Illustration by Laura Aitken

When the lights of health go down

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The perception of an illness changes when the doctor becomes the patient, as I learned when I developed a medically incurable disease. It began as an intermittent, dry, hacking cough—more an annoyance than a concern—until it became persistent. I had been in good health, although recently on two occasions, I became unusually winded while swimming laps and had to hold on to the side of the pool to catch my breath.

I consulted a medical colleague, who other than the swimming episodes, found nothing of concern in my history; however, on physical examination he heard crackles over my posterior lung bases. There were diffuse bilateral infiltrates on my chest X-ray and on the high-resolution CT scan, which also showed "honey comb" cystic changes and traction bronchiectasis at the periphery of the lower lung fields. My pulmonary function tests showed both a reduced total lung capacity and a functional residual capacity. As the conflation of my clinical symptoms, imaging studies, and pulmonary function tests snapped into focus, I realized that I had idiopathic pulmonary fibrosis (IPF), a progressive, interstitial lung disease with a median survival of approximately three years.[1] The moment hung there, as the spectrum of the disease filled my mind, leaving me with a sense of entrapment. Like normal

people, I took a breath about 20,000 times a day and never thought about it, but from the time I was diagnosed with IPF it seemed that breathing was all I thought about.

The disease

Although the cause of IPF is unknown, there are known risk factors, such as men of advanced age, a history of inhaling environmental irritants, such as tobacco smoke, asbestos, stone or mineral dusts, or agricultural aerosols; or past treatment with ionizing radiation or certain therapeutic drugs. Like most patients with IPF, I had none of these risk factors. In the United States, the incidence, prevalence, and age adjusted mortality rate of IPF have increased over the last decade, and will continue to do so as the population ages.[2,3]

In the early stage of IPF, histologic sections show patches of fibrosis amid a bed of normal lung tissue, but as the disease progresses it destroys wide swaths of lung, including the membranes across which oxygen diffuses into capillaries. Lung biopsy provides the definitive diagnosis of IPF, but because the procedure may accelerate the disease, many physicians forego lung biopsy in patients, such as I, who have a typical clinical picture and characteristic imaging studies.[4]

The natural history of IPF is variable. From 5 percent to 15 percent of patients, most often men with physiological and functional evidence of severe disease, have a rapidly progressive course and die within weeks or months of diagnosis; conversely 20 percent to 25 percent of patients live five years or longer.[5,6] In the majority of patients, the disease pursues an indolent but relentless course, ending in death from respiratory failure within three to five years.[1]

The clinical course

In my case the question was not the diagnosis, but the velocity at which the disease would progress. My physician emphasized the importance of maintaining a blood oxygen saturation above 90 percent, so I purchased a digital pulse oximeter. As the disease progressed, and my exercise tolerance decreased, I found it difficult to maintain my oxygen saturation at the desired level. Foolishly, not wanting to walk around in public tethered by nasal cannulas to an oxygen canister—which I should have done—I developed an alternate strategy. If my oxygen saturation dropped below 90 percent I would stop walking and pretend to talk on my cell phone; after my oxygen saturation rose above 90 percent I would continue on. In time, I would pay a price for this behavior.

The progression of my disease was monitored by pulmonary function tests, including spirometry and lung volume studies, and a six-minute walk test that measures endurance, distance walked, and concomitant changes in oxygen saturation. Although my initial tests showed mild dysfunction they progressively worsened, and I realized that my purchase on life was dwindling.

I had to decide either to do nothing and let my life play out—not an unreasonable decision, considering that I was more than 76 years old—the average life expectancy for white American males—or to consider treatment with an unproven experimental drug, or the rather drastic option of lung transplantation, the only cure for IPF.

The treatment

I learned that the efficacy of two drugs, pirfenidone and nintedanib, was being evaluated in clinical trials of patients with IPF. I tried to enlist in each trial but the advanced stage of my disease made me ineligible. Based on the results of the two trials, which showed a significant decrease in the decline of forced vital capacity and a trend toward lower mortality, the FDA approved each drug for the treatment of patients with IPF.[7,8]

The lung was the last major, vital, solid organ to be transplanted successfully. In 1963, Dr. James Hardy (AΩA, Raymond and Ruth Perelman School of Medicine at the University of Pennsylvania, 1941) performed the first unilateral lung transplant at the University of Mississippi. His patient lived 18 days.[9] In 1968, Dr. Fritz Derom from Ghent, Belgium, performed a unilateral lung transplant in a patient who lived 10 months.[10]

Over the next two decades there were multiple attempts at lung transplantation, but it was not until 1986 that Dr. Joel Cooper (AΩA, Washington in St. Louis School of Medicine, 1998, Faculty), of the Toronto Lung Transplant Group, reported long-term survival in patients transplanted with a single lung.[11] Two years later, Dr. Alexander Patterson, also of Toronto, described the first en bloc transplantation of both lungs, an operation that was subsequently modified to one where the right and left lungs were transplanted sequentially.[12]

Following the Toronto reports, lung transplantation was adopted worldwide. Fortunately, Dr. Cooper and Dr. Patterson were recruited to the Division of Cardiothoracic Surgery at Washington University where I chaired the Department of Surgery. They established one of the first successful lung transplantation program in the United States. I used to marvel at seeing their patients, near death one day, casually walking around the hospital a few days after a lung transplant. Little did I know that Dr. Patterson's

life and mine would intersect over two decades later.

Based on Organ Procurement and Transplantation Network (OPTN) data from 2016, surgeons in the U.S. performed 19,060 kidney transplants, 7,841 liver transplants, 3,191 heart transplants, and 2,327 lung transplants.

Lungs are suitable for transplantation in fewer than 20 percent of organ donors. This is primarily due to damage from the catecholamine storm that occurs during brain death, and to the abrasion, microbial infestation, and gastric reflux that occur during intubation and mechanical ventilation at organ procurement.

Because of the life time exposure to environmental pathogens, the lung, like skin and intestine, has a heightened immune response to foreign antigens, thus lung transplant recipients, compared to recipients of other organ grafts, have a higher incidence of acute and chronic rejection, and a shorter overall survival. According to OPTN data from 2008 to 2015, the five-year survival of patients receiving lung transplants was 53 percent, compared to 79 percent, 78 percent, and 73 percent for patients receiving kidney, heart, or liver transplants.

There has been controversy regarding the age limit for lung transplant recipients. One study found that from 2006 to 2012 there was no significant difference in one-year post-transplant survival among patients older or younger than 70 years of age; however, there were marked differences in survival at three years (49 percent in patients over 70 years, compared to 64 percent in patients younger than 70 years), and at five years (28 percent compared to 48 percent).[13] Professional medical societies have not endorsed an upper age limit as a contraindication to lung transplantation, but adults older than 75 years of age are unlikely to qualify as candidates because of associated comorbid conditions. There is a report of a lung transplant in an 81-year-old man with IPF.[14]

I was reluctant to proceed with a lung transplant for several reasons. I was 77-years-old and knew the risks associated with the procedure, and the potential chronicity of postoperative recovery, especially if things did not go well. Also, I was seronegative for cytomegalovirus (CMV). Activation of CMV, a common opportunistic infection in immunosuppressed lung-transplant recipients, is associated with acute and chronic rejection, as well as early and late mortality. Considering that the seroprevalence of CMV ranges from 50 percent in individuals 20 years to 29 years of age to 90 percent in individuals 70 years to 79 years of age, I was likely to receive a lung from a CMV positive donor, putting me at risk for an active infection.[15]

There were also societal and ethical issues to consider. Given the scarcity of organ donors, was it right for me to have a lung transplant, and a less than 50 percent chance of surviving five years, or for a younger patient with a dependent family to receive the transplant and have a chance of prolonged survival? I wrestled with this question, but reasoned that I had been active and functioning well before the illness, and had unfinished work to complete. I also had an innate desire to stay alive.

To be certain that I was in sound physical condition, I had several studies, including hematology and metabolic profiles, cardiac catheterization, ultrasound of the carotid arteries and abdominal aorta, 24-hour monitoring for gastric reflux, colonoscopy, and physical strength tests. There proved to be no contraindication to my being a transplant candidate, so with the consent of my family, the approval of my physician and surgeon, and with an amalgam of despair, reservation, hope, and optimism, I was added to the transplant list. I began a required rehabilitation program to ensure that I was in optimal physical condition and could withstand the operation and possible perioperative complications.

By the middle of my second year from diagnosis I required intermittent supplemental oxygen and by the end of that year, I needed oxygen 24 hours a day; 30 liters a minute when I showered or walked to the breakfast table, and 50 liters a minute, straight from the wall source, when I walked slowly on the treadmill. The worsening of the disease, along with the waiting, brought on severe depression. I wasn't at my lowest, but I was heading there and exploring a depth of despondency that was new to me.

As I entered the end stage of my disease, I had no appetite, had lost 40 pounds, had no exercise tolerance, and was totally dependent on my wife, who was burdened with pushing me around in a wheelchair. In my age group, the average waiting time from candidate listing to transplantation is 186 days. I was on the list for 210 days; this was partly due to my choosing to wait for a CMV negative donor. As the disease progressed and my condition worsened I waived this option.

The donor

As typically happens in organ donation, a tragic event at a remote site intersected with my deteriorating state. Early on a Sunday morning, one week after my 78th birthday, I received a call from the transplant coordinator telling me that lungs were available from a "high-risk" donor.

Ten percent of organ donors are considered high-risk because their life style increases the likelihood that they will transmit hepatitis B, hepatitis C, HIV, or other

infectious agents. Care is taken in screening donors to minimize the chance of such an such an occurrence, and the medical center where I was treated had had no case of such disease transmission in a transplant patient. The lungs were in excellent condition and, surprisingly, the donor was CMV negative. I agreed to accept the lungs.

In some ways, organ transplantation is like a lottery. The transplanted lungs need to be the right size and in sound physiological condition, and the donor and recipient need to be ABO blood group compatible; otherwise, there are no exclusion criteria, although a favorable histocompatibility match between the donor and recipient, and other factors, currently unknown, influence how the transplanted organ will get along in its new host.

The transplant

At the hospital, I was in the preoperative area talking with the anesthesiologist while she put in an epidural block. She asked me if I could taste anything, concerned that the anesthetic might have entered my blood stream. I said "no," and then remembered nothing else until I awoke in the intensive care unit.

During seven hours in the operating room the pulmonary wreckage was removed and a new pair of lungs were masoned in. The operation was uneventful except that I was found to have pulmonary artery hypertension, which required cardiopulmonary bypass. The pulmonary artery pressures, normal at cardiac catheterization 12 months earlier, had increased, most likely because I failed to use supplemental oxygen judiciously during the early stage of the disease.

After surgery, I was in the recovery room for 24 hours, and then, harnessed to intravenous lines, catheters, and an assortment of monitors, I was moved to the step-down unit. The apprehension, anxiety, and depression present before the operation, began to melt when I awoke with pink mucous membranes, a heightened mental alertness, and an oxygen saturation of 99 percent on room air. After one day, I moved to the main hospital.

My recovery was uneventful, except for a brief period on the morning of the third postoperative day when I saw platoons of red ants marching on the ceiling. I pointed out this unusual drill formation to the nurse who was taking my blood pressure. She denied seeing the ants and explained that temporary hallucinations often occur in postoperative patients. As she predicted, the ants disbanded by late afternoon to bivouac elsewhere.

During the first few days, I walked progressively longer distances in the ward hallway, and on the fifth postoperative day I began walking on the treadmill. On the eighth postoperative day I went home, and within a week I was walking the sidewalks in the neighborhood.

Like most patients recovering from a life-threatening illness, I wanted to know something about my prognosis, but when I asked the pulmonologists and surgeons about this on postoperative visits, there was always a quick deflect. Given the unpredictable outcome of patients receiving a lung transplant, I understood their guarded responses and quit asking.

The donor's family

Before discharge from the hospital I asked the transplant coordinator what she knew about my organ donor. She said, "All I can tell you is that your donor was a 26-year-old white male who was brain dead."

While recuperating at home, thoughts of the donor replayed in my mind. What kind of person was he? How had he died? What influenced his family to declare him an organ donor?

Some donor families do not wish to hear from the recipient, feeling that such communication would sustain unbearable memories of their loss. Most families, however, appreciate hearing from the recipients or their families. One would expect an outpouring of gratitude from deathly ill patients who receive a life sustaining transplant; however, less than half of recipients write to thank the donor family for the gifted organ.

Wanting to contact my donor's family, I followed the transplant center protocol and over several months exchanged anonymous letters with my donor's mother. Once we were allowed to exchange contact information, I phoned her and told her how grateful I was to have received her son's lungs, and be alive. I said that I would like to meet her, and thank her in person. She said that she would welcome my visit.

On a spring day, under a cloudy, bruised Missouri sky, I drove southwest to a rural community more than 300 miles from St. Louis. I arrived at the mother's apartment complex before the scheduled time of our meeting and sat in my car going over what I was going to say to her. When I saw her step from her apartment onto the sidewalk, I got out of the car to introduce myself. My attempt to shake hands turned into a hug, as she cried softly and said how much she appreciated my coming. Within the first moments of our meeting, I sensed the permanency of her deep grief at losing her son.

Over coffee in her apartment, she told me that because her son was smaller than his grammar school classmates

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he had been the target of jokes and ridicule. After the eighth grade, she home-schooled him, and he received a General Education Diploma. He began work as a dry wall contractor; however, it was a time in his life when he was vulnerable to the lure of an ominous attraction, and "He got in with the wrong crowd and began using drugs." He was arrested twice and incarcerated in federal prison for producing, selling, and using methamphetamine. Upon release from his second imprisonment, he resumed his habit, and would have been homeless had not his mother, brother, and two sisters cared for him. He lived intermittently, and in rotation, with each sibling—an arrangement that one described as "living with a tornado."

Shortly after moving in with his older sister, he became violent and drew a pistol. When she threatened to call the police, he walked into an adjacent room and shot himself in the right temple. He was transported to a trauma center where after failed resuscitation he was pronounced brain dead. His mother granted permission for him to be an organ donor, something that she had never discussed with him, but knew it was what he would have wanted. He was transported by helicopter to the Midwest Transplant Service where his organs were procured, and his lungs were sent to a hospital 15 minutes away—where I waited.

It is extremely difficult for a family, grieving the loss of a loved one, to be confronted with the decision of organ donation. The gifting of organs is one of the most delicate social transactions, which does not take place in an atmosphere of warmth and gaiety, such as that surrounding family members in their exchange of holiday gifts; rather it occurs under the most impersonal and stressful circumstances, where the donor and recipient are unknown to one another, and a surrogate acting on behalf of the donor makes the decision to gift the organs. Federal law prohibits payment to an organ donor's family, recognizing the perverse incentive that might stimulate one family member to take the life of another for monetary gain. Such payment would also be an incentive for a poor individual to sell a paired organ to a wealthy recipient. The organ procurement center, the hospital, and medical personnel caring for the patient receive payment for their services, and it seems unfair that the donor's family receives nothing, especially in cases where homicide can be excluded as a cause of death.

I had lunch with the mother and her other son, but her two daughters were not ready to meet me. I did meet them on a second visit, and the family and I had a pleasant lunch together, during which there was no mention of the deceased sibling, although, the fresh memory of his tragic ending permeated the atmosphere surrounding us. In the parking lot, after we left the restaurant, the younger sister showed me a commemorative tattoo occupying most of her right arm. She had planned to have her deceased brother's ashes blended into the ink for the tattoo, but ultimately decided not to do so. The children had stable and productive lives, and were close to, and protective of, their mother.

On a third trip, I visited the mother's new home, situated in a copse of hardwoods adjacent to an expanse of farm land. Her deceased son's remains were buried on the property, and she told me that every day she visited his grave and wept.

My gratitude to the donor family continues unabated. In more ways than one I have become part of them.

Epilogue

I write this near the fifth anniversary of my operation, and think back to the time before surgery, when I was told that if I had a lung transplant I would be exchanging one set of problems for another, as if the two sets were evenly balanced. For me, lung transplantation has been a resurrection. I am fully functional and back at work, yet ever mindful of the natural history of patients with lung transplants, especially those in my age group. I keep looking over my shoulder knowing that I am being stalked by the sinister triad of chronic graft rejection, malignancy, and vital organ damage from prolonged immunosuppression.

I am deeply grateful and appreciative for the donor and

his family. I am also indebted to the many unfortunate patients who died during the early attempts at lung transplantation, and how their sacrifices led to the ultimate success of the procedure, due primarily to the creative work of surgeons at the University of Toronto. I am indebted to the doctors and nurses who cared for me. They went about their highly complex work with a default setting of competence and disarming ease that only comes from long hours of study, hard work, and repetitive technique refinement. I know and respect the primary surgeon and pulmonologist who cared for me. They have been in lung transplantation from the beginning, and I am alive because of their knowledge and expertise.

Throughout the ordeal, my wife and two daughters were ever present, especially during the postoperative period, when their care and concern helped to shorten my hospital stay and recovery.

Since my transplant, I have often thought about the brief time period from the conception of organ transplantation to its wide application as an established therapy. It is a miraculous story of advances in basic biology and immunology, drug development, surgical technique, critical care, and sensible government regulations. The five-year survival of patients receiving organ transplants for end stage kidney, liver, or lung disease, is nearly ten times higher than the five-year survival of patients treated for end stage cancer of the kidney, liver, or lung.

On the day that I write this, 75,513 listed patients are awaiting an organ transplant, yet year-to-date only 23,091 patients have received a transplant from 10,869 organ donors. Every 10 minutes someone new is added to the transplant list, and every day 22 patients die for lack of an available organ.

Knowing that organ transplantation yields such high success rates, one can only wonder, where are all the organ donors? It is imperative that more citizens become organ donors if we are to save the lives of desperately ill patients awaiting a transplant. The success of the smoking cessation program in the U.S. saved thousands of lives, and is a case study in behavioral modification. We need a similar national program to increase the number of organ donors.

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