

# Use of preimplantation genetic diagnosis for serious adult onset conditions: a committee opinion

Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

PGD for adult-onset conditions is ethically justified when the condition is serious and no safe, effective interventions are available. It is ethically allowed for conditions of lesser severity or penetrance. The Committee strongly recommends that an experienced genetic counselor play a major role in counseling patients considering such procedures. (Fertil Steril® 2013; ■: ■–■. ©2013 by American Society for Reproductive Medicine.)

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## KEY POINTS

- Preimplantation genetic diagnosis (PGD) for adult-onset conditions is ethically justifiable when the conditions are serious and when there are no known interventions for the conditions or the available interventions are either inadequately effective or significantly burdensome.
- For conditions that are less serious or of lower penetrance, PGD for adult onset conditions is ethically acceptable as a matter of reproductive liberty. It should be discouraged, however, if the risks of PGD are found to be more than merely speculative.
- Physicians and patients should be aware that much remains unknown about the long-term effects of embryo biopsy on any developing fetus. Though thought to be without serious side effects, PGD for adult onset diseases of variable penetrance should only be considered after patients are carefully and thoroughly

counseled to weigh the risks of what is unknown about the technology and the biopsy itself against the expected benefit of its use.

- It is important to involve the participation of a genetic counselor experienced in such conditions before patients undertake PGD. Counseling should also address the patient-specific prognosis for achieving pregnancy and birth through in vitro fertilization (IVF) with PGD.

In both the United States and Europe, preimplantation genetic diagnosis (PGD) for adult-onset conditions has been used with increasing frequency. Post-conception diagnosis and pregnancy termination have also been increasingly employed for serious single-gene diseases that are manifested principally in adulthood. In 2008, the Practice Committee of ASRM recommended PGD with IVF as a significant advance over post-conception diagnosis and pregnancy

termination in the case of single-gene disorders (1). A 1999 ASRM ethics opinion concluded that PGD for sex selection should be recommended only when based on the need to identify sex as a means to prevent transmission of sex-linked genetic diseases and should not be legally prohibited in other cases (2). This opinion concludes that PGD is ethically permissible in the case of genetically transmitted conditions that are highly serious and manifest in adulthood.

PGD was initially developed to identify IVF embryos that carried genes for serious, childhood-onset diseases. More recently, PGD has been used for serious single-gene diseases that do not develop until adulthood, such as Huntington disease and early-onset Alzheimer disease; for cancer predisposition genes, such as BRCA1; and for non-fatal conditions that are apparent at birth, such as cleft palate (3–5). The use of PGD for these and other conditions is growing rapidly (6).

Huntington disease is an autosomal dominant condition that is uniformly fatal, although the age of onset varies with the mutation. In the cases of some other serious adult-onset conditions for which PGD has been used, such as breast cancer associated with

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the BRCA1 gene, however, the presence of the identified gene or genes does not predict with certainty that an individual will ever develop the disease. Moreover, in many cases, the disease can be treated successfully and is thus not ultimately fatal. The uses of PGD technology for serious adult onset conditions thus raises challenging policy and ethical questions, given what we know about the human genome, disease etiology, and embryo biopsy procedures. The complexity of these issues demands that an expert in genetic counseling be involved in counseling a patient considering the procedure.

To the best of current knowledge, PGD is not linked to fetal malformations or other identifiable problems for the offspring (7–9). Although pediatric follow-up data are reportedly ready for analysis, long-term safety data are not available. PGD does appear to be associated with reduced rates of pregnancy and delivery in IVF. IVF itself is associated with an increased risk of multiple births, in addition to a small risk of ovarian hyperstimulation syndrome, potential complications associated with the oocyte retrieval, and an increased risk of adverse perinatal and obstetrical outcomes (5, 10). Thus, long-term consequences for the offspring after PGD cannot be ruled out with certainty at present. With the available PGD technology, moreover, testing is only available for single-gene diseases, and risks of diagnostic error remain (1, 7).

## ETHICAL ANALYSIS

Arguments offered in support of PGD for serious adult-onset conditions include the right to reproductive choice on the part of persons who seek to bear children, the medical good of preventing the transmission of genetic disorders, and potential social benefits of reducing the overall burden of disease. Arguments advanced against the use of PGD include expense, the questionable value of the medical benefits obtained in light of our inability to predict medical progress over the longer term, the possibility of misdiagnosis, and the unknown risks of the procedure. In addition, arguments offered against expanded uses of PGD portray the changes that genomic medicine is bringing to the practice of reproductive medicine as the beginning of a slide down a “slippery slope” toward unacceptable uses of genetic technology to control the non-disease related characteristics of children and future generations.

### Arguments in Favor of PGD for Serious Adult-onset Conditions

In the case of adult-onset diseases, parents may have many reasons for the reproductive choice of PGD. Reproductive liberty is an important, albeit not absolute, right.

Parents may wish to avoid the worry associated with the uncertainty that their offspring may be affected with serious adult-onset conditions. Professional organizations such as the American Academy of Pediatrics currently recommend that genetic testing for adult-onset conditions for which interventions are unavailable is inappropriate until children reach adulthood (11–13). Families may thus experience the stress of not knowing about a possible adult-onset disease during the entire period of a child’s minority. Critics have argued that this recommendation against testing fails to

understand autonomy and to appreciate the harms that may be associated with uncertainty (14), but the recommendation was reaffirmed in 2009 (11).

Parents may also wish to avoid the stress of medical management during childhood. With some later-onset conditions, testing may be medically indicated before the child reaches adulthood. For patients who carry the familial polyposis gene (P-53), for example, testing and polyp removal may be important before adulthood. Some patients with BRCA1 are also at risk of the development of cancer before adulthood.

Additionally, concerns may expand beyond the parents and the affected child. Parents may wish to use PGD to avoid the impact on other family members of learning that some are at risk for or affected with adult onset conditions while others are not.

The goal of preventing serious disease also supports the liberty to use PGD for adult-onset conditions. PGD is an effective intervention for identifying genes that can lead to disease (1). Parents may wish to try to avoid the possibility that their offspring become afflicted with the conditions.

Finally, cost reasons also support the reproductive liberty to choose PGD in cases of some adult-onset conditions. This is particularly relevant given the growing lifetime cost of health care for chronic medical conditions. With PGD, the expenses are borne at the outset; the costs of managing later-onset conditions may be significantly greater in comparison. Patients with a genetic condition must undergo repeated testing and treatment, often from early adulthood or beyond. The social costs of Huntington disease include lost wages and long-term medical treatment. The psychological impact of these diseases should also be considered, as many individuals who have these genes must live with the ongoing burden of fear and concern about the development of disease. An individual whose embryos are undergoing PGD for Huntington disease may also request that his or her carrier status not be disclosed to him or her. It is ethically acceptable to honor such requests.

### Arguments against PGD for Serious Adult-onset Conditions

There are ethical reasons on the other side of the argument as well. The medical benefits of PGD for adult-onset conditions are speculative. It is impossible to predict whether effective treatment modalities will be available long before the manifestation of conditions in adulthood. Individuals with the genetic trait may live healthy lives for several decades before a disease may become an active concern in adulthood. Moreover, some of these genes may have variable expressivity, manifesting as a much milder form of illness than anticipated, or perhaps not even expressing as illness at all, as in the case of some mutations that increase the lifetime risk of cancer. Cancer predisposition genes such as BRCA1 present a unique set of challenges. Our current understanding of the complex interactions between DNA and the environment is limited. A woman who carries the BRCA1 gene has an increased risk for the development of breast and ovarian cancer but may never develop cancer for reasons that are not yet understood.

Critics of PGD also argue that utilizing the procedure for embryo selection risks devaluing certain lives (15). They contend that PGD has the potential to send a negative message regarding the value of those individuals living with the disease, including those who have the mutation for the disease but have not yet developed it (16). Other critics put forth a “slippery slope” argument that, although utilized with the good intent to avoid illness in the future, this form of prospective risk assessment opens the doorway to the use of PGD to identify genetic characteristics that in and of themselves are not predictors of illness: the so-called “designer baby” concern (17). An additional criticism is that PGD may foster inaccurate identification of gene with disease and thus inadvertently reinforce problematic views of genetic causation and responsibility. Moreover, PGD operates by preventing the birth of people with the disease, not by treating a disease condition in the same person. This scenario has been called the “non-identity” problem (18). Interventions that interrupt or reverse disease processes on the other hand, such as a treatment that derails the process of plaque formation in Alzheimer disease, would not encounter the non-identity problem. Despite ongoing medical progress, the availability of safe and effective interventions for many adult onset conditions remains speculative, even over a time frame of 30 or more years. In addition, misdiagnosis remains a possibility for technical reasons, and the procedure is only available at present for conditions associated with a single gene (1, 7, 19, 20).

IVF with PGD also is an expensive procedure with no certainty of live birth. Indeed, the likelihood of achieving a successful pregnancy and birth in such cases may be lower than in IVF performed without PGD (7, 19, 21). One study of single embryo transfer in IVF, however, concluded that pregnancy and delivery rates were not reduced with PGD versus without PGD (22). In addition, as mentioned previously, IVF, with or without PGD, is associated with an increased risk of multiple pregnancy and other potential complications, including an increased risk of adverse perinatal and obstetrical outcomes.

## SUMMARY

After careful review and consideration, the Committee concludes, based on the arguments outlined above, that PGD for adult-onset conditions is ethically justified when the condition is serious and no safe, effective interventions are available. The Committee further concludes that reproductive liberty arguments ethically allow for PGD for adult-onset conditions of lesser severity or penetrance. In the latter cases, the application of the technology hinges on the evidence that PGD is a relatively low-risk procedure; this evidence may change. The complexity of the scientific, psychological, and social issues involved in this arena compels the Committee to strongly recommend that an experienced genetic counselor play a major role in counseling patients considering such procedures.

**Acknowledgment:** This report was developed by the Ethics Committee of the American Society for Reproductive Medicine as a service to its members and other practicing

clinicians. While this document reflects the views of members of that Committee, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment in all cases. This report was approved by the Ethics Committee of the American Society for Reproductive Medicine and the Board of Directors of the American Society for Reproductive Medicine.

This document was reviewed by ASRM members and their input was considered in the preparation of the final document. The following members of the ASRM Ethics Committee participated in the development of this document. All Committee members disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients. Members of the Committee who were found to have conflicts of interest based on the relationships disclosed did not participate in the discussion or development of this document.

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**1 Use of preimplantation genetic diagnosis for serious adult onset conditions: a committee opinion**

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This document discusses the ethical considerations of performing preimplantation genetic diagnosis to deselect embryos for transfer in order to prevent future adult onset conditions in the offspring.