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Pig kidneys to the rescue? Groundbreaking transplant a step toward solving organ shortage

More than 100,000 Americans are waiting for an organ replacement. A breakthrough surgery offers hope animals may help fill the void.

Karen Weintraub, USA TODAY
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NEW YORK — Dr. Robert Montgomery planned for this moment for three years.

On an operating table in front of the transplant surgeon was a woman's body donated precisely for this purpose. The kidney he was about to attach to her came from a pig bred for this day.

If the surgery worked, it would show pig organs could be safely used to save human lives.

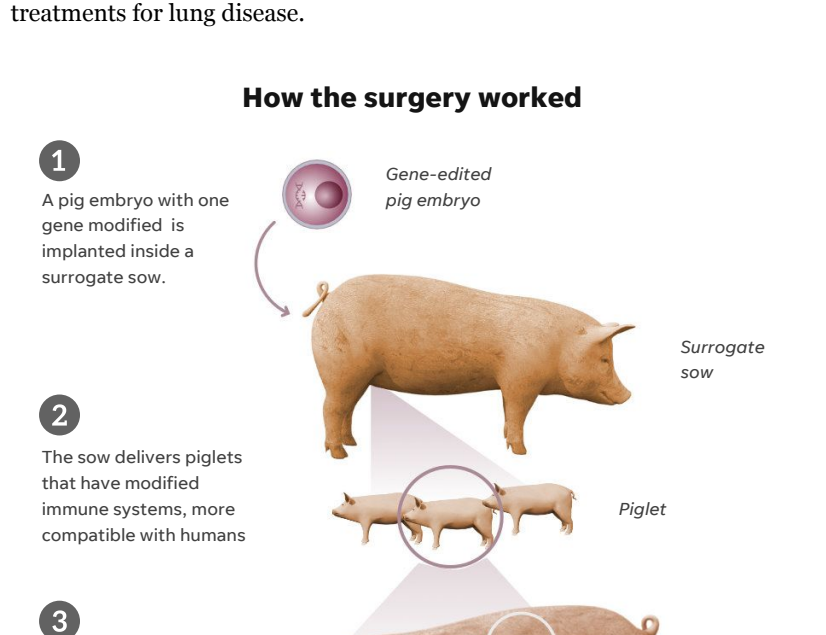
Clamps separated her bloodstream from the pig kidney.

Once he released them, the organ would fill with blood. In the worst case scenario, it would rapidly turn blue, a sign her immunity "soldiers" were flooding in to fight off the foreign organ. That could set his field back for years.

"No matter what happens when I take these clamps off, we will learn something very important that no one could have known before," Montgomery told the transplant team.

Scientists for decades have dreamed of xenotransplantation: using animals to solve the shortage of organs available for human transplant.

Today, people in need of a new kidney or a new heart have to wait for someone else's tragedy — a motorcycle accident, a drug overdose, a drowning — to get a replacement. More than 100,000 Americans sit on the national organ transplant waitlist, the majority for kidneys, and about 6,000 of them die every year. Others never qualify at all or wait years, often enduring terrible symptoms, emotional distress and difficult treatment.



Surgeon transplants a pig's kidney into a brain-dead human in groundbreaking surgery

ROBERT DEUTSCH, USA TODAY

Pigs, whose organs are about the right size and can be bred easily and quickly, offer a promising alternative.

But before tying a person's fate to a pig's organ, Montgomery, head of the Transplant Institute at NYU Langone Health, wanted to prove that the procedure wouldn't trigger an immediate immune attack.

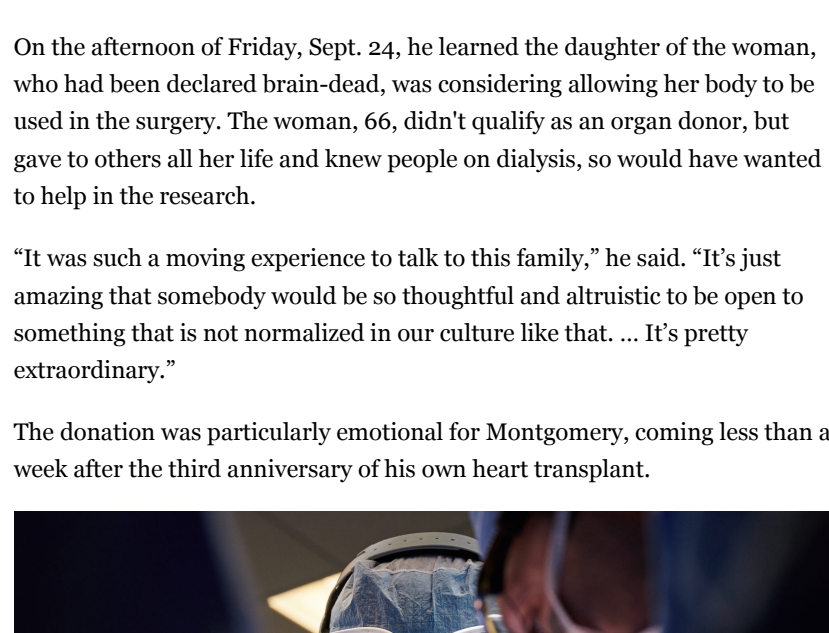
Jumping the species barrier is perilous. In 1984, after years of study, Leonard Bailey, a transplant surgeon at Loma Linda University Medical Center in California, thought he had overcome the immune system's rapid rejection of foreign organs.

He transplanted a baboon heart into a 12-day-old baby born with a deformed heart. Nicknamed "Baby Fae," she died 21 days later because her blood type was incompatible with the monkey's.

Though unsuccessful, the experience was pathbreaking. The next year, Bailey performed the first human-to-human heart transplant in a baby. Bailey died in 2019 at age 76; many of his transplant patients have outlived him.

Montgomery's pig had Type O blood, which made it a universal donor. The surgery was funded by a \$3.2 million grant from United Therapeutics, a biotechnology company based in Silver Spring, Maryland, involved in treatments for lung disease.

How the surgery worked



SOURCE: NYU Langone. GRAPHIC: Javier Zaracina/USA Today

If the procedure worked, the next step would be to test a pig organ in a living person, probably someone with a short life expectancy or whose life is in immediate danger.

"It's going to give us that confidence that something's not going to go wrong immunologically in these first couple of days," Montgomery said, as surgical nurses prepared the operating room. We still are assuming a lot until we actually do this."

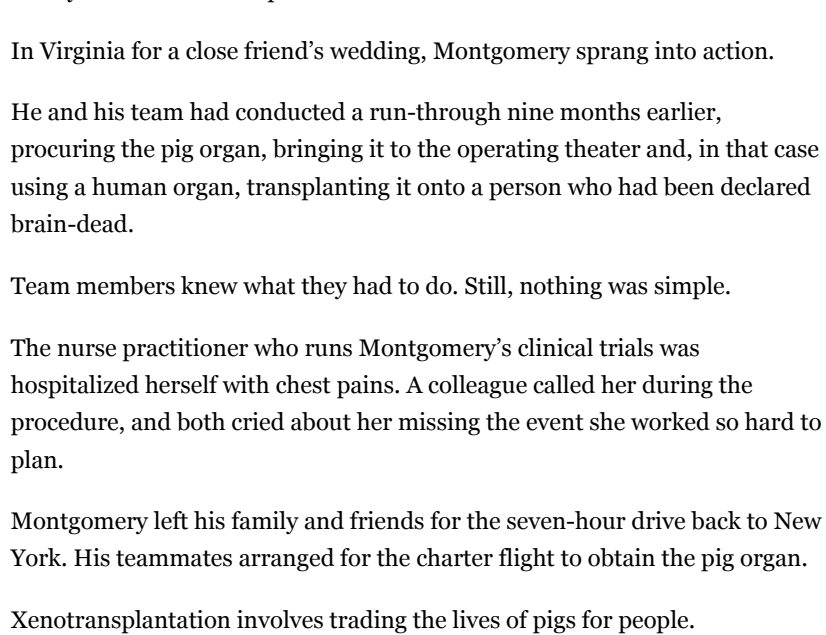
Getting consent

A cowboy of a man, Montgomery, 61, is 6-foot-1 with a thick moustache and a preference for boots. He strides rather than walks into a room.

On the afternoon of Friday, Sept. 24, he learned the daughter of the woman, who had been declared brain-dead, was considering allowing her body to be used in the surgery. The woman, 66, didn't qualify as an organ donor, but gave to others all her life and knew people on dialysis, so would have wanted to help in the research.

"It was such a moving experience to talk to this family," he said. "It's just amazing that somebody would be so thoughtful and altruistic to be open to something that is not normalized in our culture like that. ... It's pretty extraordinary."

The donation was particularly emotional for Montgomery, coming less than a week after the third anniversary of his own heart transplant.



Dr. Robert Montgomery, chair of the Department of Surgery at NYU Langone and director of its Transplant Institute, performs the first xenotransplantation of a genetically engineered nonhuman organ to a human at NYU Langone Health on Sept. 25, 2021. JOE CARROTTA FOR NYU LANGONE HEALTH

An inherited heart condition ended the lives of his father at age 52 and brother at 35. Montgomery had a defibrillator implanted when he was still in medical school.

Decades later, after collapsing at a medical conference in Italy in 2018, Montgomery knew his own heart was on the verge of giving out.

He was able to get a donor heart quickly by agreeing to take one from a man who had died of a drug overdose and was infected with hepatitis C.

Montgomery had started a program at NYU allowing such donations. Many people remain uncomfortable accepting an organ from someone with hepatitis C, but treated and cured of the dangerous liver infection before he had any symptoms, Montgomery remains immensely grateful for the gift.

"I always felt there was some reason or purpose that I'm still around," Montgomery said. "Maybe this is it."

The daughter of the woman lying in front of him died at 3:30 p.m. that Friday to consent to the procedure.

In Virginia for a close friend's wedding, Montgomery sprang into action.

He and his team had conducted a run-through nine months earlier, procuring the pig organ, bringing it to the operating theater and, in that case using a human organ, transplanting it onto a patient who had been declared brain-dead.

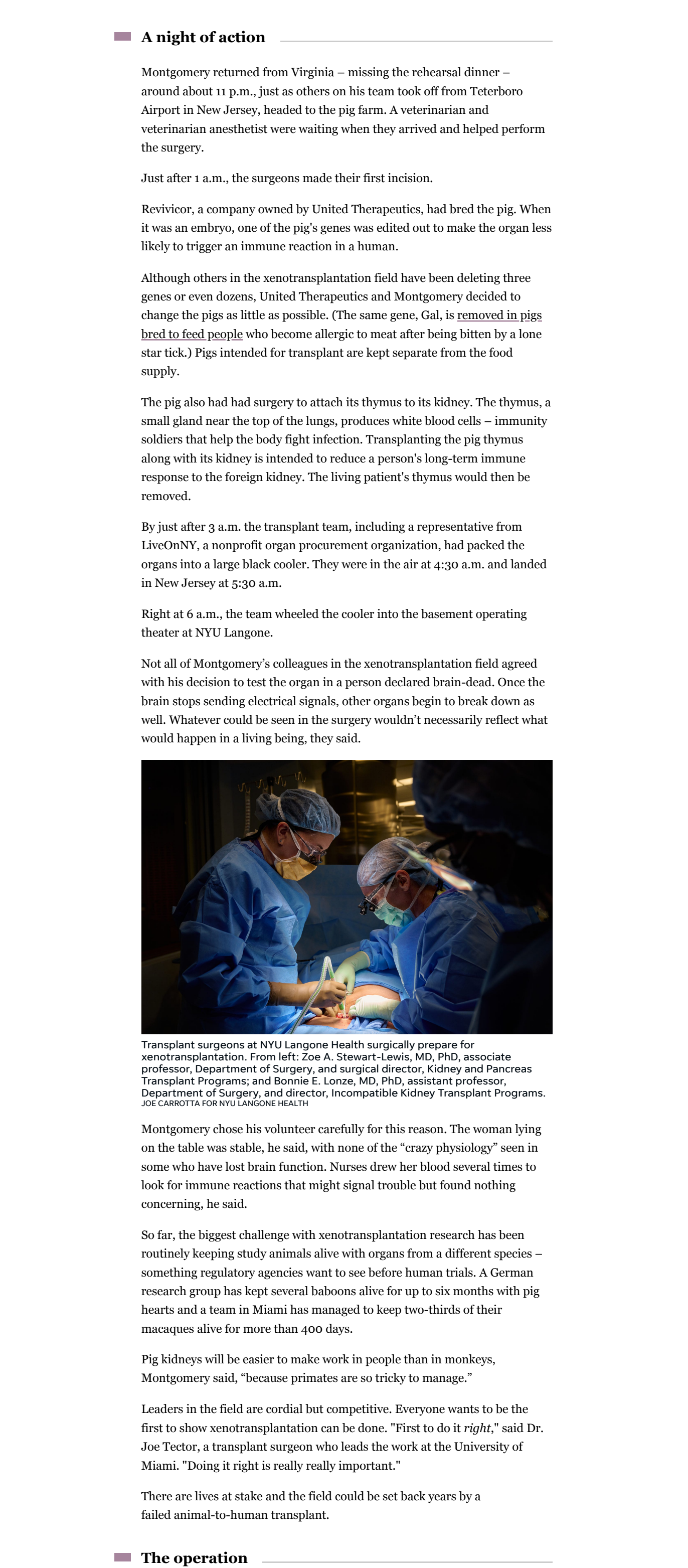
Team members knew what they had to do. Still, nothing was simple.

The nurse practitioner who runs Montgomery's clinical trials was hospitalized herself with chest pains. A colleague called her during the procedure, and both cried about her missing the event she worked so hard to plan.

Montgomery left his family and friends for the seven-hour drive back to New York. His teammates arranged for the charter flight to obtain the pig organ.

Xenotransplantation involves trading the lives of pigs for people.

People for the Ethical Treatment of Animals, an animal rights group, says the organ shortage could be solved without killing animals. If the U.S. switched from its "opt in" organ donation system to one that was "opt out," requiring people to say they didn't want to donate, there would be plenty of organs, the group says.



The surgical team at NYU Langone Health examines the pig kidney for any signs of rejection. The organ was implanted outside the body to allow for observation and tissue sampling during the 54-hour study period. JOE CARROTTA FOR NYU LANGONE HEALTH

"From an ethical perspective, PETA has always been opposed to the use of sentient animals as warehouses for human spare parts. Animals are removed in laboratory investigations cases, said in an email.

The Rev. Tadeusz Pacholczyk, a Catholic priest, neuroscientist and bioethicist, sees no insurmountable ethical problems with the surgery or pig-to-person transplant. Animals have long been sacrificed for human benefit.

More than 120 million pigs are killed for food every year in the United States alone. For years, doctors have implanted heart valves from pigs and cows into their patients. Those implants are considered safer for older adults than mechanical valves, because the patient doesn't need to take risky anti-clotting medications. Animal cells are removed from the valves before implantation, so it's not considered an organ transplant.

Pacholczyk, director of education at the National Catholic Bioethics Center in Philadelphia, said he's also comfortable with the idea of operating on a person whose brain function had ceased as long as the family consents, as they did in Montgomery's case.

"To my mind there's not a fundamental concern there," Pacholczyk said, "since this would be an instance of 'donating one's body to science' after death."

A night of action

Montgomery returned from Virginia — missing the rehearsal dinner — around about 11 p.m., just as others on his team took off from Teterboro Airport in New Jersey, headed to the pig farm. A veterinarian and veterinarian anesthetist were waiting when they arrived and helped perform the surgery.

Just after 1 a.m., the surgeons made their first incision.

Revivior, a company owned by United Therapeutics, had bred the pig. When it was an embryo, one of the pig's genes was edited out to make the organ less likely to trigger an immune reaction in a human.

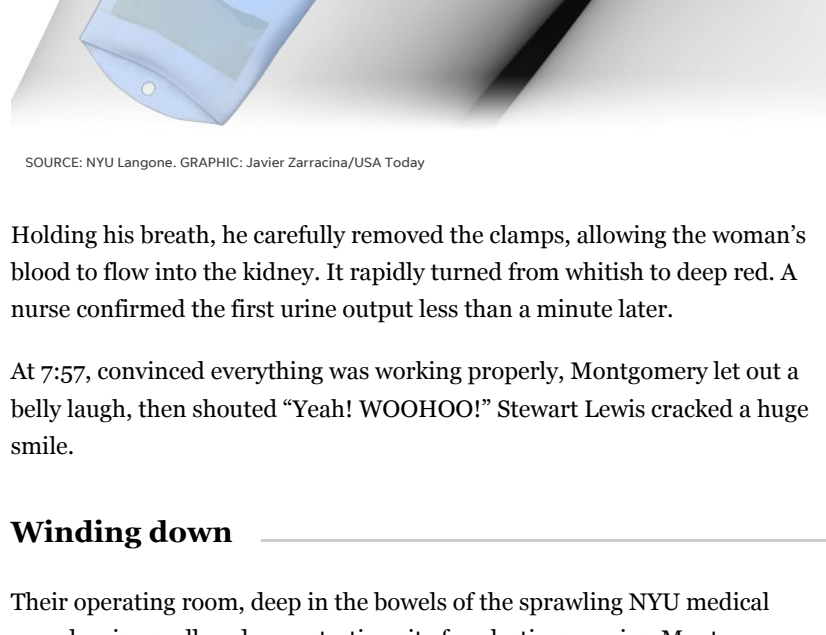
Although others in the xenotransplantation field have been deleting three genes or even dozens, United Therapeutics and Montgomery decided to change the pigs as little as possible. (The same gene, Gal, is removed in pigs bred to feed people who become allergic to meat after being bitten by a lone star tick.) Pigs intended for transplant are kept separate from the food supply.

The pig also had surgery to attach its thymus to its kidney. The thymus, a small gland near the top of the lungs, produces white blood cells — immunity system cells that help the body fight infection. Transplanting the pig thymus along with its kidney is intended to reduce a person's long-term immune response to the foreign kidney. The living patient's thymus would then be removed.

By just after 3 a.m. the transplant team, including a representative from LiveOnNY, a nonprofit organ procurement organization, had packed the kidneys into a large black cooler. They were in the air at 4:30 a.m. and landed in New Jersey at 5:30 a.m.

Right at 6 a.m., the team wheeled the cooler into the basement operating theater at NYU Langone.

Not all of Montgomery's colleagues in the xenotransplantation field agreed with his decision to test the organ in a person declared brain-dead. Once the brain stops sending electrical signals, other organs begin to break down as well. Whatever could be seen in the surgery wouldn't necessarily reflect what would happen in a living being, they said.



Transplant surgeons at NYU Langone Health surgically prepare for xenotransplantation. From left: Zoe A. Stewart-Lewis, MD, PhD, associate professor, Department of Surgery, and surgical director, Kidney and Pancreas Transplant Programs; and Bonnie E. Lonze, MD, PhD, assistant professor, Department of Surgery, and director, Incompatible Kidney Transplant Programs. JOE CARROTTA FOR NYU LANGONE HEALTH

Montgomery chose his volunteer carefully for this reason. The woman lying on the table was stable, he said, with none of the "crazy physiology" seen in some who have lost brain function. Nurses drew her blood several times to look for immune reactions that might signal trouble but found nothing concerning, he said.

So far, the biggest challenge with xenotransplantation research has been routinely keeping study animals alive with organs from a different species — something regulatory agencies want to see before human trials. A German research group has kept several baboons alive for up to six months with pig hearts and a team in Miami has managed to keep two-thirds of their macaques alive for more than 400 days.

Pig kidneys will be easier to make work in people than in monkeys, Montgomery said, "because primates are so tricky to manage."

Leaders in the field are cordial but competitive. Everyone wants to be the first to show xenotransplantation can be done. "First to do it right," said Dr. Joe Tector, a transplant surgeon who leads the work at the University of Miami. "Doing it right is really really important."

There are lives at stake and the field could be set back years by a failed animal-to-human transplant.

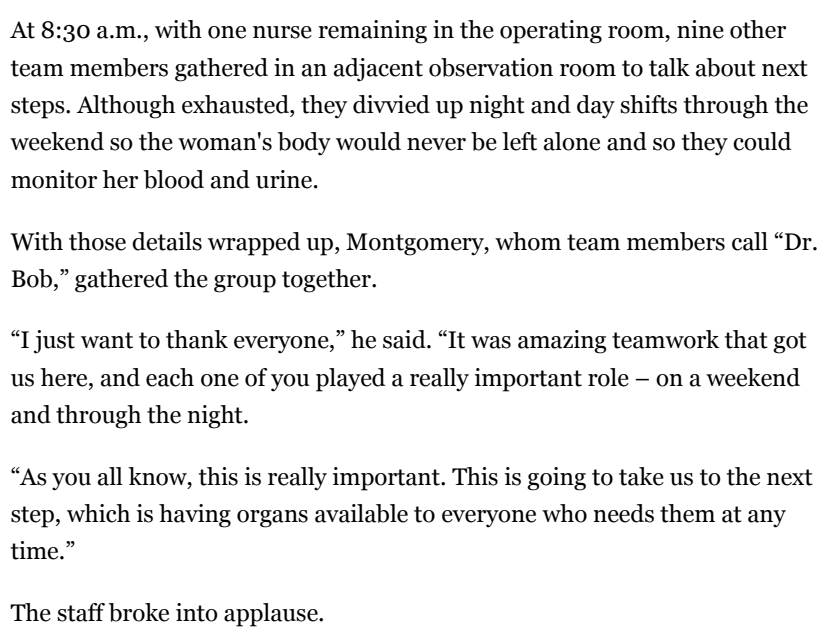
The operation

At 6:05 a.m., shortly after the cooler arrived, Montgomery indicated he was ready to begin.

"All right, does anyone know how to turn the lights on?" Montgomery said. Two gigantic round lights abruptly illuminated the woman's pelvic area. Nurses had raised her body so only the surgical site was visible. Her chest continued to rise and fall with the push of the ventilator.

Montgomery washed his hands for the second time, and a nurse helped him don a gown over his scrubs and then two layers of brown plastic gloves. He began cleaning a pig kidney while surgeons Bonnie Lonze, and Zoe Stewart Lewis prepped the woman's body.

In a typical kidney transplant, surgeons don't remove the damaged organs, they simply add the new one. Once the transplanted organ is working, the old ones essentially become scar tissue and usually don't need to be taken out.



A genetically engineered pig kidney is cleaned and prepared for transplantation to a human. JOE CARROTTA FOR NYU LANGONE HEALTH

At 6:22 a.m., Montgomery called a timeout, the pause made before every surgery to ensure the safety and accuracy of the procedure.

The team held a moment of silence to honor the woman they were about to operate on. The steady beeping of a heart monitor pierced the quiet.

At 7:02 a.m., Montgomery carried the organ — about the size of an outstretched hand — from a nearby table and began carefully stitching the pig kidney into place. He left it nestled against the woman's right leg and would carefully sew a plastic "silo" around it. For this trial, he wanted the kidney to stay outside the body so he could easily biopsy it to check for problems as well as keep out germs and watch its coloration.

A half hour later, he stood on a stepstool to get a better position. At 7:45 a.m., he threaded a plastic tube into the ureter, the duct that carries urine from the kidney to the bladder.



SOURCE: NYU Langone. GRAPHIC: Javier Zaracina/USA Today

Holding his breath, he carefully removed the clamps, allowing the woman's blood to flow into the kidney. It rapidly turned from whitish to deep red. A nurse confirmed the first urine output less than a minute later.

At 7:57, convinced everything was working properly, Montgomery let out a belly laugh, then shouted "Yeah! WOOHOO!" Stewart Lewis cracked a huge smile.

Winding down

Their operating room, deep in the bowels of the sprawling NYU medical complex, is usually a demonstration site for plastic surgeries. Montgomery couldn't tie up a typical operating room for the 72 hours he wanted to keep the body hooked up to the pig kidney.

But even that proved too long. Plastic surgery residents needed their classroom by Tuesday morning, almost exactly 72 hours away. And the room had to be thoroughly cleaned first. Not to worry, Montgomery told a nervous transplant team member, who brought the time constraint to his attention. It would all work out.

During the procedure, anyone who set foot in the operating room or came into contact with the pig organs had to have their blood drawn and frozen.

Pigs carry viruses in their genes called porcine endogenous retroviruses, or PERVs. When these were identified in the early '90s, as the full scope of the HIV epidemic was being recognized, regulators worried that PERVs would spark the next lethal outbreak. For years, xenotransplantation research was sidelined by these fears.

Concerns have ebbed, though, with HIV now a treatable disease and hundreds of people safely exposed to pig cells and tissues since.

Members of the xenotransplant surgical team at NYU Langone Health. JOE CARROTTA FOR NYU LANGONE HEALTH

Still, in an abundance of caution, nurses collected blood from everyone in the operating room in case the deceased woman was found to have PERVs in her system. If that happened, they would all need to provide new samples to ensure they hadn't been infected.

As another precaution, the body would be embalmed right there — a funeral home director was on call — to kill any remaining pig germs before moving it to a funeral home for cremation. Then the scrubbing would begin.

At 8:30 a.m., with one nurse remaining in the operating room, nine other team members gathered in an adjacent observation room to talk about next steps. Although exhausted, they divided up night and day shifts through the weekend so the woman's body would never be left alone and so they could monitor her blood and urine.

With those details wrapped up, Montgomery, whom team members call "Dr. Bob," gathered the group together.

"I just want to thank everyone," he said. "It was amazing teamwork that got us here, and each one of you played a really important role — on a weekend and through the night."

"As you all know, this is really important. This is going to take us to the next step, which is having organs available to everyone who needs them at any time."

The staff broke into applause.

Leaving the hospital a little after 9 a.m., Montgomery got back into his car for the seven-hour drive back to the wedding. He arrived just in time to hear his wife — a singer with the Metropolitan Opera — perform and the couple exchange vows. "I made it for the high points," he said on the drive back to New York the next day.

Then he spent his third nearly sleepless night watching over the body.

Urine output from the pig kidney was strong, and the organ effectively filtered her blood as a normal kidney would. Her immune system didn't seem to be responding at all to the foreign kidney carefully stitched to her thigh.

At 2 p.m. Monday, 54 hours after the connection between human and pig was made, the team turned off the ventilator. Within minutes her heart stopped.

Later, after reviewing the data, Montgomery said he was pleased with the results. "It's even better than I'd hoped."

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