The Very Early Embryo & Its Moral Significance

Andrew J. Prunty

Keywords: reproductive ethics, early embryo, zygote, clonote, embryonic stem cells, stem cell ethics

ABSTRACT

By clarifying and correlating beginning of life biomarkers with those already established and accepted for end of life, we can begin to facilitate discussion about when life begins and the ethical and legal limits of medical research and practice. There is an ethical imperative to establish consistency and develop parameters to guide appropriate research and medical practice that is ethically acceptable. If ethical standards of embryonic rights and beginning of life remain undefined or debated, it will remain difficult to establish sufficient guidelines to regulate new scientific medical technology.

INTRODUCTION

As technology and biological research continue to develop in the twenty-first century, it is necessary to address and further define the ethical considerations of embryonic research and the appropriate rights that may limit the extent of human research on zygotes, blastocysts, and fetal scientific advancement. Because the area of harvesting embryonic stem cells remains significantly undefined, both legally and morally, there are vastly different opinions between researchers and bioethicists, mainly because of ethical limitations, on the rights that should be granted to cells with the potential to develop into human beings and the consequences of neglecting significant scientific research or advancement.

ANALYSIS

Current laws in the United States differ at the federal and state level, but there is no consistency in recognizing human embryos as humans, or affording them the same legal rights granted to a child; in fact, legal precedent actually detracts certain rights from developing embryos, favoring a human's ability to destroy a potential human being (i.e. *Roe v. Wade*[1]) or the categorization of embryos as property (i.e. *Davis v. Davis*, *A.Z. v. B.Z.*, *Marriage of Dahl*, or *Reber v. Reiss*).[2] These case law samples suggest the courts' inability to reach a conclusion as to what is the status of an embryo.

The debate is not only circumscribed to matters of research, but to fundamental controversial and intertwined issues of bioethics such as: when life begins, embryonic stem cells, fetal rights, abortion, et cetera. All these topics are contentious and when one topic arises, they begin to comingle.

© 2017 Andrew J. Prunty. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction, provided the original author and source are credited.

Embryonic stem cells are valuable to medical research and advancement because of the plasticity of the embryoblast – that is, the ability to adapt in response to changes in the environment.[3] Compared to somatic stem cells, which have less plasticity and at this point have little ethical controversy, embryonic stem cells are much more versatile and able to develop into a broader range of potential cells.[4] Therefore, despite somatic stem cells having qualities that allow it to develop into multiple variants of tissue cells, they are significantly limited compared to embryonic stem cells. Future development and research surrounding the abilities of somatic stem cells may change if current research is successful in attempting to improve the pluripotent potential of somatic cells. Cell potency is the cell's ability to differentiate into various types of cells; the more variations in which a cell can differentiate, the greater the potency. Cell potency is a scale, where if a stem cell has the ability to differentiate into every type of cell, it is pluripotent, whereas if it can only differentiate into one type of cell, it is unipotent. The potential for cell potency is the most significant factor in utilization of stem cells and pluripotency is the primary factor embryonic stem cells are desired for medical research and advancement.

In response to the legal ambiguities surrounding the morals and ethics of this new scientific technology, Robert P. George authored the 2005 article *Acorns and Embryos*, which states an imperative that zygotes and blastocysts be afforded rights comparable to those of humans. Because these cellular clusters may eventually develop into human beings, he finds it a necessity to develop a set of ethical standards that limit scientific research and establish restrictive guidelines to protect the rights of embryos, future human beings, that are congruent with generally accepted practices of human testing and research. George's argument is developed on the grounds that embryos are humans, but in a different stage of life. Similar to how infants and adolescents are all humans, but in different stages of physical and mental development, so too are human embryos, but in the embryonic stage of development. To understand how George believes embryos should be afforded human rights, he voices the following opinion: specifically, those who support destruction of human embryos fail to understand that they support a blind injustice towards human beings who happen to be in the embryonic stage. According to George, this represents a form of ageism – that is, discrimination and the withholding rights based solely on age of an embryo's state of maturation. George further argues that our society, "would not tolerate the killing of a retarded child, …a person suffering from brain cancer, [or]…the killing of infants," implying that we should therefore not tolerate the blatant destruction of humans in the embryonic stage.[5]

However, as our society changes, we are in fact starting to become more accepting of these scenarios. Multiple states have passed "death with dignity" legislation allowing a variant of euthanasia for those suffering from a terminal illness;[6] our society tolerates the killing of infants born with significant genetic birth defects by withholding pediatric nutrition and hydration,[7] and continues to stand behind the legalization of abortion. In closely related ethical similarities, our society also allows and supports in-vitro fertilization, where 97% of fertility clinics reported fertilizing more eggs than would be implanted in a given cycle and 84% of those clinics dispose of the extra embryos. [8]

Despite his push to increase limitations on research involving the creation of embryos with no differentiation in the zygote's cellular composition, a morula comprising a spherical cell mass 3-4 days post fertilization, and blastocysts 4-5 days evolved from fertilization into embryo, George contends that individual gametes should not be afforded the same rights or treated the same as embryos. He argues that an individual gamete does not have the potential to develop into a human being on its own accord as there has yet to be a case of spontaneous human parthenogenesis. However, just as a sperm cannot develop into an embryo independently, an embryo cannot develop into a human independently either; in the context of both, they are in need of 'another half' to successfully develop: a sperm cannot develop into an embryo without an egg,

and an embryo cannot mature into a human without a suitable environment to grow and develop. While the two are different in the context of being a haploid versus diploid cell – that is, one complete set of chromosomes such as a sperm or egg versus two complete sets of chromosomes represented by every cell in the body besides sex cells – the fact remains that neither is viable independently.

George also asserts that individuals do not first exist without any rights and only later acquire certain features that qualify us to become the bearers of rights. However, every person passes through phases of development and these stages also bring changes in their rights. Further consistent with George's viewpoint, just as a child has fewer rights than an adult (due to age and maturation), an embryo would certainly have fewer rights than a newborn infant. Since the moment of conception cannot be known with any sense of certainty, the beginning of the rights for an assemblage of cells can also not be certain. Therefore, an arbitrary timeframe needs to be established where rights would be conferred progressively to coincide with the development of the embryo, fetus, and infant.

Acorns and Embryos was written to counter Michael Sandel and Paul McHugh's perspectives written in their 2004 New England Journal of Medicine articles, *Embryo Ethics – The Moral Logic of Stem-Cell Research* and *Zygote and "Clonote" – The Ethical use of Embryonic Stem Cells*, respectively, in response to questions raised by the President's Council on Bioethics regarding federal funding of embryonic stem cell therapies. Both Sandel and McHugh, to different extents, support the development and use of embryoblasts to further medical research. McHugh poses a distinction between the ethical considerations given to a blastocyst derived from natural production or in-vitro fertilization compared to one derived from somatic-cell nuclear transfer (SCNT) – dubbing it a 'clonote.' Contrary to most viewpoints from members of the President's Council on Bioethics, McHugh believes there to be a distinct difference between the ethics of a zygote versus a clonote: a zygote (regardless of derivation from natural fertilization or IVF) being protected from harvesting embryoblasts from blastocysts for use in stem cell research and therapies, and a clonote being free for use in stem cell research or therapies.

Stem cells are only controversial when they are embryonic – and thus potential human beings. There is no ethical opposition to stem cells derived from an umbilical cord, bone marrow, adipose tissue, etc.[9] Thus, the solution to solving the ethical qualms of embryonic stem cells lies not within arguing the ethics surrounding embryonic stem cells, but instead defining the parameters about the beginning of life and associated fetal rights. McHugh emphasizes that, "if a source other than embryos can provide pluripotent stem cells – and harvesting them requires no killing – then this shadow vanishes."[10] If we can define when human life begins, we can effectively define the rights associated with a human at that stage of development.[11]

With the lack of clarity encompassing moral and ethical acceptability of beginning of life issues, it often seems easiest to establish standards through correlation to similar topics. Therefore, if congruency is defined between beginning and end of life ethics, and similar criteria established, it would allow ethicists and researchers to further formalize appropriate guidelines and regulations surrounding embryonic stem cell research and therapies. Current law, the Uniform Determination of Death Act (UDDA),[12] states that life ends at the irreversible cessation of organismic functioning; the two accepted death criteria are cardiorespiratory arrest and absence of brain stem function. Using these criteria for end of life, we can identify correlating biological markers to help determine the beginning of life. Three significantly distinct markers that correlate to accepted end of life definitions are: when the heart begins to beat, neuromaturation – functional development of the central nervous system – which can be separated into whole brain or higher brain 'birth', and fetal viability.

Fetal viability is the measurement of a fetus that has reached such a stage of development as to be capable of living, under normal conditions, outside the uterus. This marker of fetal viability is a comparable marker to assist in defining the beginning of human life. Markers of neuromaturation and the appearance of lower and higher brain waves in fetal development parallel whole and higher brain death. The first appearance of brain waves from the brain stem appear at the six to eight-week mark and higher brain waves in the cerebral cortex appear after approximately 22-24 weeks of gestation. Available evidence suggests that the neocortex does not become a functional part of the neuraxis until at least mid-gestation, and it is not until then that the thalamus – the major gateway for sensory input to the cerebrum – makes its first afferent contacts with the neocortex.[13]

If life is unsustainable in an adult, it will inevitably result in one of the two criteria discussed earlier under the UDDA. Similarly, despite embryonic cardiac or neurological development and detectable biological markers, embryonic viability and fetal life may still be unsustainable even if these criteria are met. According to studies conducted by *Breborowicz and Tyson, et al*, results showed that only 20-35% of babies born at 23 weeks gestation survived, while 50-70% survived when born at 24-25 weeks.[14] Unfortunately, fetal viability is not limited to biological factors, but significantly linked to technological abilities and therefore exists only as a function of biomedical and technological capabilities. Consequently, fetal viability in developed countries is significantly different from that found in underdeveloped parts of the world. Furthermore, as technology and medical abilities develop and continue to improve, this may change premature fetal survival rates.

While biological markers remain unchanged for embryonic development, it is hard to develop a set of ethical standards based on a specific stage of development associated with current technological limitations. This ability to show significant differentiation in fetal viability based on geographic location, economic status, and technological medical care available make fetal viability a difficult criterion to use.

Robert George and those who agree with the theory that human life begins at conception believe that because there is one living cell with the potential to develop into a human being, the embryo should be protected and afforded the same rights as a human being after birth. However, in applying this logic to end of life, death would be defined when the last human cell has lysed. While the time for complete cellular death to occur is insignificant compared to the time associated with fetal development, studies have shown that 5% of leukocytes are still alive 70 hours after clinical death, skin cells can live for days, and neurological electrical activity can occur in brain dead patients as much as 168 hours after clinical onset.[15] It is imperative to keep the definition of beginning and end of life criteria congruent, otherwise it appears to be random ad hoc choices of when human life begins and ends.

It is difficult to determine which side has a stronger argument when no basic standard exists for fetal rights. While it is difficult to agree with the notion that a human being begins existing at the precise moment of zygote formation, there should be limitations on research, clinical application, and non-reproductive use of embryos past a certain stage of development. Dr. McHugh suggests limiting blastocyst development not past the 14th day, although he does not cite specific reasons as to why he chose the 14-day mark as a limit when he discussed clonote development limitations. At the latest, one could conclude that development should be allowed until, at most, 22 weeks because it not only marks neuromaturation to higher brain function, but also because of current limitations of fetal viability. However, despite any support of embryonic development to 22 weeks for non-reproductive purposes and regardless of what maturation timeline is chosen, embryonic development should be limited only to that necessary for embryoblast harvesting. If limitations allowed embryonic development to 22 weeks, but successful research and embryoblasts could be

harvested by the 14th day, there should be no support for further unnecessary embryonic development – hence, the pressing need for standards.

Despite the significance and untapped potential of this research and clinical abilities, it is necessary to develop standards and limitations prior to authorization and potential federal funding of such research. While this work is rich in therapeutic promise, we cannot allow it to proceed before establishing a set of morals and ethics to guide the research. Therefore, practitioners and clinical ethicists should support a moratorium on further embryonic stem cell research until those within the community can agree on ethical limitations of new science. Even though this paper was not intended or designed to address the ethics of defining beginning or end of life criteria, it is crucial to understand its necessity and integration into other concepts, such as embryonic stem cells and embryonic rights, to help us adequately discuss the morals and ethics of surrounding concepts.

CONCLUSION

By clarifying and correlating beginning of life biomarkers with those already established and accepted for end of life, we can begin to facilitate discussion about when life begins and the ethical and legal limits of medical research and practice. There is an ethical imperative to establish consistency and develop parameters to guide appropriate research and medical practice that is ethically acceptable. If ethical standards of embryonic rights and beginning of life remain undefined or debated, it will remain difficult to establish sufficient guidelines to regulate new scientific medical technology. As scientific capabilities increase and new research develops, it is compulsory to ensure discussion of ethical tolerability in a prompt manner to allow researchers the ability to understand and develop increased potential of new research.

[1] *Roe v. Wade*, 410 U.S. 113, (1973)

[2] *Davis v. Davis*, 842 S.W.2d 588 at 597, Tennessee (1992); *A.Z. v. B.Z.*, 725 N.E.2d 1051, 1059, Massachusetts (2000); *Marriage of Dahl*, 194 P.3d 834, Oregon (2008); *Reber v. Reiss* 38 FLR 1279, (2012)

[3] Hans R. Schöler. (2007). "The Potential of Stem Cells: An Inventory". In Nikolaus Knoepffler; Dagmar Schipanski; Stefan Lorenz Sorgner. *Human biotechnology as Social Challenge*. Ashgate Publishing, Ltd. P. 28. ISBN 978-0-7546-5755-2.

[4] Illmensee K, Mintz B. Totipotency and normal differentiation of single teratocarcinom cells cloned by injection into blastocysts. Proc. Natl Acad. Sci. USA. 1976;73:549–553.

[5] George, R.P., Lee, P. (2005). Acorns and Embryos. *The New Atlantis,* 90-100.

[6] ABX2-15 *End of Life Option Act*, California, (2015); Proposition 106: *End of Life Options Act*, Colorado, (2016); DC ACT 21-577 *Death with Dignity Act of 2016*, District of Columbia, (2016); *Baxter v Montana*, Mont. Sup. Ct., 2009 MT 449, 354 Mont. 234, 224 P.3d 1211 (2009); Ballot Measure 51: Death with Dignity Act. Oregon, (2008); *Gonzales v Oregon*, (04-623) 546 U.S. 243 (2006) 368 F.3d 1118; Act No. 39. An act relating to patient choice and control at end of life. Vermont. (2013); Ballot Initiative 1000: Death with Dignity Act. Washington. (2008).

[7] Johnson, J., Mitchell, C. (2000). Responding to Parental Requests to Forego Pediatric Nutrition and Hydration. *The Journal of Clinical Ethics, 11*(2), 128-135; *Barber v. Superior Court*, 147 Cal.App.3d 1006 (1983) 195 Cal. Rptr. 484.

[8] Gurmankin, A.D., Sisti, D., & Caplan, A.L. (2004). Embryo disposal practices in IVF clinics in the United States. *University of Pennsylvania Center for Bioethics*.

[9] Lo, B., Parham, L. (2009). Ethical Issues in Stem Cell Research. *Endocrine Reviews,* 30(3), 204-213.

[10] McHugh, P.R. (2004). Zygote and "Clonote" – The Ethical Use of Embryonic Stem Cells. *The New England Journal of Medicine, 351*(3), 209-211.

[11] Sandel, M.J. (2004). Embryo Ethics – The Moral Logic of Stem-Cell Research. *The New England Journal of Medicine, 351*(3), 207-209.

[12] *Uniform Determination of Death Act*, National Conference of Commissioners on Uniform State Laws, (1981).

[13] Fowler, M.J. (1985). Neuromaturation and the Moral Status of Human Fetal Life. *J Med Philos, 10*(3). 237-252.

[14] Breborowicz, G.H. (2001). Limits of fetal viability and its enhancement. *Early Pregnancy, 5*(1). 49-50; Tyson, J.E., et al. (2008). Intensive Care for Extreme Prematurity – Moving beyond Gestational Age. *The New England Journal of Medicine, 358*, 1672-1681.

[15] Can, I., et al. (2014). Distinctive thanatomicrobiome signatures found in the blood and internal organs of humans. *Journal of Microbiological Methods*, 106, 1-7; Bernat, J.L., et al. (2006). Report of a National Conference on Donation after Cardiac Death. American Journal of Transplantation, 6: 281–291. doi:10.1111/j.1600-6143.2005.01194.x; Grigg, M.M., et al. (1987). Electroencephalographic Activity After Brain Death. *Arch Neurol*, 44