

The Animal In Us

The Latest Advances in Xenotransplantation

Two developments last year in xenotransplantation—the technique of moving tissue from one species of animal into another—have brought closer the prospect of engineering and manufacturing animals for the purpose of routinely providing spare parts for human beings.

First, researchers announced that they had genetically engineered pigs to be more compatible with humans, in the hope of transplanting pig organs and tissues into people. In January 2002, two competing companies (Immerge BioTherapeutics and PPL Therapeutics) revealed that they had knocked out one of the two copies of a pig gene, GGTA1, that makes an enzyme believed to trigger an immune response in humans. One of those companies—PPL Therapeutics, the Scottish firm that created Dolly the cloned sheep—then succeeded in knocking out the second copy of the gene. On July 25, a cloned litter of these so-called “double-knockout” piglets was born at the company’s lab in Blacksburg, Virginia.

Those cloned pigs, however, may be too large to serve as sources of human organs. Early this year, Immerge, working with researchers at two universities, announced the creation of smaller cloned double-

knockout pigs. The creation of these potentially transplant-compatible “miniature swine” suggests that herds of made-to-order pigs may someday be manufactured for the specific purpose of supplying replacement organs for human beings. If the PPL and Immerge piglets turn out to be healthy—no one yet knows how the genetic modifications will affect them—and if the organs are deemed safe for transplants into humans, we might see such herds within a decade.

Second, in August 2002, an international team of researchers announced the results of a controversial two-year experiment in which they inserted pig cells into adolescents with diabetes. In this study, an updated version of experiments first attempted in the early 1990s, a team of researchers from Mexico and Canada treated a dozen Mexican children suffering from Type 1 diabetes (formerly called juvenile diabetes). First, the doctors created a pouch of human tissue inside the abdominal wall of each child. Then, without giving the children immunosuppressive drugs, the doctors filled those pouches with insulin-producing pancreatic cells from newborn pigs. Then—and here’s the new twist—the researchers also inserted certain cells taken from the pigs’ testicles

into the children, in the hope that these cells would quiet the children's immune systems.

The results were promising. None of the children needed to take immunosuppressants, according to the researchers. After two years, half of the children were producing at least some insulin on their own, reducing their need for insulin shots. One of the children was off insulin for six months, and another has remained off external insulin altogether—thus possibly becoming the first diabetic patient to be taken off external insulin without requiring the use of immunosuppressants.

Still, the study has come under criticism. Whenever pig-to-human xenotransplantation is attempted, there are concerns that certain genetic material from the pigs could have dangerous side effects on humans. Theoretically, porcine endogenous retroviruses (PERVs) could damage the human immune system, with results similar to the effects of AIDS or leukemia. Although no human or animal receiving pig tissue has so far shown any PERV-related problems, scientists have seen PERVs affect human cells under laboratory conditions.

Beyond the fear and uncertainty about PERVs, the diabetes study has been condemned for insufficient preclinical research. The “approach has not been properly tested in animals,” according to critics cited in the journal *Nature*. The lead researcher says that he obtained approval from the Mexican government, even

though Mexico apparently has no rules regarding xenotransplantation research. He also says he followed FDA guidelines—although “other researchers say that the FDA would not have approved” this research because of “the lack of pre-clinical studies and the fact that his work was in patients too young to give proper informed consent,” according to *Nature*.

While it's true that animal parts have been medically inserted into people for some time—for example, pigs are already commonly used as a source of insulin and heart valves—the prospect of routine xenotransplantation raises two broad ethical concerns, which may seem at first to contradict one another. One group of critics argues that engineering animals for use as organ factories is too callous an abuse of human power. Meanwhile, others worry that xenotransplantation may erode the dividing line between man and beast and thus degrade its human beneficiaries. Xenotransplantation is therefore criticized as both too high and too low for humanity.

One or both of these concerns likely lie behind the disgust many Americans initially have at the idea of harvesting animal organs. In the end, the medical benefits may give us adequate reason to cross the lines that separate species, just as they gave us reason to begin the project of moving organs between humans. But we should step cautiously as we approach yet another medical, moral, and biological boundary.