Designing babies: what the future holds

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Abstract

Advances in reproductive technology have opened new opportunities to avoid inherited diseases in offspring. The preimplantation genetic diagnosis (PGD) of human embryos permits those embryos carrying gene disorders or a non-diploid chromosome constitution to be identified. Numerous disease genes including those with a late onset have been identified and the conditions averted in children. Risks of abortion have been reduced, and the incidence of live births raised after PGD. It is also possible to select embryos with human leukocyte antigens (HLA) identical to those of a sick elder sibling, and then use stem cells from cord blood at birth to supply the necessary therapy. This form of treatment has alleviated the inherited disease in many recipients. The outlook and ethics of this approach to the alleviation of human disorders are discussed.

Keywords: assisted human reproduction, designer babies, HLA typing, preimplantation genetic diagnosis

Introduction

There are many and various debates on the ethics of the techniques and technologies I will introduce here. I was asked to speak about human designer babies. The background of the term 'designer' baby has been initiated by journalists and not by scientists to describe several different reproductive technologies. These technologies have one thing in common. They give the parents more control over the characteristics of their offspring than other forms of conception. The problem is whether it is ethical for doctors and parents to design babies by selecting or altering an embryo and bring it to a full-term fetus. Should this procedure be made illegal? Should there be limits to such practices? And what exactly are the different techniques for designing babies?

Unfortunately, the term is very imprecise and it is difficult to untangle its various meanings in the public mind. It can mean various things. Human embryos can be assessed for various disorders or for unknown diseases. The sex of a child at birth can be prearranged by choosing embryos for this specific sexual trait. Genetic testing can be done for therapeutic or for cosmetic reasons. All these features come out of one basket, and this raises the nature of the argument for designing the babies. It can help to prevent certain genetic diseases, so reducing the financial and emotional strains on the parents if they want the best for their children. Why shouldn't we use this technology? As of today, these techniques are used only by those parents who need the help of a fertility clinic to have their children. Since they are investing so much time, energy, money and effort to have a baby shouldn't they have a healthy one? In any case, a great number of naturally conceived embryos are rejected naturally because of their disordered growth. Many such defects can also be identified by scanning embryos in their preimplantation development. They may simply be discarded if it is discovered that their inheritance can lead to anomalous forms of growth. Many such defects can also be identified by scanning embryos in their preimplantation development. They may simply be discarded if it is discovered that their inheritance can lead to anomalous forms of growth. In such cases, we are replacing Nature, who routinely takes care to reject such cases.

Arguments against designing babies could lead to objections about our attempting to produce healthy babies. Once we start down the slippery slope of eliminating embryos because they are diseased, what is to stop us from choosing babies for their physical, physiological or psychological traits? There is always a looming shadow of eugenics, involving the practice of improving the human gene pool by eliminating undesired embryos. This motivation has, in the past, spurred some governments in Europe and in the US to use various methods
such as modifying fertilization, selective breeding and racial hatred to apply such eugenic systems to their citizens. On the other hand, could we breed races of supermen? Who is to criticize the various sources of genetic enhancement? Will this new technology only be available to the wealthy, who will hence avoid problems inflicted on lower classes due to their suffering from inherited disabilities and diseases? Worst of all, will the discrimination against people already born with such a disability increase as they are perceived as genetically inferior?

Economic factors and pressures might also come to have a significant role in making choices regarding the nature of characteristics in newborn babies. Insurance companies, for example, may refuse to cover newborn malformations that could have been corrected before implantation. They may also have concerns over parents designing their child. Widespread concerns apply to such matters, which began when transferring the process of procreation from home to the laboratory and turning it into a sort of manufacturing process. What is happening in this field today is highly practical and possible, while everything whatever that was said before is now just simply speculation. Deeper questions must be answered about this new and burgeoning field. Have we really designed anybody? The answer is no. Have we really designed anything? The answer is yes. What have we designed? PGD is a medical diagnostic procedure allowing the design to avoid the pregnancy with congenital disease. Is there a need to apply it? It can offer an alternative to prenatal diagnosis. If this is not done by PGD, it can be achieved only by aborting the affected fetuses.

What is bringing us to enlarge our programmes of PGD, and what advantages does it give us? Data from our centre using PGD to identify translocations before implantation showed that PGD contributes to a sevenfold reduction of abortion rates for the same group of patients, improving the number of patients taking healthy babies home tremendously: 80% of our patients delivered a normal baby, healthy and free of the familial impairment. There is also another benefit of PGD as compared with prenatal diagnosis performed for pre-existing Mendelian disorders. We performed PGD for 92 single-gene disorders covering various types of different mutations. By now, we have performed 560 cycles for single-gene disorders and have achieved embryo transfer in 90% of these cases. Currently, we have established 195 pregnancies. Expanding applications of PGD are possible, and decisions must be taken about ethical approval to use PGD rather than prenatal diagnosis, such as in PGD for genetic predisposition for late-onset disorders, as it is doubtful if termination of pregnancy will be acceptable after prenatal diagnosis identifies that the baby carries such disorders.

For example, PGD for the p53 tumour suppressor gene mutation confers long, disease-free life on the embryo. Examining pedigree history reveals the dreadful state of many close relatives who have succumbed to this particular disease gene (Figure 1). Similar histories arise for different cancers. No alternatives to PGD exist for these parents or future parents. Do they wish to continue the previous form of life for their future children? PGD will precondition their genetic diagnosis and measure the outlook for a healthy child. Is it therefore ethical? Will the family then realise they have

![Blastomere analysis for G524A in Exon 5](image)

**Figure 1.** PGD for p53 tumour suppressor gene mutations. Left panel: Duplex blastomere analysis for G524A mutation in exon 5 (top) and corresponding short tandem repeats (STR) in intron 1 (bottom), showing that embryo numbers 1, 4, 5 and 9 are affected, while embryo numbers 3, 7 and 8 are mutation-free and suitable for transfer. ADO (allelic drop-out) of three repeats in intron 1 STR was detected in blastomeres from embryo numbers 4 and 9. ET: embryo transfer. Right panel: Family pedigree for three generations, with the resulting birth of a healthy mutation-free child.
modified pedigrees in their more distant family to avoid the frequencies of children with these inherited conditions? A family carrying a gene for early onset disease may already have a sibling who is affected by a disease gene at the age of 33 and 42. In this situation, the family had decided to have children, but when the time comes they may regret their choice. Today, they do not have to deliver such children with severe inherited disorders. The choice is up to them. They could move to PGD and have two or three healthy children without risk of disease. Who sees any ethical problem with that? One might think that a mother whose family has been rigorously affected with a specific inherited disease and had to face it itself is in a better position to decide.

Surely it is a kinder moral attitude for parents while in their younger or middle ages to spare their children from such a terrible fate. The mother would certainly know what such a life involves. Some forms of designing babies offer longer, healthier, more pleasant lives. The presence of a disease gene in a child, and the fearful knowledge that a parent also carries it, has been removed by PGD for the whole of their life.

Another and quite different PGD approach involves alleviating disease and death in a young member of the family. This occurred with a family who are now very well known to have treated one of their children using stem cells from a later newborn baby. It involved diagnosing embryos for transfer that had a specific set of genes. This set would not include any disease genes in the family. The embryo was also typed for its HLA antigens to ensure its cord blood could be taken at birth and injected into a matched sick sibling. Cord blood is well known to be full of stem cells. In this case, the embryos had been selected as being free of Fanconi anaemia and HLA-matched with those of the sick sibling called Molly (Verlinsky et al., 2001). Molly had Fanconi anaemia, was very ill, and cord blood stem cells from her newborn PGD sibling could save her life. Otherwise, she would soon be dead. After this treatment, her life, and that of the newborn donor, will be continuous and free of disease.

A British couple was also treated in a similar manner. This time a younger child saved the life of an older one who had Diamond–Blackfan anaemia (Verlinsky et al., 2004). Without PGD, the parents had no choice, except for a horrible life for their child while they tried using natural conception to have another baby matching their sick child and hopefully helping to save its life. The chances of saving it in these circumstances would have been very low. The couple applied to the UK Human Fertilisation and Embryology Authority (HFEA), who did not give approval for the PGD to be carried out in UK. Hence, they came to our Chicago laboratory to use the approach of designer babies. A successful treatment was achieved for this couple and their older sibling was safe. The HFEA, the British fertility watchdog, announced very recently that it will broaden the rules on embryo screening to allow of birth of designer babies for wider cures of sick siblings. Our clinic has received increasing numbers of requests for HLA typing with PGD throughout the whole of this year.

There is also another wider application for PGD in assisted reproductive technology: considerably improving pregnancy rates and substantially reducing spontaneous abortion rate. This is our goal at present and it involves scoring the number of chromosomes in embryos before they are transferred to their mothers. According to our data, the reproductive history of couples prior to PGD showed an abortion rate of 68% after natural conception, or IVF not involving PGD. In contrast, their abortion rate after PGD was reduced to 28.4%, improving implantation and take home baby rate, which was 70.7% after PGD, compared with 32% in the same group of patients prior to PGD. It is of interest that PGD also reduces considerably the frequency of multiple pregnancies, as by avoiding the transfer of chromosomally abnormal embryos we can now transfer one embryo or a maximum of two to decrease the possibility of multiple births. So we have gained many benefits by implementing PGD in our IVF practice. Overall, we have carried out 3000 PGD cycles, which resulted in >600 pregnancies and >450 babies born free of disease.

A dynamic future?

What is the future? In a recent article in the London Times (29 September 2004) about stem cell therapy, it was stated that Dr Wilmut has received permission to clone human embryos with genetic disorders in order to be able to develop the possible treatment. We have a different approach. We created a repository of human embryonic stem cells, including some carrying various types of inherited disease (Verlinsky et al., 2005). Many of them are derived from afflicted embryos and were donated by patients who did not wish to have them for transfer. So we have their permission to create stem cell lines, which will provide a source of cells helping to create new therapies for existing disease. I think this is one of the ways to go. Other different and equally provocative approaches are also being proposed. For example, we could make better human beings by knowing how to add good genes to their embryos. Should we do this — what is wrong with it? It is a complex question to ask.

How far can this technology take us? Will technology inevitably lead to a world of human beings who are partly man-made? Suppose parents could add 30 points to their children’s IQ. Who would want to do it? And if parents did not, would their children have a low IQ as compared with other treated children in the neighbourhood? A final point. We know now how powerful gene therapy can be. We can turn monkeys into workaholics. Maybe some employers would like to put in an application form. I would.

References


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