

## Science Makes Sex Obsolete

<http://www.wired.com/news/technology/1,68970-1.html>

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02:00 AM Dec, 01, 2005

When the U.S. government decided to ignore the field of assisted reproduction, it unwittingly created the perfect conditions for bold -- some would say risky -- science and medicine.

Free from having to satisfy strict federal oversight, and supported by eager patients wanting children, some doctors performing [in vitro fertilization](#), or IVF, turned their clinics into quasi-research centers. As a result, a string of innovations over the past three decades has stretched the boundaries of fertility science.

Most IVF doctors and researchers are not pursuing esoteric science. They tend to focus on tweaking existing techniques -- finding better ways to use drugs and trying out new gear -- because they'd rather focus on what they can offer patients sooner rather than later. But what may seem like a small alteration could altogether change what it means to make a baby, and who can make a genetically related baby (think same-sex couples).

Let's take a look at some of the possibilities coming down the pike.

### **Designer babies**

The idea of "designer babies" is one of those concepts that is fun to discuss over a pitcher of Mojitos, but the practical reality is sobering.

Designer babies have already been born. Well over 1,000 children have been screened as embryos by [preimplantation genetic diagnosis](#), or PGD. In PGD, a cell taken from an embryo is analyzed to see if the chromosomes or genes are normal. Families use PGD to weed out genetic diseases and to make a baby who will be immunologically [compatible](#) with an existing sibling in need of a blood or bone-marrow donation. More controversially, it can be, and has been, used to select the sex of babies.

But the term "designer baby" could become more literal.

In the Nov. 1, 2004, issue of the [Proceedings of the National Academy of Sciences](#), a team led by [Ralph Brinster](#) at the University of Pennsylvania [managed to grow](#) mouse "spermatogonial stem cells" in a dish. Also known as SSCs, they are the type of stem cells that eventually become sperm.

It gets even more interesting when you learn what Brinster did with sperm stem cells in 2001. In that study, he and his team changed the genetic program of SSCs. Because these are sex cells, any changes scientists might introduce to their genes will be carried from

generation to generation. This is called a "germ line" change, and it's a line that the majority of bioethicists agree should not be crossed, because it raises the specter of DNA eugenics.

So in theory, this technology could lead to a way to make sperm for infertile men, which most people would agree would be a great outcome. But scientists would also have the ability to alter the sperm genes so every succeeding generation would carry the change.

"SSCs provide an alternative method to modify the germ line of animals," Brinster and his team wrote, adding that changing the soup the cells soak in could change their genetics, and "identical or similar signaling mechanisms and culture requirements are likely to be applicable to other species," including humans.

Brinster wants to use the technology as a therapy, as a study tool and to make new kinds of lab animals. But it doesn't take many Mojitos to come up with a whole lot of other possibilities, too.

### **Ovarian transplants**

In the July 7 issue of [\*The New England Journal of Medicine\*](#), St. Louis IVF specialist [Dr. Sherman Silber](#) announced he had [transplanted](#) ovarian tissue from one woman into her identical twin sister who had undergone cancer chemotherapy as a girl. The cancer treatment left her infertile, but after receiving the transplant she became pregnant and delivered a healthy baby. Because the ovarian tissue came from her twin, the baby is genetically her own.

The limitation, of course, is that not everybody has a twin-in-waiting. And Silber's technique used strips of ovarian tissue that could be easily damaged by harvesting, storage and insertion into a recipient.

On Sept. 14, however, Israeli scientists at the [Institute of Animal Science](#) announced they had transplanted entire ovaries into sheep, that the ovaries functioned normally and that eggs produced by the ovaries made embryos.

"We conclude that immediate and long-term hormonal restoration and normal ovulation is possible after cryopreservation and transplantation of whole ovaries in sheep," the researchers [wrote](#). If the technique works for humans, women could have their ovaries removed before cancer treatment, screened for the presence of cancer cells, stored and then replaced after their recovery.

But Dr. Marcelle Cedars, who directs the University of California

at San Francisco [Center for Reproductive Health](#), and others say [freezing eggs](#) could be a better solution. While that is one technique she believes was introduced [prematurely](#), the technology is improving and will likely replace ovarian tissue preservation.

Then again, egg freezing itself may ultimately be replaced.

### **Manufactured eggs and sperm**

One of the most common causes of infertility is that men often make wimpy sperm -- or no sperm at all -- while women often make eggs that refuse to hum along like the little factories they were meant to be. This is especially true for women who are older or have undergone cancer treatment. So for about the past six years, scientists have tried to do an end run around misfiring eggs and missing or weak sperm.

Teams in France, the United Kingdom, New York and Japan are [working](#) to morph regular human cells into egg cells.

The major obstacle researchers face is that regular cells have a full complement of chromosomes (two copies of each, or diploid). In order to become reproductive, a cell must eject half its chromosomes and become haploid (a process called "haploidization") in order to receive the other half from sperm and create a new organism. So, researchers are pursuing methods to achieve "artificial haploidization."

In 2001, [Dr. Gianpiero Palermo](#) of the [Weill Medical College](#) at Cornell University in New York [announced](#) that his team created artificially haploid eggs by borrowing techniques from cloning. The scientists removed the nucleus of a donor egg, then inserted a somatic (adult body) cell. When the somatic cell fused with the egg, researchers fertilized the egg with sperm. Fifty-two percent of the reconstituted eggs fertilized normally.

But at some point along their path to development, the engineered embryos' chromosomes went awry. Ever since, Palermo and others have been trying to figure out why. In his team's most recent experiments, [published](#) in September in the journal [Reproductive BioMedicine Online](#), "blastomeres (cells) isolated from cleaving embryos showed a chaotic distribution of chromosomes." Chaos isn't good in biology.

So Palermo's team is switching tactics and inserting embryonic stem cells instead of adult cells into eggs. Last month, at the annual meeting of the [American Society for Reproductive Medicine](#) in Montreal, the team reported that by using that approach, the cells underwent haploidization and became, in effect, sperm. The combination not only made embryos, but those new embryos yielded a second generation of embryonic stem cells.

Scientists from the University of Pennsylvania [announced](#) at the same meeting that they had created egg-like cells from mouse embryonic stem cells by basting them in a special chemical marinade.

Soon, Palermo says, it may be possible to use so-called therapeutic cloning to custom-make sperm and eggs for infertile people. "In theory, such stem-cell differentiation should be the most promising." In fact, a research group at the [University of Sheffield](#) in

the United Kingdom reported in June that it had made precursors to human eggs and sperm using this technique.

This could literally cure infertility. Of course, it also raises possibilities that may alarm some, like, say, enabling two gay men to create a child genetically related to both of them. A cell from one man could be turned into an egg and fertilized with sperm from his partner. [Dr. Alan DeCherney](#), an IVF pioneer, UCLA professor and editor of the journal *Fertility and Sterility*, says such a scenario is about five years away from reality, and when it happens "there will be an outcry. There's lots of homophobia. But eventually, it'll be accepted."