# How Death Becomes Life

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*Notes from a Transplant Surgeon*

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*For G, S, K, and P.*
*And for the donors, living and dead.*
*You are true heroes.*

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# Note from the Author

The following book is neither a memoir nor a complete history of transplantation. I am not old enough to write a memoir, and a few excellent complete histories of transplantation exist already (and are listed in the bibliography). My goal is not to provide a chronological depiction of my coming-of-age as a surgeon, but rather, to use my experiences and those of my patients to give context for the story of the modern pioneers who made transplantation a reality.

The remarkable events that allowed mankind to successfully transplant organs between two individuals that are not genetically identical occurred relatively recently. In the early 1950s, the idea of transplantation remained in the realm of science fiction. By the late '60s, multiple organs were being transplanted, with a few poignant successes and many failures. True success with organ transplantation was realized in 1983, with the approval of cyclosporine. These accomplishments were achieved on the backs of a relatively small number of truly incredible people.

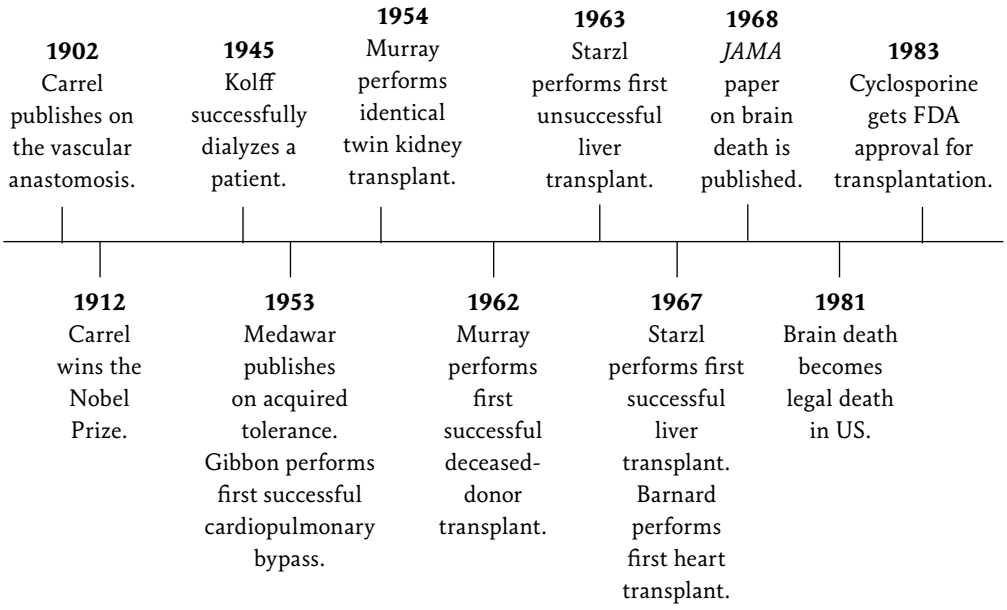
My own training began with four years of medical school at Cornell University Medical College in New York City. I then did my surgical internship and first year of residency at the University of Chicago Hospital and Clinics. After that, I spent the next three years performing transplantation research at Massachusetts General Hospital. I then returned to the University of Chicago for three more years of surgical residency. Thereafter, I came to Madison, Wisconsin, where I completed a two-year fellowship in organ transplantation. I have

been in Madison ever since, performing organ transplants and running a basic science lab studying the immune system.

By illustrating what it took for me to practice transplantation, and by painting a picture, with the stories of my patients, of how the discipline has touched so many, I hope to highlight the incredible gift transplantation is to all involved, from the donors to the recipients to those of us lucky enough to be the stewards of the organs. I also will show the true courage of the pioneers in transplant, those who had the courage to fail but also the courage to succeed.

All the details in this book are historically accurate and factual to the best of my knowledge, with some minor patient details changed in a few cases to protect the identity of an individual, if requested.

# Milestones in Transplantation



# Part I

# Out of Body

I have great respect for the past. If you don't know where you've come from, you don't know where you're going. I have respect for the past, but I'm a person of the moment. I'm here, and I do my best to be completely centered at the place I'm at, then I go forward to the next place.

—MAYA ANGELOU

We are not makers of history. We are made by history.

—MARTIN LUTHER KING JR.

# 1

# A Perfect Organ

*In a Small Plane over the Hills of La Crosse, Wisconsin,*
*September, 2:00 a.m.*

While I'd been on planes many times, I'd never experienced the full power of a thunderstorm at ten thousand feet. The small King Air, a six-passenger dual prop, was bouncing around uncontrollably. Every few seconds, it would go into free fall and then hurl itself back up violently. The two pilots in the cockpit were hitting knobs and dials, trying to silence the various alarms that sounded as we rocked violently back and forth. It didn't help that our physician's assistant Mike, who had been on hundreds of flights in small planes before, was screaming uncontrollably, "We're gonna die! We're gonna die!"

Given that Mike was such a seasoned member of our team, I could only assume that this particular flight was going badly. When the pilots glanced back to see the source of the screaming and cursing, I could make out the fear in their eyes. I looked at the spinning altimeter and noted that our plane was popping up and down as much as a thousand feet at a time. Outside the window, the lightning was shooting horizontally. The rain was constant and loud, and I was sure I heard pieces of hail hitting the windshield.

IT WAS THE third month of my transplant fellowship at the University of Wisconsin. I hadn't chosen transplant surgery so I could fly through thunderstorms in the middle of the night over the fields of central Wisconsin. Hell, I'd grown up in New Jersey, spent most of my life in the Northeast, and had never known anything about the Midwest. I had been drawn to Madison because it is one of the best places to be a transplant fellow. I was learning how to perform kidney, liver, and pancreas transplants, and how to take care of these complicated patients while they waited for organs and then recovered from their surgeries.

One unique part of the discipline of transplantation is the procurement of organs from donors. While we do perform transplants, particularly kidneys, with organs from living donors, the majority comes from people who have just died. Rather than transporting donors, who typically remain on a ventilator, brain dead but with a beating heart, we send a team out first, to meet with their families to thank them for their gift and then to perform the surgery to remove their organs. We then take those organs back for transplant into waiting patients.

On this particular day, I'd received a phone call at around 5:00 p.m. telling me to come to the OPO (organ procurement organization) at 9:00 p.m., for wheels up at 9:30. The thirty-minute flight from Madison to La Crosse had been without incident. We arrived at the donor hospital at around 10:30. The donor was a young man (almost a boy) who had died in a motorcycle accident. That detail is easy to remember, as Wisconsin, being the land of Harley (not to mention a state where wearing a helmet is frowned upon), produces a never-ending supply of donors who've died in motorcycle accidents. In the winter, it's snowmobile accidents, the snowmobile being the vehicle of choice for bar hopping in the evenings—which

sounds like fun but is also incredibly dangerous, given the power of those machines.

After we examined the donor at the hospital in La Crosse, confirming his identity and blood type, and went over the paperwork, including the declaration of brain death, we met with his family.

This continues to be one of the most difficult and, at the same time, most rewarding aspects of my job. No matter how tired I am, the interaction with the donor family always reminds me how wonderful and cathartic the donation process is. These people are going through the worst experience of their lives, as most donors die far too young and unexpectedly. Often, the family members have not even had the opportunity to say good-bye. Perhaps the one positive notion that family members can hold on to is this: with this ultimate gift, their loved one will save the lives of, and live on in, as many as seven other people. Their gift of life will be a legacy their families can cherish amid the brutal pangs of loss they have to endure.

We have a picture in our transplant unit of a mother whose teenage daughter died in a tragic car accident. This young girl saved at least seven lives. Some years later, the mother met the heart recipient at a transplant picnic we sponsored, and a picture was taken of her using a stethoscope to listen to her daughter's heart beating in the chest of the man she had saved.

This family tonight in La Crosse was no different. They asked how and when they could possibly make contact with the recipients, a process that we can help facilitate down the road if all parties agree. Then, once all their questions were answered, they said their final good-byes.

Once the donor was transferred to the operating table and prepped, we scrubbed in and placed the sterile drapes. At this point, all emotions from the encounter with the donor's family were pushed

out of our minds. We had a job to do: to get all the transplantable organs out and flushed so that they would spring to life when placed in their new "owners." Our team, which had come for the abdominal organs, was not the only one in the operating room that night; there were two others: heart and lung teams, waiting to take their respective organs. We stood around the operating table, separated by the patient's diaphragm. They focused on the chest, and we focused on the belly.

I took a scalpel and made a long incision from "stem to stern," or from the notch at the bottom of the neck down to the pubis. As I dissected through the tissues and entered the belly, the cardiac team took a saw and began opening the chest. I quickly grabbed a malleable (a long, bendable steel retractor) and held it in front of the liver, to make sure they didn't get a little careless with the saw and injure this beautiful organ.

There is a natural conflict between a cardiothoracic team and an abdominal team. We all realize the importance of the incredible gifts the donor is giving, and we are all the stewards of these organs. At the same time, the procurement team always gets blamed for anything that goes wrong with the recipient operations that follow.

"Why is the upper cuff of the liver so short?"

"Why didn't I get more vena cava below my heart?"

We're all trying to bring back the best organs we can. So, everyone protects his turf.

I think about operations in steps. Step one: open the belly. Step two: mobilize the right colon and duodenum, and expose the aorta and vena cava. Step three: loop the aorta to prepare for cannulation (i.e., the insertion of a plastic tube into an artery that will allow us to flush the blood out).

That night, we got through our steps, which included freeing up

attachments to the liver and separating the liver from the diaphragm and retroperitoneum. We dissected out the porta hepatis, identifying the hepatic artery and the bile duct. We divided the bile duct, letting the golden bile pour out into the abdomen. Then we cleared off the portal vein. Next, we mobilized the spleen and exposed the pancreas. As we neared the end, we identified the renal veins and arteries, which lead to the kidneys.

By now the cardiac team had scrubbed out and was standing behind us anxiously. Our portion of the operation is always much more involved than theirs, and as usual, they were constantly asking us when we would be ready. In their defense, their recipient surgeons (often hundreds of miles away) typically have already taken their patients to the operating room and begun opening their chests and getting them ready to be placed on bypass for removal of their sick hearts or lungs.

Finally, we were ready. We placed our cannula in the aorta. The cardiac team then placed a cross-clamp on the aorta and started infusing cardioplegia solution (which causes the heart to stop beating). Then they got ready to cut into the vena cava right before it entered the heart. (We made sure to protect as much vena cava as we could from those bastards. They didn't need it for their transplant, but we did for ours.) Once they cut it, the blood started to well up and out of the chest cavity. We started our flush through the aorta and then placed a second cannula in the portal vein. In poured the cold "University of Wisconsin solution," the wonderful solution, invented at our own institution, that preserves the organs and helps make all this possible.

The blood turned clear as it flushed out into our suction devices. We then poured buckets of ice into the abdominal cavity. Our hands began to cramp and ache from the ice as we held our cannulas in

place. The good news was that, after a couple of minutes, the pain dissipated (as did all other feeling in our hands). The organs were cut out, flushed some more, and placed in bags.

Then we all went our separate ways.

That evening, I called Dr. D'Alessandro on the way out and told him we had a perfect liver. Of course, he was sleeping soundly in his bed. He would direct the OR team back in Madison to take the recipient patient to the operating room and start removing the old liver.

We took a cab back to the airport. It was about 1:45 a.m. at this point. We were all exhausted, but also filled with the satisfying feeling that always accompanies an operation gone well. The added bonus was that our cooler was filled with four organs that would go into three separate patients—a liver, a kidney, and a combined kidney and pancreas (called "simultaneous pancreas and kidney," or SPK). At the airport, we walked out onto the tarmac, where the pilots were waiting.

FOR SOME REASON I remember this vividly, even though it was more than ten years ago. It felt windy and cool that morning, quite different from the stifling summer weather we'd experienced when we landed a few hours before. There was the unmistakable feeling that a storm was coming.

The pilot turned to me and asked if I thought we should go. We both looked over at the cooler with the sticker reading "Organs for Transplant." I mentioned to him that he shouldn't worry about the organs; thanks to UW solution, the carefully designed preservation solution that would allow the organs to be metabolically inactive, they could wait awhile. I could always call Dr. D'Alessandro and tell him to delay the recipient.

Instead, I asked the junior pilot if he thought it was safe. I say "junior" because he looked all of about ten years old.

"It should be," he said. I detected a slight tremor in his voice.

Not that convincing, but I agreed to go.

We took off, and everything seemed pretty smooth. But about ten minutes in, things started to get crazy.

As the plane bucked and the alarms sounded, I really did think this was it. I thought about my family, particularly my little girl, born two weeks before we moved to Madison for my fellowship. I was bothered by the idea that someone at my funeral would say I'd died doing what I really loved. That's bullshit. There is really no great way to die, certainly not in a stupid little plane in the middle of the night.

We finally got through the storm, and as quickly as it started, it stopped. The pounding rain and the turbulence subsided, the plane settled, and we sat in silence for the last five minutes of the flight.

After we landed, I asked one of the pilots how commercial planes could possibly be landing in this weather. He said, "Oh no. The airport is totally closed, only open for emergencies." I remember feeling somewhat pissed about this, but in a way, what we had just done qualified as an emergency.

I OPENED THE bag with the liver and dropped it into the sterile bowl filled with ice. I was in the operating room back in Madison, and Dr. D'Alessandro and my co-fellow Eric were almost done with the hepatectomy, or removal of the diseased liver.

The donor liver was truly a perfect organ. I cleaned the extra tissue off it and meticulously tied off all the small vessels that came off the cava (though, of course I would still be blamed for any bleeding

they got into after reperfusion). I then separated the pancreas (which we'd also use) from the liver, making sure not to injure either and to leave enough portal vein and artery for both transplants. I placed the pancreas in its own bag, which I would bring back down to the "lab." This organ would be prepared and transplanted in the morning into a type 1 diabetic, along with one of the donor kidneys we'd just procured. The other kidney would go into a different recipient. In two other states, two different patients were receiving the heart and the lungs from our donor in La Crosse.

I never cease to find this remarkable.

Once the liver was ready, I brought it into the recipient room, where the team was waiting. When they saw me, Dr. D'Alessandro took the Klintmalm clamp and placed it on the last remaining attachment to the liver, the hepatic veins going into the vena cava. He cut the recipient's liver out. I watched over his shoulder.

There is no more amazing sight in surgery than the abdomen once the liver has been removed. The vena cava—the large vein that brings blood from the legs back to the heart, which is normally enveloped by the liver—is fully exposed, coursing from bottom to top, and there is a huge, empty space around it. It is an unnatural but weirdly beautiful sight.

Dr. D'Alessandro took the new liver and started sewing it in—in steps. Upper cuff first. Then portal vein. Then flush. Then reperfuse. The liver pinked up and looked beautiful. Everyone looked happy.

Then Dr. D'Alessandro mentioned that I needed to go. There was another procurement, up in Green Bay.

# 2

# Puzzle People

> If you think of physical genius as a pyramid, with, at the bottom, the raw components of coordination, and, above that, the practice that perfects those particular movements, then this faculty of imagination is the top layer. This is what separates the physical genius from those who are merely very good.
>
> —MALCOLM GLADWELL, "THE PHYSICAL GENIUS," *THE NEW YORKER*

*Madison, Wisconsin*

My kids love to do art projects. They sit at the kitchen table and draw, cut, and glue princesses and animals and houses. The projects go on for weeks, cluttering up multiple rooms in our house, but in the end, the kids get a real sense of satisfaction as they play with their creations—until they are ready to move on to the next project.

My projects are my patients. Each one requires something cut out, glued in, or fixed up until it's time for me to move on to another. Cindy was a particularly memorable "project." When I first did a liver transplant on her, she was gravely ill, probably within a day or two of dying. I had gone to bed early the night before. At

around two o'clock in the morning I got the phone call. I answered it on the first ring because, when I'm on call, as I was that night, I sleep with one eye open.

It was one of our coordinators for organ offers, Pamela. "We have a liver offer. It looks like a good one. He is a forty-four-year-old male, died of a drug overdose. Twenty minutes of CPR. Perfect liver numbers." Pamela spent the next five minutes giving various details about the donor's stability, previous medical history, and other lab values. I half-listened, partly because as long as the liver looked good, we were going to use it.

I asked Pamela who'd come up first for the liver.

"Cynthia R. MELD forty. Should I have the coordinator call you?" The MELD (or "Model for End-Stage Liver Disease") score predicts how sick a patient's liver is, and how likely she is to die without a transplant. A scoring system based entirely on lab values, the MELD score determines where a particular patient's name will fall on the transplant list. The scores range from 6 to 40. When your score is below 15, it typically means your risk of having a bad outcome during a liver transplant outweighs your risk of dying without a transplant, and we typically will not proceed. As the score gets higher, it means your liver is becoming more dysfunctional and you are at greater risk for dying without a transplant. Allocation of livers is based entirely on risk of waitlist death, with no consideration of quality of life, ability to work, or some prediction of your likelihood of returning home or to a "valuable" life afterward.

So begins the round of endless phone calls involved in coordinating every transplant, from identifying the potential recipients, who can be at multiple programs around the country; to bringing them into the hospital and making sure they are healthy enough to receive the organs; to running numerous tests on the donor to rule

out infection risks; to running tissue typing to identify blood type and genetically match the donor and recipient; to setting up OR times at both the donor and recipient hospitals; to getting planes ready to fly all the donor surgeons and teams to the donor hospital; to, of course, making sure the donor family is comfortable with the timing so they can say good-bye to their loved one and talk to the transplant team. Each time there is a hiccup, and the timing has to change, all this has to be reset.

At 3:15 a.m., the phone rang again. (This second call is when I focus on the recipient.) Jaime, the transplant coordinator who focuses on our patients before and after transplant, gave me some more information on Cynthia, who goes by "Cindy." She had been admitted multiple times over the last few months. She had recently been treated for pneumonia and had spiked a fever the day before. She had gone into renal failure during this hospitalization and was now on dialysis. She was obtunded (i.e., confused from her liver failure to the point of almost being in a coma) and yellow as a banana. Her blood wasn't clotting at all, and she was oozing from her gastrointestinal tract (in her bowel movements), her nose, and around her IV lines. She was getting blood transfusions every day.

I trust Jaime, but given the severity of Cindy's illness, I decided to do my own chart biopsy. I turned on my computer and maneuvered through all the firewalls to log into the hospital system. I kept Jaime on the phone through this, since I might have to decide to call in a backup patient in case Cindy seemed too sick.

This crazy concept of calling a backup in case I deem Cindy too sick and skip her highlights the emotional challenge of being on the liver transplant list. When you are waiting for a liver, you want to be as healthy as possible going into this massive operation, but at the same time, you need to get sicker to get the liver, but not too

sick that you get passed over when the time comes. When I evaluate an offer, I need to decide if I can get the patient through without killing her in the OR, fully aware that if I skip someone because she seems too sick, I am likely signing her death warrant.

Nowadays, we are willing to push things pretty far. I will take patients with breathing tubes, renal failure, fevers, and on medication to support their blood pressure. I will take patients who are having active GI bleeds, who have tumors growing in their liver, who have blood vessels that are clotted, and who may need bypasses of these blood vessels or some other heroic measure. But if I think someone is too sick, I'll have the backup recipient brought to the hospital, where the coordinator will tell this person that he will get the liver only if something happens to the person it is intended for. What must that be like for a patient—driving to the hospital in the middle of the night, getting prepped for surgery, even being wheeled down to the pre-op area, knowing he will receive this gift of life only if the intended recipient dies? It's horrific to contemplate, but from my point of view, I don't want to waste a healthy liver.

I looked over Cindy's data. I felt as if I knew her at this point, having gone through her history, labs, films. I have seen her digital insides, have examined her lungs and her liver and her spleen and her bowel and her blood vessels. If I saw her on the street, I wouldn't recognize her, but if I looked into her open abdomen, I would know her immediately, from her shrunken liver to her large spleen to her massive varices (big, swollen veins), which are carrying blood in the wrong direction (because of so much resistance to flow caused by that shrunken liver) and led to her GI bleeding, confusion, kidney failure, and now her imminent death.

I told Jaime it's a go. Let's not bring in a backup.

I finally met Cindy and her family at 4:30 p.m. I would come to

know them quite well, particularly her daughter, Ally, and husband, Michael. I could see how much they loved Cindy, and how worried they were. I talked to them about the surgery and told them how sick she was. I told them the donor organ looked like a good liver. I went through some data—*x* percent chance of this, *y* percent chance of that, the possibility of bleeding, a bile leak, the clotting of blood vessels, organs being injured, the liver not working. But the questions they cared about most I couldn't answer.

First, I couldn't tell them much about the donor. We avoid giving too much information about donors, since it would be too easy to figure out their identities on the internet. And of course, Cindy's family wanted to know when the operation might take place. I had no idea. The various coordinators were busy trying to place all the organs. We had a good brain-dead donor (but with a heartbeat), so that meant being able to place the heart, lungs, liver, kidneys, pancreas, and maybe even the small bowel and skin, bones, and eyes. Some of the recipient surgeons involved probably wanted more tests done on this donor—a cardiac catheterization, an echocardiogram, a liver biopsy (which we'd requested), a bronchoscopy. That meant the donor would be wheeled down to the cath lab, where a cardiologist would stick a needle in his groin and snake a catheter in his heart to shoot pictures of his coronary arteries; another doctor would stick a needle into his liver for a biopsy; and a third would send a scope down into his lungs to look at his airways.

My phone rang just before midnight. Pamela again, back on her shift. An OR for the donor had been booked for 1:00 p.m. tomorrow. At 3:00 a.m. Pamela called again. The OR time had been moved to 3:00 p.m.

At 7:00 p.m. we were finally in the OR. The anesthesia team put Cindy to sleep. I sat in the room watching them put gigantic IV lines

into her neck, to pour blood in when I began exsanguinating her. I noticed that her systolic blood pressure was starting at 60 mmHg, dangerously low considering I hadn't even started the bloodletting. I watched them dial up the blood pressure meds. I considered whether I should call in a backup recipient now, as the likelihood of Cindy not making it had risen a little bit. *Nah, forget it.* Our team was packing up at the outside hospital, a thirty-minute flight away. Our fellow had sent a picture of the donor liver to my phone; it looked perfect. *I'm putting this thing into Cindy. It's hers now. If she gets buried, it will be buried with her.*

At 8:15 p.m. we finally made the incision. My second-year fellow Emily sliced through Cindy's skin. Everything was bleeding. This was not surprising, given that she had absolutely no clotting factors in her body and was already bleeding from every IV site and orifice. But she was not Cindy to me anymore. I no longer thought of her life, her family, whether she was male or female, young or old. I don't think I would have been able to do to her what I was about to do if I thought about that. I had seen her films, had a mental image of what everything in there should look like, but now I needed to put together the puzzle.

A liver transplant can involve anywhere from a thousand to a million pieces. Despite the exquisite quality of CT scans and MRIs these days, you never quite know what a liver transplant, or any operation, is going to be like until you start. But shortly after opening, you have a pretty good idea. If the diseased liver is shrunken and mobile, and you can reach in and pull it up right away, you know it won't be that difficult to get it out. If it is stuck to the tissue around it from years of inflammation and damage, however, you know you're in for a battle. If you lose 2 liters of blood just cutting through the skin, you know you're screwed.

We got into Cindy's belly and sucked out 8 liters of beer-colored fluid—we call this fluid ascites; it bathes the organs in most patients with advanced liver failure. (I congratulated Steph, our scrub nurse, for guessing 7.5 liters—the closest to the actual number without going over. Good, clean OR humor.) We put our retractors in and looked at the liver. I could tell right away this was going to be bloody but not that bad. We got two suctions ready to suction the ascites and blood we were going to be swimming in throughout the operation. Emily and I had both put knee-high waterproof "booties" over our OR clogs, so we wouldn't be standing in soggy socks by the end of the operation (something we have all learned the hard way).

The surgery itself went quite well. Cindy's beautiful new liver worked right away, and we were able to stop the bleeding without too much trouble. We finished at around 3:30 a.m.—a little long for some surgeons, but I believe in taking my time and making sure everything is perfect before I leave. I went downstairs to talk to the family, leaving Emily and "anesthesia," as we refer to the anesthesia team in the OR, to move the patient to the ICU and to complete all the never-ending paperwork. I told the family the case had gone well. I mentioned that Cindy's pressure was pretty saggy throughout, but I was hopeful that would correct itself over the next day or so. She would go to the ICU with a breathing tube in. She was critically ill, but I thought she would be okay. They asked me if her kidneys would recover, and I said I hoped so.

EMILY CALLED ME at around 8:00 a.m. on post-op day five. "Hey, Josh, it looks like there is bile in Cindy's drain." Damn. My stomach immediately jumped into my mouth. Every time something goes wrong with one of my patients, I get this incredibly awful feeling,

something like guilt mixed with nervousness mixed with depression. Bile can't be good. It had to be leaking from where we'd sewn her bile duct together. The two ends of the duct had seemed fine in the OR, but she had been so unstable over the last couple of days that perhaps her low blood pressure had caused the ducts to fall apart. Bad blood flow can lead to bad healing.

In the shower, I pictured the operation we would need to do—most likely a Roux-en-Y hepaticojejunostomy. In other words, we would divide her small bowel, pull one end up to the bile duct, sew that onto the bowel, and then plug the other end back into the bowel so it looked like a *Y*.

Now the guilt was seeping in. You really have one shot at getting surgery right on a sick patient, particularly one who is on immunosuppression (i.e., drugs to prevent the immune system from attacking the new organ). Once you have a complication, you're backpedaling.

I could already see that Cindy would now be hospitalized for months, would likely get numerous infections, have prolonged intubation, have an open wound, need various antibiotics, probably grow fungus out of her belly, get line infections and deep vein thromboses (DVTs), and probably never come out of renal failure. Nice thoughts.

I drove to the hospital and headed directly to the ICU. Cindy's drain looked like shit. I don't mean it looked bad. I mean it actually looked, and smelled, like shit. I wasn't sure what I'd screwed up, but I couldn't help wondering if another surgeon could have avoided this. Emily got the OR ready, and we rushed Cindy off for surgery. I was super anxious until we got her into the operating room. As a surgeon, when you have a complication, you're dying to fix it. Waiting to go to the OR is agonizing, and sometimes it seems like every-

one is putting up barriers to your doing so—missing paperwork, delayed lab results, absent staff.

We opened Cindy up and scooped out what seemed like a liter of poop. We saw that the liver looked great (other than being poop-stained) and the blood vessels were fine, as was the bile duct. As we looked around, we found a large hole in her right colon. I had no idea how that got there. Maybe it was from a retractor; maybe it was from her low blood pressure and high-dose steroids. It wasn't directly my fault—but did that make any difference?

Emily and I removed Cindy's right colon and gave her an end ileostomy and long mucous fistula that she would keep for the next year. In other words, we pulled the end of her ileum (small bowel) right through her abdominal wall so that her stool would come directly out into a bag; we also pulled the disconnected colon out as well as a double-barreled ostomy, so it couldn't leak into her belly. After that repair, Cindy had a pretty tough course—a three-month stay in the hospital; an open, gaping wound; several readmissions; rounds of nursing home care. But she finally got better and made it home. And we were able to reconnect her bowels so she could poop like the rest of us again.

Her family was with her every step of the way, and it was definitely tough on them, but they weren't done giving. Cindy's kidneys never recovered. She was going to dialysis three days a week, four hours at a time. It is a miserable existence, but it was keeping her alive. The good news was this was something we could fix. We just needed a kidney. And immediately, her daughter, Ally, stepped forward to give it. Once that kidney was in there, she would be as good as new, ready to get on with her life.

This is why I love the field of transplant. Since I began taking care of sick people, I have noticed that one of the hardest things

about getting sick, really sick, is that you are separated from the people you love. Even when families are dedicated to the patient, illness separates the well from the sick. The sick suffer alone, they undergo procedures and surgeries alone, and in the end, they die alone. Transplant is different. Transplant is all about having someone else join you in your illness. It may be in the form of an organ from a recently deceased donor, a selfless gift given by someone who has never met you, or a kidney or liver from a relative, friend, or acquaintance. In every case, someone is saying, in effect, "Let me join you in your recovery, your suffering, your fear of the unknown, your desire to become healthy, to get your life back. Let me bear some of your risk with you."

I saw Cindy in my office on a Tuesday in October, about a year and a half after her liver transplant, the day before I was planning to perform her kidney transplant. She was with Ally. Cindy tearfully asked me what the chances were that the operation would be successful.

"Of course it's going to work," I told her. I didn't say this out of a surgeon's narcissism. The reality is that she was getting a young, living-donor kidney from a healthy donor, all the immunologic tests we had performed indicated no evidence for risk of early rejection, and the procedure has become quite commonplace. I just needed to put the last piece of the puzzle in place, and she would be on her way.

It really was that simple.

How did we get here? How is it possible that we can take organs from someone who has just died, plug them into someone who is in the process of dying, and have those organs suddenly start working? Livers begin making bile, kidneys start peeing on the table, pancreata start secreting insulin and regulating blood sugar, hearts start beating, lungs start breathing. It has all become so straightforward

and predictable, but it wasn't always like this. There was a time when sane people thought transplant was a pipe dream, something that could never happen.

*Lyon, France, June 24, 1894*

Marie-François-Sadi Carnot, the popular French president, had just given a speech at a banquet in Lyon, and was back in his carriage, when a man ran at him from the crowd. Sante Geronimo Caserio was a twenty-one-year-old Italian anarchist who had made up his mind to kill the president. He'd purchased a knife. He'd studied the program for the president's visit to the city. When the perfect moment arrived, he jumped onto the president's carriage and stabbed him. Carnot was taken to the town hall, where prominent local surgeons examined him. They probed his wound, and he briefly came out of his unconscious state, exclaiming, "How you are hurting me!" Shortly thereafter, he died. An injury to the portal vein was identified as the cause.

One can only imagine the chaos and emotions that this assassination inflicted on the people of France, heightened by the complete inability of surgeons at that time to offer Carnot anything resembling treatment. His murder had a major impact on one young student, Alexis Carrel. An extern in Lyon (the equivalent of a medical student), Carrel wondered whether he could somehow improve the management of these types of injuries and decided to become a surgeon. He was a natural surgeon, ambitious, driven, and hungry for fame. He reportedly told people that doctors should have been able to save Carnot, that there should be a way to sew severed vessels back together. Surgeons of the day thought the idea was crazy.

In 1901, once he finished his initial training in surgery, Carrel obtained space in a lab with access to surgical equipment and dogs. His focus was on designing a method to join together two blood vessels. It is hard to imagine that surgery ever existed without this, but at the time, there was no inkling of peripheral vascular disease, no real understanding of atherosclerotic plaques, no consideration given to operations on the heart, and most people didn't live long enough to develop these types of problems anyway. While vascular injuries were seen secondary to battle wounds or trauma, the standard management of these injuries was to try to ligate (tie off) whatever might be bleeding; this remained the practice well into World War II. The main vascular issue surgeons saw in those days involved aneurysms (or the outpouchings of arteries), which nowadays are associated with smoking and atherosclerosis. Back then, though, these were often secondary to syphilis. If an aneurysm was found before it ruptured, causing certain death, surgeons would ligate the artery. Mortality was high, but not that much higher than the outcomes seen with virtually any abdominal operation in those days. Thoracic operations weren't even attempted.

Carrel recognized three things: First, he needed to find better needles and thread to sew vessels together, thus minimizing injury to the inner wall (intima); the needles in use then were causing clots to form at the needle holes. Second, he wanted a technique that would protect the intima more than he could do just by improving his suture material. Third, he needed to find a setup that would allow the repair to be done quickly, as he knew that clamping the vessel for too long would inevitably lead to clotting. Knowing that the needles and thread available for surgery were woefully inadequate, he visited a local haberdashery in Lyon to obtain finer material, which included straight needles and fine cotton thread.

In addition, legend has it he took embroidery lessons at the home of Madame Leroudier, a world-famous lace embroideress, and practiced sewing with these needles on paper until his technique was perfect. He placed paraffin jelly over the needle and thread, to allow it to be pulled through the tissue more easily, and in 1902 published a paper describing his findings.

Alexis Carrel has always been described as a gifted surgeon. Most surgeons fall somewhere on a bell curve of inherent surgical skill, which is adequate to obtain good outcomes, even in technically complex cases. That said, there are natural surgeons whose hands are so good that within just a few minutes of working with them, you can tell they are off the bell curve. There are no wasted motions, the moves are so efficient, every stitch is perfect, and their instincts are unnaturally good. Carrel was in this group; he was a physical genius.

In addition to his physical skill and adoption of better equipment, Carrel was passionately committed to organ transplantation, a discipline that depends on sewing together blood vessels to supply the new organ. This is rather remarkable, given that organ transplantation was still in the realm of science fiction at this point, with a few sporadic attempts that were universally followed by rapid failure.

Carrel presented his results at local scientific meetings in Lyon, with generally good reception. He hoped that his description and demonstration of the vascular anastomosis (or reconnection of blood vessels), along with some follow-up experiments in which he sewed the carotid artery (the main artery in the neck that goes to the brain) end to end to the jugular vein (the main vein in the neck that drains the head) in dogs, would help him secure a junior faculty position. The artery-to-vein experiment was also well received,

and the technique was presented as a possible treatment for strokes or general mental decline by increasing oxygenated blood flow to the brain. We know now that this would have no beneficial effect, but it was a concept Carrel would explore over the next decade as a treatment for various failing organs. But as would become a recurring theme in the life of Alexis Carrel, some of his greatest achievements would be diminished by controversies he entangled himself in due to his diverse interests and beliefs. One local paper quoted him voicing his belief in supernatural healing forces at the shrine at Lourdes. Carrel had a mystical belief in the supernatural, and felt there existed powers that could allow the healing of various maladies and diseases in a rapid fashion. This notion was met with ridicule, and he was passed over for a staff appointment. Feeling betrayed and stifled in Lyon, he decided to emigrate to North America. After a brief stop in Montreal, he was recruited to work with Professor Carl Beck in Chicago, both working at Cook County Hospital on humans and doing experimental surgery on dogs. It soon became clear to him that he had no interest in performing human surgeries. He also had a fairly low opinion of American surgeons. He described "the crowd of imbeciles and villains who corrupt the world of medicine . . ." and declared that "to be a medical doctor in the United States is the lowest form of business." An opportunity arose at the University of Chicago, where he would not have to take care of human patients at all, and facilities were available for animal surgery. There he met Charles Claude Guthrie, a physiologist and researcher whose lab was performing dog surgery. The two men worked together for two short stints of three to four months, yet in that time, they published ten papers in American journals and almost twice that many in international ones. This productivity was certainly driven by Carrel's appetite for fame and recognition as

well as a sense of the competition that was arising in the field of vascular reconstruction and even organ transplantation in animals. It is truly remarkable how many different operations use the vascular anastomosis Carrel and Guthrie considered and described in that short period. These included connecting the femoral vein to the femoral artery in the leg of a dog (to improve blood flow to the leg); updating Carrel's original technique of the vascular anastomosis, taking full-thickness bites through the entire wall of arteries rather than just the outer layer; performing vascularized thyroid grafts, by either removing the organ from and replacing it in the same animal or transplanting an organ between different animals; and attempting multiple kidney transplants. Encouraged by their success, they also transplanted a canine heart from the chest of one dog to the neck of another (which beat for as long as two hours) and made attempts at transplanting both hearts and lungs (which invariably failed). In 1906, they published a paper on the use of the "Carrel patch," which involves cutting a vessel out along with a rim of aorta to make it bigger, a technique we still use today to perform organ transplantation.

This may have been the most critical year in Carrel's illustrious career, for two reasons. First, he focused singularly on mastering the technical demands of the vascular anastomosis. This attention, obsession even, to getting the technique perfect with repetition and focus was crucial. As a transplant fellow at Wisconsin, it took me two years of sewing in organ after organ, day and night, before my muscle memory had developed to the point where I didn't have to think at all when I sewed. When you first start sewing together vessels, you must constantly keep in mind whether you are inside or outside each vessel wall, and you are never sure how big a bite to take with your needle or how far to advance. At some point in your

training, you load the needle on your needle driver and turn your body without even thinking about it, and something that originally might have taken thirty minutes to an hour becomes a ten-minute exercise.

Of course, when I operate now, I have a scrub tech assisting me; a resident or fellow across from me; sturdy and complex retractor systems that hold everything out of my way; powerful overhead lights and a headlight to illuminate the field; super-sharp, well-designed, fine needles with even finer coated sutures that glide through the tissue; and spring-loaded needle drivers that I can operate with just my fingertips. Carrel had none of this.

The second reason 1906 was such an important year for Carrel has to do with his obsession with publishing. Some of the publications from this year remain relevant to the practice of medicine today, and his predictions about the application of the procedures he discussed in them, particularly in the field of transplantation, are shockingly prescient. By far my favorite work of his has to be "Successful Transplantation of Both Kidneys from a Dog into a Bitch with Removal of Both Normal Kidneys from the Latter," published in the premier journal *Science*, no less.

The other avenue Carrel started traveling down that year was interacting with the lay press. Although the practice was rare, and looked down upon by scientists and surgeons of the time, Carrel developed relationships with members of the press and leaked sensational information about his experiments to them. He also shared his techniques with renowned surgeons of the era. When a surgical society was convened in Chicago, Carrel had the opportunity to demonstrate his vascular anastomosis in a dog to more than twenty prominent surgeons, including the rising star Harvey Cushing. Cushing was at the Johns Hopkins Hospital at the time, working

with the great William Halsted, perhaps the father of American surgery. On April 23, 1906, Carrel traveled to Baltimore to present his findings at the Johns Hopkins Hospital Medical Society. In the audience could be found some of the premier surgeons and physicians of the era, including Halsted, William Welch (one of the founders of Johns Hopkins Hospital), and William Osler (a Hopkins founder and often considered the father of modern medicine).

Carrel spoke that day of his vascular anastomosis, the use of vein grafts to replace sections of arteries, and the importance of asepsis (the absence of bacteria or viruses) in outcomes of vascular anastomoses. (Joseph Lister had been pushing the importance of this in surgery starting in the mid- to late 1800s, but it certainly was not accepted practice, and hand washing and the use of gloves were not yet the standard of care.) Finally, he spoke of his experience with organ transplantation, its possible future applications, and how these surgeries seemed to fail after a week for unknown reasons. While he certainly did not call this "rejection," or appear to have much understanding of the immune response at this time, he did refer to possible inherited factors and discussed his plan to "perform a series of similar operations on pure bred animals" to understand this failure better. He also stated that "we intend to try and immunize the organs of an animal against the serum and organ extracts of another . . . The transplanted organ must be prepared to support the serum of the animal on which it is to be grafted." As a practicing transplant surgeon with a lab focusing on the immune system, I am pretty blown away by the topics Carrel spoke about and the predictions he made. The fact that he did most of this work in such a short time is also mind-boggling.

Carrel got a similarly positive response from the Hopkins crowd, and they tried their best to secure his appointment to their insti-

tution. But the infrastructure to support medical research was just starting to be put in place in America, and the lab space at Hopkins was just being built. Also, at the same time, another offer presented itself. Efforts were then under way to start institutes for medical research modeled after some of the great ones in Europe, institutes that could put American medicine on the map. The National Institutes of Health did exist at this point, but functioned essentially as a small laboratory and didn't start giving extramural grants for research until after World War II. Instead, two fabulously wealthy businessmen, John D. Rockefeller and Andrew Carnegie, decided to spend large portions of their fortunes to support medical research. In September 1906, the first director of the Rockefeller Institute, pathologist Simon Flexner, was successful in attracting Carrel to the gleaming labs in the newly built institute on the banks of the East River in New York City.

At Rockefeller, Carrel's most remarkable experiments were surgical in nature, involving blood vessel surgery and transplantation. In the field of transplant, he did virtually everything. He performed vascularized transplants of spleens, thyroids, intestines, and an ear (supplied with blood by the external carotid artery). He performed numerous leg transplants between dogs, sewing the blood vessels together and nailing the bones in place. Perhaps his most important transplants were kidneys. He first perfected the autotransplantation of kidneys in dogs (taking the kidney out and then transplanting it back into the same dog). He then moved on to transplants between two different animals. He thought about his occasional longer-term successes and came to the conclusion that something about the close relationship between siblings could make grafts last longer. And most impressively, Carrel grasped what might have been the next step in making transplantation a clinical reality: he considered the

idea of manipulating the donor graft prior to transplantation or applying some sort of conditioning to the recipient. It was this work that led to his Nobel Prize in 1912, "in recognition of his work on vascular suture and the transplantation of blood vessels and organs."

Shortly after this, James Murphy, working in the Rockefeller lab of future Nobel laureate Francis Peyton Rous, published a paper showing that lymphocytes (cells of the immune system) could "reject" tumors and stop their growth when they were transferred to other chicken embryos. This was essentially the first explanation of transplant rejection, and Carrel recognized this. Furthermore, Murphy showed in mice and rats that by either irradiating them or treating them with the chemical benzol, lymphoid tissue would be damaged, lymphocytes (and hence immune function) would be decreased, and tumors could be transplanted and survive in these animals. Carrel took the next step, in his mind, and considered that either radiation or chemicals such as benzol could be given to transplant recipients to extend the lives of grafts.

In 1914, when he went off to France for his summer vacation, World War I broke out. Tragically, this concept of recipient treatment and the role of lymphocytes in graft failure would essentially be lost until the 1950s.

When Germany declared war on France, Carrell was thrilled, as he loved the military and felt France had gone soft. War was just what was needed to cleanse the soul of the French people. Carrel had a particular interest in the management of wounds and wound healing, and he formed a relationship with an American chemist by the name of Henry Dakin, whom Carrel tasked with coming up with a strong antiseptic solution that could be used to wash out battlefield wounds. With it, Carrel devised an intricate and painful wound-perfusion system, which eventually fell out of favor due

to its complexity. Dakin's solution, with some modification, is still used in the management of open wounds today.

After the war, Carrel spent an additional twenty years at Rockefeller. In the lab, he moved away from surgical work and turned to cell culture and made some minor advancements in that field, which he portrayed to the press as major breakthroughs. Ultimately, some of these breakthroughs would be exposed as fraudulent. In addition, he wasted time and money on expensive experiments that were badly designed. For example, he conducted a large mouse experiment looking at the role of diet and environment in the development of cancer, but it was poorly controlled and without any testable hypotheses. But overwhelming his life at this time was a growing interest in eugenics and his relationship with Charles Lindbergh, the famous aviator and eugenicist.

From the turn of the twentieth century up until World War II, eugenics was widely popular in the United States and Europe. More than three hundred major universities offered the study of eugenics as part of their curriculum, and the scientific community considered it a legitimate science. A short list of famous people who subscribed to it includes Theodore Roosevelt, Alexander Graham Bell, John D. Rockefeller Jr., H. G. Wells, Winston Churchill, John Maynard Keynes, Woodrow Wilson, Henry Ford, and Francis Crick.

So, what does this all have to do with Carrel? In the 1920s and '30s, Carrel embraced the concept that Western civilization was in a decline. He became so focused on his concerns about mankind that he dedicated himself to the writing of his opus *Man, the Unknown*, which supports a positive version of eugenics. He wrote extensively about the loss of "natural selection" in mankind and a need to develop the strong.

The book was released in 1935 and became a best seller. Many of its themes, particularly the general decline of Western societies, the potential for improving living things with selective breeding, and getting rid of criminals and those deemed insane, were popular and mainstream. Carrel was at the absolute peak of his popularity in these years, until his retirement and return to France in 1939, where he was supported by the Vichy government.

If Alexis Carrel had followed his instincts, he very likely could have become the true father of transplantation and perhaps one of the greatest innovators in the history of medicine. If he had simply died or faded away shortly after the Nobel Prize he won in 1912, at the very least he may have been revered as one of the premier experimental surgeons of the twentieth century. Instead, as his research production dwindled and his relationship with Charles Lindbergh blossomed, Carrel focused more and more on the degeneration of mankind and how he could play a role in studying this in a scientific way. He always had a fascination with strongmen such as Mussolini and Hitler, and thought that in the 1930s, German society was taking a good approach to cleaning up its population.

Shortly after the liberation of France from the Nazis in August 1944, various rumors emerged that Carrel was under house arrest, was going to be tried as a German collaborator, or was on the run. None of this was true. He had fallen ill from heart disease, having suffered his first heart attack in 1943, and died in November 1944. Although he was not formally charged with any crimes, his name became strongly associated with Nazism, fascism, and anti-Semitism. His reputation was destroyed, and to some degree, many of his discoveries were lost. His transplant work was completely forgotten, with little mention made of it to this day.

Sir Roy Calne, the man who perhaps more than anyone moved

the field in the direction of chemical immunosuppression, had this to say about Carrel: "Alexis Carrel was a brilliant researcher, but not a very nice man." Despite that, his contributions with regard to the technical aspects of sewing vessels together and transplanting organs from one animal to another with initial graft function represent the first piece of the puzzle of organ transplantation.