Transfer of embryos affected by monogenic conditions: an Ethics Committee Opinion

Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Washington, DC

Patient requests for transfer of embryos affected by monogenic conditions linked to serious health-affecting disorders detected in preimplantation testing are rare but do exist. This opinion sets out the possible rationales for a physician's decision to assist or decline to assist in such transfers. The Committee concludes that in most clinical cases, it is ethically permissible to assist or refuse to assist in transferring such embryos. However, in circumstances in which a child is highly likely to be born with a life-threatening condition that causes severe and early debility with no possibility of reasonable function, the transfer of such embryos is ethically problematic and highly discouraged. (Fertil Steril® 2025;■:■–■. ©2025 by American Society for Reproductive Medicine.)

Key Words: Aneuploidy, preimplantation genetic testing, birth defect, embryo

KEY POINTS

- Preimplantation genetic testing for monogenic conditions (PGT-M) can be used to investigate the genetic composition of preimplantation embryos. Patients whose embryos undergo such testing should be informed about the potential uncertainties of this technique, including the possibility of variable penetrance and indeterminate or not fully predictive results.
- Patient requests for the transfer of embryos with known monogenic conditions are rare but do occur in the clinical setting, predominantly in cases where no unaffected embryos are available for transfer.
- Valid and reasoned arguments exist to support physicians as they decide to either assist in transferring an embryo with a known monogenic condition or decline to assist in such transfers. Principles of reproductive liberty, physician autonomy, professional conscience, nonmaleficence, procreative beneficence, and child welfare are potentially invoked in decision-making in this area.
- Many genetic conditions produce highly variable phenotypes, and variants of uncertain significance may or may not result in offspring with clinically significant findings. This uncertainty underscores the importance of robust counseling to support individualized decision-making, rather than reliance on categorical directives once a genetic variant is detected.
- In circumstances in which a child is highly likely to be born with a life-threatening condition that causes severe and early debility with no possibility of reasonable function, it is ethically acceptable for a physician to decline a patient's request to transfer such embryos. Physician assistance in transferring embryos in this category is ethically problematic and, therefore, highly discouraged.
- In circumstances where a child is highly likely to be born with a condition that is treatable or effectively manageable through medical interventions, it is ethically acceptable for physicians to transfer such embryos on patient request. Refusals to transfer embryos in this category also fall within appropriate ethical boundaries so long as they are made and applied in a manner that does not discriminate against the patient on any basis.
- Physicians are strongly encouraged to refer patients to experts such as genetic counselors, mental health professionals, and clinicians specializing in the specific genetic condition to help them understand the potential risks of transferring affected embryos.
- Physician counseling at the outset of treatment should address the patient-specific prognosis for achieving unaffected embryos through in vitro fertilization when used with PGT-M and convey that not all patients undergoing PGT-M will have unaffected embryos available for transfer.

Received January 29, 2025; accepted February 3, 2025.
Correspondence: Jessica Goldstein, Ethics Committee, American Society for Reproductive Medicine, 726 7th St SE, Washington, DC 20003. (E-mail: asrm@asrm.org).

Fertil Steril® Vol. ■, No. ■, ■ 2025 0015-0282/$36.00

https://doi.org/10.1016/j.fertnstert.2025.02.001

- Fertility centers should have clear policies regarding whether they will transfer embryos that carry known or potentially health-affecting genetic results.
- Information regarding a practice's policies surrounding whether they will transfer affected embryos should be made available to patients before they decide whether to pursue PGT-M.

The burgeoning field of preimplantation genetic testing (PGT) for monogenic conditions (PGT-M) enables prospective parents to screen their preimplantation embryos for specific conditions for which they are at risk, information that can both aid in and complicate their reproductive decision-making. Sophisticated diagnostic techniques can currently detect hundreds of genetic variants whose health impacts range from benign to lethal (1). Results of PGT-M include the detection of gene mutations that always lead to disease (i.e., genetic mutations that cause Tay-Sachs disease), genetic variants that increase disease susceptibility (i.e., breast cancer associated variants), diseases with variable penetrance (i.e., Huntington disease), and variants of unknown significance (VUS).

Generally, patients who use these genetic technologies do so to prevent the birth of a child at risk of carrying a health-affecting condition. Preimplantation embryos identified to carry such conditions are typically not selected for transfer into the uterus but instead donated for research or discarded. In some cases, the only embryos available for transfer are affected by the genetic condition and represent the intended parent(s)' only chance of having genetically related offspring (2). There may be rare cases in which intended parents intentionally seek to transfer embryos affected with a genetic condition that one or both intended parents carry (3, 4). The discovery of and request for transfer of PGT-M-positive embryos is likely to result in the birth of offspring with health-affecting conditions, which poses ethical dilemmas for physicians and their staff, patients, and society (5, 6).

This opinion discusses the difficulties and complexities surrounding decision-making once an embryo screens positive for a monogenic condition via PGT-M. It discusses at least four separate interests that are potentially invoked when a patient requests the transfer of such affected embryos, including the patient's reproductive autonomy, welfare of any resulting offspring, physician's professional conscience, and impact on third parties, including the patient's family as well as the larger society. These interests are considered in an ethical analysis that sets out arguments for both honoring and declining these patient requests.

DETECTION OF POSITIVE GENETIC RESULTS IN EMBRYOS

Motivations for PGT-M testing may vary; however, most intended parents elect to use this technology to avoid the transfer of embryos that are found to be positive for the condition being screened. Preimplantation genetic testing for monogenic conditions may also be used as a ranking tool, often in cases where the genetic variant is associated with adult-onset disease or variable penetrance. Although, in some instances, PGT-M can provide patients with definitive results in which positive findings always lead to disease, there are many situations in which the cause and effect are not as clear cut. In the latter case, careful counseling regarding the range of potential outcomes and the lack of certainty is critical.

Although most patients whose embryos test positive for a significant health-affecting genetic finding choose not to transfer them, some patients will request that such embryos be transferred, even when counseled about the near certainty that any resulting children will be affected by the condition. Three potential reasons for such requests are as follows: the affected embryos are the only embryos the intended parent(s) have available for transfer, such that they represent their only opportunity for genetic parenthood; the intended parent(s) has religious or other beliefs that inform their desire to transfer all embryos regardless of the future health status of any resulting children; and the intended parents or their family member(s) is/are affected by the genetic condition, and they do not wish to avoid rearing children with these same characteristics. Request for PGT to conceive a child who is affected by a specific genetic condition (in contrast to avoiding the transfer of such embryos) is known as "intentional diminishment" (6, 7). These types of scenarios have been described over the past several decades, usually involving intended parents at risk of having children with hearing loss or achondroplasia (8). In the rare cases in which a specific genetic condition is intentionally sought, patients are likely to have discussed this reproductive plan with their physician, giving them an a priori opportunity to consider whether to assist or decline to assist in their reproductive efforts. Patients whose religious beliefs or other values would guide them to seek transfer of all resulting embryos are not likely to pursue PGT. Overwhelmingly, requests to transfer embryos with positive genetic results fall under the first of these three scenarios.

No specific formal law in the United States governs the transfer of embryos with positive genetic findings. Survey research and anecdotal reports suggest that such requests are made by a very small number of patients, and clinics vary in their willingness to accommodate such requests. In the only published survey of genetic testing practices in US fertility clinics, four clinics reported that they offer PGT to select an embryo for the presence of a genetic condition (3). Law and policymakers outside the United States have issued formal regulations on the acceptability of transferring embryos with known health-affecting conditions. In the United Kingdom, the Human Fertilisation and Embryology Authority generally prohibits the selection of an embryo known to "have a gene, chromosome or mitochondrial abnormality involving a significant risk that [the child] will develop a serious physical or mental disability, a serious illness, or a serious medical condition" (9). An exception, however, is made where there is no other embryo suitable for transfer; in such cases, the transfer of such an embryo is permissible.

Assisted reproductive technology (ART) clinics that offer PGT-M should be aware of the range of choices their patients may seek to make, both in requesting genetic analysis and in seeking subsequent transfer of their embryos. They are

encouraged to develop and make written policies regarding the testing and transferring of embryos available to patients before treatment, especially when those policies preclude patients from transferring affected embryos. Developing policies that best reflect a clinic's preferred approach can be complex and challenging. In developing transfer policies, clinics should research and consider the most up-to-date data surrounding the availability and accuracy of genetic testing technologies. This document discusses some of the clinical uncertainties that impact decision-making surrounding embryo transfer. It then sets out some of the arguments that could inform a physician's decision to assist or decline to assist in transferring embryos with positive genetic testing results.

THE IMPACT OF CLINICAL UNCERTAINTY IN GENETIC TESTING OF EMBRYOS FOR MONOGENIC CONDITIONS

Outcomes following the transfer of affected embryos can be variable for several reasons. Some diseases have variable expression and severity. Nonsyndromic hearing loss and deafness are examples of such a disease. Other diseases, such as Huntington disease, will always be expressed; however, the age of onset will vary. For cancer predisposition syndromes, carrying the genetic variant is not correlated with disease certainty but instead confers an increased risk of developing one or more cancers.

Furthermore, the increased use of genetic testing in medicine has led to patient requests for PGT for VUS. Although determining the appropriateness of PGT for the detection of VUS is outside the scope of this document (1), it is important to recognize that the clinical utility of PGT in these cases is less certain because the phenotypic associations are not as clearly associated with the genetic findings. Requests for the transfer of PGT-M positive embryos in such cases require careful review, optimally in consultation with a genetic counselor or other medical genetics professional, to better understand the potential health outcomes of resulting offspring. Decisions regarding VUS may evolve as more information is available regarding their expression and whether they are disease-causing.

Research may be lacking regarding genotype/phenotype associations of various genetic findings. When evidence-based clinical recommendations are not available for a given genetic finding, physicians may require assistance to optimally counsel their patients. Arguments for and against transferring genetically affected embryos cluster around a host of factors, including whether other embryos are deemed unaffected in the cohort under consideration. What follows is a framework for developing clinic policies to either assist or refuse to assist in transferring such affected embryos.

ARGUMENTS FOR HONORING PATIENT REQUESTS FOR TRANSFER OF AFFECTED EMBRYOS

Arguments for honoring patient requests to transfer embryos with positive genetic testing results dwell primarily, although not exclusively, in the realm of reproductive liberty and patient autonomy. Described more fully in the following, these positions may be labeled by their governing value: reproductive liberty; equal protection; and preemptive dispositional authority.

The importance surrounding patient autonomy and reproductive liberty in the practice of reproductive medicine has long guided patient/physician relationships in this field. This Committee acknowledges that some requests for assistance in reproduction may include features that are material to a patient's decision-making for deeply private reasons and deserve respect. Parents who request transfer of affected embryos may so choose because it is their only opportunity for biologic parenthood, or they are willing to rear a child with a medical condition, or they desire a child who reflects their own health experience, or they are unwilling to discard embryos or donate them for research. Each of these rationales is compatible with the exercise of reproductive liberty, and infringements by physicians should generally be avoided. However, this does not imply that physicians are obligated to transfer affected embryos, so long as their refusal to accommodate such requests is performed unbiasedly and communicated to the patient before proceeding with treatment. Accordingly, robust protection of reproductive liberty may be particularly vital in the disability community where discrimination and barriers to ART access have been previously documented (10).

Applying an equality model lens, an argument arises that physicians, governments, and society should make no distinction in the treatment of fertile and infertile prospective parents. Just as fertile individuals are free to conceive and give birth to a child with serious, even lethal, health conditions without third-party interference, individuals who seek or require assistance in reproduction should likewise enjoy this same freedom. The notion that specific individuals should be prohibited from reproducing or forced to terminate ongoing pregnancies because their offspring are deemed "unworthy" of participation in the human race is deeply repugnant to our contemporary values, harkening to long-rejected eugenics-era tenets (11). Treating all prospective parents and their potential offspring as equally worthy is consistent with honoring patient requests to transfer embryos with positive genetic results.

An additional argument rests on the issue of who possesses dispositional authority over preimplantation embryos. Embryos awaiting possible transfer are, by definition, extracorporeal and, thus, theoretically subject to claims of control by the intended parents, progenitors (in the case of gamete donation), or clinic personnel. Although disputes between intended parents and physicians as to the disposition of embryos are rare, in at least one case, a court awarded complete control to the intended parents, deeming the fertility clinic to occupy the role of bailee whose sole responsibility was to exercise reasonable care over the bailment subject (12). Applying this holding to instances where the wisdom of transfer is disputed, patients could assert their superior dispositional authority over the embryos in question. However, this would not obligate any individual physician to perform the embryo transfer.

Arguments in favor of honoring patient requests for transfer of affected embryos can gain and lose in strength depending on a host of clinical factors, including whether other unaffected embryos are available for transfer, whether the child is highly likely to be born with a life-threatening condition that causes severe and early debility with no possibility of reasonable function, whether the intended parents are desirous of raising a child with conditions similar to themselves or their families, and whether the intended parents are in accord with each other about the appropriateness of transfer. Physicians who agree to honor patient requests for transfer of affected embryos should discuss the limits, if any, of their willingness to provide treatment as well as the expected health complications a resulting child may experience. This latter duty can be fulfilled by referral to a specialist trained in the particular condition at issue. Additionally, genetic counseling should be offered when there is a potential for phenotypic variability.

ARGUMENTS FOR DECLINING PATIENT REQUESTS FOR TRANSFER OF AFFECTED EMBRYOS

Arguments for declining patient requests for transfer of affected embryos focus on the principles of physician autonomy and professional duties and the welfare of ART offspring. Another considered factor is the possibility of incurring legal or professional liability in the future for assisting a patient in a way that harms another. The governing values that comprise these arguments may be summarized as follows: physician autonomy and professional conscience; reproductive nonmaleficence; procreative beneficence; offspring and societal well-being; and liability avoidance.

The concept that a physician is free to determine whether or not to enter into a doctor-patient relationship with a prospective patient is embedded in medical ethics and health law. The American Medical Association recognizes physician autonomy in the selection of patients as a basic principle of medical ethics (13). Even once a relationship is formed, physicians are not obligated to meet every patient's demand, with particular examples arising in the context of nonbeneficial treatment or treatment that harms another.

Furthermore, physicians' values, personal backgrounds, and professional experiences—informing their professional conscience—may counsel against transferring a particular embryo even in the face of a patient's firmly held desire to do so. Exercises of physician autonomy and professional conscience that are nonarbitrary and do not discriminate against the patient on any basis and that can be accomplished without inflicting harm or abandonment on the patient should be accommodated. Solutions may include transferring the patient to another willing provider or transferring the affected embryo(s) to a clinic ready to facilitate the requested transfer.

The precept of reproductive nonmaleficence describes a physician's obligation not to inflict harm while delivering reproductive healthcare. Transferring an embryo that is highly likely to result in the birth of a child with a serious disease or disability can be interpreted as the physician causing harm by facilitating the birth of an unhealthy person. At the same time, it should be acknowledged that the physician is not responsible for causing the genetic condition; it is the condition that directly causes harm to the resulting child. A further interpretation of the principle of nonmaleficence may include a duty to prevent or avoid harm. Under this configuration, a stronger argument can be made that assisting in the transfer of embryos with positive genetic findings violates the principle of nonmaleficence because the physician can avoid harm to a resulting child by refusing to transfer the particular embryo.

Philosophical discourse offers a counterpoint to the "do no harm" principle in the form of a theory known as procreative beneficence. This theory posits that prospective parents and their physicians have a moral duty to select the embryo that is expected, if successful, to have the best quality of life. This edict to "do good, whenever possible" argues against transferring affected embryos when at least one unaffected embryo remains for possible transfer. Such is the policy adopted in the United Kingdom that prohibits the selection of such affected embryos, except when there is no other embryo "suitable for transfer" (9). The acknowledged weakness of procreative beneficence is in determining what constitutes the "best child" and the "best life." If the intended parents alone are vested with this decisional authority, their good faith judgment about what would constitute their best child may be preemptive of a provider's conflicting view. A decision to transfer an affected rather than an unaffected embryo would, however, still be considered in violation of procreative beneficence, which measures the "best life" in terms of health and well-being.

Child welfare concerns occupy an important role in reproductive medicine. This Committee has previously addressed offspring health and well-being as a factor in provider decision-making about whether to agree or decline to provide treatment under certain circumstances (14). When a physician has a substantial basis for thinking that treating an intended parent will significantly harm a future child, this Committee has supported such treatment denials. Similarly, when an embryo is highly likely to give rise to a child who will experience a disease or disorder and for which no effective therapy exists, a strong argument exists that physicians can ethically decline to participate in the embryo's transfer. Additional concerns about harms to society from the birth of children with diseases or disabilities can be made but are highly problematic as arguable affronts to principles of justice and nondiscrimination. The value of child welfare concerns as a basis for declining embryo transfer is further complicated by the possibility of a physician's mistaken judgment about the prospective child's likely capabilities or quality of life.

Finally, it is reasonable for physicians to have concerns about potential legal or professional liability for assisting in transferring embryos that result in the birth of a seriously health-affected child. Although the intended parents may agree to waive any future claims against an assisting physician, no such waiver can be made on behalf of a future child or a professional licensing authority or society charged with maintaining high standards within the practice of reproductive medicine. The prospect of future liability should not deter physicians from acting in the best interests of their patients.

At the same time, physicians who are in a legitimate position to exercise discretion over treatment decisions may reasonably consider their potential liabilities. Such liability could occur both when care is provided and when it is withheld.

RECOMMENDATIONS

Patient requests to transfer affected embryos raise clinical, ethical, and legal dilemmas that impact various ART stakeholders, including patients and their partners, physicians, offspring, and society. Genotype to phenotype uncertainties including incomplete penetrance, variable expressivity, and the existence of VUS are challenges for physicians striving to counsel patients about the risks and benefits of their reproductive options. Additionally, patient preferences, values surrounding health and disease, expectations, and options for parenthood impact their decision whether or not to seek transfer or some other disposition when an embryo has positive genetic testing results.

Valid and reasoned arguments exist to support physician decisions to assist in transferring affected embryos and in declining to assist in such transfers. Principles of reproductive liberty, physician autonomy, and child welfare are invoked in this clinical setting, creating challenges in prioritizing and applying these and other principles as clinics work to establish guiding policies. Fertility clinics are strongly encouraged to draft and make available to all prospective patients their written policies on the transfer of embryos with positive genetic results from PGT. To the extent possible, these policies should be the product of an informed, deliberative, and collaborative process that includes all relevant clinic personnel directly involved in the care of patients or management of the embryos. Furthermore, patients should be informed of these policies before starting a treatment cycle so they are fully aware of their options before embryo creation in the case that no unaffected embryos are available for transfer.

The Ethics Committee concludes that in circumstances in which a child is highly likely to be born with a life-threatening condition that causes severe and early debility with no possibility of reasonable function, it is ethically acceptable for a physician to decline a patient's request to transfer such embryos. Physician assistance in transferring such embryos is ethically problematic and, therefore, highly discouraged. This conclusion is consonant with prior Committee analysis that physicians may be morally obligated to withhold services when significant harm to future children is likely. In other circumstances in which a child is highly likely to be born with a condition that is treatable or effectively manageable through medical interventions or when genetic testing has revealed findings of uncertain clinical significance, it is ethically acceptable for physicians to adopt a policy that they will transfer such embryos on patient request. Physicians who agree to honor patient requests for transfer of embryos in this category should discuss the limits, if any, of their willingness to provide treatment, as well as the expected health complications a resulting child is likely to experience, before the creation of embryos. Physician refusals to transfer embryos in this category also fall within appropriate ethical boundaries so long as they are made and applied in a manner that does not discriminate against the patient on any basis. Information regarding clinic practices and policies surrounding whether or not they will transfer affected embryos should be made available to patients before the creation of embryos. The presence or absence of one or more unaffected embryos can be considered in generating clinic policies. Physicians are strongly encouraged to refer patients to experts such as genetic counselors, mental health professionals, and clinicians specializing in the specific genetic condition to help them understand the potential risks of transferring affected embryos. Patients should be counseled that in vitro fertilization may not lead to the creation of unaffected embryos. Policies regarding the transfer of affected embryos should be discussed before treatment onset.

Acknowledgments

This report was developed under the direction of the Ethics Committee of the American Society for Reproductive Medicine (ASRM) as a service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other management plans may be appropriate, considering the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Ethics Committee and the Board of Directors of the American Society for Reproductive Medicine have approved this report.

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: Sigal Klipstein, MD; Sina Abhari, MD; Deborah Anderson; Aishwarya Arjunan, MS, MPH, CGC; Kavita Shah Arora, MD, MBE; Tolulope Bakare, MD; Zeki Beyhan, PhD; Katherine Cameron, MD; Susan Crockin, JD; Ruth Farrell, MD; Catherine Hammack-Aviran, MA, JD; Mandy Katz-Jaffe, PhD; Jennifer Kawwass, MD; Louise King, MD; Edward Martinez, MD; Joshua Morris, MD, MA; Torie Comeaux Plowden, MD, MPH; Robert Rebar, MD; Chevis N Shannon, DrPH, MPH, MBA; Hugh Taylor, MD; Michael Thomas, MD; Sean Tipton, MA; and Julianne Zweifel, PhD. The Ethics Committee acknowledges the special contribution of Ruth Farrell, MD, and Mandy Katz-Jaffe, PhD, in the preparation 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 on the basis the relationships disclosed did not participate in the discussion or development of this document.

REFERENCES

1. Practice Committee and Genetic Counseling Professional Group of the American Society for Reproductive Medicine. Indications and management of preimplantation genetic testing for monogenic conditions: a committee opinion. Fertil Steril 2023;120:61–71.
2. Besser AG, Blakemore JK, Grifo JA, Mounts EL. Transfer of embryos with positive results following preimplantation genetic testing for monogenic disorders (PGT-M): experience of two high-volume fertility clinics. J Assist Reprod Genet 2019;36:1949–55.
3. Baruch S, Kaufman D, Hudson KL. Genetic testing of embryos: practices and perspectives of US in vitro fertilization clinics. Fertil Steril 2008;89:1053–8.
4. National Council on Disabilities. Rocking the cradle: ensuring the rights of parents with disabilities and their children. Available at: https://www.ncd.gov/2012/09/27/ncd-issues-groundbreaking-report-rocking-the-cradle-ensuring-the-rights-of-parents-with-disabilities-and-their-children/. Accessed January 9, 2025.
5. Sanghavi DM. Wanting babies like themselves, some parents choose genetic defects. Available at: https://www.nytimes.com/2006/12/05/health/05essa.html. Accessed January 9, 2025.
6. Cohen IG. Intentional diminishment, the non-identity problem, and legal liability. Hastings L J 2008;60:347–75.
7. Wallis JM. Is it ever morally permissible to select for deafness in one's child? Med Health Care Philos 2020;23:3–15.
8. Kolthoff M. Assisted reproduction and primum non nocere. Virtual Mentor 2007;9:605–10.
9. Legislation.gov.uk. Human Fertilisation and Embryology Act 2008. Available at: https://www.legislation.gov.uk/ukpga/2008/22/section/14. Accessed January 9, 2025.
10. Lombardo PA. Three generations: no imbeciles. Baltimore, MD: Johns Hopkins University Press; 2008.
11. Beauchamp T, Childress J. Principles of biomedical ethics. 5th ed. New York, NY: Oxford University Press; 2001:112–5.
12. York v. Jones. 717 F. Supp. 421. E.D. Va; 1989. Available at: https://law.justia.com/cases/federal/district-courts/FSupp/717/421/1584239/#:~:text=The%20defendants%20take%20the%20position,%3B%20and%20(3)%20thawing. Accessed February 25, 2025.
13. American Medical Association. AMA principles of medical ethics. Available at: https://code-medical-ethics.ama-assn.org/principles. Accessed January 9, 2025.
14. Ethics Committee of the American Society for Reproductive Medicine. Child-rearing ability and the provision of fertility services: an Ethics Committee opinion. Fertil Steril 2017;108:944–7.