

## ETHICAL USE OF ASSISTED REPRODUCTIVE TECHNOLOGIES

### **ISSUE:**

Ethical use of assisted reproductive technologies: a call for greater transparency, reduction of a healthcare disparity and single embryo transfer to improve outcomes for mothers and babies.

### **BACKGROUND:**

The development of Assisted Reproductive Technologies (ART) is credited to the Dr. Patrick Steptoe and Dr. Robert Edwards (a Nobel Prize Recipient) who developed technology leading to the world's first "test-tube baby," a scientific breakthrough that has led to the conception of 5 million babies worldwide (1). In the United States, ART is responsible for approximately 1.4% of all infants born annually (2). While there are many unanswered questions regarding the outcomes of infants conceived outside the womb, ART and related pharmacologic ovarian stimulation has permitted children to be born to many welcoming families who would otherwise be unable to conceive due to infertility.

Infertility and subfertility are defined by various entities as failure to conceive after unprotected intercourse for one year or more (3). There are many factors that contribute to infertility in both women and men. In addition to a variety of medical factors, there are social, economic and personal pressures, as well as life circumstances that contribute to the decision of many woman and men to reproduce later in life. If the decision to delay parenthood is a personal choice, it should be done with a full knowledge and understanding of the consequences of delaying reproduction. Physicians and other health professions should begin to discuss fertility preservation early during an adult's life and help young women and men to understand all options regarding childbearing. (4). Infertility in both men and women contributes to anxiety and grief and should be recognized as a medical issue. It is the ethical responsibility of physicians and society to provide available solutions and offer support to those experiencing this life crisis (5).

There have been considerable medical and ethical concerns about the generally unregulated expansion of ART, including the use of surrogacy, international medical tourism to seek less expensive access to these technologies, and the exploitation of women in less developed countries as gestational carriers for embryos conceived in the U.S. and taken abroad. Because the use of ART is largely unregulated, there is wide variation on how the technologies are used. Although guidelines are available, compliance is purely voluntary and the

transparency of some ART practices has been questioned. A workshop of the Eunice Shriver National Institute of Child Health and Human Development in 2007 regarding Detection, Prevention, and Management of Infertility (6) developed the following recommendations:

1. Emphasis of Assisted Reproductive Technologies should be on the birth of healthy infants primarily using elective single embryo transfer.
2. Counseling of prospective parents using ART should be in a nondirective manner and provided well in advance of any invasive procedures, as well as in a relaxed and unrushed environment.
3. Couples should be informed of treatment risks and pregnancy rates, as well as of adverse pregnancy/birth outcomes for which well-documented outcome data exist (i.e. multi-fetal gestation, number of embryos transferred, congenital anomalies [including imprinting disorders], and other genetic abnormalities [parental risk factors and the use of prenatal diagnosis]).
4. Couples should be informed of maternal risk factors including increased risk for preeclampsia and risks of multi-fetal gestation, including requirement for cesarean delivery among others.

It is estimated that 36% of twin births and 77% of triplet and higher-order multiples in the United States were attributable to medically assisted conceptions. Kulkarni et al recently summarized their findings that the high incidence of multiple births in the U.S. is a consequence of two factors; 1) increased rates of advanced maternal age at delivery and 2) increased rates of fertility treatments. Some providers have begun to recognize this trend and have decreased the number of embryo transfers involving three or more embryos during IVF. These changes have resulted in a 33% decrease in the proportion of triplet and higher-order multiple births attributable to IVF since the peak rates in 1998 (7). Many IVF providers, however, have not adhered to professional guidelines regarding the number of embryo transfers. It is clear that reducing the rate of multiple-embryo transfers must be of the highest priority if we are to successfully reduce the rate of multiple births and the associated risks of prematurity and low birth weight.

Ovarian induction and hyperstimulation are also leading causes of multiple births according to Reynolds and colleagues who evaluated non-IVF fertility treatments from 1997-2000 (8). Guzik and colleagues also evaluated women who underwent ovarian superovulation and intrauterine insemination and found a large proportion of pregnancies resulted in multiple births including twins, triplets, and quadruplets (9). A clinical shift from ovarian hyperstimulation to elective single embryo transfer after IVF is likely to lower the unacceptably high rate of multiple births in women utilizing ART.

Dr. Eli Adashi, former President of the American Gynecological and Obstetrical Society declares that while “alleviation of barrenness [is] a laudable goal .multiple gestation challenge by its very nature is a public health issue,” and “our ultimate, if not immediate goal is clear: healthy singleton births.” (10). He champions the concept that “the last disabled child should be born” by using artificial reproductive technologies. Canadian ethicists Raymond Lambert and Marcel Melançon have stated that protection of the vulnerable is a physician’s moral and ethical responsibility, and that physicians are responsible for risk reduction or prevention when future generations are at stake”(11).

Prospective mothers and fathers may benefit from the experience of others who have undergone ART procedures. George J. Annas, Professor of Health Law, Bioethics and Human Rights at Boston University has suggested the book “Cracked Open” by Miriam Zoll (12), described as a compelling narrative that speaks for a generation of women who, like the author, delayed parenthood only to find themselves unable to conceive a

child using all of the benefits of contemporary reproductive science. As summarized by obstetrician and gynecologist, Dr. Christiana Northup, “the brave new world of ART isn’t nearly as rosy as we’ve all been led to believe.” (13).

Law Professor Michele Goodwin at the University of Minnesota and Judy Norsigian have described the “raw and debilitating physical, emotional and spiritual challenges created by deeply personal and life-altering procedures” experienced by some women seeking ART and support the need for additional regulation (14). In addition to the invasive processes involved in conception, the ethical quandary created by a recommendation for fetal reduction and the emotional toll on women and couples may be profound and is incompletely studied. Professor Goodwin asserts there is a “much needed public discourse that could also become the clarion call for regulation of a field of medicine that has thus far unsuccessfully regulated itself.”

## **STRATEGY**

**1) Pregnant women should receive informed consent before using ART. Note: While it has been argued that infertility itself bestows the additional risks of prematurity and birth defects, it is evident that the use of ART adds to these risks.**

- a) Informed consent should be required in every jurisdiction and should communicate information in appropriate language that conveys the relative risk or odds ratios of prematurity, low birth weight, birth defects and imprinting disorders with respect to each procedure including ovarian hyperstimulation, intrauterine insemination (IUI), in vitro fertilization (IVF), or intracytoplasmic sperm injection (ICSI).
- b) The most current data available from peer reviewed research and meta-analysis should be used when conveying relative risks and odds ratios.

**2) Prospective parents should receive counsel from a multidisciplinary team prior to initiating ART.**

- a) Multidisciplinary teams should include representatives from maternal-fetal medicine, genetics, neonatology and psychology.
- b) Thorough discussion of the potential emotional and economic costs of having a premature and/or low birth weight infant or infant with birth defects should be offered and documented. Grief counseling should be available to address issues related infertility.

**3) Prospective parents should be counseled regarding the need for adequate health insurance to assist if the pregnancy results in a child with special needs.**

- a) The well-documented higher rate of multi-fetal gestations, premature births, low birth weight infants, and a higher risk for selected birth defects (15, 16, 17) and imprinting disorders (18, 19) often results in substantially increased costs of neonatal intensive care for infants.
- b) This can lead to unforeseen economic burden for parents without adequate insurance coverage.

**4) Pregnant women using ART should receive comprehensive obstetric care.**

- a) Comprehensive care should include immediate access to specialists in Maternal- Fetal Medicine

b) Proximity to a Neonatal Intensive Care Unit should be ensured to maximize optimal birth outcomes.

**5) Insurance companies should pay for evaluations of women and men presenting with infertility. Note: Current access to ART services in most states is primarily for those with sufficient resources to pay out-of-pocket and excludes many from seeking medical help for infertility.**

**6) Insurance companies should pay only centers that meet professional standards.**

a) Professional guidelines, such as those published by the Society for Assisted Reproductive Technology, should be followed by centers receiving third-party payment.

b) This should include the substantial preference for elective single embryo transfer (20).

**7) Insurance companies should pay only centers that provide annual reports to the Centers for Disease Control and Prevention. Note: Current reporting of fertility clinic outcomes is voluntary under federal law.**

a) Reports should include number of pregnancies per patient, number of cycles required for pregnancy with live birth, infants born per cycle, birth weights, gestational age, multiples or singletons, congenital/genetic abnormalities and additional costs for infants born with special needs.

b) In unique circumstances when more than a single embryo transfer is desired, prior approval from insurance companies should be a requirement for coverage.

**8) Prospective parents and surrogates should receive independent legal counsel.**

a) Contractual arrangements should be performed prior to in vitro conception embryo transfer.

b) As the procedure for legalization of intended parents is a legal proceeding, ideally the gestational carrier and intended parents should reside in the same jurisdiction and be subject to the same legal due process.

**9) Agencies who represent women wishing to be compensated for being a gestational carrier should be governed by State regulations.**

a) Financial transactions between intended parents and surrogates should comply with federal and State taxation regulations.

b) All parties should adhere to State privacy rules.

**10) “Medical tourism” for the use of surrogacy abroad should be discouraged.**

a) Citizens of another country seeking surrogacy in the United States should be discouraged.

b) Surrogacy using a family member may be an acceptable exception.

**11) State regulatory agencies who license and provide oversight for collection and use of human tissues should provide the same level of oversight for sperm banks, the selling of human eggs and egg “donation.” Note: A bill permitting the selling of oocytes for in vitro fertilization and use in ART or research was recently vetoed by Governor Brown in California. This legislation would have made**

**human eggs just another commodity to be bought and sold.**

## **CONCLUSIONS**

The National Perinatal Association advocates the position that greater public awareness and professional transparency should assist prospective parents in making informed decisions regarding their potential choices in seeking ART as well as their options involving adoption of the many infants already born who are in need of loving parents.

Studies are urgently needed regarding every aspect of ART, including neurodevelopment outcomes, school performance, and differences in the incidence and onset of adult diseases when conceived using ART versus naturally. As with other technologies that may impact the human genome through epigenetic modification, continued research into the influences of emerging technologies on the health and well being of the infants born should be a national priority.

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