Pediatric Transplantation Committee's deliberation in July 2009 to replace the current age cut-off of 35 with a DPI cut-off. The Committee was very interested in principle in pursuing DPI as a tool in allocation. In 2008, The Pediatric Transplantation Committee conducted an analysis of the DPI characteristics that would correspond to donors <35. The Committee will review this analysis, continue its deliberation on this idea, and forward its recommendations to the Kidney Transplantation Committee.

Initial Concepts for Pancreas Allocation

Dixon Kaufman, MD, Chair of the Pancreas Transplantation Committee presented the Committee's work to develop a new pancreas allocation system (Exhibit B). In the current pancreas allocation system, approximately 66% of pancreata are allocated to simultaneous pancreas kidney (SPK) transplant candidates. Additionally, there is no uniform national system for allocating pancreata in the context of SPK transplantation. There is wide variability for SPK allocation after kidneys are allocated following pediatric candidates and after kidney debt payback. The Pancreas Transplantation Committee found that some donor service areas (DSA) require the pancreas to follow the kidney, while other DSAs allow the kidney to follow the pancreas. Some DSAs have separate SPK and PA lists and others have a mixed list (SPK and pancreas candidates are intermixed on the list).

Dr. Kaufman explained the limitations of the current pancreas allocation system including that the current policy does not maximize the utilization of the pancreas in a population of candidates that benefits the most from kidney transplantation. The Pancreas Transplantation Committee is preparing for a possible change in kidney allocation that would not allocate to SPK candidates directly.

The goals of a new pancreas allocation system would be to:

- Increase utilization of the pancreas,

- Increase access for both SPK and pancreas candidates (i.e., living donor kidney transplant/pancreas after kidney transplant) candidates,
- Reduce waiting time for all pancreas candidates without adversely affecting adult and pediatric renal transplantation candidates,
- Reduce geographic inequities of access and waiting time, and
- Reduce the burden of disease of candidates of pancreas transplants.

Dr. Kaufman asked the Kidney Transplantation Committee for constructive ideas to improve the pancreas allocation policy for the SPK transplant candidates. The Committee also was asked to help determine the conditions under which a new national system would be acceptable for a kidney follows pancreas allocation system locally. The Committee was also asked for input for SPK listing criteria and on mechanisms for monitoring and modulating a new pancreas allocation system.

The Pancreas Transplantation Committee is currently recommending that a kidney be offered with a pancreas locally and that all pancreata be allocated to a combined SPK and pancreas candidate list. Additionally, the Committee is recommending consistent SPK listing criteria so that candidates would be required to be on chronic maintenance dialysis or have a glomerular filtration rate or creatinine clearance ≤ 20 mL/min. The candidates for SPK would also be required to have a minimum C-peptide value.

Dr. Kaufman shared with the Committee the extensive analysis regarding current pancreas allocation and utilization practices around the country. Briefly, The Pancreas Transplantation Committee conducted a survey on pancreas allocation in the US and asked several questions related to local pancreas allocation practices. The Committee found that significant variation exists between DSAs on the priority given to SPK candidates. However, the vast majority of DSAs already employ a PA priority allocation system (i.e., the experiment is already largely being conducted). Additionally, the donor and recipient demographics were not notably different for SPK transplantation according to the priority (pancreas or kidney) of the allocation system. Pancreas priority was not found to increase SPK transplant in patients with Type II diabetes, those not on dialysis, those who receive a kidney-alone, or in the number of young donor kidneys transplanted into older recipients. The Committee also found that in DSAs with pancreas priority, SPK patient waiting time to transplant was significantly reduced. Additionally, both overall rate of PA transplantation and proportion of SPK transplants increased with PA priority. These data provided insights about how to develop and model a new and consistent national allocation system for PA transplant recipients that increases access and decreases waiting time for transplantation.

The Committee discussed the presentation and one member raised a concern about whether kidneys would be exported regionally with pancreata. Dr. Kaufman explained that the proposal is only to require sharing of kidneys when the pancreas is allocated locally. Otherwise, there would not be mandatory sharing of kidney pancreas. Other members expressed support of the idea to merge the SPK and pancreas-alone lists as a way of regulating the number of kidneys that go with pancreata. One member disagreed and said that there needs to be more priority given to pancreas-alone transplants and for SPK candidates who have a living donor and are willing to wait for a pancreas transplant. Since the results for pancreas after kidney are worse than for SPK, then pancreas-alone transplants have to be given the most priority. This approach was thought to incentivize people to pursue living kidney donation. A member

remarked that SPK candidates who receive a living donor kidney oftentimes opt not to receive a pancreas from a deceased donor because they are stable and doing well after the kidney transplant. A Health Resources and Services Administration (HRSA) representative cautioned that the Department of Health and Human Services (HHS) would not support overtly incentivizing living donation through OPTN policies. Mr. McLaughlin explained that HHS did not have an official policy of endorsing living donation because there is not sufficient evidence on living donor outcomes. The incentive would have to be more broadly applicable, such as awarding priority to any individual who receives a kidney, not just those who receive a kidney from a living donor. A member asked how the policy to provide prior living donors with additional priority if they ever experience ESRD and require a transplant is any different. Dr. Bowman remarked that the priority for prior living donors is in recognition of the risk that these individuals take, but it is not designed to incentivize living donors.

A number of DSAs do not have pancreas transplant programs and so there is little utilization of even excellent organs because to send someone out to retrieve only a pancreas is too large of an investment. A member recommended taking the plan one step further and requiring pancreas sharing. Another member expressed strong concerns of the impact of these ideas on pediatric kidney candidates. Locally, this member has experienced a number of kidneys going to preferentially SPK candidates rather than pediatric candidates. The Committee agreed that there will need to be a way to balance the needs between SPK candidates and pediatric candidates. As currently proposed, the SPK candidates would come before pediatric candidates. Dr. Andreoni thanked Dr. Kaufman for the update and asked that the Pancreas Transplantation Committee continue to keep the Kidney Transplantation Committee informed as it progresses with this policy initiative.

Results from Kidney Pancreas Simulated Allocation Model (KPSAM)

After Dr. Andreoni reviewed the current allocation system and the work to date to develop a new national allocation system, Keith McCullough, MS, of the Scientific Registry of Transplant Recipients (SRTR) reviewed the results from the most recent data analysis (Exhibit C and Exhibit D). Mr. McCullough explained that he conducted a total of eight runs:

- **Run 34, Current rules prior to January, 2009**
- **Run 35, Current rules after January, 2009 (without zero antigen mismatch sharing for candidates with PRA < 20)**
- **Run, 36 Run 35 + A2-B, Kidney follows pancreas locally only, no paybacks, and dialysis time in addition to wait time**
- **Run 37, Top 20% of candidates have priority for top 20% of donors**
- **Run 38, Candidates under 35 have priority for donors under 35**
- **Run 39a, Candidates within 10 years of donor age have priority**
- **Run 39b, Candidates within 15 years of donor age have priority**
- **Run 40, Top 80% of candidates have priority for top 20% of donors**

The results from these runs suggest that the allocation policy changes implemented in January 2009 to only allocate zero-antigen mismatched kidneys to pediatric candidates and sensitized adult candidates regionally and nationally reduced zero antigen mismatched transplants as expected. Additionally, this policy change may have resulted in increased allocation to African American and blood type O recipients by ≤ 1 percentage point. In the simulation modeling, the policy changes to use dialysis time to supplement wait time, A₂-B, kidney-follows-pancreas locally only, and eliminating paybacks: 1) transferred roughly 3 percent of all transplants from A₂ to B recipients, 2) reduced SPK transplants, and 3) increased allocation to African American recipients by three percentage points. However, these simulated policy changes may have also reduced access to highly sensitized (PRA 80+) candidates.

The policy changes simulated in Run 38 (Candidates under 35 have priority for donors under 35) more than doubled access for 18-34 year-olds, reduced access for candidates over the age of 35 by roughly 1,300 kidneys, may have reduced the total number of transplants and may have reduced access to Caucasian recipients by 2 percent of transplants.

The policy changes simulated in Runs 39a and 39b (priority for candidates within 10 years of donor age and 15 years of donors age, respectively) were found to shift 1,100 kidneys from recipients over 50 to recipients under 50 and increase the extra lifespan* of the candidate list from a year's worth of transplants by over 5,000 years. The differences in the results between runs 39a and 39b were negligible.

Finally, Runs 37 and 40 had differential impacts based on candidate age. Run 37 (top 20% of candidates have priority for top 20% of donors) found that for candidates ages 18-34 1,000 more kidneys were distributed to this group. For candidates age 35-49, there was an increase of 300 kidneys, for ages 50-64, the number of kidneys declined by 1,100. And for the candidates over age 65, there was a reduction of 300 kidneys. Run 40 (top 80% of candidates have priority for top 20% of donors), found that for the candidates 18-34, there was an increase of 100 kidneys, no change for the age 35-49 group, a decrease of 100 kidneys for the 50-64 group, and a decrease of 300 kidneys for the >65 candidates. Overall for runs 37 and 40, an increase in the lifespan after transplant (by 19,000 and 7,100 years respectively) and the total extra years of life (6,500 years and 3,400 years) realized from the kidneys available in a year were observed.

One member asked whether the simulation modeling took into account changes in behavior following allocation policy rule changes. Mr. McCullough explained that the simulation modeling did not take into account behavior changes. Another SRTR representative remarked that they could utilize sensitivity analysis once the Committee agrees on a proposal, to determine what effects certain assumptions have on the results. The Committee agreed that behavior would change if candidates were restricted from receiving certain types of kidneys. Michael Shapiro, MD, Chair of the Ethics Committee explained some basic ethical principles where justice is defined as fairness and utility defined as benefit. Dr. Shapiro remarked that the OPTN Final Rule calls for the use of utility in an allocation system. Chris McLaughlin, of HRSA, remarked that the access issue is critical, regardless of the direction of the Final Rule and that limited access by age groups would be very difficult for the federal government to accept. A member remarked that the policies under consideration were not restricting access and that the changes were intended to increase the use of kidneys. The Committee stated that it intends to implement a system whereby the transplant centers alter their behaviors to accept useable organs and maximize the organs available. Mr. McLaughlin explained that the Committee would have to explain these intended effects

and to include other initiatives to expand procurement from older donors. A member argued that currently, access is restricted because older candidates may not live long enough to receive a transplant so transplant centers do not list them. Another member remarked that there is no special interest group representing the younger candidates who will not have the ability to live a normal life span, even with transplant. A member asked the HRSA representatives to clearly delineate what the government would be able to support as several years have been spent in policy development, only to learn about this new constraint. Another member remarked that an allocation system would change the distribution by age because there are not any additional kidneys being added to the pool.

The Committee decided to continue the review of these simulation runs on its electronic discussion board. Based on those discussions, it was determined that additional work should be done to examine the assumptions in the acceptance model, and to combine runs 37 and 39b. The Committee requested these analyses for discussion at its next meeting.

2. **Kidney Paired Donation**

Dr. Friedewald presented the recent work of the Kidney Paired Donation (KPD) Work Group to develop a national KPD system (Exhibit E). Dr. Friedewald explained that various aspects of the KPD system were at different stages of development. The Work Group has been working to update the Operational Guidelines of the Board approved program. Dr. Friedewald explained that public interest in KPD has heightened over the last several years so to expedite the implementation of the system, the group designed a pilot program to be administered by the OPTN Contractor. By design, there is no policy language for the interim implementation of the program to allow for flexibility in the system and to allow for changes to be made in real time as experience is gained. The small scale test run is to begin in September 2009. For the full implementation of the pilot program, the system would be fully integrated into UNetsm. Dr. Friedewald asked the Committee to become familiar with the public KPD website (<http://www.unos.org/resources/KPDPP.asp>).

The Operational Guidelines describe the rules for participating in the program. The Kidney Transplantation Committee is charged with reviewing and modifying the Guidelines in real-time in response to problems. At the August 24, 2009 meeting, the Committee was asked to modify the Operational Guidelines that were approved by the Board of Directors. The current Guidelines use the terms “high stringency” and “low stringency” to describe the antigens that a recipient is sensitized against. These terms are not intuitive. Dr. Friedewald asked the committee to consider replacing high and low stringency with the following terms:

- **Unacceptable Antigens:** those antigens to which the patient is sensitized and would preclude transplantation at the candidate’s center with a donor having any one of those antigens
- **All Other Antibody Specificities:** additional, lower level antibodies against HLA-A,-B, -Bw4,6, -Cw,-DR,-DQ and DP antigens listed that may result in a positive or negative crossmatch. The rate of positive crossmatches would be expected to be higher against donors who express these antigens.

As a result, in the KPD system, a candidate would not match with a potential donor who has the candidate's unacceptable antigens. However, a candidate would match with a potential donor who has the candidate's other antibody specificities, but the match will receive a slight point penalty as they are expected to have a higher unexpected positive crossmatch rate

Dr. Andreoni remarked that this solution would allow for center flexibility in dealing with unacceptable antigens. A member asked if the antigens had to match those listed in the deceased donor system. Dr. Andreoni explained that the KPD system is completely separate from the deceased donor allocation system and so the antigens could be different.

Following the discussion, the Committee voted on the following resolution with 22 in favor, 0 opposed, and 0 abstentions:

****Resolved that the terms "unacceptable antigens" and "all other antibody specificities" replace the terms "low stringency antigens" and "high stringency antigens", respectively, in the KPD Pilot Program.**

Dr. Friedewald explained that the June 2008 KPD Proposal stated that a candidate can match with a donor who has the candidate's other antibody specificities. A match with a donor who has none of the candidate's other antibody specificities would be favored over a match with a donor who has the candidate's other antibody specificities. However, no specific point values were assigned to other antibody specificities in the proposal. The KPD Work Group recommended that a match between a donor that has a candidate's other antibody specificities would be decreased by five points. This small decrease in the number of points will favor a match with a donor who does not have any of the candidate's other antibody specificities over a match with a donor who has one or more of the candidate's other antibody specificities. A member remarked that this approach may prohibit transplants to highly sensitized candidates. Another member countered that sensitized candidates receive such high priority (120 points) that a decrement of 5 points would not adversely affect access for sensitized candidates.

The Committee considered this recommendation with the following resolution:

****Resolved that (-5) points be assigned for a match between a candidate and a donor with the candidate's other antibody specificities in the KPD Pilot Program.**

22 in favor, 0 opposed, 0 abstentions

The last issue that Dr. Friedewald asked the Committee to consider regarded match cycles, or the time periods at which new candidate/donor pairs would be allowed into the interim KPD system. Currently out for public comment were adjustments proposed for the full system. These include points for time waiting in the KPD system and a decrease of 10 points for 3-way exchanges. Dr. Friedewald asked the Committee to apply these adjustments to the interim implementation as well. The reason for excluding match cycles in the interim implementation is that any limit on the entry of donor/candidate pairs would negatively impact the ability to fully test the system. The Committee unanimously approved this request with the following resolution:

****Resolved that the following adjustments are approved for interim implementation of the KPD Pilot Program:**

- The use of only match runs (rather than match cycle)
- Pairs accrue 2 points per match run (rather than 50 points per match cycle)
- 3-way exchanges receive 290 points (rather than 300)

Dr. Friedewald concluded his presentation by asking the Committee to recommend any additional data elements that should be collected within the KPD system. Because the process for finding KPD matches is different from the deceased donor system, the same information that is available in the deceased donor system may not be available for KPD. All results from any match runs will be saved so that data can be pulled at a later time when more KPD reports are available.

Finally, as a matter of process, Dr. Friedewald asked the Committee to consider delegating to the KPD Work Group the ability to forward the Donor Chains Proposal that was currently out for public comment to the Board of Directors. Several regions had already met and were in favor of the proposal (Regions 5, 6, 7, and 10) and the individual public comment responses were largely in favor. (28-Support, 1- Oppose, 3- No Comment). If the KPD Work Group decides that public comment is favorable, the briefing paper on the KPD Donor Chains proposal will be sent to the Kidney Committee before being sent to the Board of Directors for consideration. The Committee considered this request with the following resolution:

****Resolved that the KPD Donor Chains proposal be sent to the Board of Directors for consideration if the KPD Work Group determines that public comment supports the proposal.**

****Further resolved that the KPD Work Group is charged with responding to public comment and finalizing the proposal.**

20 in favor, 1 opposed, 1 abstention

The Committee briefly discussed the financial issues associated with KPD. Dr. Friedewald explained that a finance subcommittee has been tasked with working to identify best practices. The Committee expressed an interest in involving CMS and some private insurers in the discussions.

3. Update on Minimum Listing Criteria for Simultaneous Liver-Kidney Transplantation

Dr. Andreoni updated the Committee on the simultaneous liver-kidney proposal (Exhibit F). The proposal was to set minimum criteria for candidates to receive a simultaneous liver-kidney transplant. While the proposal was well received during public comment, the proposal is very complicated to program because of a safety-net provision. Programming the provision would require modification of all alternative systems as well as the national system. The safety net would only be used a few times per year. The Committee is now trying to simplify the proposal so that transplant centers would keep its documentation for future audit, similar to how centers keep documentation for HCC exceptions. Currently, any patient may be listed for a kidney with a liver, heart or lung and if a donor is procured locally, the kidney must be shipped with the other organ. While people liked the concept of the safety-net, it was too complex to put into the computer system (mostly due to the number of variances). The Kidney Transplantation Committee is trying to find something easier to accomplish in the interim and a

subcommittee will review other options and forward to the co-sponsoring committee (Liver and Intestinal Organ Transplantation) for consideration.