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Ethical Offspring?

Bioethics and Law Forum*

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According to author Thomas H. Murray in his fine book, *The Worth of a Child*, ''adults have children for three kinds of reasons relevant to morality: for good reasons, for bad reasons and for no reason at all.''[1] He further suggested that the latter reason probably encompasses more births than the first 2 categories combined. Although I tend to agree, the children brought into the world to be discussed herein clearly do not fit into the latter category. So were they brought into the world for a good moral reason or a bad moral reason?

The Ayala Case: Anissa and Marissa, a Lucky Match

Probably the first case to capture headlines about a baby conceived with the hope of saving a sick sibling was that of the Ayalas in 1990. Mary and Abe Ayala had 2 children. At 16 years old, their only daughter, Anissa, was diagnosed with chronic myelogenous leukemia. The most promising treatment, with a 50:50 success rate at the time, was a bone marrow transplant. However, such a success rate was only possible if bone marrow from a close relative with the same immune profile as Anissa was used. Absent treatment, death was certain within a few years.

Anissa's parents and older brother were tested, but none proved to be a suitable match. In response, the Ayalas unabatedly campaigned to inform and encourage Latinos to enroll in the 1-year-old National Donor Marrow Program. They believed their prayers were answered when 1 year into their campaign a donor match was found, but those same prayers were shattered when the potential donor declined to donate. The Ayalas were unwilling to stand idly by and watch their daughter die, so, encouraged by family and friends and armed with the knowledge that a biological sibling had a 25% chance of being a compatible match, the Ayalas (who were in their early 40s) had Abe's vasectomy reversed. Despite just a 10% chance of conception, the Ayalas were blessed by conceiving a child. Whether a match or not, the Ayalas, as loving parents, were devoted and excited about the impending new addition to their family. Thus, it was not until Mary Ayala's sixth month that she had an amniocentesis and discovered that she was carrying a baby girl who was a donor match for Anissa. The baby was named Marissa. Although Marissa's umbilical cord cells were preserved for a later donation, on June 4, 1991, 14-month-old Marissa's bone marrow was transplanted into 19-year-old Anissa.

Today, Anissa is 32 years old, is fully recovered, is married to her high school sweetheart, and is the Assistant Director of the Bone Marrow Donor Program for the American Red Cross Southern California Region. In 1997, Anissa started the Anissa Foundation to help other families facing the emotional and financial burden of battling leukemia and to increase public awareness of the need for more Hispanic bone marrow donors. At 14 years old, Marissa is happy and healthy with no memory of donating her bone marrow to save her sister's life. The memory that she will always carry is that she is very special and that her family, especially Anissa, loves her very much. After all, they share a unique sibling bond, summarized by Anissa as ''If it weren't for her I wouldn't be here, and if it weren't for me, she wouldn't be here either.''[2]

The Nash Case: Molly and Adam, Preimplantation Genetic Diagnosis and Preimplantation Genetic Diagnosis Human Leukocyte Antigen Testing

Not unlike Mary and Abe Ayala, by 1999 Lisa and Jack Nash were desperate to save their 6-year-old daughter Molly's life. Molly suffered from Fanconi's anemia, a rare, recessive, genetic immune system disorder.[3] Again,

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[1] Thomas H. Murray, *The Worth of a Child*, 1996, p 4. Murray's use of the term ''adults'' should certainly be interpreted loosely given the number of teen births and those resulting from a drunken or drug-induced states, 1-night stands, and from other mindless or irresponsible actions.

[2] Leah Kohlenberg, *Designer Babies*, October 5, 2000, http://archive.salon.com/health/feature/2000/10/05/bone_marrow/print.htm. Also see Patricia Burkhart Smith, *A Gift of Life*, http://www.hispaniconline.com/vista/maygift.htm.

[3] Cecila Hall and Simon Davis, *Genetically Selected Test-tube Baby Born to Save Sister's Life*, The Daily Telegraph, October 4, 2000. Children born with Fanconi's anemia usually die by age 7 because their bodies cannot make bone marrow and, like Molly, they are born without thumbs and hip sockets.

as in the Ayala case, a bone marrow transplant from a matching donor provided Molly's only hope for survival. Her best and most effective chance at being matched was for her parents to have another child, and the doctors at the Reproductive Genetics Institute in Chicago told them so. Having more children had long been a desire of the Nashes, but because both parents carried a defective version of the Fanconi's anemia gene they did not want to risk knowingly bringing another child into the world with a fatal disease.

The doctors had another suggestion: If the Nashes agreed to conceive embryos in vitro, the doctors could use preimplantation genetic diagnosis (PGD) to not only screen the embryos for Fanconi's anemia but also as donor matches for Molly. The Nashes were thrilled by the chance to have a healthy child and one whose umbilical cord stem cells might save Molly's life. On August 29, 2000, Adam Nash was born, free of Fanconi's anemia and a perfect donor match for his sister. A month after Adam's birth, his sister was transfused with his umbilical cord stem cells. The treatment was an outstanding success; almost 4 years later Molly is in total remission and is completely free of disease and Adam is also a happy and healthy child. In the future, the Nashes hope to have more children by using some of the other disease-free embryos.

Cases in Australia, New Zealand, and the United Kingdom

Cases similar to those of the Ayalas and Nashes have been reported in Australia, New Zealand, and the United Kingdom. Unlike the United States, these countries have oversight boards that regulate assisted reproductive technologies, including PGD, and can restrict or deny access to treatment.

The Infertility Treatment Authority (ITA), which has jurisdiction in both Australia and New Zealand, has previously approved genetic disorder screening for Fanconi's anemia and sickle cell anemia and the deputy director of the Monash Institute of Reproduction and Development, Professor Alan Trounson, stated that although ''tissue match screening was legal,'' he wanted ethical approval from the ITA to screen embryos for both disease and as donor matches for a sick sibling.[4] But, rather than wait for approval, 1 couple, the Sunderlands, traveled to the United States for in vitro fertilization (IVF) and screening. They felt they had no other choice than to watch their son Brandon die.

The Whitakers of Sheffield, United Kingdom, whose son Charlie has Diamond-Blackfan anemia (DBA) were refused permission to use PGD to screen for a donor match for Charlie by The United Kingdom Human Fertilisation and Embryology Authority (HFEA). The HFEA declined permission for the procedure because the Whitakers did not carry a screenable gene for DBA, rather Charlie's disease was a result of a sporadic mutation. As such, any embryos made by the Whitakers would only be screened as a donor match for Charlie. Although the HFEA permits tissue typing coupled with screening for a serious genetic disease, they deem tissue typing alone ''unlawful and unethical because it involved some risk to the embryo but the only benefit would be to Charlie.''[5] Ultimately, the Whitakers also traveled to the United States for treatment and recently baby James became 1 of 5 healthy babies born as a donor match for an ailing sibling.

Preimplantation Genetic Diagnosis Human Leukocyte Antigen Testing With and Without Standard Preimplantation Genetic Diagnosis

Preimplantation genetic diagnosis is a means of testing an embryo in vitro for a desired genotype before implantation. Since the 1980s, more than 2500 cycles of PGD have been performed worldwide.[6] Preimplantation genetic diagnosis has been used to screen for single-gene diseases such as cystic fibrosis, thalassemia, sickle cell anemia, and muscular dystrophy, as well as chromosomal abnormalities such as Down syndrome and trisomy 18. Presently, more than 100 different conditions can be identified via PGD. In general, PGD has a tremendous advantage over traditional prenatal testing, corionic villi sampling and amniocentesis, because disease can be identified in vitro rather than in vivo, thus preventing the need to decide whether to terminate a pregnancy should the tests indicate a severe disease incompatible with life. When used in this manner, PGD raises minimal ethical concerns and has become a medically acceptable method for avoiding the birth of children with certain genetic or chromosomal disorders.

What has generated concern and controversy, as in the Nash case described previously, is the use of PGD to screen for genetic disease and to find a tissue match to a sick sibling.[7] The later technique is a specific type of PGD called PGD human leukocyte antigen (HLA) matching.[8]

[4] Designer babies could save siblings, December 24, 2001. http://onenews.nzoom.com/onenews_detail/0,1227,73521-1-6,00.html.

[5] Banned ''designer baby'' is born in United Kingdom, June 19, 2003, newscientist.com.

[6] Robert J. Boyle and Julian Savulescu, Ethics of using preimplantation genetic diagnosis to select a stem cell donor for an existing person, *BMJ* 323:1240, November 21, 2001.

[7] Since the Nash case, which was done at Chicago's Reproductive Genetics Institute (RGI), embryo tissue typing coupled with genetic disease screening has been performed more than 35 times worldwide, although most of the testing has been done at the RGI.

[8] Yuri Verlinsky, Svetlana Rechitsky, Tatyana Sharapova, Randy Morris, Mohammed Taranissi and Anver Kuliev. Preimplantation HLA testing, *JAMA* 291(17):2079, May 5, 2004. In 1994, the RGI became a Pan American Health Organization/World Health Organization Collaborating Center for the Prevention of Genetic Disorders.

Garnering even greater controversy and criticism is PGD HLA testing without PGD to identify a causative gene, but solely to find a tissue match for an afflicted sibling in need of an HLA-matched stem cell transplant.

Preimplantation Genetic Diagnosis Human Leukocyte Antigen Testing Yields 5 Perfectly Matched Potential Donors

This was the circumstance surrounding 4 babies, in addition to James Whitaker, who were born to 9 couples with children suffering from acute lymphoid leukemia, acute myeloid leukemia, or Diamond-Blackfan anemia during 2002–03. The PGD HLA testing was performed at the Reproductive Genetics Institute (RGI) Chicago, Ill, by pioneers of PGD and PGD HLA, Drs Anver Kuliev and Yuri Verlinsky and their team.[9] The first-of-its-kind protocol was approved by the RGI's diverse Institutional Review Board, as well as an independent group of volunteers who reviewed and approved the protocol. Some of the requirements for couples wishing to participate in the PGD HLA trial were having a child affected with a condition requiring a bone marrow transplant, that the condition had been successfully treated by a cord blood stem cell transplant, that the couple desired more children separate and distinct from the possibility of giving birth to a promising donor match, and, as is standard in most IVF protocols, submitting to a psychological evaluation. Interestingly, all 9 couples sought PGD HLA of their own volition after learning about its potential through their doctors or the Internet; none were recruited for the study.

Of the 5 healthy HLA-matched donor siblings born, stem cells from the cord blood of 1 infant have been transfused to the sick sibling with excellent results. However, Dr Kuliev cautioned that the donee would require close monitoring for the near future. Charlie Whitaker is presently awaiting his transplant of baby brother James's umbilical cord stem cells and because the 3 remaining donee siblings are in remission, their siblings' cord blood has been stored for possible future use. On the heels of these cases, the RGI has performed PGD HLA testing alone for more than 12 couples and has announced that demand is rising.

Is Bringing a Child Into the World to Possibly Save a Sibling's Life Morally Permissible?

Returning to our original question, we know the children discussed herein were brought into the world for a reason, but is being an HLA tissue match for an ailing sibling a good or bad moral reason?

To answer this question, we begin with the fundamental precepts of philosophy and humanity, espoused by Immanuel Kant[10]

> Every rational being exists as an end in himself, not merely as a means for arbitrary use. . . . The practical imperative will therefore be as follows: Act in such a way that you always treat humanity, whether in your own person or in the person of any other, never simply as a means but always at the same time as an end.

This edict is often misquoted and misconstrued as stating, ''Never use people as a means but always treat them as an end,'' rather then the more accurate, ''Never use people solely or simply as a means but always treat them as an end.'' What analysis results if we apply this directive to the notion of conceiving a child with the hope that it is a potential donor match for an ailing sibling?

If no form of PGD is employed and a couple uses only traditional prenatal testing to determine if a fetus is a donor match, and then aborts the fetus solely because it is not a match, then according to Kant, this would be morally unacceptable because the fetus is being treated only as a means and not as an end at all. Unfortunately, before PGD HLA testing, there were numerous anecdotal cases of such occurring.[11] However, if PGD HLA testing is used with or without traditional PGD and an embryo is selected and carried to term, then the child is not being treated solely as a means of saving a sibling, unless of course the parents killed it after saving the life of the afflicted sibling. Rather, the child is being treated as a possible means to help a sibling and as an end unto himself, especially as in the aforementioned protocol in which each couple wanted more children autonomous of producing a donor match. Thus, under Kant's construct, using PGD HLA testing to select an embryo as a tissue match for a sibling is morally permissible because the child, although being conceived as a means to save a life, also is being treated as an end unto himself.

Of course, critics and cynics may doubt the parents' true desire to have more children, but their criticism can be easily dismissed when one considers what these couples have gone through out of love for and devotion to their sick child, and the effort entailed to have another child (expensive IVF treatment, reversal of vasectomies, and painful hormone injections), one who is healthy. Furthermore, hindsight proves this prediction because the love and nurturing bestowed on siblings, such as Marissa Ayala, Adam Nash, and others, by their parents and siblings is undeniable, again adhering to Kant's ideal dictum of a child being an end unto himself.

A similar dubious criticism that surfaces in debate is that children should not be brought into the world con-

[9] Velinsky et al, op. cit., p 2079; Associated Press, Lab creates 5 babies to help save siblings: Made to order infants will serve as stem-cell donors, May 5, 2004, http://www.msnbc.com/id/4900474/.

[10] Immanuel Kant, *Groundwork of the Metaphysics of Morals,* 1964, pp 95–96.

[11] Associated Press, op. cit.

ditionally or for the benefit of another because they will not be valued in their own right.[12] Again, the realities of life defeat this lob. Some philosophers, ethicists, and theologians claim that the ideal reason to bring a child into the world is the child's own welfare, so he can be loved and nurtured. But this seemingly purely altruistic premise is not so simple because relationships, especially the parent-child relationship, are reciprocal. The children are loved and protected and the parents in return experience love, pride, and accomplishment.[13] Furthermore, in many instances, children are conceived for the benefit of others and yet are valued in their own right. For example, additional children may be conceived so a child has siblings and is not alone, so that parents will have caregivers as they age, for help on the family farm or with the family business, so that a family farm or business can be passed down generationally, and even to carry on a family name or tradition. There is no outrage at parents who have children for these reasons and many others or for no reason at all, and there should not be. Nor should there be outrage toward parents who choose to screen embryos to find a potential donor match for their dying child. Outrage should be reserved for the parents who fail to love and nurture their children and those who mistreat and abuse them. To restrict the reasons for having children or the number of children a couple can have is not only impractical but leads to deadly abuse.

Possibly the most valid concern with respect to screening embryos to be a potential stem cell donor match for an ailing sibling is the risk or harm to the new sibling, but this concern too can be allayed. Presently, there is no known risk to the embryo or resulting child from PGD HLA testing. Also, use of cord blood stem cells poses no risk or harm to the infant; instead, cord blood is considered biological waste and either discarded outright or used for research. A legitimate concern does arise if the umbilical cord stem cell transplant is not successful and a bone marrow transplant is needed, as in the Ayala's case. A bone marrow transplant, like most medical procedures, entails risk of infection and pain, and usually the child would undergo the procedure because of the consent of the parent(s). These concerns should certainly be acknowledged and addressed during the informed consent process or psychological counseling, but should not prohibit PGD HLA testing outright. The risk of infection to the bone marrow donor is minimal; young children with developing nervous systems do not experience the same intensity of pain as do adults and based on anecdotal evidence from other cases involving very young bone marrow donors, they have little if any memory of the procedure or accompanying pain; and it is a fundamental right of parents to make decisions for and on behalf of their minor children. Thus, PGD HLA testing, cord blood transplants, and bone marrow donation pose no valid constitutional challenge to defeat that right.

Finally, the use of PGD HLA testing is unlikely to slide down the proverbial slippery slope to crafting ''designer'' or ''tailor-made'' babies because despite the amazing mapping of the human genome, no technology exists to manipulate 1 multigene characteristic, not to mention constructing an entire genome of specifically chosen multigenetic characteristics; societies can and have controlled the use of certain technologies such as the atomic and hydrogen bombs; creating children with reproductive technology assistance is time consuming, painful, and expensive, and often has low success rates and therefore will not become ubiquitous; and hopefully continued advances in stem cell and medical research will decrease or eliminate the demand for this testing.

Conclusion

Thus, use of PGD HLA testing with or without standard traditional PGD is morally acceptable to create healthy children who could potentially save a sibling's life because under Kant's basic philosophical edict, the children are not treated solely as a means but as a unique end as well; because children are commonly born who benefit others for far less significant reasons than saving a life; because with the exception of minimal risk of infection and pain should a bone marrow transplant be necessary, PGD HLA testing and umbilical cord stem cell transplants pose no risk or harm to an embryo or infant; because presently the technology does not exist to grease the ''slippery slope'' and society has stopped other slides; and, theoretical philosophy aside, because in its practical results PGD and PGD HLA testing are heartily supported by public opinion, according to a large study recently conducted by Johns Hopkins University about preimplantation genetic testing. The study reported that 61% of the public embraces the idea of using PGD testing to select an embryo that could benefit an ailing sibling.[14]

Until research advances and cures are found, to those who do not support PGD HLA testing, I ask is it morally acceptable for parents to stand by and watch their child die without doing everything they can to help?

[12] Boyle and Savulescu, op. cit., pp 1240–1241.

[13] Murray, op. cit., pp 2–3.

[14] Peter Gorner, 5 babies born to save ill siblings, doctors say, Chicago Tribune Online Edition, May 5, 2004, http://www.chicagotribune.com/features/health/chi-0405050257may05,0,6628198.story?coll+chi-news-hed.