Preimplantation genetic diagnosis (PGD) is a new method of prenatal diagnosis that is developing from a union of in vitro fertilization (IVF) technology and molecular biology. Briefly stated, PGD involves the creation of several embryos in vitro from the eggs and sperm of an interested couple. The embryos are permitted to develop to a 6-to-10-cell stage, at which point one of the embryonic cells is removed from each embryo and the cellular DNA is analyzed for chromosomal abnormalities or genetic mutations. An embryo or several embryos found to be free of genetic abnormalities are subsequently transferred to the woman's uterus for gestation. Embryos found to carry a genetic abnormality are discarded or frozen. Extra normal embryos may be frozen for future transfer or donation to another couple.

The rationale for this approach to prenatal diagnosis is straightforward: "Preimplantation diagnosis for some couples at risk of transmitting inherited disorders to their children is an alternative to prenatal diagnosis and recurrent abortion." But, as with other forms of prenatal diagnosis, the use of PGD need not be restricted to couples at high risk for inherited disorders. No doubt, continued developments in molecular biology will permit a detailed genetic analysis of a potential child for a wide range of conditions, susceptibilities and, perhaps, behavioral tendencies before gestation even begins.

As an alternative to an existing clinical practice, the ethics of PGD can be considered in reference to prenatal diagnosis using better established techniques such as amniocentesis and chorionic villous sampling (CVS)—hereafter termed "traditional" prenatal diagnosis. Because PGD does not involve abortion, it has been offered as a less morally problematic alternative to prenatal diagnosis. I will argue that PGD does circumvent the problem of abortion, but it raises an interesting array of other practical and ethical issues. A primary conclusion is that PGD will not provide a solution to some of the most serious ethical concerns in prenatal diagnosis.

The emphasis of this discussion will be on the ethically relevant distinctions between PGD and traditional prenatal diagnostic techniques, and I will not develop in detail the many ethical issues involved with prenatal diagnosis in general. I also will not address the ethical issues raised by storage of embryos or the potential use of normal or abnormal embryos for research purposes—both of which are relevant to PGD.

Is there a demand for PGD?
As a backdrop to the discussion of this technology, we should consider the extent to which PGD might be utilized as an alternative to traditional prenatal diagnosis. Utilization will depend as much, or more, on the complexity of the procedures as it will on its perceived ethical advantages. The basic notions of placing eggs and sperm in a dish, testing the resulting embryos and transferring the healthy ones to a receptive uterus are, in principle, quite simple and elegant. Yet the retrieval of multiple eggs, the growing of embryos, the complexities of their analysis, and the subsequent induction of an initially fragile pregnancy require remarkable dedication by a couple and collaboration of a small army of physicians, scientists, and technicians. Willy Lissens et al. describe PGD:

Preimplantation diagnosis is ... a procedure requiring the multidisciplinary collaboration of a clinical IVF unit, a laboratory IVF unit with micromanipula-
nosis is still recommended to check the accuracy of the plantation or the loss of early pregnancies. Once a pregnancy, and it requires the will to endure the failures of implantation or the loss of early pregnancies. Once a pregnancy is established, subsequent traditional prenatal diagnosis is still recommended to check the accuracy of the process.

Related to the complexity and physical burdens and risks of the procedures are their costs. PGD remains experimental, meaning there is no established set of services provided, and there is yet to emerge a literature on its associated costs. However, there is literature on the cost of IVF for infertile couples. In a 1994 article, Peter Neumann et al. estimate that the total direct and indirect cost of IVF per cycle of egg retrieval ranges from $67,000 for the first cycle to $114,000 for the sixth cycle. In a 1997 publication, Bradley Van Voorhis et al. calculate the cost per delivery of IVF in 71 couples to be $43,000 per delivery of an infant. Assuming PGD is on the same order of magnitude, it is an extraordinarily expensive intervention. It is likely that customers for PGD will have to pay for this service out-of-pocket because it is unlikely that insurance carriers or government funding agencies will cover these costs given the nonessential nature of this intervention, the cheaper alternatives, and the controversial nature of prenatal diagnosis in general. Currently, 85 percent of the costs of IVF are not covered by insurance in the United States. Many individuals using PGD to date have their costs covered by the experimental programs developing the technology.

The market demand for PGD will depend on several factors: (1) the number of people interested in prenatal diagnosis; (2) the proportion of those interested who would strongly desire to avoid abortion; and (3) the proportion of those reluctant to consider abortion who would be willing to meet the monetary and nonmonetary costs of PGD procedures. Remarkably, despite these apparent constraints on its appeal, Yuri Verlincki notes that most experimental PGD cycles at present are being done for maternal age-related chromosomal aneuploidy (trisomy 21, trisomy 18, and so forth). For many or most of these older couples, PGD probably is being used as an adjunct to IVF for infertility. PGD by older women outside the context of infertility is an unlikely market due to two considerations. First, the risk of bearing a child with a chromosomal aneuploidy for, say, a forty-year-old women, is approximately 2.5 percent. Second, the efficiency of IVF declines significantly with age. Richard Legro et al. summarize the literature, which indicates that the pregnancy rate per cycle is 5 percent or less in women over forty years of age. Assuming future costs will not be covered by experimental programs or insurance, it is unlikely that many older mothers will be willing to undergo multiple interventions at high cost to address a modest risk that can otherwise be addressed through CVS or amniocentesis (or, perhaps, through adoption). To be more specific, how many women would spend $40,000 for a procedure with a 5 percent success rate to ensure an outcome that would occur 97.5 percent of the time anyhow? Traditional prenatal diagnosis, counseling, and pregnancy termination would avoid the same outcome at a cost of under $3,000, and this full expense would occur only if a pregnancy is achieved and a fetus with an abnormality is detected.

Further, for a number of genetic conditions, there has been a marked ambivalence about the use of prenatal diagnosis in some populations—cystic fibrosis (CF) and sickle cell disease are notable examples because they are the most common genetic conditions in Caucasians and African Americans, respectively. In 1991, a prospective trial of population screening for sickle cell disease found that less than half of those couples identified as at risk pursued prenatal diagnosis. Further, for those couples who pursued prenatal diagnosis and learned of an affected fetus, a termination rate of 39 percent was documented in a 1987 survey of U.S. and Canadian centers performing prenatal diagnosis for sickle cell disease. If these attitudes remain prevalent in the African American community, utilization of PGD for sickle cell disease is likely to be unusual. The ability to do prenatal testing for CF in recent years is being met with limited interest in the United States on the part of at-risk families. The reluctance of many at-risk couples to use prenatal diagnosis and to terminate pregnancies for these conditions is due, in part, to a reluctance to abort a pregnancy—precisely the issue addressed by PGD. But this ambivalence about selective termination is more complex than this one issue of a reluctance to abort per se. Additional dimensions include cultural attitudes about the use of prenatal diagnosis in general, the presence of other options, such as having no more children, and concerns about what abortion may imply for the value of the life of an existing affected child.

These limitations suggest that PGD in the commercial market will be a boutique service for the foreseeable future, even if the efficiency rates increase considerably. It is questionable whether many couples will believe that the added benefits of PGD will justify its costs and other burdens. This raises the broader question of whether the development of this extraordinary technology is born more of consumer demand for an alternative to prenatal diagno-
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The purpose of PGD

Despite reasons to question the future demand for this technology, there is at least a clarity of purpose for PGD compared with more established prenatal diagnostic techniques. The literature on traditional prenatal diagnosis offers a variety of potential purposes for these interventions. One purpose is to reduce the risk of bearing a child with an unwanted genetic condition or congenital malformation. This purpose is the same for PGD, although this purpose must be clearly focused and understood by clients. With all prenatal diagnostic approaches, the reduction in risk applies only to the conditions being evaluated by the technology. PGD does not guarantee that the child will be free of genetic or congenital conditions (a "perfect" baby), only that the child will be free of conditions for which testing is done. Two points are relevant here. First, the current literature is reassuring that the use of PGD does not appear to cause an increase in the risk congenital malformation in the resulting child—a reasonable concern because the procedure removes a substantial portion of the mass of the developing embryo. Joe Simpson and Inge Liebaers reviewed the literature in 1996 and report that pregnancy outcome data suggest that the prevalence of congenital malformation in infants following IVF with or without micromanipulation is about 3 to 4 percent, that is, the same as that in the general population. So although PGD does not appear to increase the overall risk, it does not decrease it below the general population level. Of course, it is important to emphasize that reduction of risk to the population level may look quite good to couples at high risk of bearing a child with a specific genetic condition.

The point here is that couples undergoing PGD should have the clear understanding that the child retains the same base-line risk of a congenital abnormality as children in the general population. More specifically, PGD is not useful for predicting congenital malformations or diseases that do not have an identified genetic basis. For couples who will not consider abortion, PGD alone will not reduce the risk of bearing a child with conditions such as spina bifida, anencephaly, encephalocele, omphalocele, hypoplastic left heart, bladder extrophy, renal agenesis, or many other conditions, because these malformations often do not have their origins in single-gene defects or in detectable chromosomal aberrations. It is interesting to note that Asangla Ao et al. report that more than 50 percent of the couples who underwent PGD for CF in their series did not want additional prenatal diagnostic evaluations of the fetus beyond routine ultrasound. Such decisions may be quite reasonable, as long as the couples understand the limitations of PGD technology.

Another purpose often mentioned for prenatal diagnosis is simply to provide couples with information about the pregnancy. This is a more neutral goal for prenatal diagnostic services consistent with the nondirective tradition of genetic counseling. Because this goal appears less problematic than goals that entail abortion, it may be promoted in patient information materials or in physician-patient encounters. Nancy Press and Carol Browner's work demonstrates how issues surrounding pregnancy termination were not explicitly mentioned in materials and initial encounters in the alpha-fetoprotein screening program in California. Many women did not understand that the principal implication of a decision to be screened was a decision about abortion if an affected child was detected. At the public policy level, it remains a challenge to decide whether prenatal screening programs are a success when at-risk couples are identified and informed of the risk, or whether success requires a significant reduction in the number of affected children born to screened couples. In the prospective screening trial for hemoglobinopathies noted above, 18,907 women were screened to identify 810 carrier women, leading to one pregnancy termination (for hemoglobin H disease). The women generally were grateful for the information—a success. Nevertheless, the limited use of the information by the women indicates that the program was largely a failure in terms of reducing the incidence of serious hemoglobinopathies—at least for the pregnancies followed in the study.

These clinical and policy problems associated with trying to provide neutral information as a purpose for prenatal diagnosis are not relevant to PGD. It would make little sense to go through IVF procedures and genetic analyses only to be nondirective about which embryos to place in the uterus. The purpose of PGD is not simply to inform couples about the genetic nature of their embryos. The explicit purpose is also to transfer healthy embryos and to discard those destined to be affected. Once a couple has chosen PGD, nondirectiveness is no longer relevant.

Similarly, a third purpose often claimed for prenatal diagnosis is that it permits parents to prepare for the birth of an affected child. Several scholars question whether emotional preparation by parents can be effective prior to actually holding and experiencing the child. Nevertheless, the claim is plausible, particularly for conditions requiring immediate surgical interventions that would be facilitated by delivery at a tertiary center. In any case, this purpose for prenatal diagnosis is not relevant to PGD.
Embryo diagnosis would not be necessary or appropriate as a mechanism to prepare for the birth of an affected child.

The explicit purpose of PGD involves the unstated assumption that couples will experience a relative psychological benefit through PGD by discarding embryos to achieve a healthy child, as compared with the abortion of an affected fetus. However, the psychological reactions to PGD remain to be evaluated. What are the psychological implications of going through IVF for this purpose and discarding affected embryos or cryopreserving others for an indefinite fate? With time, do these embryos become lost children in their parents’ minds? How often do women think about the children that might have been? How often do they challenge their own adequacy as parents—inadequacy suggested, perhaps, by a need to undergo a gauntlet of procedures before accepting a child? Do the moral distinctions between PGD and selective termination remain clear with time? Alternatively, for the majority of couples, do the lost embryos remain defective tissue or simple cells unworthy of emotional weight? In one study of couples’ attitudes at a time immediately prior to undergoing IVF concerning the status of the embryo, 25 percent of them stated they considered the embryo to be a child. Of note, however, 30 percent of the couples preferred destruction of extra embryos (including many who considered the embryo to be a child), while 92 percent would tolerate their destruction. Of course, this research does not address how couples feel after such a choice has been made. Although we would not anticipate the profound psychological effects associated with miscarriages or other perinatal losses to be induced by PGD, a careful evaluation of the effects will be essential as this technology emerges.

It is worth emphasizing here that virtually all couples who go through PGD will discard embryos or leave others in frozen limbo, while, at most, 50 percent of couples for any given genetic condition will be faced with an abortion decision per pregnancy. When traditional prenatal diagnosis is done for advanced maternal age, the great majority of older women will not face an abortion decision. So, if there are any adverse psychological impacts from embryo selection, they may be more prevalent than the psychological impacts of traditional prenatal diagnosis.

A significant issue to be addressed in the ethics of PGD, therefore, is the psychological welfare of those who go through the rather arduous process, including those who endure multiple cycles, those with early spontaneous abortions, and those who never carry a child to term, in addition to the successful outcomes. In contrast to the large volume of literature on the conceptual, philosophical, and legal issues associated with assisted reproduction and prenatal diagnosis, the literature on the psychological and behavioral implications of these technologies is relatively scant. The federal government does not support human embryo research directly, but a clear role exists for programs like the Ethical, Legal and Social Implications branch of the National Human Genome Research Institute to evaluate the personal implications of this and other new forms of prenatal genetic testing.

Ethical issues
An initial set of ethical issues to consider are ones that are shared by other forms of prenatal diagnosis and selective termination. These include the destruction of prenatal life, defining the appropriate uses of the technology, the broader social effects of prenatal diagnosis for those with disabilities, allocation of resource issues, and informed consent concerns. PGD presents some new and interesting ethical concerns in each of these familiar domains. Following this discussion, I turn briefly to two new issues that are raised by PGD alone: germ-line gene therapy and genetic enhancement.

Destruction of prenatal life
The advantage of PGD over traditional prenatal diagnosis hinges largely on the ethical distinction between discarding an affected embryo and aborting an affected fetus. The range of positions on the moral status of prenatal life will be familiar to most readers. The conservative position, consistent with the position taken by the Catholic church, is that all prenatal life post-fertilization is of full and equal moral status to that of all other persons. Under this conception, no distinction exists between discarding an embryo and aborting a fetus—both are morally unacceptable. The opposite position, characterized by the arguments of Michael Tooley, is the claim that moral status is conferred by cognitive traits that are probably lacking in newborns, and clearly absent in fetuses and embryos. Under this conception, fetuses and embryos are equal in their lack of significant moral standing. However, the majority of scholars and official bodies who have addressed the issue have adopted positions within a broad center ground. These positions are similar in that they maintain that all prenatal human life should be afforded a special moral status, but a moral status that is not equal to that of a full-fledged person. Further, these views typically hold that the relative moral status is influenced by the developmental status of the embryo or fetus. Some commentators argue that development is a seamless continuum, therefore, the moral status of the embryo and fetus increases incrementally with development. However, the predominant set of arguments confer moral status based on the achievement of certain milestones in the developmental process that have moral significance. Developmental milestones that have been promoted as conferring increased (although not necessarily full) moral status for the developing human include formation of the primitive streak at 14 days, “quickening” at
about 18 weeks, development of "brain life" at about 20 to 22 weeks, a sapient or sentient state emerging at about 22 to 24 weeks, and viability at 23 to 24 weeks of gestation.22 As Carson Strong notes, this developmental conception of moral status is in agreement with widely held moral intuitions that intrauterine devices are morally acceptable even though they destroy the preimplantation embryo, that early abortion is better than late abortion, and that infanticide is wrong.23 The recent partial birth abortion debate also illustrates the heightened ethical concern over pregnancy termination as the fetus approaches term.

The National Institutes of Health's Human Embryo Research Panel in 1994, in its review of the moral status of the embryo, observed that only the conservative position attributed personhood and full moral status to the preimplantation embryo.24 Other philosophical positions, the panel concluded, accord the preembryo either limited or no moral status. The panel preferred not to adopt any single criterion as determinative of the moral status of the embryo, but rather what it called a "pluralistic approach."

As gestation continues, the further development of human form, the onset of a heartbeat, the development of the nervous system leading to brain activity and with this at least some of the physical basis for future sentence, relational presence to the mother, and capacity for independent existence all counsel toward according an increasing degree of protectability.25

Broad recognition of this pluralistic approach in our society provides solid support for the claim that the fetus has greater moral standing than the preimplantation embryo does. A preference by individual couples for discarding embryos versus terminating a fetus is ethically justified through reference to this widely accepted social standard. Therefore, PGD is ethically acceptable on this basis as a method of prenatal diagnosis and selective termination. Conversely, however, given the debatable nature of the moral status of prenatal life and the burdens and expense of PGD, it obviously cannot be claimed that PGD is ethically obligatory as a method of prenatal diagnosis in contrast to more traditional methods.

One further point on the moral status of the preimplantation embryo deserves emphasis. For those who hold the conservative position, PGD will be seen as more ethically problematic than traditional prenatal diagnosis. PGD requires the creation of numerous embryos for each live birth produced. In a recent report by Ao et al., twelve couples utilized PGD to screen for CF. The couples produced 137 embryos, of which 26 were transferred to a woman's uterus and 5 births resulted.26 The loss of prenatal life was substantially greater through PGD than would have resulted had the twelve at-risk couples pursued traditional prenatal diagnosis and selective termination. Clearly, PGD does not resolve the ethical concerns in prenatal diagnosis for many who have fundamental objections to abortion—indeed, it makes the situation considerably worse.

Setting limits on the use of PGD

In general, there is social support for prenatal diagnosis for so-called "serious" conditions, including conditions like Tay-Sachs disease, spina bifida, CF, sickle cell disease, hemophilia, muscular dystrophy, and a number of others. There is also a general conviction that prenatal diagnosis and abortion for "trivial" or minor conditions is ethically troubling,27 although a number of professionals and commentators would permit such use of prenatal diagnosis based on a respect for parental autonomy in reproductive matters. Gender selection is often used as an extreme example of selective abortion for frivolous reasons. Nevertheless, the majority of U.S. geneticists surveyed by Dorothy Wertz and John Fletcher in 1985 would either perform prenatal diagnosis for a couple who did not want a fifth daughter or refer them to a colleague who would.29 Therefore, with traditional prenatal diagnosis, a conflict in social values arises between a reluctance to validate termination of a fetus for a less than a serious medical condition and a desire to respect parental autonomy in this most intimate of enterprises.

This fundamental problem with traditional prenatal diagnosis will be exacerbated by the rapid increase in genetic tests for a wide range of conditions, including late-onset conditions, conditions with a limited impact on health, and, possibly, behavioral or physical characteristics that fall within the normal range. This is not to suggest that genes play a predominant role in complex human behaviors and characteristics. Increasingly, it could be found that, for all but the simplest genetic conditions, dozens or hundreds of genes interact with each other and with thousands of biochemical and environmental agents over extended periods of time to produce the phenotype. Such complexity could frustrate any meaningful predictions based on genetic tests alone. Richard Strohman argues that much of the contemporary interest in genetic testing will collapse as our overly deterministic genetic paradigm progressively fails.30 Nevertheless, we only may need a popular perception of genetic determinism, fueled by creative marketing and weak regulation, to move poorly predictive tests from the lab into the clinic.

If, indeed, an extensive battery of genetic tests become available for prenatal diagnosis, what tests should be offered to couples and what tests should professionals provide on request? Should we draw a line, indicating which tests should and should not be provided by an ethical practitioner? Several general positions on the "line-drawing" question are beginning to emerge. John Robertson con-
cedes the morally problematic nature of prenatal diagnosis for "minor" conditions, but argues that our respect for procreative liberty should be paramount, at least until some definitive harm is demonstrated from unfettered use.\textsuperscript{31} Robertson places no limits on the parents' ability to obtain prenatal testing for any condition. Strong advocates use of prenatal diagnosis for all diseases or susceptibilities to diseases, but not for nondisease conditions.\textsuperscript{32} Strong's analysis places a heavy emphasis on the value of nondirectiveness in prenatal diagnostic services, suggesting that line drawing between disease categories undermines this important value. In contrast, Stephen Post, Peter Whitehouse, and I have argued that minor and late-onset conditions do not justify testing.\textsuperscript{33} Angus Clark supports prenatal diagnosis only for the most serious conditions.\textsuperscript{34} Adrienne Asch, although deeply troubled by the termination of embryos and fetuses for disabling conditions, believes that a policy of line drawing would be enormously detrimental to those in the disabled community who fall below the line.\textsuperscript{35} She, therefore, opposes line drawing, but would couple prenatal diagnosis with better education, emphasizing a fuller understanding of life's prospects with a disabled child. The Institute of Medicine has taken the position that "prenatal diagnosis not be used for minor conditions or characteristics."\textsuperscript{36} These positions illustrate a balancing of a number of considerations, including the moral status of the embryo and fetus, the limits of professional authority, the limits, if any, of our respect for parental autonomy, and the impact of individuals with disabilities on the family and society. Also to be considered in this dilemma is the impact of prenatal diagnosis on those who live with disabilities and the impact of broad choice on the parent-child relationship. Much more work needs to be done on this line-drawing question for prenatal diagnosis in general to achieve some resolution at a societal level.

PGD will serve to complicate this dilemma by reducing the concern over one significant element in the equation—abortion. The technology, by its very design, offers each couple a range of choices in offspring. Choice in offspring through PGD is not contingent on abortion. Whether to transfer an affected embryo is not a dilemma with PGD, because this is its explicit purpose; but other more subtle choices are made possible by the technology. Imagine a couple who has 8 embryos in vitro, 2 of which are homozygous for CF, 2 are heterozygous, and 4 are neither carriers nor affected (termed \textit{homozygous normal}). At the request of the parents, the embryos are sexed and three of the four homozygous normal embryos are female and both of the heterozygous embryos are male. The couple desires a son, so the homozygous normal male embryo is split—one-half (now a viable embryo itself) is implanted and the other is cryopreserved along with the other unaffected embryos.

Is there a problem with this scenario? No embryos have been destroyed on the basis of gender and the couple fulfills its wishes. Does this form of gender selection strike us as less problematic than gender selection by abortion? After all, the couple has quite a few embryos from which to choose—a primary choice has been made to discard the affected embryos, but why not choose the specific one to be implanted on the basis of secondary characteristics? By producing a number of embryos with each cycle and by eliminating the moral hurdle of abortion in the selection of offspring, PGD facilitates a broad range of possibilities for selecting the biologic characteristics of children.

If we are entering an age of genetic testing for a wide range of conditions, the extensive analysis of potential children may be a popular application. One example of a particularly interesting development is the chip technology in which tens of thousands of DNA fragments are imbedded in a glass slide that is used to analyze a target DNA sample.\textsuperscript{37} It is anticipated that these chips will enable a DNA sample to be evaluated for tens of thousands or hundreds of thousands of mutations or alleles. Backed by a powerful computer, it may be possible to correlate the results of such a DNA analysis with complex physical or psychological traits in individuals. For example, assuming intelligence has some genetic components, correlating a DNA chip analysis of, say, 100,000 random coding sites in the genome with traditional IQ scores may reveal patterns of results that are associated with higher or lower IQ scores in healthy individuals. Note that such a "test" can function with no true knowledge about the genetic influences on IQ. The same kind of testing might be used for any physical or psychological characteristic for which there are objective measures and any meaningful genetic contributions. As noted, these tests need not be very predictive to be adopted by some couples who want the very best that their sperm, eggs, and money can provide.

If such genetic tests are perceived as useful for predicting the physical and psychological characteristics of future children, some couples may pursue PGD for no other reason than to select their ideal embryo. This could well be a growth industry in the coming century for couples who can afford it.

For those who are uneasy with this notion, the challenge is to articulate the ethical problem with this approach to child bearing when abortion is no longer a concern (and assuming one does not hold the conservative position with respect to the moral weight of embryo destruction). One consistent criticism of prenatal diagnosis is the message of rejection that it sends to people with disabilities. It is feared that prenatal diagnosis will lead to heightened intolerance of disability as forces are marshaled to eliminate those embryos and fetuses with disabilities rather than to develop a society in which the disabled can live as welcomed partners. If prenatal diagnosis and PGD specifically were to have a significantly negative effect on the millions of disabled individuals in society, this would be a powerful...
argument for limiting or discouraging its use, at least for less than serious medical conditions.

The speculative nature of this concern, both in terms of whether people will use PGD or traditional prenatal diagnosis for a broad range of conditions, and whether such use will produce additional discrimination for the disabled, makes this concern difficult to weigh as a moral issue. There is no evidence of this kind of effect to date on a broad scale, despite the use of prenatal diagnosis for several decades. In contrast, individuals with disabilities have never had more social support than they do today, as reflected in the sentiment and substance of the Americans with Disabilities Act. Certainly, more social support is still due, but a generally improved social stature for the disabled has occurred in recent decades in parallel with the development and use of prenatal diagnostic techniques. Changes in technology, economics, and attitudes could adversely change the situation for the disabled in the future, but current experience indicates that society can simultaneously promote respect and opportunity for the disabled while enabling couples to prevent the birth of a disabled child through prenatal diagnosis.

However, distinctions may be made in the future between those disabled from genetic conditions that are detectable prenatally and the majority of the disabled who have limitations from a broad range of other causes (injury, stroke, infection, and so forth). Given the potential power of PGD to select the genetic characteristics of future children, it could promote societal expectations of “perfectibility” in children, thus fostering a more narrow intolerance of those disabled from genetic and congenital etiologies and, perhaps, of the parents who choose to have such a child. This is a serious concern that deserves scrutiny and persistent efforts to combat discriminatory attitudes toward the disabled.

It is likely, however, that broad changes in social attitudes concerning perfectibility and disability will be affected more by prenatal diagnostic techniques that may have much greater appeal than will PGD. For example, techniques that will enable the isolation of fetal cells from maternal blood samples early in pregnancy, in conjunction with medications to terminate early pregnancies privately and relatively painlessly, are more likely to have widespread utilization than PGD. There are even developments that may enable the determination of fetal sex through a maternal urine test. I suspect that any new approaches that make prenatal diagnosis accurate and selective termination substantially easier early in pregnancy would be widely adopted. For whatever benefits this technology may bring, widespread use could significantly reduce societal tolerance for “less than perfect” babies.

A second concern raised by the use of PGD to select against minor conditions (or for desirable characteristics) is the potential effect such control might have on the parent-child relationship. As noted, PGD facilitates the selection of children, as compared with traditional prenatal diagnosis, because it offers a range of choices with each set of embryos produced rather than the single choice of accepting or terminating an established pregnancy.

The most compelling argument from my perspective as a pediatrician is the adverse effect detailed selection may have on the parent-child relationship, whether by PGD or traditional prenatal diagnosis. Parents always have had hopes and expectations at the birth of a child, but these are layered on the knowledge that children will grow up and in directions over which they ultimately will have little control. We have all lived through our own parents’ expectations and we all understand how supportive and damaging these can be. What would it mean for parents to have very specific expectations for a child based in prenatal testing and selection?

From the age of nine months onward when an infant begins to crawl, her project becomes increasingly one of independence. Her parents’ project, in contrast, is one of control, indoctrination, and education to protect, to prepare, to bypass the mistakes made by others (often their own), and to fulfill their own conception of a life of value. This tension between the child’s striving for independence and the parents’ need for nurturing is fundamental to the parent-child relationship. Ultimately, we establish ourselves as independent—often to be quite different from what our parents had in mind. But remarkably, there need be no love lost in this clash of projects, although there sometimes is. For the most part, we continue to love our children (and our parents) as they are.

What influence could PGD technology have on this most important relationship? How might the knowledge that a child was deliberately selected for her biological characteristics affect how an individual regards her parents, how her parents regard her, and how she regards herself? Could the selection enhance the expectations of parents and alter the child’s self-perception of strengths and weaknesses? Would children be strongly channeled in directions of the parents’ choosing? To what extent would children resent such an intrusion on their own autonomy? Oscar Wilde observed: “Children begin by loving their parents. After a time they judge them. Rarely, if ever, do they forgive them.” I suspect that the greater the power parents have over the biological nature of their children, the more this observation will hold true. This is not because the child would be directly harmed by the biological selection, but because the selection may well come with a stifling set of expectations. The question is whether the child’s future autonomy—her right to an “open future”—will be sacrificed through a uncompromising respect for parental liberty in reproductive decisions.

My purpose here is to outline ethical concerns over the unfettered use of PGD that extend beyond the destruc-
tion of embryos alone. These concerns over the parent-child relationship are quite speculative and there is certainly no data as yet to support or refute these possibilities. Nevertheless, the fundamental importance of the parent-child relationship suggests that a burden of justification must rest with parents or professionals who would use PGD for the selection of offspring for characteristics other than significant health conditions. Parental desires to use technology in the fine-grained selection of children must be justified through claims of legitimate interest. Parents traditionally have had only a prima facie right to liberty in reproductive decisions—not an absolute right in the face of potential countervailing harms.

Further, in response to Strong's concern about undermining nondirectiveness through limitations on services, it should be noted that nondirectiveness in genetic services traditionally relates what couples should do with information provided to them through diagnostic services, not to what services are offered. Women under the age of thirty-five have not been routinely offered amniocentesis due to the professional judgment that the benefits do not outweigh the risks in younger women. Whether the geneticist provides prenatal diagnosis to a younger woman who requests it usually is based on individual factors in the patient-professional relationship. Geneticists do not reflexively acquiesce to such requests based on a respect for nondirectiveness. Similarly, the identification of the gene associated with CF in 1989 has not led to the offering of CF carrier screening in the general population, due to broad social and professional concerns.92 The practice of medicine in general is characterized by professional judgment on what services are offered in specific clinical circumstances. Once couples are provided with information about the embryo or fetus, then nondirectiveness is relevant to their decision over their response. Therefore, undertaking an analysis of the benefits and harms of what services should be offered or provided in PGD is quite consistent with contemporary practice in medical genetics and medicine more generally.

Why would parents want to select the biological characteristics of their children, beyond a selection against conditions causing significant disability? Is there a convincing rationale for such an intervention? If the claim is that such selections ultimately will make the resulting children happier with their lives, then the credibility of this claim can be challenged. Each of us can point to a number of biological characteristics that have influenced our lives favorably and unfavorably, but this provides little evidence for what characteristics our children will find beneficial or harmful in their lives as they unfold in very different ways, times, and places. Do we know which biological characteristics promote a contented life? If we were to look in detail at a list of genetic characteristics of a set of infants, would we presume to predict which children would experience the most fulfilling lives, by whatever definition we choose?

We probably do have a list of traits that would make our children more competitive in contemporary society, but success in competition and contentment are two very different things. There is less moral force to the claim that parents should be supported in their efforts to gain competitive advantage for their children, particularly when competitive advantage remains possible through traditional means such as education, wealth, and hard work.

The parents themselves may imagine that they would be happier if they could select just the right child. But, as I have argued, the very act of selection may mitigate against an ideal relationship, assuming that such a relationship derives in large measure from unqualified love and support. Tom Murray writes:

The quest for perfection has been spurred by a desire to escape the limitations and especially the hurts that mark indelibly our existence as finite, embodied, independent beings. The danger in that quest is that we can become so attracted to some suprahuman idea or entity that we lose sight of, or even come to have contempt for, the actual flawed and vulnerable human beings with whom we live.43

Perhaps these fears of corrupted relationships belie a cynical view of human nature. Perhaps parents and professionals will not use PGD technology for "frivolous" selections, or perhaps such selections will have no adverse impacts on complex relationships. But despite the infancy of PGD technology, there are inklings of problems already. Ao et al., reporting on PGD for CF, state:

A maximum of two embryos were transferred to each patient. In some cases, carrier embryos were transferred where only one embryo was diagnosed as normal after discussion with the patients. If more than two embryos were diagnosed as normal, two embryos were selected for transfer on the basis of morphology and advanced stages of development.44

Stated differently, heterozygous embryos were considered to be flawed in some way and there was a preference not to transfer them. CF heterozygotes are healthy and normal in all respects, so the decision not to implant heterozygotes unless necessary is, I suspect, what J.A. Raeburn has termed "technological stigmatization."45 As the power of the diagnostic technology expands in PGD, circumventing the abortion problem may make the price of technological stigmatization appear deceptively small.

It is essential that the appropriate uses and misuses of this technology be debated and defined. This is perhaps the greatest ethical challenge raised by PGD. At present, concerns over the impact on those with disabilities and the impact on the parent-child relationship suggest a limited
use of PGD (and other prenatal diagnostic approaches) for significant health concerns. (This conclusion does not necessitate legal prohibitions on some uses of the technology, only the development of standards for which tests should be offered and/or provided by the ethical practitioner.) PGD avoids the problem of abortion, but it heightens more subtle and longer-term concerns over the limits of parental control over the biological nature of their children.

Allocation of resources

The substantial cost of PGD will make it well beyond the means of most couples. Insurance and government programs like Medicaid are unlikely ever to cover the costs because, as noted previously, 85 percent of the costs of IVF are not covered by insurance in the United States and substantially less costly means of prenatal diagnosis than PGD exist. The discrepancies in the use of prenatal diagnosis between urban white women and other women in the United States are well known. This discrepancy represents both financial and cultural differences. If, or when, PGD becomes commercially available on a broad scale, it is likely to be used almost exclusively by affluent couples. (Less affluent couples who are infertile and who have their IVF costs covered by insurance may also be able to use PGD if they can afford the additional marginal costs of the genetic analysis.)

The extent to which the anticipated lack of wide availability is an ethical problem hinges on the extent to which PGD addresses important needs, or the extent to which PGD produces additional social advantages for the well-to-do. At present, the advantages of PGD are not substantial enough to require an equitable distribution in society. However, if the technology is widely used in decades hence to enhance the offspring of the well-to-do in some meaningful way (or if they are widely perceived to be enhanced), then arguments for an equitable distribution will have much stronger sway.46

Research context

Reproduction decisions are some of the most emotionally laden of any in life. The very existence of IVF has been termed coercive for infertile couples.47 If this is the feeling of many who use IVF technology, then it suggests that the manipulation of couples who are struggling with reproductive concerns is a real possibility. What are couples told about the risks, burdens, and possibilities of success with PGD? The literature on PGD explicitly states that it is an experimental intervention, yet the literature reveals few acknowledgments of institutional review board (IRB) review. Are these projects being subject to peer review and acknowledgment of institutional review board (IRB) review? If this is the feeling laden context of PGD, peer review through an IRB is highly desirable to ensure appropriate human subject protections. Many PGD programs may not be required to undergo IRB review if they are not federally supported or regulated, or if they are not part of an institution that requires IRB review of all human subject research. One solution to this problem is passage of federal legislation to require peer review for human subject concerns for all human subjects research.48 Absent new federal legislation, voluntary submission of PGD protocols to an IRB would reassure subjects and colleagues of the integrity of this work. As an additional incentive, journal editorial boards should strongly consider requiring IRB review for publication of this innovative work using human subjects.

Issues unique to PGD: germ-line gene therapy and genetic enhancement

PGD could be a component of two controversial interventions that are not relevant to traditional prenatal diagnosis: germ-line gene therapy and genetic enhancement. The ability to manipulate the in vitro embryo will greatly facilitate the insertion of genetic material, either to treat a medical condition or, potentially, to enhance its genetic characteristics. Such gene therapy is germ-line therapy because the genetic insertion into an individual embryonic cell (or zygote), which is then grown as a separate embryo, would result in the transformation of all of the cells in the resulting individual, including the gametes. PGD could be used prior to and after insertion of genetic material in order first to identify a suitable embryo and then to evaluate the success of the genetic transfer.

Germ-line gene therapy has been the subject of a growing volume of literature, even though gene therapy in general has proven to be much more difficult than originally hoped. Leroy Walters and Judy Palmer outline eight arguments from the literature against germ-line gene therapy.49 The most compelling, at least for this purpose, is that the emergence of PGD has virtually eliminated the need for germ-line therapy. For many medical conditions in which genetic mutations produce structural or developmental abnormalities from early in gestation, successful therapy and prevention will require that the genetic material be inserted either into the gamete(s) of the parents or into the early embryo. In this circumstance, the gene therapy becomes germ-line as a by-product of the primary therapeutic intent. However, in the foreseeable future, the difficulty of reliably introducing a stable, functional genetic element into in vivo human eggs and sperm will be very difficult to surmount.50 In contrast, the possibility of introducing functional genes into an in vitro zygote or embryo seems quite reasonable in the foreseeable future.

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The basic question is why a couple would bother to treat an affected embryo with gene therapy when they could simply discard any affected embryos and transfer the ones destined to be healthy. Because embryos have little moral stature, there is no mandate to rescue them with gene therapy. Further, the failure of the gene therapy protocol would result in miscarriage or a choice over abortion later in the pregnancy, both highly undesirable in comparison with discarding the affected embryo in the first place. The only rational reasons to undertake gene therapy in an embryo would be (1) if a couple were opposed to discarding or freezing embryos, in which case PGD technology is unlikely to be attractive at the outset, or (2) if a couple were both homozygous for a recessive condition, say, a couple both of whom had sickle cell disease. This latter possibility hardly seems a solid basis for the development of an experimental gene therapy intervention for human embryos, particularly if gene therapy were developed to where somatic gene therapy could treat the affected children.

The only plausible reason to insert genetic material into embryos would be for genetic enhancement. PGD to select the best embryo followed by insertion of advantageous genetic material would be the most logical method to produce genetic enhancement. The ethics of genetic enhancement is complex and beyond the scope of this paper. Suffice it to say that, in my view, some forms of genetic enhancement may be justifiable, in principle. An enhancement of the immune system to assist in fighting infectious diseases and/or to reduce the risk of cancer or autoimmune diseases may be an example of a justifiable intervention. Enhancement of other characteristics like intelligence or physical stature or coordination, assuming such things will ever be possible, are much more problematic. In any case, enhancement created through embryo manipulation (including PGD) rather than enhancement of fetuses or children brings no new concerns to the debate, other than those created by potential differences in risk or efficacy. Research in PGD could facilitate the development of genetic enhancement, so it is imperative that we clearly articulate the appropriate uses of the technology.

Conclusions

First, PGD is ethically permissible for its primary purpose, that is, to offer couples at high risk of bearing a child with a significant genetic condition the opportunity to have a healthy child without resorting to selective abortion.

Second, PGD currently is inefficient, burdensome, and expensive. When the costs are not being subsidized by research protocols, few couples are likely to find PGD attractive for its primary purpose.

Third, as with other forms of prenatal diagnosis, socially sanctioned uses need to be defined through broad social discourse. The option to avoid aborting a fetus through PGD does not justify the selection of embryos for less than serious genetic conditions. The definition of serious in this context needs much more work.

Fourth, research on the psychological effects of PGD is essential to validate the implicit claim that couples fare better through PGD than they would through prenatal diagnosis and selective termination.

Fifth, IRB review of PGD protocols should be strongly encouraged on a voluntary basis, or mandated by federal legislation, and documented in published articles.

And, sixth, PGD provides a logical avenue for genetic enhancement, but ethical concerns over enhancement possibilities do not invalidate PGD for its contemporary use. PGD provides a new opportunity for couples who desire prenatal diagnosis, but who want to avoid abortion of an affected fetus. Yet the potential power of this technology to manipulate human embryos raises a host of new concerns about the nature of the parent-child relationship and the limits of our biological control over succeeding generations. It remains to be determined whether this is a good trade of ethical concerns.

Acknowledgments

An earlier version of this paper was presented at a meeting titled “Introducing Innovation into Practice: Technical and Ethical Analyses of Preimplantation Genetic Diagnosis and Intracytoplasmic Sperm Injection Technologies,” which was sponsored by the National Advisory Board on Ethics in Reproduction and the National Institute of Child Health and Human Development on June 18, 1997. I am grateful to participants in the conference, and to Jay Jacobson, M.D., Leslie Francis, J.D., Ph.D., and Margaret Battin, Ph.D., for their suggestions. My thanks also to Sara Taub for her assistance with the research. This work was supported, in part, by a grant from the National Human Genome Research Institute (Grant No. P50 HG00199).

References

3. Lissens et al., supra note 1, at 719.
5. See J.A. Collins et al., “An Estimate of the Cost of In Vitro Fertilization Services in the United States in 1995,” Fertil-
ity and Sterility, 64 (1995): 538-45.


23. See Strong, id.


25. Id. at 30.

26. See Ao et al., supra note 14.


29. See Wertz and Fletcher, supra note 27.


32. See Strong, supra note 22, at 133-58.


36. See Andrews et al., supra note 27.


44. See Ao et al., supra note 14.

50. The technical difficulties of inserting functional genetic material into in vivo eggs and sperm are significant. Primary oocytes are produced from cell division while the woman is still a fetus herself and the meiotic divisions occur near the time of ovulation and fertilization. Because the insertion of genetic material generally requires an actively dividing cell, primary oocytes are a difficult target in their dormant state. The challenge with sperm is to insert successfully the genetic material into virtually 100 percent of billions on billions of sperm stem cells. Further, the insertion must be in a stable fashion that leaves the sperm functional and otherwise unimpaired. Given the limited success to date with any gene therapy, prospects for such success in humans are not on the horizon.