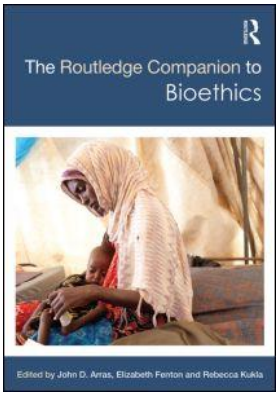


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## Human Embryos for Reproduction and Research

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# HUMAN EMBRYOS FOR REPRODUCTION AND RESEARCH

*Françoise Baylis*

## Introduction

*Ex utero* (i.e., extracorporeal) human embryos created by *in vitro* fertilization (IVF) are now widely used for reproductive and research purposes. Individuals or couples who are infertile or who are at risk of having a child with a genetic disorder can use IVF, with or without third-party gametes, to create embryos for reproductive use. In addition, individuals and same-sex couples who are not infertile, but who want a genetic link to their child, can avail themselves of this reproductive technology.

Typically, more IVF embryos are created per cycle than can reasonably be transferred in the cycle in which they were created. While practice differs between IVF clinics, in many countries the current norm is to transfer no more than three IVF embryos per cycle (unless there are sound clinical reasons to increase this to four or five), and increasingly there is a move towards single embryo transfer (which is now legislated in some jurisdictions). IVF embryos not transferred in the cycle in which they were created can be discarded; donated or sold for reproductive, teaching, or research use by others; or cryopreserved (hereafter, frozen) for later own reproductive use (provided they are deemed suitable for transfer). If, at some later date, these frozen IVF embryos are no longer wanted by the prospective social parent(s) (i.e., those who planned to care for the child(ren) born of IVF and embryo transfer), then they can be transferred to a third-party for their reproductive use; an IVF clinic to improve assisted human reproduction or to provide instruction in assisted human reproduction; or a research team to pursue basic science or clinical research. Not all human embryos used for research purposes are IVF embryos in excess of reproductive need. In some jurisdictions it is legal to create human embryos expressly for research purposes, using IVF or other technologies.

A brief review of some of the ethical issues associated with the reproductive and research uses of human embryos follows, but first, some (very) basic biology and terminology. In science, the term "human embryo" refers to the developing human organism from day 14 after fertilization is complete until day 56. Prior to 14 days, the developing human organism is, according to some, a pre-embryo. When a human egg is fertilized by human sperm a new cell, called a zygote, is created. The zygote contains genetic information from the egg and sperm providers. As this cell continues to divide it becomes a

morula, then a blastocyst, and only once implantation is complete (approximately 14 days after fertilization) is the developing human organism technically a human embryo. More commonly, however, in guidelines, regulations, and laws, the term human embryo refers to the developing human organism from the completion of fertilization (i.e., the appearance of the two cell zygote) until eight weeks' gestational age (i.e., 56 days). Potentially, however, human embryos need not be created by fertilization. For example, they could be created by parthenogenesis, somatic cell nuclear transfer (hereafter, cloning), single-cell embryo biopsy, and the reprogramming of somatic nuclei. In what follows, the term human embryo is used to describe the developing human organism from the time it is created (whether by fertilization or some other means) until it becomes a fetus at eight weeks' gestational age.

## The Moral Status of the Human Embryo

In the years surrounding the 1978 birth of Louise Brown (the first human born using IVF technology), debate on the ethics of this technology focused primarily on the moral (and legal) status of the developing human embryo, including the right to life. In many respects, this early debate mirrored the abortion debate insofar as one's view on abortion typically informed one's view on the moral status of the IVF embryo, despite there being important differences in developmental stage (embryo versus fetus) and location (outside or inside the woman's body) (Robertson 1986). Particular attention was given to religious claims about ensoulment, philosophical claims about potentiality and personhood, and biological claims about human development.

For some, the developing human embryo "from the moment of conception" has the same moral status as all other humans (be they infants, children, or adults). This view is defended in particular by the Catholic Church. In the 1987 *Instruction on Respect for Human Life in its Origin and on the Dignity of Procreation (Donum Vitae)* the Church reaffirmed its view that "[h]uman life must be absolutely respected and protected from the moment of conception" (Congregation for the Doctrine of the Faith 1987). From a secular perspective, similar arguments have been advanced on the basis of human origin and potentiality. The human embryo is undeniably of the species *Homo sapiens* and it has the potential to become what everyone recognizes as a human person with full moral status—provided the embryo is of "good quality" and placed in a physiologically receptive uterus. Proponents of this view believe that with the completion of fertilization there is protectable human life. Many scientists, however, suggest that fertilization is "only incidental to the beginning of life" as there are other processes from which humans could potentially develop, including parthenogenesis and nuclear transfer, and that "potentiality for life must therefore reside in the unfertilized egg and all of its precursors" (Edwards 1974: 13).

For others, the developing human embryo is just human material; it is a collection of cells, similar to skin, blood, bone marrow, and other bodily tissues; it has no moral status. Rather (in)famously, Helga Kuhse and Peter Singer (1990) have compared the early human embryo to a lettuce. Proponents of this view insist that species membership (i.e., genetic humanity) is neither necessary nor sufficient for moral status. Personhood is a sufficient condition for moral status, but not all humans are persons, and not all persons are humans. Persons are beings to whom we have moral obligations; they are beings endowed with rights, dignity, and value. Sentience (the capacity to feel pain), rationality (the powers of reason), and relationality (being part of a particular social and

biological community) are among the criteria that have been proposed for assigning moral status (Warren 1998; Strong 1997).

Between these extremes (of full moral status for human embryos on the one hand and near complete disregard for human embryos on the other) are those who believe, for different reasons, that the developing human embryo has special moral status, but not the same moral status as a full-fledged person. The proponents of this view maintain that the human embryo is deserving of "profound respect" but that such respect does not preclude the use of human embryos for reproductive and research purposes when the anticipated benefits outweigh the harms of embryo death and destruction (Ethics Advisory Board 1979a). The United States National Institutes of Health Human Embryo Research Panel, for example, concluded that "the preimplantation embryo warrants serious moral consideration but not the same as that due infants or children" (National Institutes of Health 1994: 50). In support of this view, the Panel noted "[t]he very high natural mortality, the absence of developmental individuation, the lack of even the possibility of sentience and most other qualities considered relevant to personhood" (National Institutes of Health 1994: 50). Others, however, insist that the hoped-for benefits in scientific knowledge and human health do not justify the wholesale destruction of human embryos. They note that a majority of the human embryos used for reproductive purposes will not survive, and typically all of the human embryos used for research purposes either will be destroyed during the course of experimentation, or will be destroyed thereafter owing to prohibitions on the transfer of human embryos that have been the subject of experimentation so as to avoid harm to future offspring.

Against this backdrop, and in an effort to side-step the intractable debate about the moral status of the developing human embryo, some have suggested that human organisms created through the reprogramming of somatic nuclei, parthenogenesis, cloning, and altered nuclear transfer would be different in kind and moral status from human embryos created by joining egg and sperm and thus could be used for research without any moral qualms (for a summary overview, see Baylis 2008; Green 2007). Others contest such claims. They insist that human origin and potentiality, not the means of creation, determine moral status.

An important feature of the contemporary debate on the moral status of the developing human embryo is the unwavering attention to the physical/material properties of the embryo as if there were biological facts about the embryo amenable to discovery that would authoritatively resolve the moral status debate. This is not so, however, as the debate is ultimately about values not facts.

## Reproductive Use of Human Embryos: Beyond the Moral Status Debate

With the development of IVF technology and *ex utero* access to the developing human embryo concerns about procreative liberty (and marital privacy), potential harms to embryos manipulated outside of the body, informed choice, equitable access to reproductive technologies, resource allocation, slippery slopes, and impact on the family were added to early concerns about the moral status of the human embryo (Ethics Advisory Board 1979b). Concerns about procreative liberty focused on the right to reproduce and found a family. Concerns about potential harms to embryos focused on the risk of congenital defects as a direct result of *ex utero* manipulation, and on the potential for long-term physical and psychological harms to children born of IVF and embryo transfer.

Concerns about informed choice focused on the obligation to disclose the potential harms of IVF and embryo transfer to improve reproductive decision-making, and on the importance of ensuring voluntariness. Concerns about access focused on discrimination, typically on the basis of marital status and sexual orientation, as originally IVF and embryo transfer were limited to lawfully married couples. Concerns about resource allocation—a thorny issue in countries with government-funded health care systems—focused on whether to include IVF and embryo transfer in the basket of services paid for by the state, given competing health care priorities. Concerns about slippery slopes focused on the possibilities of surrogacy (hereafter, contract pregnancy); undesirable genetic interventions (e.g., cloning to produce children or for biomedical research), altering the cellular and genetic composition of embryos, and creating part-human hybrids and chimeras; and the commercialization of reproductive materials (e.g., gametes and embryos). Finally, initial concerns about impact on the family highlighted the splintering of parental roles. At that time, it was understood that as many as five individuals could have a parental role *vis-à-vis* a child born of IVF and embryo transfer—a biological mother and a biological father who each make a genetic contribution, an additional biological mother who provides a gestational service, and two social parents who together plan to care for the child. Today, there is the prospect of further splintering as many families have more than two social (and sometimes legal) parents and as two women may be involved in providing the genetic contribution, using mitochondrial replacement technology—the woman who provides the nuclear DNA (removed from an egg with "unhealthy" mitochondrial DNA), and the woman who provides the enucleated egg containing the "healthy" mitochondrial DNA.

From a practice and policy perspective, some of the ethical issues identified above are more or less settled in some jurisdictions. In other jurisdictions, these issues remain contentious and ethical debate continues. In addition, as the range of assisted human reproductive technologies has expanded beyond IVF and embryo transfer to include pre-implantation genetic diagnosis (PGD) (and, more recently, comprehensive chromosome screening, embryo and oocyte (hereafter, egg) freezing, *in vitro* maturation of eggs, and (pending) mitochondrial replacement technology), so too the range of contentious ethical issues has expanded.

For example, concerns about PGD (a technique used to diagnose a range of chromosomal and single gene traits in the eight-cell IVF embryo prior to transfer) focus on how we choose our children—most commonly, what kind of children we choose not to have, or not to have again (Glover 2007; Scott 2007). Initially, this technology was available to "select against" human embryos at significant risk for incurable, early onset, sex-linked, seriously disabling traits. Now, it is used to "select against" less serious early and late onset disorders. One example in the category of late onset disorders is heritable breast and ovarian cancer associated with two abnormal genes: BRCA1 and BRCA2 (Krahn 2009). Critics of the use of PGD to identify embryos "affected" with late onset disorders compared with early onset disorders insist that these embryos could become people with rich lives if they were transferred to a uterus, successfully implanted and were born. By the time their condition manifested, treatments (even cures) might be available. These same critics argue that the ever expanding use of PGD reinforces the false belief that embryos are fungible (i.e., completely replaceable/interchangeable with nothing lost in choosing between one embryo and another). The fact is, however, that different people would be born of so-called "healthy" and so-called "affected" embryos and the difference would not be reducible to the presence or absence of one undesirable

trait. Critics of PGD also argue that use of this technology not only expresses disvalue for persons with disabilities, but ultimately could result in diminished support for persons with the disabilities targeted by PGD (Parens and Asch 2000).

From another perspective, if one chooses to avail oneself of PGD and there are embryos identified as "affected" it would be foolish (if not morally wrong) to transfer these "affected" embryos, regardless of the severity of the diagnosed condition or the age of onset. And yet there are some, who would "select for" what others might consider "affected" embryos. Deaf parents, for example, may want a child who will also be a member of the Deaf Community. PGD to "select for" human embryos with desired traits has also been used to select for HLA compatibility (when parents want a child who will become a donor for a sibling in need of a cell transplant—i.e., savior sibling) and could be used for social sex-selection (Wilkinson 2010).

Concerns about embryo freezing initially focused on potential harms to the offspring and on decisional authority and control over frozen embryos. With time and clinical experience, concerns about potential harms to children born of frozen–thawed embryos have diminished, though there are still conflicting reports on the potential harms of embryo freezing. As regards the relevant decision-making, particular attention has been given to the "who," "what," and "when" of informed choice. Who should decide whether embryos are frozen? Who should decide whether frozen embryos are discarded or donated/sold for reproductive, teaching, or research use? What information should be available to those who will make this decision? And, when should the decision about the eventual disposition of unused frozen embryos be made—before embryos are created, before they are frozen, when they are no longer needed for their original reproductive purpose, or when they are to be "handed over" to another? And, in relation to this point in time, if an option other than discarding frozen embryos is chosen, when and if so, how often, should there be the option to renew or withdraw consent?

In answer to the first of these questions, IVF clinics typically allow the prospective social parent(s) to decide whether to freeze good quality embryos for later use. Possible objectives in choosing embryo freezing include: reducing multiple gestations, avoiding embryo destruction, reducing costs, and preserving future options. Some clinics, however, until quite recently would only allow this if there were more than two good quality embryos to freeze. If there were only one or two such embryos, then embryo freezing was not available, but donation for human embryonic stem cell (hESC) and other research was an option (Haimes and Taylor 2009). In answer to the second of these questions, there are those who insist that the gamete providers (i.e., the sperm and egg providers) should be the ones to determine the disposition of any frozen embryos created using their genetic material. This perspective is ethically non-controversial when the gamete providers and the prospective social parents are the same people. When third-party gametes are used, however, the situation is more complicated as the prospective social parents (who are prospective embryo providers) may not be authorized to consent to the research use of embryos created with someone else's genetic material. Consider, for example, a situation in which a woman donated her eggs to create embryos for an infertile heterosexual couple to have a child using the sperm of the male partner. When that couple has finished their reproductive project, what should happen to any remaining frozen embryos? While it is clear that the sperm provider (who is one of the prospective social parents) should be involved in decision-making regarding the disposition of these embryos, the roles of the egg provider and the prospective social mother are contested. What if, for example, the egg provider consented to the use of her eggs to create an

embryo to assist an infertile couple, but expressly objected to embryo research (Schaefer et al. 2012)? In some jurisdictions (e.g., Canada), only the gamete providers have dispositional authority over frozen embryos. In other jurisdictions (e.g., the United States), the gamete providers typically have no control over embryos created using their gametes; the prospective social parents have sole dispositional authority over frozen embryos.

With egg freezing, dispositional authority is not (yet) a contested ethical issue, but it may become one should there be large quantities of abandoned eggs in storage. Initially, egg freezing was offered to women with cancer prior to chemotherapy or radiotherapy. Now, it is also widely offered to women as insurance against ovarian insufficiency when pregnancy is delayed because of educational pursuits, career goals, or later age of establishing committed relationships. It is anticipated that so-called "social egg freezing" will amount to an expensive and unnecessary form of insurance as many of the women who will have frozen large numbers of eggs for their future reproductive use will become pregnant without using their frozen–thawed eggs (Darnovsky 2008). Should there be large quantities of unused, unwanted eggs in storage, these could become a valuable resource for embryo research.

On the horizon is mitochondrial replacement technology using pronuclear transfer or maternal spindle transfer to avoid the transmission of disease-linked mitochondrial DNA (mtDNA). Typically, babies are made from the sperm of one man and the egg of one woman. But, some women's eggs include unhealthy mtDNA. If these women reproduce using their own eggs, their children could be affected with a mitochondrial disease and this could result in serious health problems, including neurodegenerative disease, stroke-like episodes, blindness, and muscular dystrophy. The plan to avoid the vertical transmission of mtDNA mutations involves replacing disease-linked mtDNA with healthy donor mtDNA to create children with three genetic parents: the man who contributes nuclear DNA; the woman who contributes nuclear DNA; and the woman who contributes healthy mtDNA. In addition to concerns about the further splintering of parentage (noted above), concerns with this technology focus on the potential harms to the eggs providers and the increased risk of coercion and exploitation, the potential short- and long-term harms to offspring and their progeny, the move to embrace germline genetic modification, and the opportunity costs associated with the technology which ultimately will benefit very few (Baylis 2013).

## Research Use of Human Embryos: Beyond the Moral Status Debate

In 1998, James Thomson and colleagues reported on the successful derivation of hESCs. This research, with the attendant promise of future treatments for everything from Alzheimer's, to burns, to cancers, and so on reenergized the debate on the moral status of the developing human embryo. It also introduced new ethical concerns focused on the source of eggs and embryos for research, the potential harms to the providers of eggs and embryos, the need for regulatory and research ethics oversight, and the ethics of volitional evolution (i.e., willful control of inheritable genetic traits through research involving cloning, human admixed embryos, and mitochondrial replacement, all with a view to changing the genetic inheritance of future generations).

*Should human embryo research be permitted?* This question has been answered in the affirmative in countries that permit (and in some cases fund) both fertility treatments involving IVF (which is the fruit of early and ongoing embryo research as new methods

are developed, applied, and perfected) and hESC research in pursuit of clinical applications in regenerative medicine. Indeed, tolerance for, if not active endorsement of, these practices continues to shape the ethical debate. Ethical questions of pivotal importance include: What embryo research should be permitted? And, which embryos should be used for research?

*What embryo research should be permitted?* The proponents of human embryo research typically agree that such research should not exceed 14 days after fertilization. The 14-day limit on human embryo research was proposed by the Ethics Advisory Board of the United States Department of Health, Education, and Welfare (1979a). Writing in support of research involving IVF and embryo transfer, the Ethics Advisory Board recommended that human embryos not "be sustained *in vitro* beyond the stage normally associated with the completion of implantation (14 days after fertilization)" (1979a: 107). Underlying this recommendation was the belief that moral status could only be conferred on individuals, and that until implantation was complete the developing human organism might or might not be an individual, as both twinning and recombination were possible. With twinning, two genetically identical individuals could be created from one embryo. With recombination, two genetically different twin embryos could fuse together to create a chimera, or one twin embryo could envelop (wrap around) the other twin embryo (which ceases development during gestation) to create what is called a fetus *in fetu*.

Five years after this recommendation, in 1984, the Committee of Inquiry into Human Fertilisation and Embryology (the Warnock Committee) in the United Kingdom also recommended a 14-day limit on human embryo research, using the formation of the primitive streak (the precursor to brain development) as the "reference point" for individuality (a presumed necessary condition for moral status). At the time, most authorities placed this developmental process at about 15 days after fertilization, and on this basis the Warnock Committee endorsed a precautionary 14-day limit on human embryo research (Department of Health & Social Security 1984). That same year, the Committee to Consider the Social, Ethical and Legal Issues Arising from In Vitro Fertilization in Victoria, Australia (the Waller Committee) also endorsed a 14-day limit on human embryo research (Victoria 1984). Some Australian scholars, however, advocated a different (later) time limit. Kuhse and Singer (1990), for example, suggested a 28-day limit. On their view, sentience (the capacity to feel pleasure or pain) determines moral status and prior to 28 days the embryo is not sentient and so does not have moral status.

The 14-day limit is now widely entrenched in legislation and research ethics guidelines around the world. In important respects, however, this limit (from the time it was first proposed to this day) is mostly irrelevant because researchers typically do not have the ability to maintain an *ex utero* human embryo beyond approximately six days (Edwards 1974), at which time the embryo (at the blastocyst stage) hatches. Once this happens, the embryo needs to implant and get access to a blood supply. If the embryo is in a petri dish (not a uterus) it will attempt to "implant" on the bottom of the dish and it will fail to develop. So, from a practical perspective, the 14-day limit at most serves a political purpose. In anticipation of new science, however, it has been suggested that if it were possible to maintain a human embryo in culture up to and beyond 14 days, there should be national (or perhaps international) oversight committees that determine the time limit for specific embryo research projects based on research objectives and potential clinical value. Instead of an arbitrary 14-day limit for all embryo research, some such research would be limited to a few days (perhaps as little as 3 or 5 days), whereas other

human embryo research could be permitted beyond 14 days. For example, it might be permissible to do cancer research until day 21 of embryonic development (beginning of closure of the neural tube).

In addition to specifying the length of time during which human embryo research is permitted, countries that regulate human embryo research typically also specify the scope of permissible research. The most liberal of the regulated regimes is the United Kingdom. In 1990, the *Human Fertilization and Embryology Act* (1990) was introduced. Schedule 2 of the Act identified the following research activities as "necessary and desirable":

(a) promoting advances in the treatment of infertility,
(b) increasing knowledge about the causes of congenital disease,
(c) increasing knowledge about the causes of miscarriages,
(d) developing more effective techniques of contraception, or
(e) developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation.

Ten years later, this list was expanded in recognition of the potential of regenerative medicine (following the first successful derivation of hESCs). In January 2001, the *Human Fertilization and Embryology (Research Purposes) Regulations* were passed to specifically expand allowable embryo research beyond reproductive purposes. Currently, the *Human Fertilization and Embryology Act* (2008) (Schedule 2) permits the following research:

(a) increasing knowledge about serious disease or other serious medical conditions,
(b) developing treatments for serious disease or other serious medical conditions,
(c) increasing knowledge about the causes of any congenital disease or congenital medical condition that does not fall within paragraph (a),
(d) promoting advances in the treatment of infertility,
(e) increasing knowledge about the causes of miscarriage,
(f) developing more effective techniques of contraception,
(g) developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation, or
(h) increasing knowledge about the development of embryos.

In reviewing this list of legally permitted research, one might wonder "what research is excluded"? The "not-so-facetious" answer would be "nothing that could not somehow be described (or re-described) as relevant to health care." Why then expand the list of permitted embryo research instead of eliminate the list altogether? Some speculate that this approach better fits with the overarching goal of having a permissive regime with the appearance of robust national oversight.

*Which embryos should be used for research?* In the early days of human embryo research for reproductive purposes, it was suggested that non-viable embryos—embryos with no potential for ongoing growth and development because of a genetic or metabolic disorder—were morally equivalent to other human somatic cells and could be used for research (Baylis 1990). This idea was revisited in the late 1990s and early 2000s in debates about hESC research, at which time it was suggested that organismically dead embryos (embryos with irreversible cessation of cell division), and "pseudo-embryos" (embryos created by altered nuclear transfer to ensure that certain essential elements of

embryogenesis are lacking) were non-viable and thus could be used for research (President's Council on Bioethics 2005). These specific proposals did not gain much traction. Meanwhile, researchers around the world continue to use embryos classified as "poor quality" on the basis of appearance or progress, as well as embryos identified as genetically "affected" through the use of PGD, for hESC research (Ehrich et al. 2010).

Another proposed distinction is between "spare" embryos (embryos originally created for reproduction, that are no longer wanted for this purpose) and "research" embryos (embryos specifically created for research purposes). In some countries only "spare" embryos—an ethically contentious category—can be used for research. Typically, this means that only women and couples undergoing fertility treatment who have embryos in storage and have completed their reproductive project can provide embryos to research. Beyond this, in some instances, embryos that are abandoned (as when the women or couples neglect to pay their storage fees and are lost to follow-up) can be made available for research. In other countries it is permissible to create human embryos specifically for research. So doing is ethically contentious, however, because of the need to access eggs from fertility patients or healthy volunteers. Women normally produce one egg a month. To increase the number of eggs potentially available for treatment or research, hormones are administered to women to stimulate the production of multiple eggs. These eggs are then removed by a needle inserted through the vagina.

Technologically assisted egg production is widely recognized as an onerous, invasive, and potentially harmful activity (Schaefer et al. 2012). The primary physical risk of hormonal stimulation is ovarian hyperstimulation syndrome. This may only result in abdominal bloating and mild abdominal pain, but in rare instances it can produce life-threatening complications including hemorrhage from ovarian rupture and thromboembolism. There have also been anecdotal reports of ovarian cancer, breast cancer, and colon cancer that suggest an increased risk of these cancers among those who undergo hormonal stimulation. In addition to the physical risks of hormonal stimulation, there are the physical risks of egg retrieval including bleeding, infection and adverse responses to the anesthesia. Other surgical risks include acute ovarian trauma, infection, infertility, vaginal bleeding, and lacerations.

It has been suggested that if the egg providers are fertility patients, they have presumably consented to the potential harms of ovarian stimulation and egg retrieval in pursuit of their own reproductive project and, as such, there are no potential physical harms specifically attributable to their decision to provide some of their eggs for research. This is inaccurate, however. Fertility patients who provide eggs for research and who do not become pregnant in their treatment cycle may have to undergo additional cycles of hormonal stimulation and egg retrieval to produce more eggs—eggs that would otherwise have been available to them (as either frozen eggs or embryos). In this situation, egg providers who are fertility patients would experience additional physical harms. In the alternative scenario, if the egg providers are healthy volunteers, then clearly the potential physical harms of hormonal stimulation and egg retrieval are solely a function of the decision to become an egg provider. It is one thing for infertile women to assume the potential harms of egg production in the hope of having a child using IVF, but quite another to encourage healthy volunteers to expose themselves to these potential harms for no potential benefit to themselves. From this perspective, restricting embryo research to "spare" embryos protects women (both healthy volunteers and fertility patients) from potential physical harms.

In those jurisdictions where human embryo research is limited to "spare" embryos, a further distinction can be drawn between fresh and frozen embryos. By definition,

"spare" embryos are embryos "in excess of reproductive need." Following Carolyn McLeod and Françoise Baylis (2007), this category includes fresh embryos that are unsuitable for transfer and thus unsuitable for freezing (for example, embryos classified as "poor quality" as well as "affected PGD" embryos); and frozen embryos that are surplus to fertility treatment. As it is in the best interest of women pursuing fertility treatment to freeze their good quality fresh embryos for future reproductive use, good quality fresh embryos that are suitable for freezing are not "in excess of reproductive need" (unless it is known that there will be no subsequent embryo transfer cycle using frozen–thawed embryos). Others reject this distinction. In their view, "spare" embryos are any and all embryos not transferred in the cycle in which they were created, including good quality fresh embryos suitable for freezing. Interest in defining "spare" embryos in this way was originally motivated by a desire to have access to these embryos for hESC research, in the belief these embryos were superior to frozen embryos. Notwithstanding efforts to popularize this definition of spare embryos, the fact is that IVF clinic staff and embryo research staff appear "more 'comfortable' with donation of frozen, not fresh, embryos to hESC research" (Ehrich et al. 2010: 2206) and so the debate about whether fresh embryos count as "spare" embryos is, in some sense, moot.

*Providing eggs for hESC research.* While some jurisdictions limit human embryo research to "spare" embryos, other jurisdictions permit the creation of embryos specifically for research purposes. Typically, where creating human embryos for research is permitted, so too are payments, cash or in-kind (e.g., reduced IVF fees), to provide eggs to create embryos. These could be cash payments to healthy volunteers, or in-kind payments to women undergoing fertility treatment. Well known and controversial is the Newcastle "egg sharing for research" scheme (NSER) funded by the United Kingdom's Medical Research Council (Haimes 2013). With this scheme, IVF patients were eligible to receive a £1,500 reduction in fees for one IVF cycle (at a cost of £3,000 to £3,700) if they agreed to provide 50 percent of their fresh eggs for nuclear transfer research.

With the buying and selling of eggs, the ethical debate is about commodification, commercialization, and exploitation on the one hand, and rights, freedom of choice, and dignity on the other (Widdows 2009; Baylis and McLeod 2007). Some jurisdictions, such as the United Kingdom, Canada, Australia, New Zealand, and Israel prohibit payment for eggs (whether for reproduction or research) on the grounds that such payment is likely to induce financially disadvantaged women to assume serious risks they would not otherwise assume. These (and other) countries allow egg donation, however, and they generally permit compensation for out-of-pocket expenses incurred as a direct result of donation.

Other jurisdictions, most notably the United States, distinguish between eggs for reproduction and eggs for research. Some states (e.g., Massachusetts and California), allow payment for eggs for reproduction, but not for research. Other states (e.g., New York), allow payment for eggs irrespective of intended use. Those who support commercial trade in human eggs argue that women should be compensated fairly for egg production whether the eggs are for reproduction or for research. It should not be the case that women who undergo ovarian hyperstimulation and egg retrieval procedures to produce eggs for reproductive purposes are paid, while those who undergo the very same procedures with the same attendant risks to produce eggs for research purposes are not (Spar 2007). As well, it should not be the case that researchers may benefit financially from embryo research while those who provide the essential research

material and services are prohibited from doing so. On this view, if there is exploitation, it is in expecting women to undergo hormonal stimulation and egg retrieval without fair compensation.

But what is fair compensation and what is unfair inducement? In the United Kingdom, patients undergoing ovarian stimulation and egg retrieval for their own reproductive project can provide eggs for research in exchange for a £1,500 reduction in treatment fees. Is this "egg sharing for research" scheme fair compensation? The market price in the United States for human eggs for reproduction is supposed to be around US$5,000 per cycle, as recommended by the Ethics Committee of the American Society for Reproductive Medicine and this has been used as a reference point for compensation for eggs for research. Meanwhile, there are advertisements soliciting elite egg donors from college students at Ivy League schools in the United States for as much as US$100,000 per cycle (Subrahmanyam 2008), and reports of student egg providers in Romania receiving as little as €600–800 per cycle (Zeiger 2013).What then is fair compensation for women in the United Kingdom or the United States who sell their eggs for research use? And, in the context of globalized trade in human eggs, what is fair compensation for women in middle income or poor countries who provide the same "services," for the same "product," with the same attendant risks?

Notwithstanding efforts to increase the number of eggs available for embryo research through various compensation/payment schemes, human eggs for research remain in short supply relative to the increasing demand. In 2007, in a further effort to address the problem of supply and demand, the Human Fertilisation and Embryology Authority—the national regulatory body responsible for licensing embryo research in the United Kingdom—granted several licenses for stem cell research involving the creation of cytoplasmic hybrid embryos—embryos created by inserting a human nucleus into a non-human enucleated egg. Shortly thereafter, in 2008, the United Kingdom passed legislation specifically permitting the creation of human admixed embryos as defined in Section 4A(6) of the *Human Fertilisation and Embryology Act* (2008).

For various reasons, the proposed use of enucleated animal eggs to create research embryos has had no impact on the problem of supply and demand. This problem may be time limited, however, given increasing enthusiasm for social egg freezing, at least in North America. Not all of the eggs being frozen will be used for reproduction, as many of the women with eggs in storage likely will become pregnant without using assisted human reproduction. And, of those who do reproduce using their frozen–thawed eggs, many likely will have considerably more frozen eggs than they will use. This means that, *de facto*, we are in the process of creating human egg banks, thereby obviating the need to create part-human cytoplasmic hybrid embryos for research purposes.

## Conclusion

The promises and perils of human embryo manipulation, whether for reproduction or for research, are considerable. But this need not be so. With more informed debate and discussion that critically engages the moral imagination, we should be able to direct the reproductive and research use of embryos in ways that will serve the interests of human kind. This is not to suggest that consensus or even harmonization is possible. It is to say that in the context of global health and global science we need to critically examine the range of ethical issues remaining attentive to the broader, global implications of national policies and practices.

## Related Topics

Chapter 28, "Regulating Reproduction: A Bioethical Approach," Isabel Karpin
Chapter 32, "Reproductive Testing for Disability," Adrienne Asch and David Wasserman

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