

PGD in Practice

Laurence Udoff, M.D.

Preimplantation Genetic Diagnosis (PGD) is one of several reproductive options for couples that carry a serious genetic disorder and want to decrease their chances of having an affected pregnancy. PGD involves testing embryos conceived through in-vitro fertilization (IVF) for a specific genetic disorder prior to implanting them in the uterus. Consequently, when a couple conceives, there is a likelihood that the pregnancy will be unaffected by the genetic problem of concern. However, prenatal diagnosis is commonly recommended to confirm the PGD findings, since all clinical tests have an error rate (estimated at less than 5%). Couples choose PGD for various reasons, the most common being either to avoid terminating a pregnancy or because they have infertility as well as a genetic issue. Even though fertile couples utilize PGD, there is no guarantee that a PGD treatment cycle will produce a pregnancy. More than half of couples require additional treatment cycles, with some couples never achieving pregnancy.

It has been my experience that PGD is a very stressful and emotional process. Factors contributing to stress include: financial pressures; multiple doctor's visits and IVF procedures, especially for couples who do not need IVF to conceive; and feelings of guilt, blame and resentment associated with being a carrier of a genetic disorder. To address some of these issues, I have found it very helpful to include a psychologist as part of the PGD team to help select appropriate candidates for treatment, as well as be a resource during and after treatment.

Although PGD can be a difficult and complicated process to endure, when it works it is truly a miracle of modern science. One of the most rewarding aspects of my job is holding a healthy baby born to parents who have previously suffered the loss of a child to an inherited disease. There are also many challenges associated with PGD, such as consoling a couple that has failed to conceive through PGD despite multiple attempts. Additional challenges are awareness and cost. On the one hand, many couples are simply not aware of this reproductive option. On the other hand, I often meet couples that would be excellent candidates for treatment, but lack the financial resources.

The role for PGD has greatly expanded since its introduction over a decade ago, with some IVF programs offering PGD to infertility patients as an additional tool to select the "healthiest" embryos for transfer. Research has shown that women over the age of 35, with a history of recurrent pregnancy loss, or with a history of multiple failed IVF attempts, produce a higher proportion of embryos with the wrong number of chromosomes. Standard IVF procedures do not accurately identify these abnormal embryos, which, if transferred, are associated with lower pregnancy rates and a higher

incidence of miscarriages. Furthermore, if a child is born from a chromosomally abnormal embryo, there is a greater risk of it having a genetic condition such as Down's syndrome. Though very promising, most IVF programs have not embraced PGD because only a small proportion of the total number of chromosomes can be tested. Additionally, results from clinical studies have been mixed, suggesting a benefit only in specific situations.

PGD has also been successfully used for controversial applications. Recently, a couple used PGD to conceive a child who would be an exact bone marrow match, and subsequently a donor, for their other child who is suffering from a genetic disorder. The fear of using babies for "spare parts" or requesting PGD for "designer babies" has been the subject of many editorials in the lay press, as well as in the medical literature. At the University of Maryland, where I teach, we have recently completed a survey of physician attitudes towards the controversial applications of PGD. Preliminary results indicate that physicians are very unlikely to offer PGD to couples unless it involves reducing the risk of a serious medical problem.

Although very bright, PGD's future will hinge upon several important developments. First, advances in DNA analysis are needed to expand the scope of testing. Second, advances in IVF are pivotal to improving pregnancy and live birth success rates, as well as reducing the patient burden from complicated procedures. Unfortunately, at present, research in IVF and PGD is primarily funded by private sources, thereby significantly hindering progress. As a result, most of the medical literature either comes from PGD centers outside the U.S., or privately supported, mainly non-academic programs within the U.S. Finally, access to PGD services needs to be significantly improved. PGD is an amazing technology that unfortunately is only available to the few patients who are aware of it and have the financial resources to pursue it. Despite these hurdles, I remain hopeful that PGD will live up to its promise of greatly improving the human condition.

Dr. Udoff is an assistant professor at the University of Maryland's Division of Reproductive Endocrinology and Infertility.