

## *Art and Pat Joseph—New Immunosuppressant Approaches to Kidney Transplantation*

**H**usband and wife Art and Pat Joseph are a perfect match in more ways than one. In 1990, at age 26, Art was diagnosed with a serious kidney disease, called focal segmental glomerulosclerosis, or FSGS. FSGS describes the regional scarring or hardening of a portion of the million or so tiny clusters of looping blood vessels, or glomeruli, that serve as filters within the kidneys. These glomeruli are essential for processing about 400 quarts of blood a day to sift out an estimated two quarts of waste products and extra water that eventually leave the body as urine. FSGS hampers the filtering process. The bottom line is that most patients with the disease progress to kidney failure, often referred to as end-stage renal disease (ESRD), within five to 20 years after diagnosis. In Art's case, 11 years passed from the time he was diagnosed until the time he was in desperate need of a kidney transplant. But thanks to a loving wife able to give one of her kidneys to her husband, as well as NIDDK-sponsored scientific research that has led to advances in immunosuppressant drug therapies to prevent rejection of transplanted organs, this is a story with a happy ending.

### THE SIGNS AND SYMPTOMS OF GLOMERULAR DISEASE

There are several warning signs that can signal glomerular disease, including:

- Large amounts of protein in the urine (proteinuria), which may cause foamy urine.
- Blood in the urine (hematuria), which may cause urine to be pink or cola-colored.
- Inefficient filtering of waste from the blood.
- Low blood protein (hypoproteinemia).
- Swelling in parts of the body (edema), including hands and ankles, especially at the end of the day, or around the eyes when awakening in the morning.

Often, however, these symptoms go undetected.



*Art Joseph (right) was diagnosed with serious kidney disease in 1990. He successfully received a donor kidney from his wife Pat two years ago, under a newly developed transplantation protocol. The two are now counselors for other patients considering the procedure, and look forward to “traveling and growing old together,” as Pat says.*

Such was Art's case. Had it not been for a medical exam while he was stationed in Japan with the U.S. Navy, the then Petty Officer Second Class may never have learned that he had FSGS until years later. “They discovered large amounts of protein in my urine,” says Art. A biopsy of his kidneys led to a confirmed diagnosis of FSGS. To decrease the protein in his urine and improve his kidney function, Art was placed on a cortisone-like steroid to reduce kidney inflammation. However, steroids can promote insulin resistance in a significant number of patients. Six weeks after being put on steroids Art was in a near coma in a Scottish hospital, the result of steroid-induced type 2 diabetes. “I

## PATIENT PROFILE

was feeling real bad, so my wife made me go to the doctors,” he says. A glucose test indicated Art’s sugar level to be off the charts—856 (normal blood sugar levels are between 60 and 110 if an individual is fasting, and between 80 and 120 following a meal). He was immediately taken off steroids and given daily injections of insulin to control his sugar level. Within weeks his glucose started to come back into the normal range, and within six months he no longer needed to take insulin. For a while, life for Art returned to almost normal.

### DIAGNOSING KIDNEY DISEASE

Urinalysis provides information about kidney damage by indicating levels of protein and red blood cells in the urine. Blood tests measure the levels of waste products such as creatinine, a waste product in the blood that results from the normal breakdown of muscle (healthy kidneys filter creatinine from the blood), and urea nitrogen to determine whether the filtering capacity of the kidneys is impaired. If these lab tests indicate kidney damage, a doctor also may recommend ultrasound or an x-ray to see whether the shape or size of the kidneys is abnormal.

### LIVING WITH THE DISEASE

As kidney function becomes impaired, most people with a glomerular disease, including FSGS, lack energy, feel listless, and lose their appetites. Many must periodically take time off from work. Fortunately for Art, aside from regularly scheduled exams to monitor his kidney function and having to take medication to control his blood pressure, he was able to go for years without any fundamental lifestyle changes. “I continued to work, play football, basketball, lift weights, ride my bike,” he says. “My doctors were amazed that I was able to sustain such a high activity level for so long.” But over time, the disease started to take its toll. In 1994, Art’s creatinine level started to creep up, and by 1999, it was obvious that Art would require a kidney transplant within a year. Once again, Art was extremely fortunate. When they learned of his need, about 20 of his friends and relatives said they would be willing to donate one of their kidneys to him. As fate would have it, tests showed that

a kidney taken from Art’s wife, Pat, would be the best option. Despite the risks, including a slightly increased risk of high blood pressure or kidney failure of her own, Pat says, “I was delighted to learn that mine was the best match, and I never gave donating one of my kidneys to Art a second thought.”

### FACTS ABOUT KIDNEY DISEASE AND TRANSPLANTS

In recent years, National Basketball Association superstars Alonzo Mourning of the Miami Heat, and Sean Elliot of the San Antonio Spurs (retired) have raised awareness of kidney disease as a result of their being diagnosed with focal segmental glomerulosclerosis (FSGS). The facts are:

- More than 50,000 Americans die each year because of kidney disease.
- More than 260,000 Americans suffer from chronic kidney failure, and to stay alive require either an artificial kidney machine (dialysis) or a kidney transplant.
- More than 35,000 patients are waiting for kidney transplants, but only about 11,000 will receive them this year because of a shortage of suitable organ donors.

### TYPES OF KIDNEY DISEASE

**Glomerular diseases—including glomerulonephritis (inflammation of the membranes in the kidney), and glomerulosclerosis (scarring or hardening of the tiny blood vessels within the kidney)—interfere with the kidneys’ ability to filter body fluids. Focal segmental glomerulosclerosis (FSGS) refers to a regional glomerulosclerosis of the kidney. All can lead to kidney failure, or end-stage renal disease (ESRD). These diseases may be the direct result of an infection or a drug toxic to the kidneys, or may result from diseases that affect the entire body, like autoimmune diseases such as type 1 diabetes or lupus.**

### NEW EXPERIMENTAL PROTOCOL

But Art and Pat Joseph were faced with yet another major decision. Once transplanted with his wife's kidney, Art could decide to either go on a standard therapy of immunosuppressant drugs, which includes steroids, to prevent his body from rejecting the new organ or undergo a new protocol developed by NIDDK researchers. "Because I already had had an episode of steroid-induced type 2 diabetes, if I chose the standard therapy I ran a fifty-fifty chance of becoming a life-long diabetic," says Art. He and Pat talked it over. Another major consideration was the fact that he would be only the second person to undergo the new protocol. They decided on the new protocol. Art's case was immediately transferred from Walter Reed Army Hospital to NIDDK. Tests showed that he was a good candidate for the new protocol, and his transplant took place February 8, 2000.

Art was treated using a new approach to kidney transplantation. Researchers at NIDDK have hypothesized that one of the main reasons that people reject a kidney transplant is that the immune system is activated by the surgical trauma necessary to put the new kidney in. Since the immune system has evolved to protect people from infection at the time of injury, it is likely that there are trauma-associated triggers that spur on the immune system to seek out foreign tissue. Thus, if the immune system could be sequestered until the trauma from the surgery was healed, NIDDK researchers postulate that the rejection response will be greatly reduced and controlled with a minimal amount of immunosuppression, hopefully avoiding the need for steroids and other harmful drugs.

As part of a new treatment protocol, Art received an experimental drug called Campath-1H. This drug temporarily removes T cells (the cells that cause organ rejection). Rather than putting Art on multiple anti-

rejection medications from the start, he was given no medication, watched closely, and placed on the amount of immunosuppression necessary only when the Campath effect wore off. For Art, that was a single daily dose of a liquid called sirolimus. He did not need steroids or cyclosporine. As this document goes to press, Art is two years from his transplant and has had no signs of rejection. He has required about 15 percent of the immunosuppressive drugs that he would have received under standard therapy. Importantly, given his history, he has not required any steroids.

Today, Art, who received a medical discharge from the U.S. Navy in 1996 and now works at the Office of Naval Intelligence in Suitland, Maryland, says that he is "back to normal." Other than having experienced a slight fever immediately after the first dose of the drug protocol, he says he has had no other side effects. "The only kidney medication I take is a liquid called sirolimus, which I drink each morning with orange juice to slow down the activity of my white blood cells," says Art. "I went back to work three weeks after my transplant. I could have gone back in two, but my wife and mother didn't want me to," he adds.

Art and Pat now volunteer as counselors for other patients who are considering undergoing the new protocol for organ transplantation. "We were treated wonderfully by everyone at NIDDK," says Pat, who adds that her operation to donate her kidney went flawlessly. "They answered whatever questions we had and were available to Art and me all hours of the day and night. Counseling others is our way to give something back." Since the transplant, Pat, who will be retiring from the Navy in a few years, says she's more protective of and feels a closer bond to her husband. "I can now look forward to our traveling and growing old together," she adds happily.