Embryo Screening and the Ethics of Human Genetic Engineering

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What if you could screen embryos for diseases before they became babies? What if you had the power to choose the traits your baby would have? Would you use it?

In April 2008, Dartmouth College ethics professor Ronald M. Green's essay, "Building Baby from the Genes Up," was published in the Washington Post. Green presented his case in support of the genetic engineering of embryos, arguing that tinkering with genes could eliminate disease or confer desirable features onto our future progeny. "Why not improve our genome?" he asked. Two days later, Richard Hayes, executive director of the Center for Genetics and Society, rebutted, warning of a "neo-eugenic future" and "the danger of genetic misuse."

These practically polar opposite opinions are two sides of a debate taking place around the world. The controversy revolves around what scientists are calling reprogenetics: the combined use of reproductive and genetic technologies to select, and someday even genetically modify, embryos before implantation—not for health reasons, but for the sake of "improvement."

Reprogenetics and Preimplantation Genetic Diagnosis (PGD)

Can we define a perfect baby?

Everyone has a different idea of the perfect baby. Consequently, questions about how to regulate the use of PGD raise complex issues about the definition of embryo "improvement".

Reprogenetics is an offshoot of an established medical procedure called preimplantation genetic diagnosis (PGD). Also known

as embryo screening, PGD allows couples at risk of transmitting a genetic disease to ensure their future children are unaffected by the disease without going through the process of prenatal diagnosis (i.e., testing of fetal tissue for the presence of disease genes) and being forced to make the difficult decision regarding pregnancy termination. Basically, PGD involves extracting a single cell from an eight-cell embryo (created via *in vitro* fertilization) and analyzing theDNA of that single cell for the presence of one or more disease-associated genetic alterations. Then, only those embryos without the disease mutation are implanted in themother's uterus.

Introduced into clinical care in the early 1990s, PGD was first used for determining the sex of embryos to minimize the likelihood of transmitting fatal sex-linked disease genes tooffspring. If there were a family history of Duchenne muscular dystrophy (DMD), for example, parents might choose to undergo embryo screening to identify female versus male embryos and then have only the female embryos implanted. (DMD is a recessive X-linked disease that affects mostly males.) Since the 1990s, clinical use of PGD has expanded from embryo sexing to single-gene diagnostic testing, such as for Huntington's disease. Today, reproductive clinicians regularly use PGD to diagnose some 170 different conditions, with two of the more common being cystic fibrosis and hemoglobin disorders (e.g., Cooley's anemia).

A third and more controversial use of PGD involves screening for chromosomally abnormal embryos in an effort to improve the relatively low pregnancy rates and decrease the relatively high miscarriage rates associated with *in vitro* fertilization procedures (which are often due to chromosomal abnormalities). While some experts have gone so far as to suggest that this type of PGD should be routine for *in vitro* fertilization procedures because it increases their success rate, others warn that data have yet to show that PGD actually improves pregnancy rates or decreases miscarriage rates following *in vitro* fertilization (Kuliev & Verlinksy, 2003; Gleicher *et al.*, 2008). The latter group argues that the use of PGD for chromosomal screening is still "experimental."

Screening Embryos to Eliminate Risk for a Single Disease

Most recently, and even more controversially, at least two British couples have relied on PGD to screen embryos for the presence of *BRCA* mutations associated with increased risks of breast cancer. Both couples came from families that had suffered several generations of breast cancer, and both couples wanted to eradicate breast cancer from their lineage once and for all. In Britain, all PGD procedures must be approved by a formal regulatory agency, the Human Fertilisation and Embryology Authority (HFEA), and these cases initially stumped the HFEA. Debate among HFEA members centered around the fact that testing positive for the *BRCA1* or *BRCA2* variant associated with breast cancer means only that an individual is at risk for developing breast cancer. Not all embryos with breast cancer-associated *BRCA* mutations necessarily develop breast cancer as adults. Moreover, most individuals who eventually develop breast cancer have 40 or 50 years of healthy life before becoming ill. After lengthy deliberation, the HFEA finally approved the couples' requests.

Professor Green alluded to the HFEA's decision in his *Washington Post* article. "To its critics, the HFEA, in approving this request, crossed a bright lineseparating legitimate medical genetics from the quest for ‘the perfect baby,'" he remarked. "Like it or not, that decision is a sign of things to come—and not necessarily a bad sign."

It is not a bad sign, Green argues, because "knowing more about our genes may actually increase our freedom by helping us understand the biological obstacles—and opportunities—we have to work with." Green foresees a day when our scientific understanding of the genetics of obesity, for example, will be so advanced and our technology so sophisticated that, "eventually, without discarding embryos at all, we could use gene-targeting techniques to tweak fetal DNA sequences. No child would have to face a lifetime of dieting or experience the health and cosmetic problems associated with obesity. The same is true for cognitive problems such as dyslexia. Geneticists have already identified some of the mutations that contribute to this disorder. Why should a child struggle with reading difficulties when we could alter the genes responsible for the problem?"

Many scientists are doubtful that a day like this will ever come, given that most human traits are influenced by multiple genes interacting not just with each other, but also with the environment. Just as not all embryos with breast cancer-associated BRCA mutations will necessarily develop breast cancer as adults, embryos with altered genes may not necessarily develop the desired traits. The journey from embryo to adult is extraordinarily complex and impossible to predict.

What do you think?

But suppose science surprises us and that day does arrive. Green argues, "[T]he critics' concerns may be less troublesome than they appear." He insists that parents will not love their children any less in the quest for perfection, and children will not feel pressured to live up to perfectionist expectations; if they do, the problem is with the parenting, not the genetic manipulation. While Green concedes that certain social effects might be worrisome, such as the production of a "genobility," or a ruling genetic class, he also sees PGD as a tool for reducing the class divide by "genetically vaccinating" individuals against potential hardships like obesity and dyslexia.

Dr. Hayes vehemently disagrees, arguing that while the technology of PGD has the potential to eliminate many horrible diseases, it could also do some real harm: "If misapplied, [these technologies] would exacerbate existing inequalities and reinforce existing modes of discrimination. .
.the developmentand commercial marketing of human genetic modification would likely spark a techno-eugenic rat-race. Even parents opposed to manipulating their children's genes would feel compelled to participate in this race, lest their offspring be left behind." Will all couples, regardless of their fertility issues, go the arduous route of PGD? How will they decide what to do when the likelihood of the "perfect baby" is pitted against the financial and emotional costinvolved?

Hayes points to Green's own cited statistic—that 80% of Green's students indicated in a survey that society should not move in the direction of human genetic engineering, a figure in agreement with public opinion polls on the subject. Hayes writes, "[Green] would be wise to listen to what medical

students, the great majority of Americans, and the international community appear to be saying. . .[W]e don't want to run the huge risks to the human community."

What do you think these risks are?