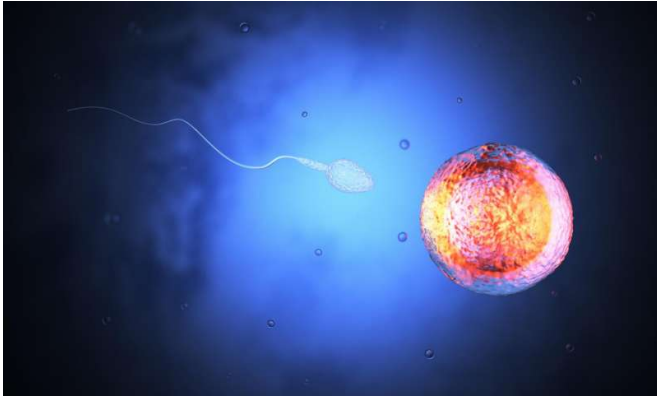


# Paper examines potential—for better or worse—of 'in vitro gametogenesis'

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In the future, the two cells that start us all might sometimes get their start in the lab, rather than in reproductive organs. Credit: istockphoto/Brown University

Even in such game-changing reproductive advances as in vitro fertilization or mitochondrial replacement therapy, what has remained necessary is that the gametes—the sperm and the egg—come from the father's testes and the mother's ovaries, respectively. But a new lab technology rapidly advancing in mouse studies could upend that biological imperative by, at its hypothetical endpoint, creating embryos from sources such as repurposed skin cells.

The implications of "in vitro gametogenesis" (IVG), three experts write in a perspective essay in *Science Translational Medicine*, could be helpful for infertility patients and for research, but also deeply vexing for society and policymakers.

IVG holds the promise of radically advancing fertility and the ability to intervene against disease at the pre- or post-embryonic stage, wrote Dr. Eli Adashi of Brown University, I. Glenn Cohen, professor at Harvard Law School, and Dr. George Daley, dean of Harvard Medical School. But it also

could lead to ethical nightmares—if people become empowered to create and choose among scores of embryos in the pursuit of ideal children, for example.

"There's something troubling about an inexhaustible supply of gametes that can be fertilized into an inexhaustible supply of embryos," said Adashi, professor of medical science and former dean of medicine and biological sciences at Brown University.

IVG arises from the ability of scientists to manipulate [stem cells](#), either derived from embryos or induced from normal adult body tissues. Working with mice in the lab, scientists have reported key successes. They have created fertilizable egg cells from [embryonic stem cells](#) and have generated sperm-like cells as well. They've also created fertilized embryos from stem cells. In that case, the scientists coaxed stem cells into an early stage of gamete development and then finished their development within the reproductive organs of mice before accomplishing fertilization.

So far it is not feasible—technically or legally—to create a human baby via IVG, and depending on many remaining technical, economic and regulatory hurdles, Adashi said, it might never be. But it does now seem at least prospectively plausible.

"These things may happen, and it may just be a question of time," said Adashi, who has been tracking the development of IVG, mostly in Japan and the United Kingdom, since 2005.

## Opportunities and dilemmas

The most straightforward benefit of IVG might be that producing sperm or eggs without the need for functioning reproductive organs could help patients for whom reproductive function has been lost, for instance because of chemotherapy, the authors wrote.

Moreover, they continued, IVG could revolutionize in vitro fertilization because it could vastly expand the supply of eggs, which currently must be drug-induced and then surgically harvested in very small quantities and at great expense.

Healthy men have no trouble producing sperm by the millions, but the possibility of an abundant and maybe even cheap supply of eggs, derived in the lab from sources such as sloughed skin or a cheek swab, raises many of the biggest opportunities and dilemmas of IVG, Adashi said.

If IVG can indeed produce many eggs in the lab, then combined with rapidly advancing genome editing techniques, future physicians could root out some inherited diseases even before fertilization occurs, the authors wrote. With an abundant source of gametes, researchers could also more easily study disease and development at the molecular and cellular level.

And with readily available eggs, people could also generate personalized embryonic stem cell lines for future medical needs. That would harness an existing technology in which they create stem cells by transferring a nucleus from one of their mature body cells into an enucleated egg cell.

But ethical minefields abound. Many people are adamantly opposed to creating embryos for research or therapeutic use and in an IVG-enabled scenario in which that's done easily in a lab, the ethical questions are magnified.

Current U.S. law prohibits public funding for the creation of embryos for research. Clinical uses of IVG will certainly undergo tough regulatory scrutiny in most any country.

But even if IVG proves safe and effective, what would policymakers do, for instance, in the case where a couple wanted to use it to purposely generate scores of embryos—many more than IVF allows—merely to select the "best" among them to become their baby?

"IVG may raise the specter of 'embryo farming' on a scale currently unimagined, which might exacerbate concerns about the devaluation of

human life," Cohen, Daley and Adashi wrote. "IVG could, depending on its ultimate financial cost, greatly increase the number of [embryos](#) from which to select, thus exacerbating concerns about parents selecting for their 'ideal' future child."

In the most speculative scenario, one that Adashi believes will forever remain far-fetched, IVG might enable single-parent babies, in which one person produces both sperm and egg, leaving no need for a second parent (though men would still need a surrogate mother to carry the embryo to term). It's not yet clear, however, that a person can produce the other gender's gametes via IVG, and that producing a baby with just one parent's genes—the ultimate in inbreeding—would be to risk the baby's health.

Finally, to the extent that gametes could be derived from easily harvested sources such as skin, it's conceivable that people could be made parents without their knowledge or consent.

"Should the law criminalize such an action?" Cohen, Daley and Adashi asked. "If it takes place, should the law consider the source of the [skin cells](#) to be a legal parent to the child, or should it distinguish an individual's genetic and legal parentage?"

### **Not too soon to contemplate**

In the nearest term, the authors wrote, the likelihood is that IVG will merely remain a subject of research and that its first impact would most likely be in aiding basic studies of gametes and those earlier-stage gametes, "[primordial germ cells](#)."

"Given the stringent safety imperative, clinical applications are less likely to be pursued any time soon," they wrote. "Still, with science and medicine hurtling forward at breakneck speed, the rapid transformation of reproductive and regenerative medicine may surprise us. Before the inevitable, society will be well advised to strike and maintain a vigorous public conversation on the ethical challenges of IVG."

They may prove to be many.

**More information:** "Disruptive reproductive technologies," *Science Translational Medicine*, [stm.sciencemag.org/lookup/doi/ ... scitranslmed.aag2959](https://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aag2959)

Provided by Brown University

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