THE ETHICS OF ASSISTED REPRODUCTIVE TECHNOLOGY

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Summary

Assisted Reproductive Technology (ART) generally is divided into three fields (gametes [spermatozoa and oocytes], embryos, and third party reproduction). These topics can be subdivided into such techniques as husband insemination, in vitro fertilization and embryo transfer, gamete intrafallopian transfer, and zygote

intrafallopian transfer. In addition, these aforementioned methodologies also can be used with donor gametes making it third party reproduction. There are other topics of interest that fall within the purview of ART that include human immunodeficiency virus, stem cell research, preimplantation genetic diagnosis, adoption, and rights of children. A general discussion of each of these topics is included in this narrative as well as the ethics that are involved with each of these topics. Furthermore, the pros and cons of each of these topics are offered as well as the medical indications for the use of each of these methodologies, research that is still needed in each of these areas and general references, should the reader desire further knowledge on any of these specific topics.

1. Gametes

1.1. Ethics as It Relates to Gametes

Gametes (sperm and oocytes) belong to the individual and it is the individual's right to decide the fate of these cells. An individual can have "fertility insurance" by preserving his or her gametes via cryopreservation. With cryopreservation, testicular or ovarian cancer patients have the potential to become a parent (to many having children is the most important contribution to society). While it may sound simple to those who do not have reproductive problems, to those who are infertile, cryopreservation becomes a huge benefit. It is about personal rights to parenthood. However, one has to weigh rights of the provider with rights of those to come.

While one must respect a person's autonomy, individuals within each ART center must keep in mind the good of society, and, as the Hippocratic oath states, "…never do harm to anyone." If one takes "anyone" to mean future generations, then personnel in ART centers must look beyond the present individual and consider the potential future generation. Thus, even a practice with a strong ethic to treat all persons in need must have the right, under physician and professional autonomy, to withhold treatment when deemed necessary.

It may be the right of a 22-year-old female to cryopreserve her oocytes until she is 60 years olds and then use these oocytes to have a child, but one must weigh this autonomy with the potential offspring in mind. Is it in the best interest of the offspring to have a mother who has a significant chance of dying before the child reaches adulthood?

It may be the wishes of the spouse of a deceased partner to have a surgeon aspirate her partner's sperm from his testicles upon his death so that she might have a child with her partner's genes. However, is it ethical to produce a child without someone's permission even if that someone is deceased? Furthermore, a child born from a conception after a man's death may not be legitimate or entitled to the man's inheritance. At the least, the child is born with the burden of having lost one genetic parent.

With oocyte cryopreservation comes the potential for a similar scenario for the male partner of a deceased female partner. It is not without possibility that, in the near future, if a woman dies in an accident, her partner could ask an ART program to cryopreserve immature oocytes from the deceased woman's ovaries with the anticipation of having

offspring from the deceased female partner. The legal issues that the author described in the previous paragraph now apply to the child from the deceased "mother." In addition, because the male partner needs a "surrogate" uterus to achieve a pregnancy, additional issues come into play.

If gametes (sperm and oocytes) are frozen before death in anticipation of their being used for procreation, partners of the deceased have fewer complications. However, if surgeons have to retrieve gametes after death and no directives exist to indicate wishes of the deceased, then the Ethics Committee of the American Society for Reproductive Medicine indicates that this scenario need not be honored.

With the development of cryopreservation techniques comes more potential for parenthood. In the last thirty years, the number of sperm banks has increased to meet the increased demand for this particular gamete. However, with this increased demand comes a concern that men could be exploited or coerced into providing semen specimens, especially if exorbitant fees are paid. Therefore, sperm bank personnel keep the payment for this renewable resource to a minimum (approximately $50), with the idea that the cost helps offset the man's time and expenses (e.g., travel).

Harvesting of donor oocytes, unlike that of donor sperm, is a relatively new technique and requires more time, hardship, and expense. Therefore, the cost for this nonrenewable resource becomes much greater than the cost for donor sperm. However, the same financial concerns are still in place for the female just as they are for the male. How much is a woman paid for her oocytes before the payment becomes more than a charitable gift? Obviously, most ART center personnel think that a minimum amount of money needs to be paid for a woman's time and expenses, just as for a man's, but is $2,500 enough and $10,000 too much?

While donor sperm and donor oocytes may be considered "anonymous" in most cases, the fact that health issues now revolve around genetics makes it more likely that "anonymous donation" will become a thing of the past. Children from an "anonymous" donation, whether it is sperm or oocytes or both, will soon voice their right to know their genetic background. Cures will be based on genetic information, so individuals may coerce or manipulate the "anonymous donor" into a loss of anonymity for the sake of the child.

Research on cryopreservation of oocytes is limited. While much of the above information is applicable for cryopreservation of human spermatozoa, one must remember that cryopreservation of human oocytes has not been perfected. In 2003, a review of literature indicates that, while babies are being born from cryopreserved oocytes, numbers are small and the ratio of oocytes frozen to babies born is low – 1.8% (13 babies/737 oocytes) and 5.6% (5 babies/90 oocytes). Furthermore, no long-term outcomes exist for the few babies already born. Because there is a lack of scientific data, medical organizations do not recommend cryopreservation of oocytes for routine use; it should be considered only for a patient who is undergoing chemotherapy and only then if the patient is under a research protocol approved by an Institutional Review Board. Currently, ovarian tissue cryopreservation is even less successful than oocyte cryopreservation (no human offspring have been born from its use). Therefore, medical

organizations do not recommend ovarian tissue cryopreservation except in rare cases.

In summary, ethics surrounding the use of gametes revolves around autonomy, benevolence, and justice for all parties involved. With the advent of new forms of biotechnology, all three of these principles are testing boundaries of our current ethics and will require flexibility from all who are involved.

2. Embryos

2.1. Ethics as It Relates to Embryos

What is an embryo? According to *Dorland's Illustrated Medical Dictionary*, a human embryo is a "…developing organism from the fourth day after fertilization to the end of the eighth week" and then it becomes a fetus. The writers for *Dorland's* call the first three days of cellular development "preembryos." In contrast, *Webster's New World College Dictionary* defines a human embryo as the early stages of its development, "… from conception to about the eighth week." It is obvious from these two varying definitions that individuals do not agree on what an embryo is.

In their attempt to determine where life begins (and ultimately what had to be protected under law), the British government established the Committee of Inquiry into Human Fertilization and Embryology and selected Dame Mary Warnock as chair. The committee decided that up to 14 days after fertilization, cells were "pre-embryos" and did not need to be protected. The American Society for Reproductive Medicine (ASRM) adopted this term and then defined an "embryo" as a "developing organism from two weeks after fertilization to the end of the seventh to eighth week."

Regardless of the exact definition of a human embryo or where life begins, this book focuses mainly on early cellular development before implantation – the first six to seven days of development. These first six to seven days are before implantation or the onset of the notochord (the rudimentary beginning of the spinal cord that includes the brain) and almost two months before one would consider the structure a fetus.

The most adamant and derogatory response to the in vitro development of embryos came in 1987 from the Vatican in a document titled "Instruction on Respect for Human Life and Its Origin and on the Dignity of Procreation." The document recognizes the good of the human person and the role of science and medicine to help obtain the good of human beings; it cautions individuals not to reject all new technology and recognizes the suffering of childless couples. After having made these statements, the document denounces all forms of reproductive technology to assist couples in becoming pregnant. (One exception is gamete intrafallopian transfer, provided the husband collects his semen in a specialized condom and the male and female gametes never come in contact with one another until they are inside the reproductive tract.) The Vatican advocates making it a crime to perform artificial insemination with a partner's sperm, conducting any form of in vitro fertilization, performing research on the embryo (except for therapeutic reasons and only if not disproportionately risky), or using donor or surrogate aid.

Contrarily, the Ethics Committee of ASRM finds artificial insemination and basic in vitro fertilization with a partner's sperm or donor sperm ethically acceptable, provided that medical specialists follow particular precautions and guidelines. Furthermore, the committee sees that research with embryos is ethically acceptable if medical personnel follow approved policies and guidelines. This same committee finds it disturbing that laws should be made without supportive scientific data. Besides, in the United States, the Constitution protects the rights of privacy of an individual as fundamental, and these rights include privacy pertaining to the right to procreate. The British government put a similar scenario in place under HR Act, Article 12.

If one looks at the science of how a child develops, one has to start with the haploid state for the sperm (23 chromosomes) and the oocyte (23 chromosomes). Steps that change these two haploid gametes into a diploid (46 chromosomes) entity are continuous. Likewise, so is the development once the oocyte is fertilized (zygote). For the sake of explanation, discussion, and understanding, scientists define specific events along the way from the haploid states to the child. Such states include zygotes, embryos, fetuses, etc. However, none of these states simply stop and another simply starts; the process is continuous. Thus, to say that one particular moment is the point at which life begins or in which the soul enters this group of cells seems impossible.
As the haploid state turns to a diploid state and development ensues, concerns and moral values increase. There is little objection if laboratory personnel discard excess sperm or oocytes, but the disquieting consequence over discarding cells increases as cells increase in number and diversity. A pluralistic society such as the one that exists in the United States allows individuals to weigh their beliefs and decide for themselves the point at which this disquietude becomes too great for them to accept discarding these cells. Another way to state this is that most of us will assign some special status to this group of cells, but eventually we will shift the designation from "special status" to "full moral status." However, except for the Vatican's document, no other large, organized body appears willing to give full moral status to the embryo.

During the 1980s, individuals discussed, in great detail, the ethical issues surrounding basic Assisted Reproductive Technology (ART) procedures (e.g., in vitro fertilization, gamete intrafallopian transfer, zygote intrafallopian transfer)[8] and, for the most part, accepted them by the beginning of the 21st century. However, as new technology emerges, ethical issues that relate to these new advances also surface. Three techniques that deal directly with the embryo, which still have major issues surrounding them, are embryo splitting, embryo cryopreservation, and intracytoplasmic sperm injection (ICSI).

In the 1980s, individuals in the livestock industry bisected or even quartered embryos in an effort to produce more offspring, mainly calves. While the news media considered this cloning, in reality it was only embryo splitting because no direct manipulation of the genetic pool (genome) took place. Embryologists could mix embryo splitting with preimplantation genetic diagnosis (see Section 4.3) to produce a child. In such an instance, an embryologist could split a blastocyst that was diagnosed as free from a specific genetic disease and a physician could transfer both halves (demi-embryos). (Data indicate that pregnancy rates increase when physicians transfer two or more embryos.) This would be helpful especially if the couple has only one embryo that is

diagnosed free from a specific life-threatening disease.

The main ethical problem in splitting embryos is whether the progenitors request that the physician transfer one demi-embryo, while the embryologist retain the other demi-embryo (by cryopreservation) for later use (as a source for stem cells to replace damage or diseased organs), after the first offspring is born. While this scenario is realistic and leads to philosophical and psychological issues for all individuals involved, medical personnel can easily remedy this scenario by mandating that the physician transfer all demi-embryos at one time.

While the concept of saving embryos through cryopreservation sounds like a good idea, pitfalls do exist. For those individuals that think that life begins at conception, when the embryologist cryopreserves embryos, life is put on indefinite hold. However, if the physician prohibits embryo transfer at the regularly scheduled time (hyperstimulation of the patient) or if excess embryos exist after transfer, cryopreservation does offer the opportunity to preserve embryos for use at a later time.

One of the major problems with cryopreservation of embryos arises when couples leave embryos unused and unclaimed (abandoned). The Ethics Committee of the ASRM recommends that every ART Center address this issue in their consent forms before the start of oocyte retrieval. Patients need to have written instructions as to the fate of their cryopreserved embryos in case of death, divorce, separation, failure to pay storage fees, inability to agree on disposition, or when the patients fail to contact the storage facility. The Ethics Committee of the ASRM has stated that the ART center that stores a couple's embryos does not have an obligation to store these cells indefinitely and as such can, after an appropriate length of time of abandonment, discard these cells. The Committee designated this length of time to be five years. However, these cells, destined for disposal, cannot be donated to other couples or used for research. Perhaps John D. Biggers said it best, "… that very early embryos may not have the same moral value as older fetuses, and that the spare unused embryos were at least necessary to ensure the birth of a healthy baby."

Intracytoplasmic sperm injection does present some ethical considerations of interest. Nature has a built-in mechanism to ward off many genetic problems that could arise simply with the development of the construct that it takes millions of sperm to traverse the female reproductive tract and penetrate the support cells to the oocyte. From there a single sperm must penetrate the thick shell of the oocyte (called the *zona pellucida*) and the subsequent membrane to get to the cytoplasm, the site of fertilization. The mechanical technique of ICSI circumvents this entire process and allows a man with few sperm to fertilize an oocyte.

Often the reason for producing so few sperm is genetic in nature and so ICSI allows for poor genetic traits to continue unfettered as opposed to Nature's way to only permit the fewest genetic defects ("strongest") to propagate. Long-term follow-up of children produced with the use of this relatively new technique is being conducted and the results compared to more conventional in vitro fertilization and to naturally conceived children. Thus far, the data indicate that ICSI is a safe procedure with an acceptable level of risk. However, ICSI patients may have an elevated level of inherent risk for some disorders.

In summary, our pluralistic society honors individual liberty and privacy above all else, no matter how we define a group of cells or how we try to determine when and how much respect/moral status to assign these cells. In the end, it is a personal issue for those involved with the ART procedure.

3. Third-Party Reproduction

3.1. Ethics as It Relates to Donor Spermatozoa

A number of issues are linked to the use of donor sperm. The weakest part of donor sperm usage is the lack of proper record keeping. If society deems it necessary to control the number of offspring produced by a single donor and if organizations such as the American Society for Reproductive Medicine (ASRM) cannot or do not wish to tighten controls, it may require federal intervention.

Before the patient uses donor sperm, the semen donor should undergo rigorous screening and selection. This process should reduce the risk of psychological and physiological problems. If screening is not undertaken, the donor sperm could be obtained through manipulation and undue influence.

When family members donate the spermatozoa, ethical issues magnify greatly. In such a scenario, incest is a concern (sexual relations between two closely related individuals), as is consanguinity (reproduction between two closely related individuals), or even the appearance of such situations.

Often the rationale for intragenerational and intergenerational arrangements is to preserve the family's genetic inheritance, reduce the risk of genetic or sexually transmitted infections, reduce the time, or reduce the cost. While the Ethics Committee of ASRM does not think that many of these familial combinations are unethical, it does not condone relationships in which offspring would have the same genetic relationship to the parents as would children from an incestuous or consanguineous union (son-to-mother or daughter-to-father [this includes adopted children and stepchildren]).

What if there is a familial donor involved and what if the pregnancy is not successful; will there be anger directed towards the donor? Using the same scenario, what if the child is born with a birth or genetic defect; will family direct their anger towards the donor?

With familial sperm donations, other potential issues are brought about as well. A partner to the donor may have emotional problems with the donation of sperm to a relative. Likewise, the sperm donor may find it difficult to detach himself from the offspring. Furthermore, the offspring produced via donor sperm may become confused with the genetic link.

In the mid-1990s, there was a trend to more openness about sperm donation and to allow the progeny who request it more access to non-identifying information. However, this is a parental decision. On the one hand, perhaps offspring need to know their biological origin to complete their identity or their genetic information for health

reasons. Another rationale for telling children comes in the fact that if they accidentally find out, this will be more damaging than being told initially. In April 2005, The United Kingdom's Department of Health enacted a plan to enable children conceived through donor sperm to learn the identity of their biological father when they become 18 years old. Conversely, knowing such information may lead to psychological and social turmoil, especially if the children cannot find out more about their donors. Furthermore, it may be important for nondisclosure if family members do not approve.

One thing is for sure: if parents plan on telling the child about the donation, then the parents must inform the donor so he can decide if there is any risk posed by relinquishing privacy. About the release of information the donor and the recipient need to have similar expectations.

In summary, medical personnel intended donor insemination to be provided by an unnamed source; however, just as other reproductive techniques have evolved over time, so has donor insemination. It is no longer uncommon for a familial member to offer support in this area. Once individuals broach donor insemination (regardless of the source of the donor semen), all individuals involved have to be sure that the rationale for the donor's contribution is purely altruistic and that the child produced from such a donation will be exposed to minimal risk, physiologically as well as psychologically. Finally, lack of communication brings about new issues that must be resolved by parties involved before the use of such gametes.

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Biographical Sketch

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