Should embryos with a hereditary disorder be transferred if no unaffected embryos are available?

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The numbers of cycles of preimplantation genetic diagnosis or screening are rising steadily in Europe with over 2,700 reported in 2004 (the most recent year for which data are available). Fertility centres are able to screen for a growing number of genetically related conditions, but what should doctors do if no embryos without the targeted condition are available for transfer and the parents request that affected embryos should be transferred instead?

Ethicist Dr Wybo Dondorp told the 24th annual meeting of the European Society of Human Reproduction and Embryology in Barcelona today: "Parental requests for transferring affected embryos should not be dismissed beforehand as a sign of irresponsible capriciousness. As the couple's primary wish may be for a child, they may reason that if a non-affected, healthy child is not what they can get, they will also be happy with, and good parents for, a child with a condition they at first intended to avoid. Respect for autonomy at least requires taking such requests seriously, even if, in view of all other considerations, doctors decide not agree to the requests."

Dr Dondorp, who is a senior research fellow at the faculty of Health, Medicine and Life Sciences, department of Health, Ethics and Society at Maastricht University (The Netherlands), said that before couples have preimplantation genetic diagnosis (PGD), fertility clinics should discuss the decision-making process and the particular clinic's policy in their pre-

test counselling sessions with prospective parents, so that everyone was clear about what the options were in cases where no unaffected embryos could be obtained.

He said the most important consideration was the welfare of the child, particularly taking into account doctors' professional responsibility "to do no harm". "A high risk of serious harm is a contraindication for transferring affected embryos. The present consensus is that where the classical indications for PGD are concerned, doctors should, as a general rule, not transfer affected embryos where no non-affected ones are available. In pre-test counselling it should be explained that if no non-affected embryos are available, the only options are trying a new cycle or being advised to reconsider one's reproductive plans such as refraining from reproduction, using donor eggs or sperm, or adoption.

"The welfare of the child is closely connected to the classical indication for PGD: a serious disease caused by a single gene mutation for which there are no, or limited, treatments, and, in most cases, presenting early in life. An example is an embryo that is homozygous for cystic fibrosis, where the child will definitely have the disease. In such cases it is inconceivable that doctors would agree to transfer these embryos as it would be at odds with their professional responsibilities."

However, as the use of PGD is being extended increasingly to conditions outside the classical range of indications, transferring affected embryos need not always involve a high risk of serious harm. This is obvious where treatable diseases are concerned, such as MCAD deficiency (where people with a faulty medium-chain acyl-CoA dehydrogenase gene are unable to metabolise fat, but can lead a healthy life by observing a strict diet).

"Things are less clear where PGD for hereditary cancer syndromes is concerned. Debate about this is urgent, as centres are already confronted

with parental requests to transfer embryos found to have the targeted mutation (e.g. BRCA1 or BRCA2 genes for hereditary breast cancer) in cases where no non-affected ones turned out to be available. How should they respond? That there seems to be more room here to at least discuss the issue has everything to do with the nature of the conditions in question: serious but later onset, incomplete genetic penetrance (not all individuals with the mutation will also have the disease) and availability of some therapeutic options," said Dr Dondorp.

"In the case of PGD for hereditary cancer, room for manoeuvre will depend on a case-sensitive evaluation of aspects relevant to the 'high risk of serious harm' criterion, also in view of the family history. If this approach is acceptable and if further debate leads centres to decide that they would not categorically rule this out, pre-test information about centre policy should be adapted accordingly. It must be made clear that there may be, with conditions, room for shared decision-making about transferring affected embryos. But that does not amount to leaving it to the parents, as doctors cannot avoid their professional responsibility for the welfare of the future child."

He concluded: "However, professionals may still find it difficult to respond to such requests that lead not only to the deliberate conception of a child in need of special care, but also to the very outcome they set out to prevent when offering PGD to a couple. Is it acceptable to use PGD just for trying to have a better result than one is eventually prepared to accept? This fits in with a wider debate about the morally charged nature of PGD and the proportionality of its uses: is it acceptable to use PGD for avoiding treatable disease, such as MCAD, in the first place?"

Together with Professor Guido de Wert, also from Maastricht University, Dr Dondorp is writing a paper to be published in Europe's leading reproductive medicine journal, Human Reproduction, on these

issues. This is the first time ethicists have considered the questions that arise as a result of extending the use of PGD to hereditary symptoms such as cancer and MCAD.

Source: European Society for Human Reproduction and Embryology