Embryological Perspectives on Gamete and Embryo Donation

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ABSTRACT

This article addresses the issue of gamete and embryo donation from the perspective of the assisted reproduction laboratory, where the so-called “clinical” embryologists work making all the current variants of in vitro fertilization including the andrology laboratory, oocyte collection, conventional insemination or through ICSI, embryo culture, gamete and embryo quality evaluation, embryo transfer, cryopreservation of gametes and embryos, preimplantation genetic studies, results analyses and quality control, assessment and improvement. To think that the responsibility of an ART laboratory only attains the strictly technical or logistical areas is an error or a simplification that excludes embryologists from other important matters. Clinical embryologists have the obligation to ensure that procedures follow strict ethical rules, highlight deviations or errors from these canons, and refuse to act in cases of violation of said standards. Donating embryos to assist in others’ efforts on building a family is an important option for patients who are considering the disposal of cryopreserved embryos, in excess those needed to meet their own fertility goals.

Gamete donation, a more widespread procedure, can help us to better understand certain aspects of embryo donation. Donation must be a free transaction, not influenced by guilt or any other type of pressure or coercion of any kind.

We are facing a totally new issue because we are the only species on the planet that can manipulate our own gametes and embryos in a context where assisted reproduction represents a dramatic challenge to the social values that govern our way of being born, without precedent in human history.

KEYWORDS: Fertility, Embryology, Laboratory, Bioethics.

MANUSCRIPT

The International Glossary on Fertility and Infertility Medical Care, agreed upon by the main fertility societies in the world and published in each of their scientific journals in 2017 [28], establishes that the embryo donation for reproductive purposes is an assisted reproduction treatment (ART) cycle that consists of the transfer of an embryo resulting from the union of gametes that did not originate from or are not 1

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specific to the woman who receives that embryo or her male partner, if any.

The definition seems obvious but the clarification "if any" places it in another arena: it refers to the new infertility definition also provided by this consensus: "a disease characterized by the impossibility of achieving a clinical pregnancy after 12 months of regular sexual intercourse and without protection or by a person’s inability to reproduce, either as an individual or with his or her partner. Infertility is a disease that produces an inability due to an impediment of the reproductive function".

It is then clear that the "recipients" of an embryo-donation can be the partners made up of a woman and a man, two women, two men or a woman or a man. Assisted reproduction with third party intervention (that is, people other than those who wish to reproduce) has made it possible for infertile people to have more options when it comes to starting a family. That is medicine: in the face of the wonderful but severe nature (Darwin called it the nature of bloody teeth and claws) we oppose vaccines to diseases, crops to hunger and, in our case, assisted reproduction to infertility and forms of reproduction that do not follow the traditional canon of a man, a woman and two children (one of each sex, if possible...).

This modern definition coincides with the Pronouncement of the Inter-American Commission on Human Rights regarding the "Costa Rica Case", a country that prohibited assisted reproduction techniques (Artavia Murillo et al. Case - In Vitro Fertilization - Vs. Costa Rica, http://www.corteidh.or.cr/cf/Jurisprudencia2/ficha_tecnica.cf m?nId_Ficha=235):

- Infertility is a disease. The prohibition of assisted reproduction is discrimination.
- Reproductive rights are human rights.
- The embryo is not subject to the right to life as people are. Access to rights is a gradual process and is not established immediately after fertilization.
- The woman is the right holder, not the embryo.

This article addresses the issue of gamete and embryo donation from the perspective of the assisted reproduction laboratory, where the so-called "clinical" embryologists work making all the current variants of in vitro fertilization including the andrology laboratory, oocyte collection, conventional insemination or through ICSI, embryo culture, gamete and embryo quality evaluation, embryo transfer, cryopreservation of gametes and embryos, preimplantation genetic studies, results analyses and quality control, assessment and improvement. To think that the responsibility of an ART laboratory only attains the strictly technical or logistical areas is an error or a simplification that excludes embryologists from other important matters. Clinical embryologists have the obligation to ensure that procedures follow strict ethical rules, highlight deviations or errors from these canons, and refuse to act in cases of violation of said standards.

Donating embryos to assist in others’ efforts on building a family is an important option for patients who are considering the disposal of cryopreserved embryos, in excess those needed to meet their own fertility goals. Another way to receive donated embryos is through their in vitro origin after the double donation of oocytes and sperm, a procedure that raises ethical questionings different from those stated herein [19]. The embryo donation cannot be equated to the adoption of minors because the embryos are not simply minors. It is important to use the appropriate terminology to refer to this procedure. The use of the term "adoption" for embryos is inaccurate, misleading, and could place an inappropriate burden on infertile recipients. Since adoption refers to a specific legal procedure that establishes or transfers the parentage of existing children, the term donation should be used for embryos [9]. The adoption of girls and boys is another important option available to help women and men who want to start their families, also providing loving homes for those in need [9].

Neither a zygote (a fertilized oocyte that shows two pronuclei) nor an embryo are "minors" [15,13,12] mainly because:

- They have individual cells that are too independent to constitute an individual.
- They lack a structured constitution.
- They are a cluster of cells (embryonic tissue) that can potentially develop into a new individual, or into more than one individual, as in the case of a set of twins. [27] demonstrated this potential by dividing 4-cell embryos into 4 parts on day 2 (placing 1 cell in each of the 4 receiving zonas pellucidas, emptied of their original cells), originating 4 blastocysts at the sixth development day.
- They can generate a tumor, a hydatidiform mole or a chorioepithelioma, and not a person.
- An embryo generally carries several genetic abnormalities that cause many embryos to fail implantation or, if they do so, to be lost very early in their development.
- Depending on maternal age, between 40 and 90% of “good quality” embryos have been reported as aneuploid [18].
However, embryos deserve a “special status” between simple cells and human beings, being an entity that can potentially develop into a person [6]. Moral philosophers have argued about the moral status of the human early embryo as a “special entity, an intermediate stage between an object and a person, which deserves respect and protection but which can be used for research, therapeutic purposes or be destroyed if it is not going to develop into a child” [5,11]. The human embryo deserves greater respect than other human tissues because of its potential to become a person and its symbolic value to many people. However, it cannot be treated as a person because it still has not developed its characteristics as an individual, it still has not established itself as an individual, and may never develop its biological potential [7] We are holders of a deep moral intuition that tells us that human embryos are not just things, they are something more than the sum of sperm and oocytes or a simple accumulation of cells, and they shall not be treated as products or commodities (raw materials). Clinical embryologists must know that in ethics language is never neutral: there is a big difference between the fact of feeling owners of a life and the fact of having been entrust a life in custody (which will potentially develop, or not, into a person) [21].

The use of embryos for therapeutic purposes is not the same as their use as if they were raw materials [1].

**Compensation**

The sale of embryos is then ethically unacceptable, and donors shall not be compensated for their donated embryos. However, it is legal for the clinic to charge a professional fee to potential recipients for embryo thawing, embryo transfer procedure, and screening of infectious diseases on both recipients and donors. Physicians and employees of an infertility clinic shall be excluded from participating in embryo donation (as donors or recipients) within said clinic.

Gamete donation, a more widespread procedure, can help us to better understand certain aspects of embryo donation. In procedures that involve egg or sperm donation, it is customary to financially compensate the donors (“loss of earnings compensation” for absences or “travel expenses”). This expense compensation often poses an ethical dilemma since, although the service offered by fertility clinics is far from being an event where rich women buy eggs from poor women, it is also far from being a mere compensation of expenses, since what to some people may be a “per diem” for expenses, to others it is certainly a salary. Participants in a symposium on ethical and legal aspects that took place in Buenos Aires in 2011 [2] were asked if they thought that it was a donation or a sale, since all the people who give their gametes to be used in the extraction of embryos receive financial compensation. About a third of those surveyed answered that it was a donation, a third said it was a sale, and the remaining third said they did not know or did not want to answer. When asked if they should be financially compensated in a different way according to the donor’s phenotype (that is, if it is not clear, that those with certain more socially “valued” phenotypes should be paid more), an 85% answered no but a 15% said they didn’t know. No one said yes, although some later commented that they usually did it that way at their workplaces.

In fact, an advertisement for an oocyte bank announces that its donors are “physically perfect and mentally healthy, without bad habits or vices” and that “they have a strong desire to share the happiness of being a mother with other women”, since most of them are mothers “of at least one healthy child”. Furthermore, the same clinic offers “VIP” egg donors, possessing “extraordinary beauty and high educational level”.

Thus, it is essential to be clear that:

- Both gamete and embryo donation must not be for profit or commercial purposes.
- Compensation must be intended to repair the physical discomfort and travel and labor expenses that arise from the donation; In no case can it be an economic incentive for the donor.
- Any advertising campaign or other activities, aimed at promoting the donation of tissues, gametes or embryos by authorized specialized centers, must respect the altruistic donation nature, and may not, in any case, encourage donation by offering financial benefits.
- The financial remuneration that exceeds the mere compensation for the donation of tissues, gametes and embryos, as well as the promotion or advertising that encourages the donation of cells, tissues and gametes by specialized health centers, authorized by offering compensation or economic benefits contrary to the provisions of law, shall be considered serious offences.

While The Practice Committees of the American Society for Reproductive Medicine (ASRM) and the Society for Assisted reproductive Technology (SART) advised in one of its most important guidelines (2008, then replaced by a new document in 2013) that vitrification was still an experimental technique, the proliferation of oocyte banks in the United States, the advertisements for apollonian men in sperm banks or “VIP” women in reproductive egg donation programs, or the cover stories in certain popular magazines where the interviewees answered as if they were providing cryopreserved oocytes for donation comparable to selling frozen asparagus or sardines, were clear.
examples of the misuse of things that cannot be sold, such as blood or transplant organs.

The concept res extra commercium derived from Latin ("something outside of commerce") is a doctrine originated in the Roman law that states that certain things may not be the subject of private rights and therefore, they can neither be sold or purchased. The donation must be a free transaction, not influenced by guilt or any other type of pressure or coercion of any kind. The use we give to language will play an important role in this decision-making.

Language

The first term that should be of concern to us is the one that we ourselves, embryologists and reproductive health doctors, have used in some occasions to refer to the biological structure that we are donating, and that we precisely did not know how to define. "Pre-embryo" was used along with "concept" (only in the United States) or "early embryo" to define the stage of development that occurs between the end of fertilization (zygote) and the emergence of the primitive embryonic line, from the 12th to the 14th day of life. From day 12-14 onwards, biological individualization is guaranteed, and we could then call it "embryo", and from the third month of gestation until birth, "fetus". While for some authors this term has been invented by some of them to avoid moral accusations or pressure from the tabloid press, for others "pre-embryo" is a "fabricated" term that no embryologist has approved and that no textbook uses.

Some national dignitaries that are critics of techniques that involve "human life" are epitomes of the Manichaean use of the language and do not blush when instituting "the day of the unborn child" or when attacking research work with stem cells derived from donated embryos (a technique that uses embryonic tissue in order to study how to improve the lives of millions of people suffering from incurable diseases), at the same time that carry out fraudulents casus belli (that is, an act or event that causes a war or is used to justify it) that brings about the loss of countless human lives, including many civilians, ignoring international humanitarian laws and international conventions, cutting off funds for critical social plans, while proclaiming to defend "a culture of life where the strong protects the weak and where we recognize the image of our Creator in every human life".

"Donation" is a gift without payment involved (a definition that is obvious) or, more specifically, the "liberality of someone who freely transmits something that belongs to him in favor of another person who accepts it". From Ethics, "Egg donation" then seems correct.

Another way to use language erroneously is through its "domestication". This is how a fertility clinic advertises its services on the local subway with drawings of a blue female bird, wearing a pearl necklace, a purse and outstanding eyelashes, and a kind of male bee (a drone) carrying an office briefcase. The drawings represent the following idea: "when the little bird and the bumblebee can’t have babies, turn to our clinic". We could think of a certain tendency to "infantilize" language, rather than domesticate it, but it happens that even a child knows that bees and birds do not procreate, and that, because of this, they are infertile among themselves. We should perhaps be less severe in our assessment and alternatively think that the clinic or those responsible for the propaganda have wanted to soften and provide a dose of humor to a topic that is thorny or painful for patients.

Other advertisements from some clinics that offer egg donation services seem to use language that is somehow between altruistic and childish. An advertisement says that donating oocytes is a "very small gift" (it doesn’t even say "small"), treating the donors as if they were girls who do not understand what the matter is about. Others say: "giving is the best way to receive; donate eggs"; "everything that is not given is lost; your eggs too... we will compensate your generosity"; "it pays me to donate eggs" and "it pays me to donate semen". What is it that you are going to receive, according to the advertisement? The thanks, the inner satisfaction for the altruistic duty fulfilled or simply money? "You are young and you have thousands of them... become an egg donor". She also has a lot of hair and could donate it to a wig factory. Surely, since you are young, you also have thousands of minutes left over, and you could donate them to another charitable activity. It is essential to notice the difference between donating eggs and donating hair, time, or money.

The way we handle certain altruism in our society has been masterfully revealed by biologist Robert Trivers, when he writes: "The proof that self-deception acts in the service of deception is the denial of deception, the unconscious management of selfish and deceptive tricks, the establishment of a public image that looks as if it was altruistic and as a beneficial and useful person to other people’s life".

On some occasions, the term “recruiters” has been used as slang to refer to those women, generally former donors, who in turn look for new donors. This unfortunately coincides with the negative opinion of certain general public and some members of the medical profession who see all this as something negative. This extreme distortion of the language in the form of jargon can be harmful and the only thing it achieves is that the donors’ efforts are not rewarded, that their genuine interest in helping is not recognized.
(although at the same time they feel that it is correct or necessary to be economically compensated), nor the good intention and performance of many professionals involved and that, in the end, those people who need to complete a family are harmed.

Embryo donation is not exactly the same, nor has it been handled by clinics or advertising in the same way, as gamete donation. The donation of oocytes or sperm is an individual act, in theory, independent. The decision to donate eggs or sperm could be influenced by the opinion of the donor's partner. However, the decision to destroy or cease the egg or semen cryopreservation is the exclusive responsibility of the person who originated those cells, never of his or her partner or other family members. Likewise, the act of donating embryos already produced in vitro and cryopreserved does not involve the woman in the same way: while one is subject to ovarian stimulation and undergoes surgery, the other only must sign a consent or, at most, agree to certain additional studies. Despite these significant differences, it is illustrative and instructive to relate both types of donations because the experience accumulated with gametes can shed light on a less frequent practice which, in general, we have less experience with. Furthermore, in the same way that there are "VIP" oocyte donors, there could also be "VIP" embryo donors.

Consent

Patients who decide to donate their embryos to other people or couples must clearly know their motivations and understand without confusions the meaning of what they are going to do. All embryo donors must sign an informed consent document indicating their authorization to use their embryos for donation. Couples who may potentially be embryo donors should be informed about all aspects of their medical treatment and the psychological and ethical issues relevant and inherent to embryo donation. Embryo disposal options should be discussed with their doctor prior to cryopreservation. Current options include:

- the future use of embryos by the couple through cryopreservation,
- the donation of cryopreserved embryos to other infertile couples,
- the donation of embryos for research, including stem cell research,
- the cessation of cryopreservation, which means the destruction of the embryos.

All potential donor couples should be notified that additional testing may be necessary if they choose to donate their embryos and, if necessary, offered psychological counseling. After couples have completed their own reproductive attempts, embryo disposition options should be reevaluated.

Informed consent is also essential for embryo recipients, who must take full responsibility for the embryo and any child or children who may result from the transfer. Recipients must release both the embryo donors and the assisted reproduction clinic from any liability for any possible pregnancy complication or other unforeseeable embryo donation complications.

By no means can a general IVF consent include the "fine print" formula that states that, when patients do not specify their embryo donation, it is then automatically interpreted that they do donate them. On the contrary, there must be a specific consent where all the details are clearly stated but not in small print.

In special cases in which the couple has not specified what to do with the leftover embryos and contact with them has been lost, or they have left the decision of what to do with them in the hands of the ART clinic, said embryos are called "abandoned" embryos[10]. These situations pose an indefinite storage problem to the ART clinic, including the space and cost that this implies. For these particular cases, it is important that the consent clearly states that the ART clinic can dispose of those embryos if no patient has contacted the clinic for a specified period of time even though the clinic has attempted to contact them, without success[10].

Then, the issue of what to do with these "abandoned" embryos arises. A clinic can choose to continue cryogenic storage indefinitely or discard the embryos. Given the legal uncertainty of these embryo status, many clinics around the world choose the indefinite storage. By no means could embryos be donated to other couples or given for research[10], since no one has agreed upon said intention.

The right to be informed

The right to be informed about genetic origins, and in particular the right to know that one was born through assisted human reproduction with donor gametes or donated embryos, is unavoidable, since every person has the right to know that he or she was born through assisted human reproduction with gametes or embryos from a donor.

Likewise, although donations are anonymous to guarantee the privacy of both donors and recipients, the right to know must also be guaranteed, since every person, who has been born through assisted human reproduction techniques with gametes from a donor, is of age and mature enough to request from the specialized center involved, information related to the donor's medical data, when relevant to his or her health.
The use of genetic platforms or panels to genetically explore the donors’ genome is a more distant possibility because the donors’ will is needed to undergo such studies (in the case of oocyte or sperm donors it is different because for some centers this is essential and the donor would be listed among the mandatory studies) and because the interpretation of these results may lead to confusion and baseless fears, such as studies for late-onset diseases [17]. In other words, beyond the essential and mandatory studies required before a donation, the rest is an area still under discussion. We are all mutants and, if we search information, we will find out that we all have some predisposition to suffer from something, mild or severe, serious, or benign.

Conclusion

We are facing a totally new issue because we are the only species on the planet that can manipulate our own gametes and embryos in a complete de novo way.

We know that males of some fish species can imitate females (changing color and behaving as them) and release their sperm exactly at the moment when true females are spawning, mixed among themselves. The territorial male believes that two females have laid eggs for him, but in fact he has been deceived: the “cross-dressing” male has inseminated the eggs before he has [4,25].

Although some fish like the one in the example and other animals may have behaviors that in some way represent a form of gamete manipulation, technology has allowed humans to do it much better than fish [8]. Within only 50 years we have gone from a reproduction system where conception was largely unpredictable, sex was closely related to conception and there was a natural inheritance of genes, to another where (at least in societies with access to technology):

- There are effective contraception methods and female independence from non-planned pregnancy,
- There are alternatives to natural reproduction,
- The offspring sex could be open to selection,
- Gene therapies could modify natural gene inheritance.

We find ourselves, then, in a context where assisted reproduction represents a dramatic challenge to the social values that govern our way of being born, without precedent in human history.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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