Preimplantation genetic diagnosis (PGD) represents an alternative to prenatal diagnosis and allows selection of unaffected IVF embryos for establishing pregnancies in couples at risk for transmitting a genetic disorder.

Embryo biopsy and genetic analysis can be performed on the oocyte/zygote (polar body analysis), blastomeres from cleavage stage embryos, or blastocysts. PGD can be applied for monogenic disorders or chromosomal abnormalities, using diagnostic protocols based on the polymerase chain reaction (PCR) or fluorescence in situ hybridisation (FISH), respectively. Although it is more than a decade since the first PCR-based clinical PGD cycles were performed, clinical application of PGD has remained limited for several reasons. Firstly, it is a multistep procedure which requires combined expertise in reproductive medicine and genetics. Secondly, the genetic diagnosis of single cells is technically challenging at all stages. In addition, several pitfalls which may compromise the accuracy of diagnosis have come to light, including a phenomenon known as allelic drop out (for PCR-based analyses) and the frequent occurrence of chromosomal mosaicism in preimplantation embryos. Efforts continue to improve protocols and develop new technologies for genetic analysis of single cells for an ever-increasing spectrum of genetic disorders. Several practical and ethical issues need to be addressed before a wider application of PGD in clinical practice, but it is a valuable procedure in preventive genetics, especially for couples who have an unsuccessful reproductive history and, additionally, a high risk of transmitting a severe genetic disease.

In developed countries, genetically determined disorders account for up to one-third of admissions to paediatric wards and are a significant cause of childhood deaths. Although the Human Genome Project and related advances in molecular biology promise means for the long-term curative treatment of many severe genetic disorders, the current approach for controlling these disorders remains prevention, including application of prenatal diagnosis (PND) which is an accepted procedure in most populations.

PND aims to provide an accurate, rapid result as early in pregnancy as possible. A prerequisite involves obtaining fetal material promptly and safely, and current methods include trophoblast sampling or amniocentesis. Fetal cells and free fetal DNA are also present in the circulation of the pregnant mother and provide a potential source for “non-invasive” fetal sampling, but reliable protocols have yet to be established for clinical application. Termination of affected pregnancies is the major disadvantage of PND. Although PND promotes reproductive confidence for couples wishing to avoid the birth of an affected child, the trend of starting families later and the increasing recourse to assisted reproduction means that pregnancies may be initiated with some difficulty, and termination in these cases is an even less acceptable option.

Preimplantation genetic diagnosis (PGD) represents a “state of the art” procedure which potentially avoids the need to terminate affected pregnancies through identification and transfer of only unaffected embryos established from in vitro fertilisation (IVF). The feasibility of PGD was initially facilitated by developments during the late 1980s in assisted reproduction and embryology, along with the discovery of the polymerase chain reaction (PCR), and it is more than a decade since the first pregnancies were achieved following biopsy and genetic diagnosis of human preimplantation embryos. Although a growing number of centres worldwide offer PGD, it is still not widely performed as a clinical service since it requires combined expertise in the fields of reproductive medicine and molecular genetics and/or cytogenetics. Additionally, genetic diagnosis of single cells is technically demanding, and protocols have to be stringently standardised before clinical application. We present an overview which highlights many of the technical, practical, and ethical issues associated with performing PGD as a part of a clinical service for preventive genetics.

**SOURCES OF GENETIC MATERIAL FOR PGD**

There are potentially three types of cells suitable for PGD analysis including polar bodies (PBs) from the oocyte/zygote stage, blastomeres from cleavage stage embryos, or trophectoderm cells from blastocysts.

The expertise of an embryologist is fundamental to ensure successful biopsy while maintaining embryo viability. The first stage of any biopsy procedure is to make a hole in the zona pellucida that surrounds the oocyte or embryo until the expanded blasocyst stage. Acid Tyrodes drilling was the first method used, but for PB biopsy acid Tyrodes may adversely affect subsequent oocyte development, and mechanical means that tear the zona are preferable. The most recent development is the use of a laser for zona drilling, potentially the most precise and safest method.

**Abbreviations:** PGD, preimplantation genetic diagnosis; PND, prenatal diagnosis; PB, polar bodies; ADO, allelic drop out; PGS, preimplantation genetic screening; CGH, comparative genomic hybridisation
**Polar body (PB) biopsy**

PB biopsy was initially considered advantageous since manipulations involve oocytes rather than embryos, precluding ethical and safety debates concerning human embryo biopsy, and the genetic material removed is not destined to become part of the developing embryo.

For PGD of monogenic diseases, the simplest model predicts that the genotype of the oocyte is indirectly derived from the opposite diagnosis of the first PB (IPB). However, PB analysis may be complicated by recombination events, whereby a crossover event occurs in a heterozygous primary oocyte which includes the region around the gene under analysis, the two daughter chromatids in IPB will have a “heterozygous” genotype. In this case, analysis of the second polar body (II PB) is essential to define the status of the secondary oocyte, whereby the genotype of II PB is opposite to that of the oocyte. This evaluation may be further complicated by the phenomenon of allelic drop out (ADO), which may occur during PCR analysis of single cells (see section on PGD for monogenic disorders), such that detection of a single allele in IPB cannot distinguish between a “true” genotype (when there has been no recombination event) or ADO (unless the gene maps closely to the centromere of a chromosome, where recombination is less likely to occur). The analysis of both IPB and II PB doubles the number of manipulations and samples for analysis, and furthermore many oocytes must be tested, despite the fact that a significant number will fail to fertilise or form embryos suitable for IVF. Finally, the genotype of the paternal allele remains unknown.

PB analysis is useful for detecting numerical chromosomal abnormalities, since the majority of aneuploidies are maternally derived. In clinical PGD cycles, PB biopsy has been used mainly for age related aneuploidy (also known as preimplantation genetic screening) or chromosomal analysis where the female carries a translocation, but is not preferred by most centres offering PGD.

**Cleavage stage embryo biopsy**

On the third day post-insemination, the fertilised embryos are usually six to eight cells (cleavage stage embryos). At this stage the cells are still totipotent and the embryos are usually not yet compacting. The quality of cleavage stage embryos in culture is variable but they can be evaluated morphologically as grade 1 (correct stage of development, regularly shaped, evenly sized blastomeres, and no fragmentation) to grade III (slow development, unequally sized blastomeres, at least one degenerate blastomere and/or a high level of fragmentation). Biopsy of blastomeres from cleavage stage embryos is preferred by most centres performing PGD.

The original protocol was described by Hardy et al and is illustrated in fig 1. Subsequent modifications to the protocol include the use of the same pipette for zona drilling and blastomere aspiration, the use of a laser for zona drilling and blastomere aspiration, and in addition the use of calcium and magnesium free media during the biopsy to reduce cell-cell adhesion, especially if the embryos have begun to compact. One of the main disadvantages of blastomere biopsy is the limited amount of material available for analysis. Many PGD centres recommend the biopsy and replicate analysis of two blastomeres from each cleavage stage embryo, although this approach is often limited by suboptimal embryo quality and/or development in culture.

**Blastocyst stage biopsy**

The blastocyst is a cavitated structure that contains approximately 100 cells and it develops about five to six days post-insemination. Biopsy of the blastocyst has a potential advantage over blastomere biopsy in that more cells may be removed for analysis, and the biopsy procedure is technically less demanding than that of blastomeres or PBs. The trophoderm cells do not contribute to the embryo proper, but eventually form the placenta and other extra-embryonic tissue (comparable to an early chorionic villus sampling), partially reducing ethical considerations. The removal of up to about 10 cells from the trophectoderm does not appear to alter the early development of human embryos, but to date there have been no reports on blastocyst biopsy for clinical PGD cycles and it is not known whether later fetal development is affected. Furthermore, although the use of sequential media for embryo culture supports the development of embryos to the blastocyst stage, only up to about 40-50% of preimplantation embryos develop to this stage in vitro with present protocols, limiting the application of this biopsy method for PGD.

**PROTOCOLS FOR GENETIC ANALYSIS**

For clinical PGD cycles, the outcome of IVF treatment and quality of embryos available for biopsy depends upon many case specific factors, including whether the couple is fertile or not, the underlying cause of infertility, and the age of the woman, and clinical application allows little choice in these factors. It is only the stage of genetic analysis that can potentially be optimised for accuracy and reliability, and technically single cell diagnosis has proved to be the most difficult part of PGD. Furthermore, genetic diagnosis has to be completed within about 48 hours to allow embryo transfer before embryo viability is compromised.

PGD can be applied for monogenic disorders or chromosomal abnormalities (including aneuploidies or translocations), using diagnostic protocols based on the polymerase chain reaction (PCR) or fluorescence in situ hybridisation.
(FISH), respectively. PGD can theoretically be performed for any genetic disease for which there is enough sequence information to facilitate the design of specific primers or probes. To establish a diagnostic protocol, preclinical experiments are carried out using single lymphocytes, fibroblasts, or single blastomeres from research embryos. The former cell types are not completely representative of embryo derived cells (for example, for evaluating the cell lysis protocols which precede PCR based diagnoses), but have the advantage that they are easier to obtain and can be selected with variables such as mutation(s) in the gene(s) under study. On the other hand, spare embryos from completed IVF cycles are in limited supply and have variable, often suboptimal genetic quality, making comparisons and experimental controls difficult. Despite these obstacles, efficient protocols for many disorders have been established and applied, as outlined below.

**PGD for monogenic diseases**

Protocols for genotyping single cells for monogenic disorders are based on PCR. Since the first PCR based PGD cases were performed, several inherent difficulties associated with single cell DNA amplification have become evident. These include potential sample contamination, total PCR failure, and allelic drop out (ADO, when one of the alleles fails to amplify to detectable levels), all of which should be minimised for any PGD PCR protocol before clinical application. In addition, the chosen method must reliably and accurately characterise the genotype of the embryo relative to the disorder under investigation.

PCR based analysis of a single cell requires many cycles of amplification and thus accidental introduction of contaminating DNA should be carefully guarded against. Potential contaminants that are specific for the PGD procedure include the cumulus cells that surround the oocyte (maternal origin) and excess sperm that may be embedded in the zona following fertilisation. Thus, when establishing embryos, the oocytes must be stripped of their cumulus cells and intracytoplasmic sperm injection is recommended for fertilisation of oocytes.

Other sources of contamination include cells from the operators performing the IVF/PGD procedure or PCR amplions within the system of the genetics laboratory. For these reasons, biopsy and PCR reaction set up should be carried out in separate, isolated, UV treated areas under stringent conditions, using exclusive equipment and stringently prepared reagents. Pre- and post-PCR procedures should be strictly separated, and each PGD analysis should be monitored by the inclusion of negative controls and blanks at all stages.

The PCR reaction must be optimised to minimise PCR failure and ADO and in preclinical experiments most centres accept a single cell amplification rate of above 90% and an allelic drop out (ADO, when one of the alleles fails to amplify to detectable levels), all of which should be minimised for any PGD PCR protocol before clinical application. In addition, the chosen method must reliably and accurately characterise the genotype of the embryo relative to the disorder under investigation.

PCR based analysis of a single cell requires many cycles of amplification and thus accidental introduction of contaminating DNA should be carefully guarded against. Potential contaminants that are specific for the PGD procedure include the cumulus cells that surround the oocyte (maternal origin) and excess sperm that may be embedded in the zona following fertilisation. Thus, when establishing embryos, the oocytes must be stripped of their cumulus cells and intracytoplasmic sperm injection is recommended for fertilisation of oocytes.

Other sources of contamination include cells from the operators performing the IVF/PGD procedure or PCR amplions within the system of the genetics laboratory. For these reasons, biopsy and PCR reaction set up should be carried out in separate, isolated, UV treated areas under stringent conditions, using exclusive equipment and stringently prepared reagents. Pre- and post-PCR procedures should be strictly separated, and each PGD analysis should be monitored by the inclusion of negative controls and blanks at all stages.

The PCR reaction must be optimised to minimise PCR failure and ADO and in preclinical experiments most centres accept a single cell amplification rate of above 90% and an allelic drop out (ADO, when one of the alleles fails to amplify to detectable levels), all of which should be minimised for any PGD PCR protocol before clinical application. In addition, the chosen method must reliably and accurately characterise the genotype of the embryo relative to the disorder under investigation.

PCR based analysis of a single cell requires many cycles of amplification and thus accidental introduction of contaminating DNA should be carefully guarded against. Potential contaminants that are specific for the PGD procedure include the cumulus cells that surround the oocyte (maternal origin) and excess sperm that may be embedded in the zona following fertilisation. Thus, when establishing embryos, the oocytes must be stripped of their cumulus cells and intracytoplasmic sperm injection is recommended for fertilisation of oocytes.

Other sources of contamination include cells from the operators performing the IVF/PGD procedure or PCR amplions within the system of the genetics laboratory. For these reasons, biopsy and PCR reaction set up should be carried out in separate, isolated, UV treated areas under stringent conditions, using exclusive equipment and stringently prepared reagents. Pre- and post-PCR procedures should be strictly separated, and each PGD analysis should be monitored by the inclusion of negative controls and blanks at all stages.

The PCR reaction must be optimised to minimise PCR failure and ADO and in preclinical experiments most centres accept a single cell amplification rate of above 90% and an allelic drop out (ADO, when one of the alleles fails to amplify to detectable levels), all of which should be minimised for any PGD PCR protocol before clinical application. In addition, the chosen method must reliably and accurately characterise the genotype of the embryo relative to the disorder under investigation.

PCR based analysis of a single cell requires many cycles of amplification and thus accidental introduction of contaminating DNA should be carefully guarded against. Potential contaminants that are specific for the PGD procedure include the cumulus cells that surround the oocyte (maternal origin) and excess sperm that may be embedded in the zona following fertilisation. Thus, when establishing embryos, the oocytes must be stripped of their cumulus cells and intracytoplasmic sperm injection is recommended for fertilisation of oocytes.

Other sources of contamination include cells from the operators performing the IVF/PGD procedure or PCR amplions within the system of the genetics laboratory. For these reasons, biopsy and PCR reaction set up should be carried out in separate, isolated, UV treated areas under stringent conditions, using exclusive equipment and stringently prepared reagents. Pre- and post-PCR procedures should be strictly separated, and each PGD analysis should be monitored by the inclusion of negative controls and blanks at all stages.

The PCR reaction must be optimised to minimise PCR failure and ADO and in preclinical experiments most centres accept a single cell amplification rate of above 90% and an allelic drop out (ADO, when one of the alleles fails to amplify to detectable levels), all of which should be minimised for any PGD PCR protocol before clinical application. In addition, the chosen method must reliably and accurately characterise the genotype of the embryo relative to the disorder under investigation.

PCR based analysis of a single cell requires many cycles of amplification and thus accidental introduction of contaminating DNA should be carefully guarded against. Potential contaminants that are specific for the PGD procedure include the cumulus cells that surround the oocyte (maternal origin) and excess sperm that may be embedded in the zona following fertilisation. Thus, when establishing embryos, the oocytes must be stripped of their cumulus cells and intracytoplasmic sperm injection is recommended for fertilisation of oocytes.

Other sources of contamination include cells from the operators performing the IVF/PGD procedure or PCR amplions within the system of the genetics laboratory. For these reasons, biopsy and PCR reaction set up should be carried out in separate, isolated, UV treated areas under stringent conditions, using exclusive equipment and stringently prepared reagents. Pre- and post-PCR procedures should be strictly separated, and each PGD analysis should be monitored by the inclusion of negative controls and blanks at all stages.

The PCR reaction must be optimised to minimise PCR failure and ADO and in preclinical experiments most centres accept a single cell amplification rate of above 90% and an allelic drop out (ADO, when one of the alleles fails to amplify to detectable levels), all of which should be minimised for any PGD PCR protocol before clinical application. In addition, the chosen method must reliably and accurately characterise the genotype of the embryo relative to the disorder under investigation.

<table>
<thead>
<tr>
<th>Table 1: Monogenic diseases for which PGD has been more commonly applied</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Autosomal recessive</strong></td>
</tr>
<tr>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td>β thalassaemia (β globin gene)</td>
</tr>
<tr>
<td>Sickle cell anaemia (β globin gene)</td>
</tr>
<tr>
<td>Spinal muscular atrophy (type I)</td>
</tr>
<tr>
<td>Tay-Sachs disease</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia</td>
</tr>
<tr>
<td><strong>Autosomal dominant</strong></td>
</tr>
<tr>
<td>Myotonic dystrophy</td>
</tr>
<tr>
<td>Huntington’s disease</td>
</tr>
<tr>
<td>Charcot-Marie-Tooth disease IA</td>
</tr>
<tr>
<td>Marfan syndrome</td>
</tr>
<tr>
<td>Familial adenomatous polyposis coli</td>
</tr>
<tr>
<td>X linked</td>
</tr>
<tr>
<td>Duchenne/Becker muscular dystrophy</td>
</tr>
<tr>
<td>Haemophilia</td>
</tr>
<tr>
<td>Fragile X syndrome</td>
</tr>
<tr>
<td>Wiskott-Aldrich syndrome</td>
</tr>
<tr>
<td>Lesch-Nyhan syndrome</td>
</tr>
</tbody>
</table>

**PGD for chromosomal abnormalities**

Fluorescence in situ hybridisation (FISH) allows chromosome enumeration to be analysed in interphase nuclei in single cells. FISH was first applied for PGD to avoid X linked monogenic diseases, subsequently for assessment of unbalanced chromosomal complements (aneuploidies), and more recently for chromosomal translocations.

Preimplantation diagnosis of chromosomal abnormalities is applicable for two distinct groups of patients: women of advanced maternal age undergoing IVF treatment, or couples who have a high risk of aneuploid pregnancy owing to specific parental chromosomal rearrangements (translocations).

Approximately half of the PGD cycles carried out to date have been for age related aneuploidy. The selection of embryos following aneuploidy assessment in women of advanced maternal age or with repeated IVF failure may help to increase reproductive success (in addition to preventing the birth of affected babies), since it has been observed that aneuploidy correlates positively with increasing maternal age. This application is essentially a screening procedure to detect those aneuploidies most commonly observed postnatally or in spontaneous abortions (involving chromosomes X, Y, 13, 16, 18, 21, and 22). In the absence of familial predisposition, this application of preimplantation genetic diagnosis is distinguished by the name preimplantation genetic screening or PGS. Most cases of PGS have been performed by polar body analysis, appropriate since most chromosomal abnormalities are of maternal origin. However, there are limitations of PGS to routine clinical application. Firstly, older women or women with repeated IVF failure may have limited numbers of good quality IVF embryos (or oocytes). Secondly, the maximum number of chromosomes that may be analysed in single blastomeres or PBs by FISH is limited to about seven to
nine. Finally, the error rate of aneuploidy assessment may be as high as 15%. Errors are mainly caused by inherent technical difficulties of FISH which include background staining, signal overlap, weak signals, split spots, and loss of nuclei when spreading single blastomeres.

Reciprocal translocations (usually an exchange of two terminal segments from different chromosomes) and Robertsonian translocations are estimated to occur in 1 of every 500 live births. Carriers of these translocations are nearly always phenotypically normal, but may be detected when the person presents with recurrent pregnancy loss and/or phenotypically abnormal offspring owing to production of genetically unbalanced gametes. Analysis of reciprocal chromosome translocations for PGD is difficult since each translocation is effectively unique to the family or person within which it occurs, and the breakpoint may have arisen at any point on any chromosome. To overcome the need to find case specific probes distal to the breakpoints of the chromosomes involved in the translocation, chromosome specific subtelomeric probes have more recently been used. Analysis of Robertsonian translocations is simpler, involving the use of chromosome specific probes for the patient specific chromosome imbalance.

Methods to improve accuracy and reliability of chromosomal analysis are being investigated, and the most promising is comparative genomic hybridisation (CGH). This involves cohybridisation of DNA from the test and control sample (labelled with different fluorescent dyes) to a normal metaphase spread and is appropriate for analysis of minute quantities of DNA and single cells, as for PGD. The limited quantity of genetic material available for analysis requires a first step to amplify the whole genome of the sample under test, which introduces potential error into the method because of amplification bias. Additionally the CGH method at present takes four to five days to complete, and thus when applied for clinical PGD cycles, embryos have to be frozen after biopsy while awaiting CGH results. 

**PRACTICAL AND ETHICAL ISSUES**

As data have accumulated from chromosomal analysis of human preimplantation embryos, it has become apparent that there is a high rate of chromosomal abnormalities in cleavage stage embryos and blastocysts detected by both FISH and CGH. Results show that only a minority (<35%) of human embryos derived from IVF have a normal chromosome complement in all cells, with the remaining embryos observed to be abnormal non-mosaic, mosaic, or less commonly “chaotic”. Furthermore, there is no apparent correlation between embryo morphology and chromosomal analysis. These findings have important implications for potential inaccuracy of PGD analysis for chromosomal and monogenic dominant disorders, since the nucleus of one cell may not be representative of another. In addition, the full relevance of these findings for the success of assisted reproduction per se is not yet unclear.

The positive outcome of any PGD cycle, that is, the birth of a healthy, unaffected baby, depends upon success at each of the multiple stages of the assisted reproduction procedure, as well as an accurate genetic diagnosis. Generally, about 70% of all oocytes collected will fertilise and about 70% of these will develop to the cleavage stage, of which not all will be suitable for biopsy. PGD is successful in about 80-90% of successfully biopsied embryos and about half of these are diagnosed as suitable for transfer (unaffected). Reported pregnancy rates vary, but rarely surpass about one third of all cycles initiated. The relatively low overall success rate of PGD should be evaluated by any couple considering the option of PGD as an alternative to PND. Furthermore, for couples without fertility problems, a major practical disadvantage of PGD is the need to undergo IVF. Thus, although PGD was initially intended to provide couples with an alternative to conventional PND, it may be considered that PGD is most appropriate for couples with a high risk of transmitting a (severe) genetic disease, who also have fertility problems. In addition, couples who have experienced a selective pregnancy termination following PND, have an affected child, or who have an ethical or moral objection to terminating an ongoing pregnancy may find PGD an appropriate option.

The safety of PGD for children born is of major concern, but initial evaluation of about 250 babies born world wide after PGD indicates that the procedure has no adverse consequences on early development. There is also public concern about the use of PGD for social or eugenic reasons, and although the majority of centres are only willing to perform PGD to prevent the birth of children with severe genetic disorders, there are a few centres which have begun to offer PGD for “social” sexing (personal communication, through the ESHRE PGD Consortium). Thus, it is imperative to establish appropriate ethical guidelines and legislation as soon as possible.

**CONCLUSIONS**

The initial concept of PGD appeared fairly simple, especially following the development of PCR based DNA methodologies. However, a decade of practical application has proven that this is not the case, and although experience, research efforts, and some technological advances have led to many improvements, PGD remains a technically challenging, multistep, labour intensive procedure which requires the close collaboration of a team of specialists. Efforts continue to ameliorate and simplify protocols, particularly for genetic analysis and to develop methods for more disorders, but present technologies still limit wider application.

Other limitations to the wider application of clinical PGD cycles include the necessity to involve IVF, even if the couple are not infertile, the relatively low pregnancy and birth rate, and the high cost of a complete PGD cycle. For many couples, PGD has already proved to be a valuable and worthwhile procedure. With close ethical attention and the continuous trend of technological advancement, it can be foreseen that PGD could have an ever widening role to play in averting serious inherited diseases, alongside (but probably not in place of) PND.

**ACKNOWLEDGEMENTS**

The authors wish to thank Dr C Vrettou, Dr M Tzetzis, and G Palmer for their collaboration in the field of PGD.

**Authors’ affiliations**

E Konavakis, J Traeger-Synodinos, Medical Genetics, University of Athens, Aghia Sophia Children’s Hospital, Athens 11527, Greece

**REFERENCES**


by DNA amplification.

- Single gene disorders by DNA amplification.

- Application of the simplified two-pipette technique is more efficient than the conventional biopsy procedure for preimplantation diagnosis.

- The reliability of single blastomere analysis for preimplantation diagnosis.

- The development of preimplantation genetic diagnosis.

- A technique for eliminating allele specific amplification failure during DNA amplification of teratocarcinoma cells for preimplantation genetic diagnosis.

- ESHRE Preimplantation Genetic Diagnosis (PGD) Consortium. data collection (May 2000).


- Blennow E, Jones B, Nordenskjold M, Ahrlund-Richter L. Application of the biopsy of human preimplantation embryos and sexing by DNA amplification.


- Chen SU, Chao KH, Wu MY, Chen CD, Ho HN, Yang YS. The effect of silver-stained SSCP analysis: an application for preimplantation diagnosis.

- Dummol JC, Bron M, Coonen E, Dreesen J, Geraedts JP, Evers JL. Effect of Ca2+/Mg2+-free medium on the biopsy procedure for preimplantation diagnosis.


Preimplantation genetic diagnosis in clinical practice

E Kanavakis and J Traeger-Synodinos

doi: 10.1136/jmg.39.1.6

Updated information and services can be found at:
http://jmg.bmj.com/content/39/1/6

These include:

References
This article cites 65 articles, 21 of which you can access for free at:
http://jmg.bmj.com/content/39/1/6#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Ethics (220)
Reproductive medicine (519)
Clinical genetics (256)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/