Doctors learn how to transplant organs without the worries of rejection.

By Kirsten Weir

PERFECT FIT

Demi-Lee Brennan isn't the girl she used to be. After receiving a new liver several years ago, her body underwent an astonishing transformation. Her blood type and her immune cells changed to match those of her liver donor. In a medical first, the 15-year-old Australian girl had acquired her donor's immune system.

Even before Demi's story came to light last winter, U.S. researchers had been trying to encourage the immune systems of transplant patients to do what Demi's did on its own. In January, a team of scientists and surgeons at Massachusetts General Hospital in Boston announced that it had pulled off the trick. The team's new technique could improve the lives of the nearly 30,000 Americans who receive organ transplants each year.

RESISTING AN ARMY

Demi's tale began when she was 9 years old and became seriously ill. Doctors determined that an unknown virus was attacking her liver. Surgeons performed a transplant, replacing her failing liver with a healthy one taken from a boy who had recently died. The surgery saved her life.

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The biggest challenge to any transplant's success is usually the patient's own *immune system*. The immune system protects the body from foreign cells such as bacteria and viruses. To do that, it employs an army of *white blood cells*, some of which keep watch for foreign invaders while others attack and destroy them.

Unfortunately, white blood cells identify transplanted organs as foreign entities and attack them the way they would viruses and bacteria. To prevent such attacks, transplant patients are prescribed *immunosuppressant drugs*. The drugs damp down the immune system, keeping the white blood cell soldiers in check.

Demi began taking immunosuppressant drugs immediately after her transplant. Several months later, though, her doctors made a startling discovery. Before her transplant, Demi had type O-positive blood. Now, her blood was O-negative—the blood type of the boy whose liver she had received. All of Demi's blood cells, including the white cells, had changed to match those of her organ donor.

What had happened? *Stem cells* in the transplanted liver had made their way into Demi's *bone marrow*. Stem cells are immature cells that have the ability to mature into many different kinds of adult cells. Bone marrow is

Demi-Lee and her doctors, Stephen Alexander (left) and Stuart Dorney

the spongy tissue in the center of the bones that produces new blood cells, including immune cells. Inside Demi's bones, stem cells from the donated liver began churning out new blood cells. Eventually they replaced her native cells.

Demi's new immune system identified the transplanted liver as part of her own body, rather than a foreign invader. Her liver became safe from an immune attack. She was able to stop taking immunosuppressant drugs.

TRICKING THE SYSTEM

Those drugs have made transplants possible, says David Sachs, director of the Massachusetts General Hospital Transplantation Biology Research Center. "The drugs have saved many lives," he notes. Yet the drugs aren't perfect. After all, they weaken the body's defense system. Although that weakened state protects transplanted organs, it also puts patients at risk for infections and some types of cancer, he says. Worse, half of all transplanted organs are rejected within 10 years, even with immunosuppressant drugs.

Recently, Sachs and his colleagues developed a new technique to prevent organ rejection. They tested it on five kidney transplant patients. Each patient received a kidney plus a bone marrow transplant from his or her kidney donor. After the procedure, Sachs says, the donors' bone marrow cells mixed with each patient's own cells. The patients took on a kind of hybrid immune system—a condition known as *mixed chimerism.*

The result is similar to Demi's case, though not exactly the same. "She became a complete chimera," Sachs explains, wholly taking on her donor's immune system. Sachs's mixed chimeras, on the other hand, retained their own immune cells in addition to those of their donors.

Sachs's patients remained mixed chimeras for only a few weeks. Then their original immune systems took over. Still, that was long enough to trick the patients' immune systems into tolerating the transplanted kidneys indefinitely. "Even though chimerism disappears," Sachs says, "[the patients' bodies] don't reject their organs." One patient experienced complications, but the other four were able to stop taking immunosuppressant drugs. The patients are doing well today, two to five years following their transplants.

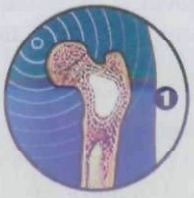
The next step for Sachs and his team will involve testing the technique on other types of organ transplants. One day, all organ recipients may be able to live without immunosuppressant drugs and the risks they pose. "I hope this will improve the quality of life for [transplant] patients," he says. **CS**

Trick Transplant

By performing double transplants, doctors at Massachusetts General Hospital were able to keep their patients' immune systems from rejecting transplanted kidneys.

PREPARATIONS

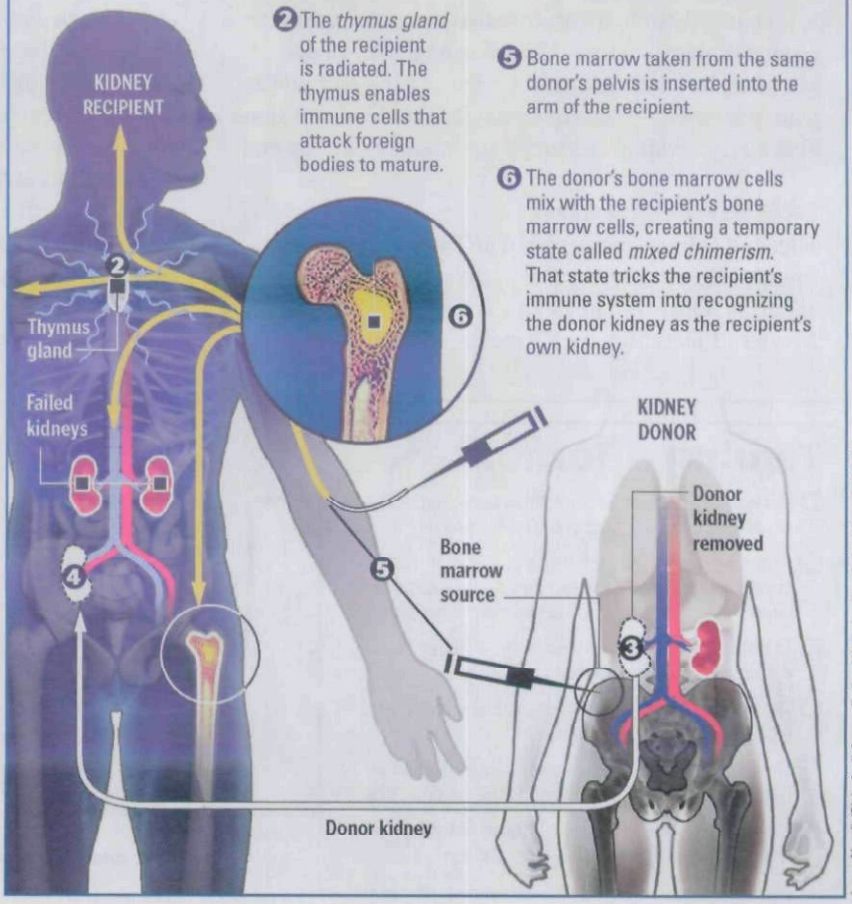
1. Starting five days before the transplant, the organ recipient receives a low dose of chemotherapy to kill off bone marrow cells.



2. The *thymus gland* of the recipient is radiated. The thymus enables immune cells that attack foreign bodies to mature.

TRANSPLANT

3. A kidney is removed from the donor (who needs only one kidney to live).
4. The kidney is transplanted into the recipient's pelvic area and attached to blood vessels.
5. Bone marrow taken from the same donor's pelvis is inserted into the arm of the recipient.
6. The donor's bone marrow cells mix with the recipient's bone marrow cells, creating a temporary state called *mixed chimerism.* That state tricks the recipient's immune system into recognizing the donor kidney as the recipient's own kidney.



James Abundis/Globe Staff; Source: Dr. David H. Sachs, *New England Journal of Medicine*