Preimplantation genetic diagnosis (PGD), also known as embryonic screening, allows parents and doctors to screen fertilized embryos and pre-fertilized oocytes for numerous characteristics, particularly genetically inherited diseases. PGD is an extension of in vitro fertilization (IVF). In IVF, oocytes are obtained, fertilized outside of the body, and implanted in the woman’s uterus. While IVF facilitates fertilization of eggs and implantation of embryos, PGD goes a step further than simply assisting couples to become pregnant. It screens these embryos and selects only those with desired traits to be implanted and eventually grow into a baby: scientists look for genetic flaws and actively select embryos for implantation that are disease-free.

However, the development of PGD opens up a Pandora’s Box of opportunities to dictate a child’s future traits. As PGD becomes more widespread and successful, it presents a moral dilemma: where is the line between creating a healthy child and trying to mold a “perfect” child?

Development of PGD

The development of embryonic screening began in 1967 with Edwards and Gardner’s ability to determine the gender of live rabbit blastocysts while retaining their viability (1). Their ability to harvest embryos and identify future traits without harming the embryos set the stage for application of PGD in humans. In 1989, Coutelle et al. established a preimplantation diagnostic test for cystic fibrosis for human embryos (2), and in 1992, Handyside et al.’s IVF and PGD testing led to the successful birth of a healthy, cystic-fibrosis-free girl (3).

Throughout the past 2 decades, PGD has made rapid progress as the development of efficient PCR techniques has allowed for more varied, accurate, and cheaper diagnoses. Since Handyside’s first PGD baby, the list of genetic conditions which can be tested is rapidly expanding; the UK’s Human Fertilisation and Embryology Authority currently lists over 60 conditions that are testable by PGD (4).
The science behind PGD

Embryonic screening has 3 main components: obtaining an embryo, taking a biopsy of it, and completing a genetic analysis of the biopsy. The procedure for obtaining embryos for PGD is identical to that used in IVF. Controlled ovarian stimulation uses a set of timed hormone supplements to stimulate production of surplus oocytes for harvesting. Finally, to fertilize the oocyte and create an embryo, sperm is directly injected into the oocyte, a procedure called intracytoplasmic sperm injection (5).

One of the most controversial procedural components of PGD is the biopsy. Depending on the personal, religious, and legal definitions of which embryonic stage constitutes a living being, the following three biopsy options present varying scientific and moral trade-offs.

The first and most popular biopsy method (used in 94% of embryonic screens) is the “cleavage-stage biopsy” where 1 or 2 cells from a blastomere (8 cell or later development stage) are sectioned out for analysis. The obvious advantage to this method is that it allows analysis of the DNA contributed by both the mother and the father, since the cells were taken from a fertilized embryo. Nonetheless, there are several scientific and moral cons to this method.

Scientifically, this sectioning disrupts development and can cause the biopsied cell to develop abnormally, defeating the purpose of the screen. Also, chromosomal mosaicism is common at this stage, which can make results of the tests irrelevant (5). Cleavage stage biopsies obtain far less tissue than the other two techniques, forcing scientists to rely on diagnostic techniques that present their own problems. Although it is a preferable method from a scientific perspective, it has been rejected on a moral basis by individuals or countries that consider these embryos to be living and thus forbidden to probing, selection, and disposal (6).

The second available method is called a “polar body biopsy.” Oocytes develop via a two-step meiotic oogenesis, during which uneven division of cytoplasm results in one large oocyte and two smaller polar body byproducts. (Figure needed here). Since the polar bodies are waste products of oogenesis and not needed for embryo development, polar body (PB) biopsies provide a very safe alternative to taking biopsies of developing embryos. First used by Verlinsky (7), a polar body biopsy bypasses the ethical concern regarding the status of embryos as living beings, which is why it is used in countries such as Germany where cleave-stage embryo selection is banned. Unfortunately, this biopsy method can be misleading because it only provides information on maternally transmitted diseases (the egg has yet to be fertilized and does not contain DNA from the sperm) and genetic information may be degraded, since polar bodies are effectively “junk.” However, the ethical and safety benefits of PB biopsies have encouraged reproductive researchers to continue to develop reliable PB-based diagnoses (8).

The last biopsy method, “blastocyst biopsy,” presents many of the moral challenges that cleavage stage biopsy presents, but overcomes the limited tissue problem by taking a biopsy later in development (figure of human embryo development). While the additional tissue may lead to more accurate genetic diagnoses, since blastocysts are later in development, fewer are available for screening. Furthermore, the delaying the biopsy limits the time before implantation and the time for diagnosis (9).

Genetic Screening

There are a number of screens that can be used during PGD to detect genetic abnormalities. Fluorescent in situ...
hybridization (FISH) probes chromosomes with fluorescent DNA probes specific for various chromosomal segments and is particularly useful for detecting abnormal chromosome arrangements such as trisomy 21 which causes Down’s syndrome (10).

To detect for more specific genetic abnormalities, the polymerase chain reaction (PCR) amplifies a cell’s limited amount of genetic material to an amount sufficient for further testing (10). While traditionally a very robust assay, the use of PCR in PGD exacerbates the traditional problems of PCR due to the extremely low amount of template available in PGD (in the case of a cleavage stage biopsy, a single strand). The high number of PCR cycles required makes amplification of contaminants and misleading results more likely. Furthermore, a phenomenon called allele drop out where random non-amplification of one of the alleles in a heterozygous sample occurs may lead to many false positives and negatives depending on which allele failed to amplify. PCR and subsequent DNA analysis can provide more specific information than FISH regarding specific disease causing genetic mutations (10).

Despite all these challenges, embryonic screening has been hailed a success for helping otherwise infertile couples bear healthy children. Out of 4748 PD attempts, 754 babies have been born, and since screening eliminates embryos carrying chromosomal abnormalities that would likely abort a pregnancy, “The overall pregnancy rate per transfer is 23.3%, much higher than the rate in IVF patients in the comparable age group (average age, >39 years) without PGD.” For couples using IVF, PGD led to a fourfold reduction of spontaneous abortion (11).

**Conclusion**  
While these scientific successes validate embryonic screening as a necessary assistive reproductive technology, controversy still lurs nearby. The question of what stage of the embryo is considered a living organism has led to the various biopsy options discussed above. However, recent findings have also suggested that PGD may have detrimental effects on the children, causing parents to question whether the screen is really worthwhile (12). The success of the human genome project and the increasing accuracy and availability of PGD suggest that embryonic screening may one day go beyond simply helping parents bear healthy children and instead be used for sex selection and choosing specific traits (13). These possibilities of selecting embryos for ideal children is not far from the limits of current science and threatens to eliminate the much beloved surprise of having children.

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**References**