THE NEW YORK TIMES (RETRO REPORT)

#1

Scientists Can Design 'Better' Babies. Should They?

By Clyde Haberman
June 10, 2018

1 For nine frustrating years, Lesley and John Brown tried to conceive a child but failed because of her blocked fallopian tubes. Then in late 1977, this English couple put their hopes in the hands of two men of science. Thus began their leap into the unknown, and into history.

2 On July 25, 1978, the Browns got what they had long wished for with the arrival of a daughter, Louise, a baby like no other the world had seen. She came into being through a process of in vitro fertilization developed by Robert G. Edwards and Patrick Steptoe. Her father's sperm was mixed with her mother's egg in a petri dish, and the resulting embryo was then implanted into the womb for normal development.

3 Louise was widely, glibly and incorrectly called a "test-tube baby." The label was enough to throw millions of people into a moral panic, for it filled them with visions of Dr. Frankenstein playing God and throwing the natural order of the universe out of kilter. The reality proved far more benign, maybe best captured by Grace MacDonald, a Scottish woman who in January 1979 gave birth to the second in vitro baby, a boy named Alastair. Nothing unethical was at work, she told the BBC in 2003. "It's just nature being given a helping hand." argument 'for'

Are these welcome advances that can only benefit civilization? Or are they incursions into an unholy realm, one of "designer babies," with potentially frightening consequences?

4 In vitro fertilization, or I.V.F., is by now broadly accepted, though it still has objectors, including the Roman Catholic Church. Worldwide, the procedure has produced an estimated six million babies, and is believed to account for 3 percent of all live births in some developed countries. Designer-baby fears have proved in the main to be "overblown," said Dr. Paula Amato, a professor of obstetrics and gynecology at Oregon Health & Science University in Portland. "We have not seen it with I.V.F. in general," she told Retro Report. "We have not seen it with P.G.D."

5 P.G.D. is shorthand for pre-implantation genetic diagnosis, developed more than two decades ago and an offshoot of in vitro fertilization. Couples with family histories of serious diseases — cystic fibrosis, Tay-Sachs and Down syndrome are among the more common — can have their lab-created embryos tested for the probability of passing the flaws to their offspring. Technology in effect gives them a measure of control over their genetic fate. An embryo that looks O.K. under a microscope can be implanted in the mother's uterus for normal development. (Typically, the others are discarded, itself a morally fraught practice for some people). ← argument 'against'

6 But what if the issue isn't averting a dreadful disease? What if would-be parents, rather than leaving the matter to an old-fashioned roll of the genetic dice, resort to embryonic selection to guarantee the child is of a particular sex? It can be done with pre-implantation genetic diagnosis. Dr. Jeffrey Steinberg, director of The Fertility Institutes in New York, does it as matter of course.

argument against

"The technology was out there — it was being applied only to diseases," Dr. Steinberg told Retro Report. He continued: "I've decided to open the door and expand it and say, 'Listen, this is something that people are interested in, causes no harm, makes people happy. Let's expand it.'" Though many doctors are strongly skeptical, he also offers P.G.D. to improve the odds that a baby will have a desired eye color, practically casting himself as the Benjamin Moore of the laboratory with his "choice of 30 shades of blue eyes." ↓ argument 'for'

8 Still other gene-altering techniques are now in play. Mitochondrial transfer, for one, is intended for a woman whose genetic makeup makes it likely she will bear a child with a severe birth defect. DNA is removed from her egg and implanted in an egg from another woman that contains healthy energy-generating components known as mitochondria. This has given rise to the discomfiting term "three-parent baby." → some say this is negative/disadvantage

9 Then there is a gene-editing method called Crispr, the acronym for a mouthful of a procedure: Clustered Regularly Interspaced Short Palindromic Repeats. A team led by Shoukhrat Mitalipov, an American reproductive biologist, announced last year that it had applied the technique to change a human genome. With an enzyme called Cas9 acting as a scalpel, Crispr snipped away a mutated gene that can lead to thickened heart muscles and cause sudden death in young athletes.
└ example of how done

10 In theory, it meant that if this embryo were implanted in a womb — it wasn't in this team's research — the child eventually born would not carry the mutation, and nor would any grandchildren. In short, that family's germ line, the genetic material governing cellular lineage from one generation to the next, would have been permanently altered. → some argue an advantage

11 As Louise Brown prepares for her 40th birthday next month, moral debates over the new capabilities echo those that swirled around her parents, both now dead. Some ethicists see only good in the prospect of eliminating diseases that condemn families to misery. After all, don't childhood vaccinations amount to using technology for that very same purpose? Yet few people regard measles or polio shots as unacceptable fiddling with the natural world. ↓ argument for

12 In a different camp are those who invoke slippery slopes, fearing unpredictable genies that may be unleashed. What, they ask, is to prevent gene editing from being used someday not to combat disease but, rather, to design people who are stronger or smarter than everyone else, able themselves to produce children programmed genetically for SAT scores of 1,600 or LeBron James point totals? ← argument against

13 Then again, selecting genes to produce, say, a star basketball player is hardly a snap; height alone is influenced by tens of thousands of genetic variations. On the other hand (there is almost always another hand) the sheer expense of the procedures threatens to widen an already substantial gap between the wealthy and everyone else. ← against

14 In 2017, an advisory group formed by the National Academy of Sciences and the National Academy of Medicine endorsed gene editing in principle, but with a proviso that it be used only to deal with "serious diseases and disability" and only when no "reasonable alternative" exists. Some scientists say it is unwise to be paralyzed by fear of the unknown. But Marcy Darnovsky, executive director of the Center for Genetics and Society in Berkeley, Calif., is more skeptical. "We have to ask where is the stopping point," Ms. Darnovsky said, and she suggested that policy discussions include "a much broader range of voices" than just scientists.

15 Perhaps Shakespeare can enter the conversation. He bequeathed words often invoked to encapsulate both hope for and dread of human capability. They're from "The Tempest": "O brave new world that has such people in't."

#2

NPR

Breaking Taboo, Swedish Scientist Seeks To Edit DNA of Healthy Human Embryo

September 22, 2016
ROB STEIN

1 A scientist in Sweden has started trying to edit the DNA in healthy human embryos, NPR has learned. The step by the developmental biologist Fredrik Lanner makes him the first researcher known to attempt to modify the genes of healthy human embryos. That has long been considered taboo because of safety and ethical concerns.

argument against

What he is doing.

2 Lanner is attempting to edit genes in human embryos to learn more about how the genes regulate early embryonic development. He hopes the work could lead to new ways to treat infertility and prevent miscarriages. He also hopes to help scientists learn more about embryonic stem cells so they can someday use them to treat many diseases. The fear is that Lanner's work could open the door to others attempting to use genetically modified embryos to make babies.

argument 'for'

argument for

3 Making changes to the DNA in human embryos could accidentally introduce an error into the human gene pool, inadvertently creating a new disease that would be passed down for generations, critics say. Some also worry the experiments could open the door to so-called designer babies that would let parents pick and choose the traits of their children. Lanner, however, says he is initially planning only to study the modified embryos for the first seven days of their growth and would never let them develop past 14 days. The potential benefits could be enormous, he argues.

against

4 "Having children is one of the major drives for a lot of people," Lanner says. "For people who do struggle with this, it can tend to become an extremely important part of your life." Lanner also hopes to learn things that could help scientists who are trying to turn stem cells from human embryos into new treatments for diseases. "If we can understand how these early cells are regulated in the actual embryo, this knowledge will help us in the future to treat patients with diabetes, or Parkinson, or different types of blindness and other diseases," he says. "That's another exciting area of research."

argument for gene editing

5 NPR recently got exclusive access to Lanner's labs at the Karolinska Institute in Stockholm to watch some of his early efforts. During the visit, Lanner and a graduate student carefully thawed five embryos donated by couples who had gone through in vitro fertilization at the Karolinska University Hospital to try to have children. One of the embryos didn't survive the freezing and thawing process. The researchers gingerly placed each of the remaining 2-day-old embryos into a dish on a special microscope. "You need to be stable on your fingers and hands while doing this," Lanner said, quipping, "You don't want to be dropping the embryos while taking them out."

6 With Lanner looking on, the student injected one of each embryo's four cells with a genetic engineering tool known as CRISPR-Cas9 while holding the embryo in place with a thin glass rod. The gene-editing tool comprises two molecules that can zero in on individual genes and make very precise changes to the DNA. It lets scientists modify DNA much more easily and precisely than ever before. Lanner calls the technique a "game changer." "It's not just quicker or cheaper," Lanner says. "This actually opens the door to start to look at this for the first time, because we could not do this at all previously in the human embryo. The technology was just not efficient enough to try to look at individual gene function as the embryo develops."

could be used 'for' or 'against'

Lanner is planning to methodically knock out a series of genes that he has identified through previous work as being crucial to normal embryonic development. He hopes that will help him learn more about what the genes do and which ones cause infertility. He declined to specify which genes he's targeting until the work is reviewed and published. During the visit by NPR, one of the embryos got severely damaged when the injection needle got clogged. But the researchers successfully injected the remaining three embryos and placed them in an incubator to continue developing. One embryo divided again immediately after being injected, showing

that it could still grow. Two of the embryos survived in good enough shape to be analyzed later, Lanner explained in an email afterward.

8 Lanner has now done this on at least a dozen embryos, but is still studying his results and refining his techniques. He remains unsure how well the editing is working so far. However, he's confident he'll be able to modify individual genes in the embryos to determine their function. "It will be very exciting. We're fortunate to be in this position," Lanner says. "This is a privilege to be in this position." But just the act of attempting to edit the DNA in healthy human embryos is extremely controversial. Chinese scientists triggered an international uproar earlier last year when they tried to edit the DNA of human embryos even though they used only defective embryos that had no hope of developing. Experiments like these intensified calls for a moratorium on such research, and the National Academies of Sciences, Engineering and Medicine launched the Human Gene-Editing Initiative to sort through the complex scientific and ethical issues they raise.

could be used for argument against

9 Organizers of an international summit convened in Washington, D.C., last year as part of that process concluded that it was far too early to try to create a baby from embryos that had their genes edited. But the organizers said basic research like Lanner's could be acceptable. A final report from the gene-editing initiative is expected late this year or early next.

10 Still, not everyone agreed with the summit organizers' assessment. Some people have moral objections to doing any research on human embryos because they consider a human embryo to have the moral standing of a person. And editing the DNA in embryos is controversial even among people who think human embryonic research is acceptable. That's the position of Marcy Darnovsky, who heads the Center for Genetics & Society, a watchdog group based in California that supports human embryonic research. "The production of genetically modified human embryos is actually quite dangerous," Darnovsky says. "It's a step toward attempts to produce genetically modified human beings. This would be reason for grave concern." against

11 One fear is that scientists could make some kind of mistake, accidentally creating new diseases that would be passed down for generations. "When you're editing the genes of human embryos, that means you're changing the genes of every cell in the bodies of every offspring, every future generation of that human being," Darnovsky says. "So these are permanent and probably irreversible changes that we just don't know what they would mean."

12 But even if it's safe, Darnovsky and others still worry about what designer babies would do to society. "If we're going to be producing genetically modified babies, we are all too likely to find ourselves in a world where those babies are perceived to be biologically superior. And then we're in a world of genetic haves and have-nots," Darnovsky says. "That could lead to all sorts of social disasters. It's not a world I want to live in." against

13 Lanner says he has no interest in ever doing anything like that. In fact, at the moment it would be illegal in Sweden. And, Lanner says, much more research would be needed to make sure it would be safe before anyone tries to use a genetically modified embryo to make a baby to prevent diseases. "It's not a technology that should be taken lightly," he says. "So I really, of course, stand against any sort of thoughts that one should use this to design designer babies or enhance for aesthetic purposes." But Lanner argues that basic research is necessary and morally acceptable, and banning it would be counterproductive. "I think it's wise to be allowed to do fundamental research so we can gain more information about this technology and potentially use it in the future," he says. Lanner plans to continue attempting to edit the DNA in healthy human embryos until he develops efficient editing techniques that will allow him to study the genes involved in early embryonic development. Scientists in Britain are planning to start similar experiments later this year.

for

14 Research using human embryos is legal in the U.S., but not with the support of federal funds. U.S. labs that are known to be active in human embryo research have not announced any plans to proceed with gene-editing experiments.

THE NEW YORK TIMES (NEWS ANALYSIS)

#3

Gene Editing for 'Designer Babies'? Highly Unlikely, Scientists Say

By Pam Belluck

Aug. 4, 2017

1 Now that science is a big step closer to being able to fiddle with the genes of a human embryo, is it time to panic? Could embryo editing spiral out of control, allowing parents to custom-order a baby with Lin-Manuel Miranda's imagination or Usain Bolt's speed? News that an international team of scientists in Oregon had successfully modified the DNA of human embryos has renewed apprehensions that babies will one day be "designed." But there are good reasons to think that these fears are closer to science fiction than they are to science.

2 Here is what the researchers did: repair a single gene mutation on a single gene, a defect known to cause — by its lonesome — a serious, sometimes fatal, heart disease. Here is what science is highly unlikely to be able to do: genetically predestine a child's Ivy League acceptance letter, front-load a kid with Stephen Colbert's one-liners, or bake Beyonce's vocal range into a baby. That's because none of those talents arise from a single gene mutation, or even from an easily identifiable number of genes. Most human traits are nowhere near that simple. "Right now, we know nothing about genetic enhancement," said Hank Greely, director of the Center for Law and the Biosciences at Stanford. "We're never going to be able to say, honestly, 'This embryo looks like a 1550 on the two-part SAT.'"

↳ example of difficulty in editing genes

3 Even with an apparently straightforward physical characteristic like height, genetic manipulation would be a tall order. Some scientists estimate height is influenced by as many as 93,000 genetic variations. A recent study identified 697 of them. "You might be able to do it with something like eye color," said Robin Lovell-Badge, a professor of genetics and embryology at the Francis Crick Institute in London. But "if people are worried about designer babies, they're normally thinking of doing special — different things than the normal genetic stuff."

4 The gene-modification process used in the new study also turns out to be somewhat restrictive. After researchers snipped the harmful mutation from the male gene, it copied the healthy sequence from that spot on the female gene. That was a surprise to the scientists, who had inserted a DNA template into the embryo, expecting the gene to copy that sequence into the snipped spot, as occurs with gene editing in other body cells. But the embryonic genome ignored that template, suggesting that to repair a mutation on one parent's gene in an embryo, a healthy DNA sequence from the other parent is required. "If you can't introduce a template, then you can't do anything wild," Dr. Lovell-Badge said. "This doesn't really help you make designer babies." Talents and traits aren't the only thing that are genetically complex. So are most physical diseases and psychiatric disorders. The genetic message is not carried in a 140-character tweet — it resembles a shelf full of books with chapters, subsections and footnotes.

Supports gene editing research

↳ example of difficulty of gene editing that would likely limit idea of designer babies

5 So embryonic editing is unlikely to prevent most medical problems. But about 10,000 medical conditions are linked to specific mutations, including Huntington's disease, cancers caused by BRCA genes, Tay-Sachs disease, cystic fibrosis, sickle cell anemia, and some cases of early-onset Alzheimer's. Repairing the responsible mutations in theory could eradicate these diseases from the so-called germline, the genetic material passed from one generation to the next. No future family members would inherit them. → 'for'

But testing editing approaches on each mutation will require scientists to find the right genetic signpost, often an RNA molecule, to guide the gene-snipping tool. In the study reported this week, it took 10 tries to find the right RNA, said Juan Carlos Izpisua Belmonte, a co-author and geneticist at the Salk Institute. Dr. Greely noted that while scientists work to get human embryonic editing ready for clinical trials (currently illegal in the United States and many countries), alternate medical treatments for these diseases might be developed. They may be simpler and cheaper. "How good one technique is depends on how good the alternatives are, and there may be alternatives," he said.

6 The authors of the new study do not dismiss ethical implications of their work. In fact, Dr. Belmonte served on a committee of the National Academies of Science, Engineering and Medicine that in February endorsed research into gene editing of human embryos, but only to prevent serious diseases and conditions, and as a last resort. "In theory this could lead to the kind of intervention which, of course, I'm totally against," said Dr. Belmonte. "The possibility of moving forward not to create or prevent disease but rather to perform gene enhancement in humans."

example, supports 'against'

7 For example, soon "we will know more and more about genes that can increase your muscle activity," he said. The hormone EPO, which some athletes have been disciplined for taking, "is produced by a gene, so you could in theory engineer yourself to produce more EPO." That is the kind of genetic engineering that raises alarm.

8 "Allowing any form of human germline modification leaves the way open for all kinds — especially when fertility clinics start offering 'genetic upgrades' to those able to afford them," Marcy Darnovsky, executive director of the Center for Genetics and Society, said in a statement. "We could all too easily find ourselves in a world where some people's children are considered biologically superior to the rest of us."

concern that supports 'against'

9 Scientists and ethicists share the concerns about access. "Any intervention that goes to the clinic should be for everyone," Dr. Belmonte said. "It shouldn't create inequities in society." Unequal access is, of course, a question that arises with almost any new medical intervention, and already disparities deprive too many people of needed treatments. But there is a flip side to ethical arguments against embryo editing.

10 "I personally feel we are duty bound to explore what the technology can do in a safe, reliable manner to help people," Dr. Lovell-Badge said. "If you have a way to help families not have a diseased child, then it would be unethical not to do it." Genetic engineering doesn't have to be an all or nothing proposition, some scientists and ethicists say. There is a middle ground to stake out with laws, regulation and oversight. For example, Dr. Lovell-Badge said, Britain highly regulates pre-implantation genetic diagnosis, in which a couple's embryos are screened for certain harmful mutations so that only healthy ones are implanted in the woman's womb. "They allow sensible things to be done, and they don't allow non-sensible things," he said. "And every single embryo is accounted for. If someone tries to do something they shouldn't have done, they will find out, and the penalties for breaking the law are quite severe."

11 According to a 2015 article in the journal Nature, a number of countries, including the United States, restrict or ban genetic modification of human embryos. Other countries, like China, have guidelines — but not laws — banning or restricting clinical use, the article noted. Chinese researchers have conducted the only previously published gene editing experiments on human embryos, which were much less successful.

12 In the future, will there be nations that allow fertility clinics to promise babies with genetically engineered perfect pitch or .400 batting averages? It's not impossible. Even now, some clinics in the United States and elsewhere offer unproven stem cell therapies, sometimes with disastrous consequences. But R. Alta Charo, a bioethicist at University of Wisconsin-Madison, who co-led the national committee on human embryo editing, said historically ethical overreach with reproductive technology has been limited. Procedures like I.V.F. are arduous and expensive, and many people want children to closely resemble themselves and their partners. They are likely to tinker with genes only if other alternatives are impractical or impossible. "You hear people talking about how this will make us treat children as commodities and make people more intolerant of people with disabilities and lead to eugenics and all that," she said. "While I appreciate the fear, I think we need to realize that with every technology we have had these fears, and they haven't been realized."

against

'for'

eugenics - science of improving a human population by controlled breeding to increase the occurrence of desirable heritable characteristics.