Expanding the Donor Pool:

Using Hepatitis C Positive (HCV +) Organs in Hepatitis C Negative (HCV-) Recipients

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Individuals with end-stage renal disease (ESRD) have limited long-term options: dialysis or kidney transplantation. Dialysis is life-saving, but provides limited clearance and is associated with increased morbidity and mortality (Neovius, Jacobson, Eriksson, Elinder & Hylander, 2014). Additionally, strict dietary restrictions and four or more hours on dialysis three times per week contributes to significantly reduced quality of life. For those who are eligible, transplant is often the preferred treatment option. According to United Network for Organ Sharing (2019), there are currently more than 95,000 patients awaiting kidney transplant in the United States. With this high demand and a limited supply of suitable organs, wait times are long and only continue to grow. In San Diego, the average wait time for a kidney transplant is estimated to be upwards of 8-9 years for those with blood type O. Blood type AB experiences the shortest waiting time with an average of 3-4 years. While they wait in limbo, these patients face the difficult reality that as time goes on, they run the risk of developing a serious health condition that may make them ineligible to receive a transplant.

Previous efforts to increase the number of eligible donors and organs have included donation after cardiac death (DCD) and expanding the use of Public Health Service (PHS) Increased Risk donors, but neither have been enough to make a significant impact on the waitlist as waiting times only continue to increase.

To further complicate matters, an increasing number of young and otherwise healthy adults are dying from drug overdoses as the opiate epidemic continues. This, too, has had an impact on transplantation.

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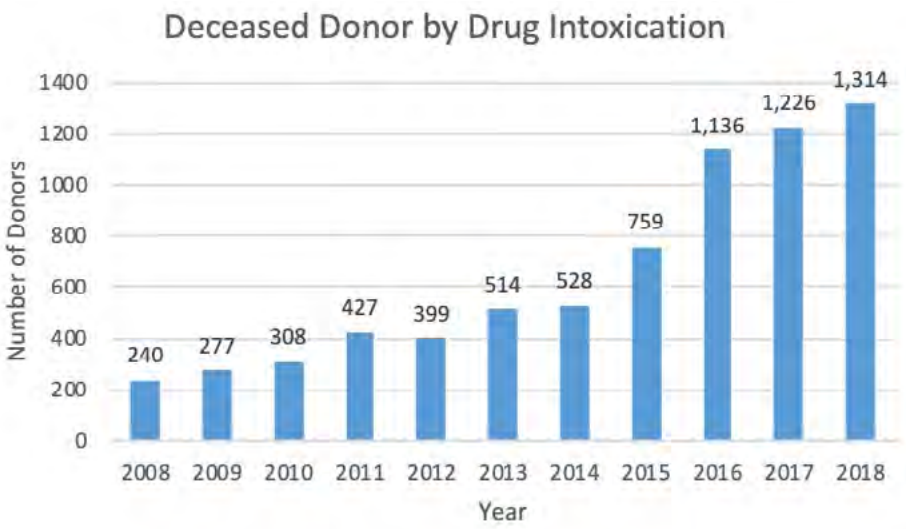

Annual cost of dialysis	$90,971
Annual costs of kidney transplant	$34,780
One time cost of antiviral drugs	$13,000 to $93,000

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In 2019 the Organ Procurement Transplantation Network reported that although drug intoxication was the cause of death for only 240 kidney donors in 2008, that number rose dramatically to 1,314 in 2018 (Figure 1). Hepatitis C infection in this population also continues to climb at unprecedented rates, with the CDC reporting in 2017 a 4-fold increase among 18-29 year olds over a ten-year period. Previous attempts at using HCV + organs were limited by poorly tolerated medication treatment regimens, low viral clearance rates, and poor patient and graft survival rates. As a result, quality organs from young HCV + donors were not even considered for transplantation.

This changed in 2014, when the arrival of direct-acting antiviral drugs (DAAs) revolutionized hepatitis C treatment. These medications have a favorable tolerability profile and provide cure rates of 94-99% following a 12-week treatment course, thus creating the opportunity to reconsider the practice of HCV + organ transplantation. Although 12 weeks of treatment is costly, ranging from $13,000-93,000 in addition to the $34,780 for the annual treatment cost for kidney transplant recipients. The national average cost of dialysis is $90,971 each year the patient is waiting on the kidney transplant list. As such, the comparative reduction in annual healthcare spending supports this initial high cost for hepatitis C treatment (Gupta, Zhang, Carroll, & Sterling, 2018).

In 2017, published data from the THINKER-1 trial demonstrated successful kidney transplantation using HCV + organs into 20 HCV – recipients. The success was based on sustained viral response at 12 weeks, stable or improved quality of life scores, and excellent kidney function in all recipients (Goldberg et al). Initially, UC San Diego Health System's Center for Transplantation began offering HCV + organs to HCV + patients that had not yet been treated with DAA regimens. With successful experience in these patients, we developed a protocol to begin offering HCV + kidneys to eligible HCV - recipients.

Prior to adding a recipient to the kidney transplant waiting list as accepting a HCV + organ, the recipient is counseled on the expected transmission of the virus and potential risk that hepatitis C may not be cleared with treatment. This is reiterated again when an offer of a hepatitis C organ is received for the recipient prior to the admission for the kidney transplant.

After transplant, there is a specific protocol for recipients who receive an organ from a HCV - donor. Polymerase Chain Reaction, or PCR, is a tool often used by labs to detect the presence of a particular gene to help identify pathogens during infection. Hepatitis C PCRs are sent on post-transplant day 3, week 1, and week 2. Once the recipient's lab results confirm they have contracted the hepatitis C virus, testing for hepatitis C genotype and

NS5A drug resistance can now be performed. These results are used to guide drug selection because certain DAAs work best with particular hepatitis C genotypes.

Since instituting the Hepatitis C protocol in January 2019, UC San Diego's Kidney Transplant Program has performed 15 HCV + kidney only transplants to HCV - recipients. The oldest kidney donor was 49 year old. Seven of the recipients are over 60 years old with three being over 70 year old. Comparing the organ quality using donor age and terminal creatinine, little difference is identified across HCV + donors versus HCV – donors. However, waiting times have been reduced on average anywhere from 5 months to 3 years, depending on blood type. Given the older age of these recipients, it is possible they may have otherwise aged out of their ability to receive a kidney transplant. At time of this publication, the kidney program has not experienced any DAA treatment or graft failures.

Though the reported waiting times are shorter for recipients willing to accept HCV + organs, the data from our center does not capture the true time-benefit, as several of our patients made the decision to accept HCV+ organs after already accruing significant amount of waiting time. Those who have seen the most significant benefit are those who face prolonged wait times, do not have living donors, and may otherwise develop sequela of long-term dialysis and jeopardize their candidacy for transplant.

The implementation of the Hepatitis C transplant protocol has been an exciting time for our kidney transplant program, and we are proud to be able to extend quality years of life for patients by making transplantation possible potentially years earlier than it would otherwise be for many patients

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