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# Organ Transplants Without the Drugs

By ALICE PARK

Thursday, Jan. 31, 2008



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Surgeons performing a kidney transplant operation through an incision in the patient's abdomen

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They are frequently called the gift of life, but organ transplants have always been plagued by a painful irony; as desperately as an ailing body needs a healthy organ to replace a faltering one, it often ends up rejecting the priceless replacement part. Decades of research have led to improved drugs to reduce this reaction, but these agents have to be taken for a lifetime and are often difficult to tolerate, leading to higher risks of both infection and cancer.

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In an intriguing but small study published in the New England Journal of Medicine, however, doctors at Massachusetts General Hospital and New York Presbyterian Hospital may have finally come up with an end run around organ rejection. They report on four kidney-transplant patients who were able to wean themselves off powerful antirejection drugs within a year of their transplants (a fifth rejected his kidney). Even more exciting is the fact that while the organ donors in the study were family members of the recipients, they were not perfect tissue

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matches.

The key, says Dr. David Sachs, a surgeon at Mass General and Harvard who led the study, is to prepare a patient's immune system well before the surgery—or, to be more exact, to deplete the immune system's T cells, which normally patrol the body looking for foreign invaders like bacteria, viruses and tissues from outside donors. Several days before the transplant surgery, Sachs' team used drugs that target and eliminate these cells to wipe the immune slate clean. Then the team transplanted the kidney along with bone-marrow cells that had been harvested from the patients before their immune cells were eliminated. What happened next was surprising: the bone marrow rebuilt the immune system but this time as a chimera—a hybrid of both the donated organ's cells and the body's own. The donated organ could then be accepted instead of rejected.

"It retrains the immune system, fooling it into thinking that the donor tissue is now part of the self," says Sachs. One patient was able to stop taking antirejection drugs as early as nine months after his surgery—though not without some discomfort as the body adjusted. "There is no question that during the initial phase, the patient has a lot more difficult time. But they trade that difficulty with what is beginning to look like lifelong suppression [of rejection]," says Sachs.

More perplexing to the team was the fact that the chimeric state is not permanent, with the immune system eventually returning to its original state. Yet the patients have nonetheless continued to tolerate their donated kidneys for almost five years. Why? Sachs believes that once the immune system is trained to accept the donated organ, sentry cells protect the organ from being recognized as foreign. The transplanted kidney exists in an immune bubble, guarded from the T cells that could still destroy it.

If that's the case, say transplant surgeons, it might even be possible in coming years to look outside our species for much needed organs. Once the human immune system can be trained to safely accept foreign tissue, then these so-called xenotransplants, from pigs or primates, could provide a welcome solution to the organ shortages that still put 98,000 patients in the U.S. each year on waiting lists.

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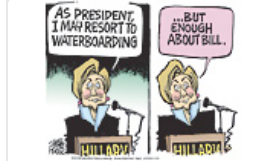
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