THE WALL STREET JOURNAL.

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Should Heritable Gene Editing Be Used on Humans?

The medical potential is enticing, but the technology raises biological and ethical concerns

Gene editing for human sperm, eggs and embryos could eliminate inherited disease—but also lead to designer babies.
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April 10, 2016 10:02 p.m. ET

The development of technology that allows human genes to be edited has stirred tremendous excitement about the potential for treating debilitating and life-threatening diseases. The technology could lead to drugs that would treat cancers and other diseases that currently are incurable.

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But another facet of this breakthrough has many scientists and others worried: the possibility that the genetic makeup of sperm and eggs could be edited so that diseases that can be inherited won't be passed on to children yet to be born. One concern is that gene editing that affects future generations, not just an individual, is too risky given our still incomplete understanding of the human genome and how changes might affect it. Another is that the ability to edit heritable traits could result in so-called designer babies, with parents choosing traits such as intelligence or physical characteristics.

Others say we can meet those challenges, and the potential benefits are too great to pass up.

George Church, professor of genetics at Harvard Medical School, favors a careful exploration of the potential of heritable gene editing. Marcy Darnovsky, executive director of the Center for Genetics and Society, says the risks to individuals and to society are too great.

YES: If Evidence Shows the Technique Is Safe and Effective

By George Church

Editing genetic material in human sperm or egg cells to restore healthy DNA can address significant unmet medical and emotional needs.

There are many genetic diseases that could be eliminated in families—Tay-Sachs disease, for example, which causes devastating progressive mental and physical deterioration, with death by the age of 4.

For this and other severe genetic diseases without cures, those who carry the harmful genetic variant currently have few choices when they want a child who won't be afflicted: adoption, egg or sperm donation or abortion of embryos that are stricken with the disease. For many couples, none of those options work.

Adoption and donation don't satisfy the strong desire of many parents to have children of their own lineage, and abortion is unacceptable to many. Genetic editing would allow couples to have healthy children who share their DNA, without harming any embryos—assuming editing is done in sperm or egg cells and not embryos, so that no embryos would be destroyed in pregnancy or using in vitro fertilization. Gene editing of sperm-producing cells could also reduce infertility and spontaneous abortions, which are important medical issues for many families.

There's every reason to expect the practice of editing heritable genes would be safe and effective. Clinical trials of gene editing that is not passed on to future generations are already showing successful cures for HIV-AIDS and leukemia. Many other applications of editing are similarly fruitful.

The notion that we need complete knowledge of the whole human genome to conduct clinical trials of heritable gene editing seems at odds with medical reality. We had a very weak understanding of the human immune system when smallpox vaccination began in the 1570s or even when the disease was fully eradicated in 1979. In the case of gene editing, it is very helpful that we can now routinely inspect the whole human genome, if not fully understand it—so that cells that give rise to sperm or eggs for each patient can

be checked to see that only the desired mutation is made, with no unwanted DNA changes.

Indeed, the latest versions of gene-editing enzymes have zero detectable off-target activities. It is also helpful to know that each edit changes the DNA from a sick version to a healthy version that billions of people share. This is far higher certainty than we have for a completely new drug that has never before been tested on humans.

Why not just use gene editing to treat diseases in adults? Gene editing in reproductive cells could be more effective than in adult cells, in many cases. When editing the more-complex adult tissues, it's hard to avoid mixing incompletely or incorrectly edited cells with correctly edited ones, which can lead to a failure to correct the targeted mutation or even the introduction of new mutations. Moreover, many genetic diseases are very hard to fix after damage is done early in embryonic development.

With the proper care, we can also avoid harmful unintended consequences. If a new technology is an improvement over previous practice, then we cautiously implement it for the clearest needs first—watching for opportunities to make it ever safer.

For gene editing, we can focus initially on fixing the most deadly, currently incurable genetic diseases in newborns. If these editing therapies are safe and effective, then we can move on to targeting other traits.

Probably the most frequently discussed of such traits are those that affect brain function. We know of many genes that affect cognitive abilities in young and old. If we are concerned that the editing of such genes will be used by the rich to get smarter, then we could regulate gene editing and any other means of achieving that outcome—drugs, prenatal genetic selection, adult gene therapy.

What seems more likely is that we'll reduce the cost of gene editing, as we have for genome sequencing, making its benefits widely available. To deal with the resulting ethical issues, we should engage citizens world-wide in a discussion of gene editing for less-severe symptoms and nonmedical uses, while we monitor the clinical trials for the most conservative applications of gene editing.

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NO: The Biological Risks and Ethical Questions Call for Caution

By Marcy Darnovsky

Gene editing in humans can refer to two very different things. One use would seek to alleviate patients' symptoms—or perhaps even cure their diseases—by targeting particular cells or tissues in their bodies. Although past experiments with this approach have been disappointing, recent advances, including new gene-editing techniques, are raising hopes that gene therapy can be made safe and effective. If so, it could be a significant and welcome medical advance.

A radically different use of gene editing would target human sperm, eggs or early embryos in an effort to alter the DNA and the traits of resulting children. These genetic changes would be irreversibly reflected in every cell of future children's bodies, and in the bodies of their children and subsequent generations—in ways that we can't possibly predict because of the complexity of the human genome. The biological risks and ethical implications of reproductive gene editing would be unacceptable.

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Indeed, the prospect of genetic modification to redesign our children or re-engineer humanity has been widely rejected since it was first contemplated decades ago. Policy makers in dozens of countries, including nearly every nation with an advanced biotechnology sector, have passed laws prohibiting heritable human genetic modification. Opinion polls consistently show large majorities of people recoiling from it.

Now, however, some scientists and futurists are pushing for reconsideration. While nearly all acknowledge that attempts to use gene editing for reproduction would be far too dangerous at present, some believe that refinements will soon make it safe enough to try. Most advocate its use to prevent the transmission of inherited diseases, but this justification is tenuous at best. That's because people at risk of passing on a genetic disease can have healthy children in several safer ways.

Using third-party eggs or sperm is one option. Alternatively, those for whom a genetic connection to both parents is important can use the embryo-screening technique known as preimplantation genetic diagnosis to identify unaffected embryos in the overwhelming majority of cases. Preselecting children who have—or who lack—specific traits raises its own ethical concerns, but it's far less biologically risky and socially

consequential than attempting to manipulate future children's genes. Of course, any effort to prevent the birth of a child with an inherited disease—including experiments with genetically engineering sperm or eggs—would require that parents know they're at risk of transmitting one, and that they're willing to use in vitro fertilization, with all its attendant invasiveness, discomforts, risks and financial costs.

A few advocates of gene editing for reproduction are openly enthusiastic about "enhancing" future generations. In the near term, they suggest inserting genes such as those correlated with larger muscles or less need for sleep. It's all too easy to imagine fertility clinics offering "offspring upgrades" to affluent parents, and competitive pressures to make sure your children aren't "left behind." Not far down that road, we could see the emergence of genetic haves and have-nots, with new forms of inequality and discrimination.

Some involved in the current controversy about human gene editing recognize the perils of genetic enhancement efforts, yet propose allowing reproductive gene editing for traits like a lowered probability of late-onset diseases. But in the real world, one genetic risk is generally traded for another—a gene that confers one kind of biological risk might also protect against another—so, again, the complexity of the genome makes this approach dangerous. And a regulatory line between traits construed as medical and those that are clearly enhancements would be impossible to draw or to hold. The Food and Drug Administration can't even control off-label use of drugs. Opening the door to one kind of reproductive gene editing would be opening the door to all kinds.

Gene editing brings us to a consequential crossroads. We need to think carefully and choose wisely between applications that lead to dangerously unacceptable social consequences, and those that can contribute to human flourishing and well-being.

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