Why Worry About Genetically Modified Babies?

The terms "genetically modified babies" and "designer babies" are attention-getters. But beyond the catchy sound bites, what do they really mean - and are they something we need to worry about?

Unfortunately, with the technical capacity to engineer inheritable traits growing quickly, and with the United Kingdom possibly on the verge of loosening its law in order to allow a limited form of inheritable genetic (germline) modification, there is ample reason for concern.

The proposed policy change in the UK would permit licensed fertility clinics to use a biologically radical technique referred to by terms including "mitochondrial replacement," "nuclear genome transfer," and "three-person IVF." This procedure would produce modifications in every cell of any resulting children, and in subsequent generations as well. In this article, we will use the term "nuclear genome transfer," as it is the most technically accurate of the various terms.

The technique is proposed as a way for women affected by a particular subset of severe mitochondrial disorders to have children who are not affected and who are mostly genetically related to them. The researchers promoting it, and some people with mitochondrial disease, have pointed out that they would not be using the technique to produce "designer babies." Understandably, some are perplexed or offended by those who object to the procedure on that basis.

But these advocates of nuclear genome transfer have missed a key element of the case against it. Those of us who oppose it on social and policy (as well as safety) grounds aren't arguing that it would in itself create enhanced humans with specified traits. Our concerns fall into two categories. The first is that an exception to the widespread prohibitions against human germline engineering will open the door to other efforts to modify inheritable traits - that nuclear genome transfer is the thin end of a wedge that would lead to a world of genetically altered human beings. The second set of concerns focuses on safety. This technique, like other forms of human germline modification, is in fact both medically unnecessary and profoundly risky to the children it would produce. Let's look briefly at each of these sets of concerns, starting with the social and policy issues.

If the UK permits nuclear genome transfer to move ahead, it would break a widely observed prohibition that has been respected by scientists globally, and codified as law in more than 40 countries and several international treaties. No other country in the world has ever explicitly sanctioned human germline modification. Just as with human reproductive cloning, it is explicitly prohibited in the Council of Europe's Convention on Human Rights and Biomedicine, and considered to be "contrary to human dignity" in UNESCO's Universal Declaration on the Human Genome and Human Rights.

Because human germline modification is illegal in the UK, proponents of nuclear genome transfer have elected to work toward carving out a narrow exception that would allow their particular manipulation methods to be implemented. A change in UK law to allow "mitochondrial replacement" in fertility clinics, without any required follow up of the resulting children, would inescapably set both a global policy precedent and a biotechnological precedent for the scientific community. If the UK, a country with one of the world's most highly developed biomedical sectors, believes this is the way forward, it would shift the scales and threaten the current international near consensus on the responsible use of genetic technologies. The UK would become an outlier, and would have to carry the burden as well as the benefit that comes with that position. And as David King explains in this issue, the way this policy process has unfolded - with numerous irregularities, misrepresentations, and cherry picking of scientific evidence - deepens our concerns that approval would be used as a wedge issue.
In the United States, a committee of the Food and Drug Administration held a day-long hearing in February 2014 to discuss human germline modification for the prevention of the transmission of mitochondrial diseases or for the treatment of infertility. Most of the experts on the committee came away deeply skeptical about the issues they were mandated to consider: the techniques' safety, efficacy, and necessity.

The United States is one of the few countries with an advanced biomedical sector that does not have any law against human germline modification. This means that if nuclear genome transfer were allowed, it could be used for any purpose. Unfortunately, there are concrete reasons to worry about this sort of "mission creep." One is that Shoukhrat Mitalipov, the U.S. researcher most notably involved with advocating for nuclear genome transfer, has made it very clear that he'd like to see the technique used in efforts to treat age-related infertility (in spite of the fact that, as several experts on the FDA committee noted, there is no clear evidence of any relationship between mitochondrial insufficiency and infertility). Mitalipov has been quoted in several articles looking forward to nuclear genome transfer being quickly adopted in fertility clinics around the country and the world. He has applied for a patent on his version of nuclear genome transfer, and has established a company presumably to commercialize its use as a fertility treatment.

Would there also be pressure to permit human germline modification techniques that would alter nuclear genes, in an effort to specify physical, behavioral, or cognitive traits? There is reason to believe there would be - in fact, a small but disturbing number of prominent scientists and futurists have advocated precisely for this vision. For example, a report produced on the basis of the 1998 UCLA conference "Engineering the Human Germline" argued for the "open exploration" of "human germline engineering." Currently, new precision gene editing techniques such as CRISPR have some scientists excited about the possibilities for the genetic modification of human embryos or adults. Will these new techniques, which will open the door to much more precise changes, be considered less drastic if nuclear genome transfer has already been approved?

Human germline modification would be of profound consequence whether it were to "succeed" or "fail." If efforts to engineer the traits we pass on to future generations succeed, they could exacerbate existing inequalities - or even introduce new forms of inequality - based on the real or perceived superiority of those whose genes had been tweaked. And we could find ourselves trapped in a kind of genetic arms race, which could lead to social disruption on a possibly massive scale.

What if such efforts fail? Germline modification in animals typically involves dozens or hundreds of non-viable offspring. If human germline modification efforts yield similar results, what would become of the people created? Who would be accountable for bouts of unnecessary human experimentation gone wrong?

With nuclear genome transfer, the policy, social and safety issues are inextricably entangled. Some proponents both insist that it would not create genetically engineered babies, and are actively trying to redefine genetic modification completely so as to exclude this particular technique. The U.K. Department of Health wants to make a distinction between changes to mitochondrial DNA (mtDNA) and nuclear DNA (nDNA), arguing that only the latter really constitutes genetic modification. While there are obvious differences between the two, this redefinition has no basis in scientific reality. mtDNA and nDNA are in continuous interaction with each other and changes to mtDNA would cause inheritable changes to every cell of a resulting person.

The notion that nuclear genome transfer is as non-consequential as "changing a battery" is entirely misleading. Scientists have known for some time that mtDNA have pervasive effects. A recent article in New Scientist reviews the accumulating evidence. The overall picture is now so clear that the magazine's editors have just reversed their earlier support for "three-parent IVF," and acknowledged that they "may have seriously underestimated the influence that mitochondria have" and that in fact, "children conceived in this way will inherit vital traits from three parents."

Which brings us to the second category of concerns about nuclear genome transfer. Like reproductive cloning and germline modification, it is scientifically interesting, but applying any of these techniques to human beings will never be medically necessary, and would pose serious safety
Nuclear genome transfer involves the removal and reinsertion of a nucleus from its own egg cytoplasm to that of another woman's. The procedure changes the environment for the nucleus, and introduces it to 37 new genes with which it will need to work in order to carry out every activity moving forward. The impacts of combining genetic material from three different people are entirely unknown, but it is certain that it will have an impact.

Safety concerns for women would include all the short- and long-term risks of egg extraction and IVF. And as members of the FDA committee pointed out, pregnancy and childbirth are often in and of themselves risky for women with serious mitochondrial disorders.

Safety concerns for resulting children would include epigenetic harm from the invasive procedure of removing and reinserting the nucleus, and "mismatch" between the nuclear and new mitochondrial DNA, which could disrupt critical biological functions. Additionally, even tiny amounts of carryover of mutated mitochondria from the first egg could lead to the occurrence of mitochondrial disease through preferential replication.

Questions of efficacy are paramount as well, given that the vast majority of mitochondrial diseases actually originate with mutations in nuclear DNA, and could not be helped by these techniques. Further, the few women who would be candidates for nuclear genome transfer - estimates are on the order of a dozen or so a year in the UK - have much safer options for having healthy and genetically related children.

Some proponents of nuclear genome transfer try to hitch it onto the coattails of the reproductive rights and justice movements, and to justify risky experiments as allowing women to make informed, personal choices about reproductive technologies. But first and foremost, these are biologically extreme technologies that would use women's and children's bodies as ground zero for their experiments. It is women and children who will be encouraged by soothing words and images, and then be asked to bear the risks while a fertility clinic collects an estimated 80,000 pounds for each attempted treatment.

Even with conventional treatments that are far less biologically extreme, the fertility industry does not have a good track record of putting evidence-based information before its customers. And the lack of required follow-up that has already been built into the UK's proposed law does not bode well for women's ability to make informed decisions about the safety or efficacy of this option, or to compare it realistically with its safer alternatives, which include preimplantation genetic diagnosis, egg donation, and adoption.

So, what is really at stake if the UK changes their law to allow a form of human germline modification into fertility clinics? Primarily, the health of women and children, and the integrity of the widespread international agreement against the most dangerous human biotechnologies. And also, perhaps, the shape of the human future.

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by Marcy Darnovsky and Jessica Cussins, GeneWatch
November 24th, 2014
Why Worry About Genetically Modified Babies?
Published on NW Resistance Against Genetic Engineering (http://nwrage.org)