

Birth of Healthy Baby from 20-Year-Old Frozen Embryo Raises Ethical Questions

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Introduction

The Jones Institute for Reproductive Medicine at Eastern Virginia Medical School (Jones Institute) pioneered the first *in-vitro* fertilization (IVF)¹ clinic in the United States in 1978.² Three years later, in 1981, the Jones Institute reported the birth of the nation's first IVF baby.³ Almost thirty years later, in 2010, the Jones Institute reported yet another milestone in reproductive medicine: the birth of a healthy baby boy from a 20-year-old frozen embryo.⁴

The 20-year-old frozen embryo, along with others, had been created by an infertile couple who had undergone IVF treatment in 1990.⁵ The couple's excess embryos were cryopreserved,⁶ or frozen at the pronuclear stage,⁷ and then placed in cryopreservation storage.⁸ After the couple was blessed with the birth of a baby boy through the IVF treatment, they subsequently decided in 1993 to anonymously donate their five remaining

¹ *In vitro* fertilization is one of the assisted reproductive technology (ART) procedures used to treat infertility. It involves aspirating eggs from a woman's ovaries, combining them with sperm in the laboratory setting to create embryos, and then implanting the embryos in the woman's uterus or donating them to another woman. See Society for Assisted Reproductive Technology (SART) and American Society for Reproductive Medicine (ASRM), *Revised Minimum Standards for Practices Offering Assisted Reproductive Technologies*, 90 FERTILITY AND STERILITY S165 (2008); Centers for Disease Control and Prev., *Assisted Reproductive Technology*, Nov. 11, 2009, available at <http://www.cdc.gov/ART/>.

² See Eastern Virginia Med. School, *EVMS Jones Institute of Reproductive Medicine*, <http://www.evms.edu/evms-dept.-of-obstetrics-gynecology/jones-institute-for-reproductive-medicine.htm>; Eastern Virginia Med. School Health Services, *Specialties: Infertility, Reproductive Endocrinology and Reproductive Medicine*, available through <http://www.evmshealthservices.org>.

³ See *Specialties*, *supra* note 2; see also *The World's First Test Tube Baby*, American Experience, available through <http://www.pbs.org/wgbh/americanexperience/>.

⁴ The frozen embryo was actually 19.7 years of age. Eastern Virginia Med. School Health Services, *Current Events: Researchers and Physicians at the EVMS Jones Institute for Reproductive Medicine Discuss Healthy Baby Conceived from 20-Year-Old Embryo*, <http://www.evmshealthservices.org/index.cfm/fuseaction/site.content/type/86576.cfm>; see also Donna Dowling-Lacey, et al., *Live Birth from a Frozen-Thawed Pronuclear Stage Embryo Almost 20 Years After its Cryopreservation*, FERTILITY AND STERILITY 1.e1-1.e3 (2010) (pending publication), <http://www.evms.edu/images/storeis/11768.pdf>.

⁵ Dowling-Lacey, *supra* note 4, at 1.e1.

⁶ Cryopreserve means to freeze at a very low temperature, such as in liquid nitrogen at -196°C, to keep the embryos viable. Am. Soc'y for Reproductive Med., *Assisted Reproductive Technologies: A Guide for Patients*, 3-22, at 18, available through <http://asrm.org>; see also Am. Soc'y of Reproductive Med., *Cryopreservation and Storage*, <http://www.asrm.org/topics/detail.aspx?id=408>.

⁷ *Cryopreservation and Storage*, *supra* note 6; The pronuclear stage is the one-cell embryo stage in which two pronuclei may be visualized confirming fertilization. One pronuclei is derived from the male gamete or sperm and the other is derived from the female gamete or egg. See *Assisted Reproductive Technologies: A Guide for Patients*, *supra* note 6, at 21.

⁸ Dowling-Lacey, *supra* note 4, at 1.e1-1.e2.

frozen embryos.⁹ The embryos were made available for donation, but remained in storage for an additional 16 years before they were finally matched with a 42-year-old woman,¹⁰ who had been undergoing infertility treatment for ten years.¹¹

Two of the five frozen 20-year-old embryos survived the thaw process,¹² and both were then transferred to the uterus of the 42-year-old recipient in August 2009.¹³ Only one embryo thrived in her womb, and in May 2010 after 41.5 weeks' gestation, the 42-year-old woman delivered a healthy baby boy, weighing six pounds and 15 ounces.¹⁴

Fertility specialists believe the 20-year-old embryo is the first of such age to produce a healthy baby.¹⁵ Until now, the previous record was held by two 13-year-old frozen embryos. In 2005, one 13-year-old frozen embryo produced a healthy baby girl in California,¹⁶ and in 2006, another 13-year-old embryo produced a healthy baby boy in Spain.¹⁷ Now, experts are claiming that frozen embryos may be stored for as long as 40 years.¹⁸ At this point, however, the oldest conceivable human frozen embryo available for IVF could be no more than 30-years-old since cryopreservation techniques were not used in human infertility treatment until the 1980s.¹⁹

Millions of healthy children have been born through IVF,²⁰ and the procedure is believed to be reasonably safe.²¹ Yet, fertility experts and researchers have long wondered whether IVF embryos—the embryos grown in laboratory petri dishes for several days—actually undergo subtle changes, and if so, whether those changes would cause adverse consequences to the health and development of the children born through IVF.²²

⁹ Dowling-Lacey, *supra* note 4, at 1.e1-1.e2.

¹⁰ *Id.*

¹¹ *Current Events, supra* note 4.

¹² As with the freezing process, the thawing process is carried out in multiple steps. See H.W. Michelmann and P. Nayudu, *Cryopreservation of Human Embryos*, 7 CELL AND TISSUE BANKING 135, 137-138 (2006), available at <http://www.springlink.com/content/997700t16h72556g?fulltext.pdf>.

¹³ Dowling-Lacey, *supra* note 4, at 1.e2.

¹⁴ *Id.* at 1.e2.

¹⁵ *Id.* at 1.e1.

¹⁶ See Alex Barnum, *Baby Thirteen Years in the Making*, San Fran. Chron., July 5, 2005, available at <http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2005/07/05/EMBRYO.TMP>; see also *Longest Frozen Embryo Baby Born*, BBC News, July 6, 2005, available at <http://www.news.bbc.co.uk/2/hi/health/4655035.stm>.

¹⁷ *Baby Born from Thirteen Year-Old Frozen Embryo*, Nov. 5, 2006, <http://www.futurpundit.com/archives/003854.html>.

¹⁸ *Current Events, supra* note 4.

¹⁹ Michelmann, *supra* note 12, at 135.

²⁰ Nobel Assembly, *The 2010 Nobel Prize in Physiology or Medicine – Press Release*, Nobelprize.org., Oct.4, 2010, http://nobelprize.org/nobel_prizes/medicine/laureates/2010/press.html.

²¹ See Gina Kolata, *Picture Emerging on Genetic Risks of IVF*, N.Y. TIMES, Feb. 16, 2009, available at http://www.nytimes.com/2009/02/17/health/17ivf.html?_r=1&nl=8hlth&emc=hlth.

²² *Id.*; see also Am. Soc'y of Reproductive Med. Press Release, *Highlights from ASRM09: ART Outcomes: IVF Kids are Healthy, Smart and Well-Behaved, Although Multiple Gestation Leads to Lower Scores on the Iowa Test of Basic Skills*, Oct. 20, 2009, available through <http://www.asrm.org> (citing Elizabeth Ginsberg, M.D., Pres. of the Soc'y of Assisted Reproductive Tech.); Am. Soc'y of Reproductive Med. Off. of Public Affairs, *Evaluation of Young Adults Conceived Via IVF at US Clinic Shows Them to be Happy and Well Adjusted*, Feb. 17, 2010, available at <http://www.reproductivecats.org/news/article.aspx?id=2490>; Denise

The news of the birth of the infant boy conceived from the 20-year-old embryo and the potential for 40-year-old embryos to emerge in the future now raise ethical questions that carry a host of medical, social, and psychological implications for the children born under such circumstances. Fertility specialists should be mindful of these ethical questions and implications and ensure that discussions concerning the same are incorporated in the informed consent conversations with their infertile patients who agree to use long-term frozen embryos.

Medical Implications

Embryos are frozen at a temperature of -196°C in liquid nitrogen with the use of a cryoprotectant agent.²³ For many years, experts have speculated that frozen embryos stored at -196°C exist in a state of cryostability²⁴ – meaning the embryos remain in suspended animation with no metabolic activity.²⁵

Since the inception of human embryo cryopreservation techniques in the 1980s, a paramount concern has been whether the cryopreservation procedure itself is safe.²⁶ There is an ongoing concern that cryopreservation may pose medical risks to embryos and resulting children. Experts estimate that approximately 20 percent of embryos do not survive the freezing process, and the combination freezing/thawing processes potentially could cause embryo injury, genetic malformations or birth defects.²⁷ But such adverse cryopreservation consequences must be clearly distinguished from the other potential risks associated with IVF that are currently being researched, such as certain birth defects, genetic disorders, or abnormal patterns in gene expression, all of which may be attributed to possible changes in the molecular biology of embryos grown in laboratory petri dishes.²⁸

During 2007 and 2008, researchers with the Jones Institute evaluated the impact of long-term cryostorage on post-thaw and implantation survival rates of frozen embryos.²⁹ They analyzed computerized data from IVF patients who had used 11,768 frozen embryos

Grady, *Birth Defects Tied to Fertility Techniques*, N.Y. TIMES, Nov. 17, 2008, available at http://www.nytimes.com/2008/11/18/health/research/18birth.html?_r=1&ref=health; Miranda Hitti, *CDC: IVF May Boost Birth Defects Risk*, WebMD Health News, Nov. 17, 2008, available at <http://www.webmd.com/infertility-and-reproduction/news/20081117/cdc-ivf-may-boost-birth-defects-risk>; Centers for Disease Control and Prevention, Nat'l Center on Birth Defects and Developmental Disabilities, Key Findings: Use of Clomiphene Citrate and Birth Defects, available at <http://www.cdc.gov/ncbddd/features/clomiphene-citrate.html>.

²³ *Cryopreservation and Storage*, *supra* note 6; see also Michelmann, *supra* note 12.

²⁴ Ryan Riggs, et al., *Does Storage Time Influence Postthaw Survival and Pregnancy Outcome? An Analysis of 11,768 Cryopreserved Human Embryo*, 93 FERTILITY AND STERILITY 109, 112 (2010).

²⁵ A. Malpani and A. Malpani, *How to Have a Baby: Overcoming Infertility: Embryo Freezing*, <http://www.drimalpani.com/book/chapter25d.html>.

²⁶ Michelmann, *supra* note 12, at 139.

²⁷ *Id.*

²⁸ See Kolata, *supra* note 21. Subtle changes in gene expression or in developmental patterns may not be obvious at birth and may not become apparent until adulthood, middle age, or old age.

²⁹ Riggs, *supra* note 24, at 109.

between 1986 and 2007.³⁰ The subject embryos had been frozen at the pronuclear and cleavage³¹ stages, with storage times ranging from 30 days to roughly 16 years.³² The researchers found that the post-thaw and implantation survival rates and the live birth rates for these pronuclear and cleavage stage embryos were similar regardless of the length of storage.³³ After assuming all storage conditions were optimal for purposes of this study, the researchers concluded that the length of storage time had no significant effect on post-thaw survival rates or successful pregnancy outcomes.³⁴

Even though the Jones Institute researchers opine that frozen human embryos are relatively stable when stored at -196°C and that duration of storage has no obvious effect on pregnancy outcomes, these researchers, nevertheless, acknowledge the need for long-term follow-up of children born from frozen embryos.³⁵ To date, there is no published data available on studies comparing the effects of long-term cryopreservation storage with normal childhood development. Normal childhood developmental milestones include gross motor, fine motor, cognitive, language, and social and emotional skills at age appropriate levels.³⁶

Of the limited studies that have been conducted on IVF-conceived children to date, the American Society for Reproductive Medicine (ASRM)³⁷ and the Centers for Disease Control and Prevention (CDC) collectively reported the results of at least five studies evaluating behavior symptoms, academic achievement, birth weight, emotional health, and incidence of birth defects in IVF children.³⁸ One study at the University of Pennsylvania compared the behaviors of IVF children with non-IVF children. In this study, the parents of IVF-children and the parents of non-IVF children were asked to complete The Child Behavior Checklist³⁹ and a questionnaire about their children's

³⁰ *Id.* at 110.

³¹ The cleavage stage denotes embryos in the process of dividing or cleaving. This initially occurs on day 3 after fertilization. Riggs, *supra* note 24, at 110.

³² *Id.* at 110-111.

³³ *Id.* at 113-114.

³⁴ *Id.* at 112. From a practical standpoint, storage conditions may be adversely affected by repeatedly accessing storage tanks to retrieve embryos or by improperly maintaining storage tanks with liquid nitrogen.

³⁵ *Id.* at 113-114.

³⁶ See Centers for Disease Control and Prevention, *Important Milestones: By the End of Five Years*, <http://cdc.gov.ncbddd/actearly/milestones-5yr.html>. There are many standardized behavioral assessment tools on the market to test early childhood development skills in infants and young children as well as pre-k through 12th grade. By way of example, the Denver Developmental Screening Test (DDST) is a widely used tool designed to assess the developmental skills of children ages 0 – 6 years. See Definition of Denver Developmental Screening Test, <http://www//medterms.com/script/main/art.asp?articlekey=9719>; see also CTB McGraw-Hill, <http://www.ctb.com.ctb.com/control/servicesMainViewAction?p=services>.

³⁷ ASRM is a multidisciplinary organization dedicated to the advancement of the art, science, and practice of reproductive medicine. Its mission is to pursue excellence in education and research and through advocacy on behalf of patients, physicians, and affiliated health care providers. See American Society of Reproductive Medicine, Mission Statement, available at <http://www.asrm.org>.

³⁸ *Highlights from ASRM09*, *supra* note 22; *Evaluation of Young Adults Conceived Via IVF*, *supra* note 22; Grady, *supra* note 22 and Hitti, *supra* note 22.

³⁹ The Child Behavior Checklist is a parent-report questionnaire on which the child is rated on various behavioral and emotional problems. It was developed by Thomas A. Achenbach and has been one of the widely used standardized measures in child psychology for evaluating maladaptive behavioral and

behavioral symptoms.⁴⁰ Investigators analyzed the parents' responses for 105 IVF children and 108 non-IVF children⁴¹ and concluded there were no significant differences in behavioral symptoms between the groups.⁴²

In the second study conducted at the University of Washington School of Medicine, researchers compared the birthweight and size of IVF newborns with spontaneously conceived non-IVF newborns and ultimately concluded there were no differences in their sizes at birth.⁴³ These results were contrary to prior study results which suggested that IVF infants were smaller at birth and had more adverse outcomes than spontaneously conceived children.⁴⁴ Now, it is believed that the underlying health of the parents may play a role in their offspring's health regardless of the mode of conception.⁴⁵

In a third study, researchers at the University of Iowa used the Iowa Tests of Basic Skills⁴⁶ to compare academic achievement test performance of IVF-conceived singletons, twins, and triplets between eight and 17 years of age.⁴⁷ The researchers concluded that, although multiple gestations appear to have a slight detrimental effect on standardized test performance, the overall test scores of IVF children were high on the standardized scale.⁴⁸

In the fourth study, researchers evaluated and compared the first cohort of IVF-conceived young adults with their non-IVF counterparts and found the IVF young adults were happy and well-adjusted with no prevalence of increased susceptibility to chronic diseases.⁴⁹ However, the researchers found there was a higher incidence of reports of clinical depression and attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) among the IVF young adults.⁵⁰

In the fifth study, researchers studied 281 women who underwent IVF treatment and found that their infants conceived through IVF were two to four times more likely to have certain birth defects than infants conceived naturally.⁵¹ The prevalent defect problems included heart problems, cleft lip and cleft palate, and esophageal and rectal

emotional problems in 1 subjects between the ages of 2–18 years. *See* Inter-University Consortium for Political and Social Research, *Project on Human Development in Chicago Neighborhoods*, <http://www.icpsr.umich.edu/icpsrweb/PHDCN/descriptions/cbcl-w1-w2-w3.jsp>.

⁴⁰ *Highlights from ASRM09*, *supra* note 22.

⁴¹ *Id.*

⁴² *Id.*

⁴³ *Id.*

⁴⁴ *Id.*

⁴⁵ *Id.*

⁴⁶ These tests consist of standardized achievement batteries used in grades kindergarten through eighth grade. The tests cover several areas including mathematics, science, social studies, vocabulary, reading comprehension, word analysis, listening, and language skills. *See* University of Iowa College of Education, *The Iowa Tests of Basic Skills*, <http://www.education.uiowa.edu/itbs>.

⁴⁷ *Id.*

⁴⁸ *Id.*

⁴⁹ *Evaluation of Young Adults Conceived Via IVF*, *supra* note 22.

⁵⁰ *Id.*

⁵¹ Grady, *supra* note 22 and Hitti, *supra* note 22.

abnormalities.⁵² However, it is not known whether IVF procedures increase the risk for these birth defects or whether infertility itself raises the risk for such defects.⁵³

None of these five studies mentioned above, however, distinguished between IVF children born from fresh embryos versus frozen embryos. It remains medically uncertain whether the processes of freezing and thawing embryos pose long-term medical and developmental risks to resulting children.⁵⁴ Thus, there is a definitive need for long-term longitudinal research and studies comparing and/or contrasting the duration of human embryo cryopreservation storage with normal childhood development.

Social and Psychological Implications

Aside from the potential medical and developmental risks associated with embryo cryopreservation, ethics experts have also raised concerns about the potential social and psychological implications affecting the overall interests and well-being of children born from frozen embryos.⁵⁵ Arguably, as the duration of embryo cryostorage periods lengthen, the adverse implications may exponentially increase, as well.

Consider for instance, the fact that the newborn baby boy born from the 20-year-old embryo and the son of the infertile couple who donated the 20 year-old embryo are biological siblings even though they were born 20 years apart. What if the non-biological parents of this newborn baby boy decide to tell him when he is older about the circumstances of his conception and the news that he has a brother?

The ASRM Ethics Committee supports the practice of parents disclosing to their children about the use of donor gametes in their conception, but ASRM also acknowledges the relative benefits of such disclosure are still under continued study.⁵⁶ Disclosure is ultimately the parents' choice.⁵⁷ If, in this 20-year-old embryo case, the non-biological parents disclose to their son about his conception and genetic origins, how would this boy take such news? Would he be confused about his place in society and where he fits in his immediate family, given that he was born 20 years after conception? Would he experience identity problems and pursue the quest to find his biological roots only to learn that his parents were anonymous donors and he cannot have access to such information?⁵⁸ Or worse yet, would he experience feelings of abandonment since he was left in storage for nearly 20 years before he was fortuitously matched with his current

⁵² *Id.*

⁵³ *Id.*

⁵⁴ Michelmann, *supra* note 12.

⁵⁵ See William J. Winslade and Judith Wilson Ross, *High-Tech Babies: A Growth Industry*, The New York Times, Feb. 21, 1986.

⁵⁶ American Soc'y of Reproductive Med., *Informing Offspring of their Conception by Gamete Donation*, 81 FERTILITY AND STERILITY 527-531 (2004); see also American Soc'y of Reproductive Med., *Patient fact Sheet: Gamete Donation: Deciding Whether To Tell*, 2008, available through <http://www.asrm.org>.

⁵⁷ *Id.* at 527. When parents disclose such information, there has been a push in recent years to allow children access to non-identifying information about the gamete donors if they request it and access to identifying information about donors if all parties agree. *Id.*

⁵⁸ Potentially, a child born from a frozen embryo may experience identity problems regardless of the length of cryopreservation storage. See Winslade, *supra* note 55.

parents? The psychological interests and well-being of the children (and later adults) born from long-term frozen embryos cannot and should not be ignored.

Conclusion

IVF patients who choose to use long-term frozen embryos, whether their own or those donated from others, must consider the medical risks and social and psychological implications for their children produced from these embryos. Fertility specialists should be especially cognizant of these risks and implications and should thoroughly discuss them accordingly with their patients during the informed consent processes. Moreover, fertility specialists should push for long-term longitudinal research and studies evaluating the impact of long-term frozen embryo storage on normal childhood developmental skills and adult emotional and psychological development.

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Birth of Healthy Baby from 20-Year-Old Frozen Embryo Raises Ethical Questions By Cynthia S. Marietta, J.D., LL.M. (Health Law)

 Introduction The Jones Institute for Reproductive Medicine at Eastern Virginia Medical School (Jones Institute) pioneered the first in-vitro fertilization (IVF) clinic in the United States in 1978.² Three years later, in 1981, the Jones Institute reported the birth of the nation's first IVF baby.³ Almost thirty years later, in 2010, the Jones Institute reported yet another milestone in reproductive medicine: the birth of a healthy baby boy from a 20-year-old frozen embryo. The frozen embryos are usually those that were donated so that the recipient could use them at a later date or they would be the embryos remaining after a successful implantation. Image Source: RWJMS IVF Program. On July 25, 1978, Louise Brown became the first human to be born after being conceived by IVF. Previously, a woman from New York gave birth to a healthy boy in 2010 after she was implanted with a 20-year-old frozen embryo. Also, in 2013, 45-year-old NASA scientist Kelly Burke gave birth to her son, Liam James, who was cryopreserved for 19 years. The frozen embryo Burke chose was actually one of the donated eggs, two of which were used by another couple from Oregon in 1994 for IVF, and the rest were frozen. Advertisements. The fate of cryopreserved embryos: an issue that raises unforeseen psychological and ethical questions. L. Karpel, N. Frydman, R. Frydman, M. Flis-Treves, R. Fanchin. OBJECTIVE: To report the successful birth of a healthy baby from a frozen embryo transfer using embryos initially frozen at the eight cell stage, and subsequently thawed, hatched, and cultured for three days, and re-frozen as blastocysts. DESIGN: Case report Setting: Private IVF center Patient: A 33 year old patient with bilateral tubal blockage Intervention: One cycle of IVF-ET followed by two frozen embryo transfers Main Outcome Measure: Clinical pregnancy with live birth. MATERIALS AND METHODS: Case Report: 52 months after a successful IVF-ET cycle.