Preimplantation diagnosis and other reproductive options: attitudes of male and female carriers of recessive disorders

Claire Snowdon1,3 and Josephine M. Green2

1 Centre for Family Research, University of Cambridge, Free School Lane, Cambridge CB2 3RF, and 2 Centre for Reproduction, Growth and Development (Midwifery Studies), University of Leeds, 22 Hyde Terrace, Leeds LS2 9LN, UK
3 To whom correspondence should be addressed

This questionnaire-based study describes in detail the attitudes of 245 carriers of recessive disorders to pre-implantation diagnosis (PID). These are compared to responses to other reproductive options for carriers, that is prenatal diagnosis (PND), adoption, donor insemination (DI) and egg donation. The positive attitudes of this sample to PID and corresponding negative attitudes to adoption, DI and egg donation are striking. Almost the entire sample indicated that they viewed early reassurance and the opportunity to avoid a termination of pregnancy as important advantages of PID. Disadvantageous aspects of PID were acknowledged, but did not result in many participants finding this approach unacceptable. The study revealed a number of differences between men and women, especially in their perceptions of the disadvantages of PID. Women saw the practical difficulties of PID as more important disadvantages than did the men, and were very much more concerned about the issues involving embryos. Men, conversely, rated the impact upon their partners as a more important disadvantage. These findings underline the importance of considering both sets of views. Despite support for PID, in an overall assessment it did not displace PND as the most useful reproductive option.

Key words: adoption/attitudes/gamete donation/preimplantation diagnosis/prenatal diagnosis

Introduction

Until very recently, those who knew themselves to be carriers of a genetic disorder had limited reproductive options: remaining childless, adopting, or playing ‘reproductive roulette’ (Fletcher, 1988). Whilst a decline in the number of available babies has made adoption more difficult, advances in the fields of human genetics and assisted conception have expanded the options for carriers. An increasing number of couples are therefore turning to the medical profession for technological solutions to their problems. Their various options are not, however, without their hazards.

Prenatal diagnosis (PND) is possible for more and more carriers as the genetic bases of disorders continue to be identified. With the refinement of early sampling techniques and the development of rapid analysis using polymerase chain reaction, PND has moved into the first trimester of pregnancy. This approach does, however, rest largely on the acceptability of selective termination of pregnancy, a stressful and traumatic experience (Blumberg et al., 1975; Donnai et al., 1981; Leschot et al., 1982; Lloyd and Laurence, 1985; Black, 1989).

Another approach, gamete donation, designed for infertile men and women, is now seen as relevant to carriers. The carrier status of one of the prospective parents can be circumvented with donated gametes, preventing the conception of a child affected by the disorder in question. The deliberate forfeit of a genetic relationship can be a difficult issue and will render this approach unacceptable to some carriers. Furthermore, whilst donor insemination (DI) is a technically simple procedure, egg donation employs the invasive techniques used in vitro fertilization (IVF). The anxiety and stress associated with assisted conception are well documented (e.g. Snowden and Snowden, 1984; Williams, 1989; Crowe, 1990).

Given the difficulties involved in adoption, PND and gamete donation, the relatively new technique of preimplantation diagnosis (PID) provides an alternative for carriers, albeit on a limited basis at present. As with gamete donation, the aim is to establish only unaffected pregnancies. With PID there is the advantage that genetic material from both members of a couple is used. Using IVF techniques, embryos are created and one or more cells are removed, amplified and checked for the genes for a given disorder. Only those which would not result in an affected child are transferred to the uterus, where a pregnancy may be established. In 1992 the first baby was born following PID to exclude cystic fibrosis (Handyside et al., 1992). To date, 34 babies have been born worldwide (Harper, 1996).

Thus PID gives couples the chance of an unaffected, genetically related child without the need to consider abortion. Furthermore, the child is known to be unaffected from the start of pregnancy. In practice, however, PID is not an easy solution; there are a number of potential difficulties for both parents and society (Robertson, 1992; Atkinson and Handyside, 1994). Access is currently very restricted and there are widely recognized physical and emotional hazards involved in IVF. Failed IVF attempts are known to be highly stressful (Mahlstead et al., 1987; Baram et al., 1988; Williams, 1989; Newton et al., 1990); several attempts at conception after PID may be necessary and some women will not conceive at all. Some users will have to decide to store, donate or destroy embryos which are not transferred. The embryo is seen as a child by some couples using IVF (Laruelle and Englert, 1995) and some members of the public (Sullivan, 1993), and the destruction of...
those which are spare or have inherited the disorder may constitute, for some, abortion in another guise.

For society there are important issues to be considered. Over time PID is likely to become more widely available. Not only will there be an inevitable increase in the number of clinics offering PID, but the service is also likely to extend to a larger population of carriers and non-carriers. It has already been seen as relevant to older women undergoing IVF on the grounds of infertility, who could have embryos checked for chromosomal disorders prior to transfer (Handiside and Delahanty, 1993; cited by Atkinson and Handyside, 1994). It has been suggested that eventually PID will ‘supplant prenatal diagnosis for several single gene disorders’ (Raeburn, 1995).

At present, the arduous procedures and financial costs involved in IVF are limiting factors but this may change as the procedures involved are refined. In a recent interview (Hodges, 1996) a PID practitioner suggested an important advance would be the maturation of eggs outside the body. Collection of immature eggs by needle biopsy would remove the need for superovulation and associated monitoring and so reduce the physical and financial cost of PID. An ethicist reflected in the same article on the impact of such a development: ‘if the IVF problem is solved then in 10 years time preimplantation diagnosis may be the technique of choice for the conscientious couple’.

Such a scenario causes concern to those who see PID as having the potential for widespread eugenic application (Testart and Sèse, 1995). Their argument is strongly rebuffed by others who describe the idea as ‘preposterous’ (Handiside, 1996) and ‘a matter of individual choice’ for the carriers involved (Schulman and Edwards, 1996).

Little is known about the extent to which PID may in fact meet the needs of carriers. Although the views of the public have been sought regarding various forms of assisted conception (Genuis et al., 1993; Shiria, 1993; Sullivan, 1993; Macer, 1994) and there are studies of the views of infertile people (Alder et al., 1986; Williams, 1992; Baluch et al., 1994; Bielawska-Batorowicz, 1994; Daniels, 1994; Kazem et al., 1995; Lyall et al., 1995), the literature describing the views of potential users of PID is small (Pergament, 1991; Miedzybrodzka et al., 1993; Palomba et al., 1994).

Pergament (1991) assessed the attitudes of 58 American women at 25–50% risk of passing on a genetic disorder and found the main objections raised to the idea of PID were damage to the embryo as a result of the procedure, low success rates and financial cost. Previous experience of PND was shown to affect attitudes to PID. Those who had been shown to have an affected fetus were more positive about PID than those who had not; 55% of the sample stated that they would be prepared to undergo PID in preference to PND.

Miedzybrodzka et al. (1993) compared attitudes and preferences for PND and PID of 474 Scottish women who had previously had: genetic counselling due to a family history of a single gene disorder, chorionic villus sampling (CVS) for a single gene disorder (and completed the pregnancy), CVS for another reason, recently given birth to a normal baby, or had previously undergone IVF. The sample as a whole favoured PND rather than PID (43 versus 38%) if they were hypothetically at risk of having a child affected by a single gene disorder. The women who had experience of genetic counselling and IVF were more likely to favour PID (48 and 70% respectively). Older women were more likely to choose PID over PND. Preferences were not related to whether or not they thought they would terminate a pregnancy if a baby was affected by a serious disease or handicap. Preferences were also unrelated to whether or not they had had a negative outcome after CVS (affected pregnancy or miscarriage).

Palomba et al. (1994) demonstrated the impact of reproductive history on attitudes to PID for 180 pregnant Italian women carrying beta-thalassaemia. All intended to have CVS and had either terminated a previous pregnancy after PND, continued with a previous pregnancy after PND or had no previous pregnancies. Only 10% of the women who had terminated a pregnancy saw PID as abortion, compared to 45% of those who had had PND but no abortion and 60% of those in their first pregnancy. The proportions who thought they would undergo PID instead of PND for the same groups were 100, 70 and 50% (73% of the sample).

These papers provide useful information, although there are some limitations. None of the studies examined the views of men. As they are not represented, there is no measure of the extent to which men and women do or do not differ in their opinions. In the case of Miedzybrodzka et al. (1993), the questions about PID for the majority of the sample who do not carry a single gene disorder are purely hypothetical and so less relevant. Pergament (1991) and Palomba et al. (1994) suggest that reproductive history shapes attitudes to PID, but this was only explored in a preliminary way. Other aspects of past experiences, such as whether or not the couple have had unaffected children or have experienced the death of a child, may also be important, as may factors such as perception of burden and attitude to abortion. A further limitation of these studies is that where comparisons of options were made they were between PID and PND, yet there are other approaches which may be considered. Attitudes to PID need to be assessed in the light of all options rather than simply with reference to PND.

This paper reports the attitudes to PID of couples known to carry a recessive disorder. The data are taken from a larger study which assessed in some detail the attitudes and experiences of carriers of child-bearing age to the range of reproductive options (Snowdon and Green, 1994a), thus allowing us to report attitudes to PID within this context.

Materials and methods

Recruitment

Couples carrying a recessive disorder were identified from the records of four genetics centres in the UK (two in London, one in Manchester, one in Cambridge). They were eligible for the study if: the couple were still together; they were of an age where they may still be considering (more) children (defined as <40 years for women and <50 years for men, unless there was evidence of a continued interest in childbearing beyond these ages); the general practitioner could be informed of the couple’s potential inclusion in the research; and the general practitioner did not indicate that contact would be
Recessive disorders and preimplantation diagnosis

Data collection

Data were collected using two postal questionnaires designed specifically for the study. Second questionnaires were sent only to those returning the first. Men and women received their own copy of each; their questionnaires differed only in the expression of gender-specific questions. The first questionnaire covered demographic information and the experience of being a carrier and included measures of existing knowledge of and interest in the various reproductive options. The second questionnaire focused on attitudes to the options and was accompanied by an information booklet for the participants to keep. The booklet described positive and negative aspects of each option as well as explaining the procedures involved.

Participants were asked to read the booklet before answering the questionnaire (see Figure 1 for extracts from the PID section and Figure 2 for relevant details for egg donation). Although this approach cannot be value-free, it meant that participants were given the same baseline of information and could make a more informed assessment of the options.

Piloting

The first questionnaire was piloted with an initial sample of 27 members of the Jennifer Trust for Spinal Muscular Atrophy. A revised version was then sent to a further 14 couples recruited via one of the genetics centres. Between them, the couples carried nine different disorders. Both members of 10 couples (i.e. 20 individuals) responded (71%). The second questionnaire was piloted with both groups, but needed very little revision.

PREIMPLANTATION DIAGNOSIS

These two approaches of prenatal diagnosis and the techniques used in assisted conception have recently been put together so that for some disorders an embryo can be checked for the faulty genes before it is allowed to implant in a woman's womb. This is called preimplantation diagnosis. (Taken from the introduction to the information booklet after the initial outline of prenatal diagnosis and assisted conception)

The purpose of preimplantation diagnosis is to check embryos for a genetic disorder before a woman has become pregnant. This is a very new technique.

The woman takes drugs which stimulate her ovaries to produce a number of eggs. The eggs are then surgically collected and fertilised by her partner's sperm. Any embryos which are created could have inherited two copies of the faulty gene and so would be affected by the disorder. One or two cells are taken from the embryo. This does not seem to affect its development. Genetic material from the cells are examined to find out if the embryo has inherited the faulty genes. Only those embryos which do not have two copies of the faulty gene are put back into the womb or fallopian tubes of the woman.

A baby conceived in this way would not have the disorder and would be genetically related to both members of the couple. As only those embryos which will not be affected are transferred to the woman's womb, there should be no need to consider a termination of pregnancy for the disorder. At the moment women who become pregnant go on to have CVS or amniocentesis to check that the fetus does not have the disorder because preimplantation diagnosis is still a new technique.

As with egg donation, couples may have to make a decision about any embryos which they will not use themselves.

As only a very small number of children have been born after using this technique, it is not possible to give success rates. It has only been used for a few disorders, one of which is cystic fibrosis. As it becomes more widely available, preimplantation diagnosis will be possible in cases where the disorder can be detected by looking at genetic material, as in CVS or amniocentesis. If the disorder can only be detected by ultrasound scanning, which looks for the physical symptoms of the disorder in a fetus, then preimplantation diagnosis will not be possible.

Figure 1. Sections from information booklet detailing preimplantation diagnosis.

At the moment it is thought that around 17 of every 100 attempts at in-vitro fertilisation (the techniques used in egg donation) will result in a pregnancy.

Clinics do not usually transfer more than two embryos because of the chance of triplets (or more). If two embryos are transferred there is still a chance of conceiving twins. Some couples may have more embryos than they can use in one attempt. It is often possible to freeze spare embryos for future attempts. If this is not possible at a particular clinic, or if the couple plan no future attempts, a decision needs to be made about the embryos: they can be donated for research or they can be destroyed.

Figure 2. Extracts from egg donation section of the information booklet.
Independent variables
A number of demographic, experiential and attitudinal variables were created primarily from items in the first questionnaire. Those created from 0 to 5 rating scales are marked with an asterisk. Further details of their composition and the rationale behind the subdivisions can be found in Snowdon and Green (1994a). (i) Demographic variables were: male or female, age (<31, 31–34, >34 years), education (minimum, some further education, higher education), influence of religion (some influence, no influence), effect of disorder carried (early death, severe, less severe), possibility of PND in their case (yes, no); (ii) experiential: experienced the death of a child (yes, no), had a pregnancy since learning of their carrier status (yes, no), terminated an affected pregnancy (yes, no), total number of children born to the couple (1, 2, >2), number of affected children born to the couple (none, 1, >1), number of unaffected children born to the couple (none, 1, >1), number of living children (none, 1, >1), firstborn child affected by the disorder they carry (yes, no); (iii) attitudinal: intention to have future pregnancies (likely, unlikely), frequency of thoughts about having (more) children* (0, 1–3, 4–5), importance attached to avoiding birth of (an)other affected child* (0–3, 4–5), perceived difficulties in coping with (an)other affected child* (0–3, 4–5), would consider a termination for the disorder they carry (yes, no).

Dependent variables
The first questionnaire contained three simple questions for each of the reproductive options: ‘How much do you know about it?’, ‘Have you thought about using it?’ and ‘Would you consider this option in the future?’. A list of response options was given for each.

The second questionnaire had separate sections covering PND analysis (134 women, 111 men; 108 couples). The data presented are based only on the 245 participants who returned second questionnaires were returned (84%). When combined with 35 pilot questionnaires, giving 305 for analysis (160 women and 145 men; 143 complete couples); 226/270 second questionnaires were returned (84%). When combined with pilot data there were 245 second questionnaires for analysis (134 women, 111 men; 108 couples). The data presented are based only on the 245 participants who returned both questionnaires.

Results
Response
A total of 618 first questionnaires were despatched and 319 were returned (52%), 270 of which were valid. These were combined with 35 pilot questionnaires, giving 305 for analysis (160 women and 145 men; 143 complete couples); 226/270 second questionnaires were returned (84%). When combined with pilot data there were 245 second questionnaires for analysis (134 women, 111 men; 108 couples). The data presented are based only on the 245 participants who returned both questionnaires.

Sample characteristics
The age range was 23–44 years (mean 32.7, SD 4.4) for women, 20–50 years (mean 35.0, SD 5.3) for men. Years spent together as a couple ranged from 3 to 20 years (mean 12.0, SD 4.2). Five couples were consanguineous: four first cousins and one second cousins.

It was found that 45% of the women and 48% of the men had left education aged 16 years or younger, while 22% of women and 29% of men had received higher education. Eighty-nine per cent of men and 17% of the women were in full-time employment; 48% of the women were not in paid employment. The majority of the sample stated that they had a religion (86% of women and 76% of men). Where a religion was given it was predominantly Christian (non-Catholic; 70% of women and 59% of men); 53 men and 71 women (37 and 44% respectively) said that their religion influenced decisions that they made about their lives.

A total of 43 different recessive disorders were represented, varying considerably in their effects. The most frequent were cystic fibrosis (34%), the infantile form of spinal muscular atrophy (SMA; 18%) and intermediate SMA (8%). Table I shows various aspects of subjects’ experiences of the disorder they carry. Forty-eight percent of the sample felt that the fact that PND was or was not possible for them had affected their decisions. There were no differences between those for whom PND was or was not available in the answers to this question. None of the participants had had first-hand experience of PND.

Only a minority gave ratings <4, so only two groups were used for analysis.
Table II. Ratings of importance (5 representing ‘very important’) of advantages of preimplantation diagnosis

<table>
<thead>
<tr>
<th>Advantage</th>
<th>% giving rating of 4 or 5</th>
<th>Higher ratings of advantage were given if:</th>
<th>Relative values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child would be genetically related to both of you</td>
<td>86</td>
<td>83</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
| Child would not inherit the disorder | 94 | 91 | PID rated > ED = DI rated > adoption  
(\chi^2 21.89, 3 df, P < 0.001) |
| Can find out whether or not child is a carrier | 56 | 44 | PID rated > CVS = amniocentesis  
(\chi^2 12.53, 2 df, P > 0.01) |
| Can know from the start that child won’t have the disorder | 94 | 94 | Not applicable |
| No need to terminate pregnancy for the disorder | 96 | 88 | PID rated > ED = DI rated > adoption  
(\chi^2 26.07, 3 df, P < 0.001) |

Knowledge, previous consideration and future consideration

At the time of the first questionnaire, 46% had ‘never heard of’ PID and 11% had thought about using it. Only four participants had investigated it and none were on a waiting list. Nineteen percent would ‘definitely’ or ‘possibly’ consider using PID in the future and 50% would ‘probably’ or ‘definitely’ not. Those who had not heard of PID were most likely to omit the question or to say that they did not know whether or not they would consider using PID.

Ratings of advantages and disadvantages of PID

Advantages and disadvantages were scored on a scale from 0 to 5 and these ratings were analysed as continuous variables. Many had very skewed distributions with the majority of the sample scoring at one extreme. In summarizing these ratings we will therefore refer to the proportion rating an advantage or disadvantage as ‘important’, by which we mean the proportion scoring 4 or 5. These proportions are shown separately for men and for women in the second and third columns of Tables II and III.

Three of the advantages: ‘no need to terminate a pregnancy for the disorder’, ‘child would not inherit the disorder’ and ‘can know from the start that the child won’t have the disorder’ are clearly linked and were accordingly given similarly high ratings by almost the whole sample. ‘Child would be genetically related to both of you’ was rated as slightly less important but was still seen as a major advantage of this technique. The feature of PID that was seen as the least advantageous was the opportunity to find out whether or not child is a carrier; it was, however, still rated as important by half the sample.

In general, the disadvantages of PID were given quite low ratings (Table III). The fact that PID may not be successful was seen as an important disadvantage by less than half of the sample. Similarly, the majority did not see the ethical issues involved in PID as important disadvantages, although 51% of the women rated ‘dilemma of what to do with spare embryos’ as important. More participants were concerned about the fate of spare embryos than about their creation.

Ratings of advantages and disadvantages × independent variables

The relationship between ratings of the advantages and disadvantages and the independent variables is shown in the fourth column of Tables II and III. The advantage that a ‘child would be genetically related to both of you’ (rated as important by >80% of the sample) was the only feature that was not significantly related to any of the independent variables. Three variables: sex, importance of avoiding the birth of an(other) affected child and willingness to consider termination for the disorder were particularly influential.

Sex

Men and women rated all advantages equally highly except ‘can find out whether or not child is a carrier’, for which the women gave significantly higher ratings (Table II). However, there were significant differences in the ratings of men and women for all the disadvantages except ‘it’s interfering with nature’ (Table III). Women saw the practical difficulties of PID (‘it may not be successful’ and ‘long waiting lists’) as more important disadvantages than did the men, and were very much more concerned about the issues involving embryos. Men, conversely, rated the impact on their partners (pain and health risks) as more important disadvantages.

Avoidance of the birth of an(other) child with the disorder

A total of 83% of the sample scored 4 or 5 on a 0–5 scale of the importance of avoiding the birth of an(other) affected child. They were compared with the 17% who gave a low rating (0–3). This variable was related to six of the 12 features of PID. Those giving higher ratings (referred to as ‘avoidance was high’) saw the fact that a child would not be affected, that this could be known from the start of pregnancy and that
there would be no need for a termination as more advantageous than those for whom avoidance was lower.

Those for whom avoidance was lower, rated the possibility of pain, health risks and ‘it’s interfering with nature’ as more important than those for whom avoidance was high.

**Attitude to termination of pregnancy**
A total of 70% of the sample would consider a termination of pregnancy for the disorder they carry and 30% would not. There was no significant difference between men and women. This variable was related to the same six features of PID as the importance of avoiding the birth of an(other) affected child and showed the same pattern of results. Those who would consider a termination gave similar responses to those for whom avoidance was high. These two variables were in fact strongly related to each other: 82% of those for whom avoidance was high were willing to consider termination compared with only 23% of those for whom avoidance was low (χ² 36.4, 1 df, P < 0.001).

Whether or not participants had actually experienced a termination of pregnancy for the disorder they carry was related to only one rating: ‘it’s interfering with nature’. Those who had not terminated a pregnancy rated it as more important.

**Comparison of ratings across reproductive options**
A number of features of PID are shared with adoption, DI and egg donation, and so it was possible to assess whether or not a common feature was valued consistently across options. Only one feature was listed in common to PID and PND (both CVS and amniocentesis). Significant differences in the ratings are shown in the final column of Tables II and III.

Four disadvantages: pain, possible health risks and creation and disposal of embryos were common to PID and egg donation and were given the same ratings in the two circumstances. Similarly, the issue of long waiting lists was rated consistently across all four options.

Attitudes to other common features were not constant. There were significant differences between the ratings of two advantages: ‘no need to terminate a pregnancy for the disorder’ and ‘child would not inherit the disorder’ across the four options. They were given highest ratings in the case of PID and lowest for adoption, with egg donation and DI falling between the two. The disadvantage ‘may not be successful’ was seen as more important in the context of egg donation than for either PID or DI. The feature ‘it’s interfering with nature’ was rated as a more important disadvantage in the context of PID and egg donation than for DI.

The common feature for PID and PND, ‘can find out whether or not child is a carrier’, was seen as a more important advantage of PID than for either of the two PND techniques.

**Acceptability**
In response to the question, ‘Would concerns about any of these things [i.e. the disadvantages listed in the previous question] be strong enough to make preimplantation diagnosis unacceptable to you?’, only 11% of the sample thought that PID was unacceptable. The most common reasons given (in an open-ended question) for finding PID unacceptable were: that it can be painful (14 women, eight men), it involves the creation of embryos (eight women, two men), and the dilemma of what to do with spare embryos (six women, five men). (Note that participants could give more than one reason.)

As Table IV shows, fewer people found PID unacceptable

---

**Table III. Ratings of importance (5 representing ‘very important’) of disadvantages of preimplantation diagnosis**

<table>
<thead>
<tr>
<th>Disadvantage</th>
<th>% giving rating of 4 or 5</th>
<th>Higher ratings of disadvantage were given if:</th>
<th>Relative values</th>
</tr>
</thead>
<tbody>
<tr>
<td>May not be successful</td>
<td>49 Women 37 Men</td>
<td>female (χ² 5.45, P &lt; 0.05) difficulty high (χ² 4.35, P &lt; 0.05)</td>
<td>ED rated &gt; PID = DI (χ² 6.86, 2 df, P &gt; 0.05)</td>
</tr>
<tr>
<td>Can be painful</td>
<td>17 Women 42 Men</td>
<td>male (χ² 15.78, P &lt; 0.001) avoidance low (χ² 4.49, P &lt; 0.05) would not consider termination (χ² 7.84, P &lt; 0.01)</td>
<td>PID = ED</td>
</tr>
<tr>
<td>Possible health risks for you (your partner)</td>
<td>46 Women 79 Men</td>
<td>male (χ² 20.19, P &lt; 0.001) received minimum education (χ² 8.7, P &lt; 0.05) avoidance low (χ² 4.79, P &lt; 0.05) would not consider termination (χ² 7.73, P &lt; 0.01)</td>
<td>PID = ED</td>
</tr>
<tr>
<td>Long waiting lists</td>
<td>60 Women 49 Men</td>
<td>female (χ² 7.06, P &lt; 0.01) no pregnancy since learned carrier status (χ² 5.2, P &lt; 0.05) have no living children (χ² 8.32, P &lt; 0.05)</td>
<td>PID = ED = DI = adoption</td>
</tr>
<tr>
<td>Involves creating embryos</td>
<td>40 Women 20 Men</td>
<td>female (χ² 17.01, P &lt; 0.001) received minimum education (χ² 11.1, P &lt; 0.01)</td>
<td>PID = ED</td>
</tr>
<tr>
<td>Dilemma of what to do with spare embryos</td>
<td>51 Women 30 Men</td>
<td>female (χ² 15.1, P &lt; 0.001) influenced by religion (χ² 4.7, P &lt; 0.05) prenatal diagnosis is possible in their case (χ² 5.75, P &lt; 0.05)</td>
<td>PID = ED</td>
</tr>
<tr>
<td>It’s interfering with nature</td>
<td>24 Women 16 Men</td>
<td>avoidance low (χ² 6.16, P &lt; 0.05) received minimum education (χ² 8.55, P &lt; 0.05) aged &lt;31 years (χ² 7.04, P &lt; 0.05) would not consider a termination (χ² 14.04, P &lt; 0.001) had not experienced a termination (χ² 9.63, P &lt; 0.01)</td>
<td>PID = ED rated &gt; DI (χ² 12.7, 2 df, P &lt; 0.01)</td>
</tr>
</tbody>
</table>
than any other option. DI and egg donation were unacceptable to the largest proportion of the sample. In both cases, more women than men seemed to find these unacceptable, although the differences were not significant. Finding PID unacceptable was significantly related to two independent variables: age and the importance of avoiding the birth of (another) affected child; those >34 years old and those with high avoidance were less likely to find PID unacceptable ($\chi^2$ 6.08, 2 df, $P < 0.05$ and $\chi^2$ 13.56, $P < 0.001$ respectively).

Ratings of some of the advantages and disadvantages were independent of finding PID unacceptable. Only one advantage, ‘can know from the start that the child does not have the disorder’ was related to this variable, with those finding PID unacceptable giving lower ratings than those who did not or were not sure ($\chi^2$ 4.41, $P < 0.05$). The disadvantages that PID ‘may not be successful’, ‘involves creating embryos’, that there is ‘the dilemma of what to do with spare embryos’ and ‘it’s interfering with nature’ were all rated as significantly less important by those who did not find PID unacceptable ($\chi^2$ 6.73, $P < 0.05$; $\chi^2$ 46.33, $P < 0.0001$; $\chi^2$ 58.14, $P < 0.0001$ and $\chi^2$ 33.33, $P < 0.0001$ respectively).

### Overall assessment

The most popular first choice was PND, given by 46% of the women and 50% of the men. The next most popular first choice was PID, given by 28% of women and 23% of men (Table V).

#### PID versus PND as a first choice

The following analyses are restricted to the 179 individuals choosing either PND ($n = 117, 65\%$) or PID ($n = 62, 35\%$) as a first choice. The choice between PID and PND showed little relationship with the independent variables. The three exceptions were: whether or not PID was possible, attitude to termination of pregnancy and whether or not more pregnancies were intended. Men and women did not differ in their frequency of choosing PID or PND.

Of those for whom PND was not possible, 64% (16/25) chose PID compared to only 26% (41/139) of those for whom it was possible ($\chi^2$ 11.1, 1 df, $P < 0.001$; 15 people did not know whether PND was possible in their case).

The relationship between choice of PID or PND and willingness to consider a termination did not quite reach significance for the whole sample ($P = 0.06$). However, the relationship was highly significant when examined for women only: 63% (12/19) of those who would not consider a termination chose PID compared to 29% of those for whom $\chi^2(22/75, \chi^2 7.51, 1\ df, P < 0.01)$. For men there was no such relationship ($\chi^2 0.01, 1\ df, P = 0.9$).

There was also a weaker relationship between choosing PID or PND and the intention to have future pregnancies. PND was chosen by 75% (50/67) of those intending future pregnancies and 60% (67/112) of those who were not ($\chi^2 4.06, 1\ df, P < 0.05$).

Comparison was made between those whose first choice was PID and those choosing PND in terms of their ratings of the advantages and disadvantages of PID. There were no significant differences in the ratings of advantages, but three disadvantages were rated differently. Those choosing PND rated health risks, creation of embryos and the dilemma of spare embryos as more important disadvantages than those choosing PID ($\chi^2 3.8, P < 0.05$; $\chi^2 6.9, P < 0.01$; $\chi^2 5.0, P < 0.05$ respectively). Men and women were also considered separately, since their ratings of advantages and disadvantages had differed. For men, the findings were the same as for the sample as a whole. For women, no significant differences were found.

Those choosing PND and those choosing PID were also compared on their ratings of the advantages and disadvantages of amniocentesis and CVS. There were no significant differences. They were also compared according to their responses to PID given in the first questionnaire, before they had received our information booklet. Those who said that they had never heard of PID were less likely to give it as their first choice, although 18% still did ($\chi^2 5.93, 1\ df, P < 0.05$). Of those who said that they would definitely or probably consider using it, 51% chose PID compared with 25% of those who probably

### Table IV. Percentage of respondents answering ‘yes’ (actual numbers of participants are in parentheses) to the question, Would concerns about any of these things be strong enough to make [option] unacceptable to you?

<table>
<thead>
<tr>
<th>Option</th>
<th>Women (%)</th>
<th>Men (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adoption</td>
<td>29 (39)</td>
<td>33 (37)</td>
</tr>
<tr>
<td>Donor insemination</td>
<td>42 (56)</td>
<td>36 (40)</td>
</tr>
<tr>
<td>Egg donation</td>
<td>41 (55)</td>
<td>32 (36)</td>
</tr>
<tr>
<td>Preimplantation diagnosis</td>
<td>13 (17)</td>
<td>10 (11)</td>
</tr>
</tbody>
</table>

### Table V. Ranking of reproductive options: percentage of participants giving each option as first and second choice. Actual numbers of participants indicating that choice are given in parentheses

<table>
<thead>
<tr>
<th>Option</th>
<th>1st</th>
<th>2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amniocentesis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adoption</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donor insemination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg donation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preimplantation diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Having no more children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Prenatal diagnosis

<table>
<thead>
<tr>
<th>1st</th>
<th>2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 (10)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>8 (9)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>3 (3)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

#### Adoption

<table>
<thead>
<tr>
<th>1st</th>
<th>2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (1)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>28 (37)</td>
<td>31 (42)</td>
</tr>
<tr>
<td>23 (25)</td>
<td>38 (42)</td>
</tr>
</tbody>
</table>

#### Donor insemination

<table>
<thead>
<tr>
<th>1st</th>
<th>2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 (1)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>17 (23)</td>
<td>13 (17)</td>
</tr>
<tr>
<td>4 (4)</td>
<td>12 (13)</td>
</tr>
</tbody>
</table>
or definitely would not and 29% of those who said ‘don’t know’ ($\chi^2 = 8.87, \text{df} = 2, P < 0.01$).

Discussion
The participants in this study were men and women for whom reproductive decision making was a salient issue. They have lived with the consequences of the disorder they carry in that almost all had had an affected child, a third had had a child die, over half had experienced PND and 19% of the women had terminated a pregnancy as a result. For the study, they were asked to consider all available reproductive options (PND, adoption, egg donation, DI and PID) and by the end had done so in considerable depth. They were in a unique position to make this assessment, as for couples carrying a recessive disorder, unlike carriers of X-linked or dominant disorders, all available options are of potential benefit.

Once the options had been considered, in spite of the fact that nearly half of the sample had not heard of PID prior to the study, and only 11% had previously thought about using it, PID emerged as a technique which was viewed very positively. Support was expressed in a number of ways. There were many enthusiastic comments in which PID was seen as ‘the perfect solution’ and ‘the way to the future’. A woman who had experienced the death of a baby and had terminated a pregnancy described PID as ‘a ray of hope in an otherwise bleak situation’. The advantages of PID were rated as highly important by the majority of the sample, while the disadvantages were generally seen as less important; in most instances, less than half of the sample gave a rating of 4 or 5 for the importance of a disadvantage. In comparison to the other options it was unacceptable to fewest participants, only 11%, and was ranked either the first or second (potentially) most useful option by 60%.

Positive attitudes towards PID extended to awarding higher ratings for some advantages and lower ratings for some disadvantages that were shared with less favoured options. While it was possible that these differential ratings were a result of participants viewing features through a filter of desirability of a technique, it was particularly notable that there were no such differences for most of the features common to PID and egg donation. This is despite marked enthusiasm for PID and a lack of enthusiasm for egg donation. When the impact of finding PID unacceptable was assessed, some disadvantages (pain, health risks and waiting lists) were shown to be independent, while others, i.e. the creation and disposal of embryos, were strongly related; those who did not find PID unacceptable gave lowest ratings for the importance of these issues. The same effect was in fact also present for egg donation in that the embryo-related disadvantages were seen as less important by those who did not find that approach unacceptable.

The fact that PID was highly acceptable despite sharing so many disadvantageous features with egg donation, an option for which there was little interest or support, emphasizes the need to focus on key differences in the advantages to account for its appeal.

There are two advantages offered by PID but not by adoption, egg donation or DI: the opportunity to know from the start of pregnancy that a child is unaffected and the fact that a child would be genetically related to both members of the couple. Early reassurance was almost unanimously seen as an important advantage, with 94% of the sample giving a rating of 4 or 5. As we have discussed elsewhere (Snowdon and Green, 1994b), the issue of genetic relationships was important to this sample. A genetic relationship with both parents was rated as an important advantage of PID by 85%. Those who found adoption, DI or egg donation unacceptable gave significantly higher ratings for the disadvantages relating to a lack of a genetic relationship for each of these options. In contrast, the importance of maintaining a genetic link through PID was not related to the acceptability of the technique, i.e. it was acknowledged as an important advantage even by those who found PID unacceptable.

Although not exclusive to PID, the avoidance of a termination is another important advantage offered by this technique. For the less favoured options, the opportunity to avoid a termination is gained at the expense of a genetic relationship. If this is too great a price to pay, then the benefit of not undergoing a termination is reduced. For PID there is no such trade-off. Instead there seems to be a cumulative effect of these advantages, resulting in a very positive view of this approach.

Despite the appeal of PID and many comments from participants about the difficulties of PND, when asked to give an overall assessment of which options would have been most useful to them, nearly twice as many chose PND as PID. This choice was unrelated to ratings of advantages and disadvantages and to the majority of the independent variables. The two exceptions were: whether or not PND was possible and whether or not they intended to have further pregnancies.

Those for whom PND was not possible were more likely to choose PID. This was not necessarily a predictable finding; it could have been postulated that those for whom PND is not available would have an idealized view of its benefits or, alternatively, there could be a tendency to play down its advantages. Inspection of the data suggests that in fact they gave somewhat lower ratings to both its advantages and disadvantages. This is probably a reflection of their greater distance from these issues compared with those for whom it is a reality.

People who were not intending to have further pregnancies were more likely to choose PID, a finding possibly stemming from the opportunity to state a preference from a hypothetical standpoint. Those intending to embark upon another pregnancy had more concrete issues to take into consideration.

It was surprising that aspects of parents’ previous experiences, such as the death of a child or having terminated a pregnancy, were not related to their choices. Even the importance of avoiding the birth of another affected child and willingness to consider terminating a pregnancy for the disorder, which were important predictors of ratings of advantages and disadvantages, did not relate to the final choice for the sample as a whole. The choice of PND or PID was related to willingness to consider terminating a pregnancy, but only for the women in the sample. Women who would consider a
termination were more likely to give PND as their first choice. Those who would not consider a termination were more likely to choose PID. This makes sense: whilst those who would consider an abortion are able to contemplate both PND and PID, those who would not are less likely to make a first choice of PND.

There is, however, an apparent paradox: those who would consider a termination were less likely to choose PID than those who would not, but they were more positive about PID in their ratings of advantages and disadvantages. In particular, those who would consider terminating a pregnancy rated avoiding a termination through PID as more important than those who would not. This may appear counter-intuitive; it could have been postulated that those who would not consider a termination would rate avoidance of termination as more important. It is, in fact, those who could envisage themselves going through the process of PND and possibly a termination who are able to see more advantages to avoiding this stressful situation.

Our findings are somewhat at odds with those of previous studies. In particular, we report a lower proportion indicating a preference for PID over PND (Pergament, 1991; Miedzybrodzka et al., 1993; Palomba et al., 1994). The reasons for this are likely to be methodological. There are crucial differences between the samples in the different studies. Participants were recruited from a variety of cultural backgrounds and, with the exception of the present study, were exclusively women. The likelihood of conceiving an affected child differed between and within samples and, in one study, context is an important issue as the women were pregnant, awaiting PND and could face terminating a pregnancy within days of completing the questionnaire. There were also differences in the information given to participants in each study. We intended that our information should go beyond technical descriptions of procedures to allow an exploration of reactions to important issues. This approach is double-edged in that it allows participants to respond from a more informed perspective, but the selection and framing of information have an unavoidable impact on attitudes. Pergament (1991) for instance addressed the issue of possible damage to the embryo and the cost of the procedure. Cost was a concern for most of the sample and so to some extent will have shaped preferences. For the present study, this was not discussed, as PID is available on such a limited and experimental basis that there are no costs which may be cited. Most importantly, our study involved very detailed questions and asked participants to give a great deal of thought to the issues raised, not just about PID but about all the other reproductive options. Given these considerations, one must be cautious in comparing the results of these studies.

In many ways, the preference for PND found in our study is quite logical in that it is the most practical option for carriers of recessive disorders. Where a reliable test is available, they do not have to cope with the complications of other options, such as limited accessibility, financial expenditure or possible problems over genetic relationships. A factor which was not addressed in this study but which is likely to be important is that for fertile couples intending to use PND, conception of their children remains a private affair rather than being placed in the public domain and assisted by doctors, scientists and technology.

Conclusion
Although there was support and enthusiasm for PID, the majority of the sample did not feel that it was the most useful option in their situation. The advantages are highly valued in theory, but in practice they are insufficient to draw most participants away from PND, despite the difficulties associated with tests, results and a possible termination. This seems to be a reasonable finding given the intensive nature of IVF required for PID and the medical and technical intrusion into conception.

Ironically, PID was often viewed most positively by those who were unlikely to use it. They were participants for whom PND and therefore PID was not currently possible and those who were not intending to have more pregnancies. Those who would not consider a termination were also those most likely to choose PID, and it is for this group that PID may really offer something new. For people wishing to avoid the birth of an affected child but who would not consider a termination, PID may provide a potentially important alternative to the remaining unpopular options. There was evidence that the creation and disposal of embryos caused some concerns in the sample, but these were no greater amongst those who would not consider terminating a pregnancy. It remains the case, however, that for those feeling that both abortion and the creation and disposal of embryos are completely unacceptable, the development of PID may not in fact have increased their options at all.

Acknowledgements
This study was supported by a grant from the Medical Research Council. We gratefully acknowledge the help of Christine Barnes and other staff of the genetics centres involved, Nina Hallowell and other members of the Centre for Family Research, the Jennifer Trust for SMA and the participating parents.

References

349
C. Snowden and J.M. Green


Received on August 23, 1996; accepted on November 8, 1996