

HAVING HOPE:

how plasma exchange
is helping more
organ transplant patients

BY LORI ALEXANDER, AABB CONTRIBUTING WRITER

AT age 18, Dachia Pinkard learned she had kidney disease, and at just 21 she had renal failure. As she went through six months of dialysis, her family was tested for compatibility. Pinkard, now 41, was lucky because, unlike many African-American families, her family had no history of kidney disease. She also was fortunate in that all three of her siblings and her father matched; she received her dad's kidney Dec. 7, 1995, "a date I'll always remember," she said. An athlete since high school, Pinkard had been forced to give up the sports she loved as she endured dialysis. After the transplant, she began to feel better and soon resumed work and her favorite activities.



But in 2006, the new kidney started to fail. "I was shocked, but I knew my siblings were a match," she said. "Then they told me that my antibodies were too high because of my first transplant, and a kidney from one of my siblings wouldn't work." Pinkard began dialysis again, while dozens of friends and family members were tested for compatibility. "Each time, they told me that my antibodies were too high." As dialysis continued, Pinkard felt sick all the time — she dealt with constant nausea, vomiting, a lack of appetite and headaches. "My whole body felt like it was shutting down. All I could

do was sleep. After about a year-and-a-half, I thought there was no end in sight. The dialysis was really wearing on me. It was very discouraging." Finally, about three years after the second kidney failure, physicians at Washington Hospital Center told her about plasma exchange. "I was willing to try anything at that point," Pinkard said. Pinkard was one of 14 people who took part in a historic paired kidney exchange over four days in July 2009 at Washington Hospital Center and Georgetown University Hospital. The largest of its kind to take place in one city, the exchange involved seven individuals receiving a kidney from a

donor, but not necessarily a donor they knew. Most of the individuals needing a kidney had a friend or family member willing to donate to another person on their behalf, and two donors with no connection to any recipient also took part. Plasma exchange was used to lower the antibody counts of many prospective recipients, allowing each to match closely enough with a potential donor. Pinkard's younger brother Bryan donated on her behalf, and Pinkard received a kidney from another recipient's husband. She had four plasma exchange sessions before the transplant surgery and four postoperatively.

The kidney exchange in which Pinkard was involved was one of three exchanges that have been done in a partnership between Washington Hospital Center and Georgetown University Hospital in Washington, D.C., since 2008. In those exchanges, kidneys were transplanted into 22 people, 70 percent of whom were of a minority race or ethnicity, groups that have traditionally received kidneys at much lower rates than whites.

Several racial or ethnic disparities are related to kidney disease and transplantation, according to L. Ebony Boulware, MD, MPH, associate professor of medicine and epidemiology at Johns Hopkins Bloomberg School of Public Health. Asian/Pacific Islanders and Hispanic/Latinos are three times more likely to have kidney disease than whites, and African-Americans are four times more likely. "Minority populations are more likely to get kidney disease and much less likely to receive the best treatment, which has a significant impact on their length and quality of life," Boulware said. "Their access to dialysis is pretty much the same, but they are less likely to be evaluated for transplantation, to move up on the waiting list and to have transplantation."

Of the more than 84,000 people on the waiting list for a kidney, 61 percent are minorities; African-Americans represent the greatest percentage among the minority populations, accounting for 35 percent of all people on the list. The average wait time for a kidney is three years for whites compared with five years for blacks. Pinkard's wait was cut to about three

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Almost a year after the transplant, Pinkard is on the way back to being her old self again. "It's amazing how you feel after a transplant. All those aches and pains go away immediately. Your life changes quickly." Although she is not yet participating in all the sports she did before, she swims, bikes and uses the treadmill. She also continues to have her antibody levels checked, now about once every three weeks — a small price to pay for the freedom she enjoys.

"Without plasma [exchange], there would have been no kidney exchange. They are able to save so many more lives with it," she said.



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years because of plasma exchange. "If it wasn't for [this procedure], I'd still be on the waiting list," she said.

One reason for the delay in transplantation among minority populations is the lack of minority-donor kidneys, which provide the best match. In general, people are more similar genetically to others of their same race or ethnicity, making the success rate of transplantation greater when kidneys are matched between members of the same racial or ethnic group.

Many minorities are unwilling to be organ donors because of either a lack of trust in the organ donation process or spiritual or religious beliefs, Boulware said. As a result, there are fewer cadaver kidneys for minorities in need of a kidney. Furthermore, minority individuals have the worst outcomes with cadaver kidney transplants, according to J. Keith Melancon, MD, director of the Kidney and Pancreas Transplant Program at Georgetown University Hospital, one of the co-leaders of the transplant teams involved in Pinkard's exchange. "However, African-American individuals have good outcomes with living-donor

kidney transplantation; the outcomes are almost the same as for white individuals," Melancon said. Living-donor kidney transplantation is preferable, but that too represents a challenge.

The issue of renal disease and kidney transplantation in the African-

American population is a vicious cycle. Because the incidence of renal disease is highest in this population, the pool of potential donors is decreased. "So these individuals have the most trouble getting a living donor to begin with," Melancon said. Adding to the

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challenge is the fact that high levels of HLA antibodies are more frequent among African-Americans and other minorities, making it even more difficult to find a compatible donor.

“Approximately 25 percent of the individuals on the kidney waiting list have high levels of HLA antibodies, and African-American individuals represent a disproportionate number of these individuals,” said Jimmy Light, MD, director of transplantation services at Washington Hospital Center and the other co-leader of the transplant teams involved in Pinkard’s exchange.

Another problem is that antibodies continue to build up as an individual receives dialysis and waits for a suitable donor match. “The longer an individual is on the waiting list, the more likely he or she is to have antibodies build up because of dialysis. The filters in the dialysis machine activate T-cells to become more sensitized. Transfusions and infection also cause antibodies to increase,” Melancon said. As was the case with Pinkard, antibodies also can build up after kidney transplantation, making it more difficult to find a suitable match if a subsequent transplant is needed.

“Many minority individuals languish on the waiting list for several years because of the large number of incompatibilities that makes finding a suitable donor for them very difficult,” Light said.

Plasma exchange has been used for more than 40 years as treatment for various types of nephritis. Melancon first used the procedure in association with kidney transplantation during his fellowship in the transplant department at the University of Minnesota from 2002 to 2004. At that time, he explained, plasma exchange and immunosuppression with intravenous immunoglobulin were used after kidney transplantation as treatment for antibody-mediated (humoral) rejection. Researchers subsequently discovered that using this approach before transplantation to reduce antibodies could decrease the likelihood of rejection.

Melancon brought his expertise with plasma exchange to Georgetown University Hospital in 2008. Before then, the procedure was rarely used with transplantation in the D.C. area, according to Light. Donor matching relies on compatibility in terms of both blood type (ABO) and HLA phenotype.

Light noted that sophisticated testing in the HLA lab is key to finding both compatible donors and donors with lesser incompatibilities that can be managed with plasma exchange and immunosuppression. Furthermore, more precise and more sensitive definitions of these antibodies allow for better monitoring after transplantation. When antibodies against the donor are identified, the levels can be lowered by plasma exchange before damage to the transplanted kidney occurs.

Research has provided cutoffs for ABO incompatibility, but those for HLA antibodies are not as well-defined, said Kirsten Alcorn, MD, medical director of transfusion services at Washington Hospital Center. “If you’re manipulating the immunology of an individual, you’re more likely to be successful with a lower number of antibodies.”

“In the transplant setting, plasma exchange is used for a short period of time, and most patients tolerate the procedure very well,” Alcorn continued. “It’s really a wonderful way to expand the pool of potential donors.” Pinkard described the plasma exchanges as “just like dialysis only not painful.”

Individuals typically undergo two to four plasma exchange sessions with immunosuppression before transplantation and again after transplantation. Postoperative plasma exchange is critical because the body makes more antibodies within 48 hours after transplantation, Melancon explained. He also noted that the plasma exchange protocol he follows is stricter than those used at many transplant centers. “We aggressively look for signs of rejection, which allows us to address



the problem early." Monitoring for the number of antibodies is carried out monthly for the first year and at three- to six-month intervals during the second year and beyond. In addition, histologic evaluation of a biopsy sample taken from the transplanted kidney is done at one, six and 12 months during the first year. "I believe the success at our center is a result of this entire protocol," he said.

Melancon noted that plasma exchange and immunosuppression offer a significant survival advantage compared with continuing on dialysis and cut the rate of humoral rejection in half. However, the procedure is not without risk. "There is a higher risk of infection because you're pushing down both B and T cells with the immunosuppression," he explained. "Therefore, you can't safely use this procedure in individuals at high risk for infection."


The procedure also is expensive, but not when the financial costs of alternatives are considered. Melancon

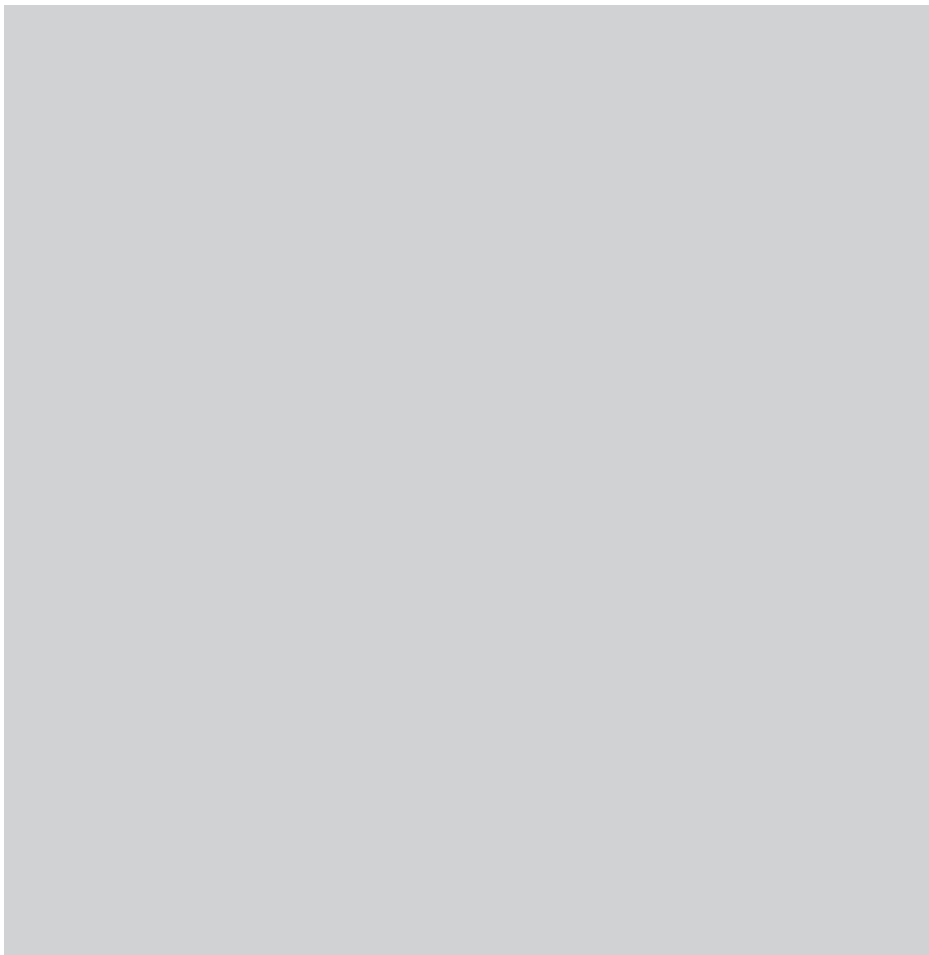
points out that dialysis costs approximately \$70,000 to \$80,000 a year and a kidney transplant (including one year of follow-up care) from \$100,000 to \$250,000. The break-even point for a transplant comes between two and three years, he said. There are additional cost savings related to the productivity of individuals who can return to work after transplantation and do not need to collect disability payments.

Melancon began efforts to increase the rate of transplantation among minority populations in Washington, D.C., a good fit considering the area has a large African-American population and the highest rate

of end-stage kidney failure in the United States. Six thousand people in the metropolitan area are on dialysis; approximately two-thirds of this group are African-American.

Overall, about 200 to 250 kidney transplants are done each year at all hospitals across the city. "We hope to double that number of transplants by using plasma exchange and kidney exchanges," he added.

"We have to provide every possible option for transplantation," Melancon continued. "Plasma exchange has enabled us to take away some of the barriers of living-donor kidneys for minority individuals." 



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