

Bioethical issues concerned with the time of human beginning in early embryo development

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Abstract:

The latest researches in biology and medicine affect dramatically the already acute debate on the moment of the beginning of human life. This debate in turn provides serious implications forming the attitude towards a cluster of Bioethical issues such as an abortion, contraception, human embryo experiments, assisted reproductive technologies, stem cells, gene editing and gene therapy. The paper investigates that the solution of those problems is directly linked with the definition of beginning of human life in embryo development. In secular science there is no consent in such a definition, because the concept ‘human’ is not only the biological or medical notion. To define it we need to use other fields of knowledge to analyze embryological data. In the paper we offer the Christian foundation for such definition. From the Christian perspective, the moment when a human comes into existence is the fusion of the sperm and the egg. We dare to believe that the arguments presented in the paper allow admitting such a perspective as the best possible bioethical consensus, not only from Christian, but also from generally human point of view.

Keywords:

embryo, human, beginning of life, zygote, Christian-Orthodox perspective

Bioethical issues concerned with the moment of the beginning of human life

The definition of time when a human begins is one of the most important problems of bioethics today. It determines the subsequent way to solve the whole cluster of bioethical issues pertaining abortion, contraception, assisted reproductive technologies, embryo experiments, cloning, stem cells, gene editing and gene therapy.

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Abortion

Obviously, the attitude to abortion and so to legislating it depends mostly on perspective on the moment when a human appears in life. After this moment the abortion becomes infanticide because the deprivation of the life who is equal to us is named a murder and infanticide, considered to be a disgusting evil that must be avoided.

But here is the room for speculation that leaves a chance for abortion to be viewed as permissible. That is someone can move the time frame for recognition of before the array of cells ceases to be as a biomass and converts into a whole entity – a human. Before such a line an abortion is considered to be permissible, and after it – forbidden.

Contraception

An abortion on the late stage is regarded as infanticide by most people, because the one who is being deprived of life has features similar to ours: a fetus has got hands, legs, eyes, heart pace, electro-activity of his brain, already after 25 weeks if he is born, he could survive with assisted help and physician's care. Even at the stage of 8 – 15 weeks when the abortion is commonly practiced, a fetus has already got human-like features – one can distinguish fetus's palms with fingers, the face with eyelids and a nose, lips. Thus, if someone does not find humanity in such an organism, he ought to try hard to prove that it is not a man.

But often abortions happen even before the woman understands she is pregnant. The reason is hormonal contraception. There are two main groups of hormone contraception – pills and devices.

The contraceptive effect of birth control pills' mostly goes with two ways. The first is concerned with estrogens, which hinder the development of an oocyte. Insofar as an egg does not mature and does not emerge into an ovarian tube, fertilization cannot occur. Although it might happen. To strengthen contraceptive effect of pills there is the second mechanism which is stipulated with progestogen effect. It influences the internal uterus layer making it thicker and inappropriate for an embryo formed implants and goes on his development. This is the way to stop a newly formed baby from living further. In this case, there is no difference between this method and the abortion.

Intrauterine device (IUD) for contraception is a small, often T-shaped birth control device that is inserted into a woman's uterus to prevent pregnancy. Its effect is concerned with changes in the internal uterus layer that prevents an embryo formed to be implanted. Sometimes such a device may have slow drug release to make implantation impossible.

The abortive effect of contraception occurs before the implantation time, i. e. before 11-14th day of embryo's life. Regarding ovulation and fertilization occur approximately at 14th day of menstrual cycle, embryo's abortion with use of contraceptive happens even before the first signs of pregnancy appear. Therefore, a woman using birth control pills or IUD cannot know whether she has done an abortion or not.

Defining the permissibility of hormone contraception depends very much on the time when human life begins. If a human appears in a womb later than 14th day, then birth control pills are OK to use. If a biomass has become a human just after fertilization, then usage of such contraception is an infanticide.

Assisted reproductive technologies

Assisted Reproductive Technologies (ART) are the methods to overcome infertility mostly by use of In Vitro Fertilization (IVF). IVF implies getting sperm and an egg, combining them in a dish ('in vitro') to form an embryo. The problem here is excess embryos. To increase the pregnancy rate, doctors derive many oocytes to fertilize them. So many embryos occur. But only 1 or 2 of them might be delivered into a womb and born. Others are frozen and kept in a freezer. There might be a chance when frozen embryo will be thawed and get a chance to achieve pregnancy. But only a few of them gets a ticket to life.

Excess embryos are being kept in a freezer while their parents pay for such service. If they disappear, a cryobank (the place where frozen embryos are stored) may eliminate embryos².

Acceptability of different variants of IVF depends on the time of human appearance as well. If we recognize the moment of human origin just after conception, we ought to admit every excess embryo is the same human as ourselves. In this case freezing of embryos, discarding them or manipulation on them should be regarded as ethical wrong and needs to be avoided.

Embryo experiments

Every experiment with a man requires his agreement in order to be ethically acceptable. But an embryo cannot give a permission for sacrifice his life for someone else's benefit. Thus, if an embryo is a real human, embryo experiments must be forbidden.

Should we notice impossibility of an embryo to give an agreement or is it more simply to reject their human status until the definite time? Thus, for the solution on embryo experiment acceptability we need to draw the line in embryo development when a human appears and every experiment on the embryo need to be stopped.

Stem cells

Every cell in our body specializes on a definite function. A muscle cell is needed for moving, a neuron cell for passing of electrical impulses and in such a way for

² Byrd W. Cryopreservation, Thawing, and Transfer of Human Embryos, *Seminars in Reproductive Medicine*, Volume 20, Number 1, 2002 – available at <https://www.thieme-connect.com/products/ejournals/html/10.1055/s-2002-23518> [accessed 01.03.19]

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delivering information, gametes for reproductive purpose. But cells get their specialization during the complex process, when different genes in chromosomes are switched on and off. To renew old cells in our body there are few non-differentiated cells, which are called stem cells. Upon some conditions an organism can make some of its genes be active and some be passive. In such a way stem cells can move to one or another path of their development and specialization. Present blood cells are a good example of the similar differentiation. In the bone marrow there are some pluripotent cells which can become red blood cells, macrophages or lymphocytes. Nevertheless, pluripotent marrow cells cannot turn into brain cells because they have already got some little specializations. The most non-differentiated cells are embryo cells. They are called totipotent and can spring into every types of tissue of our body.

Totipotency is the property of the least non-differentiated embryo cells which is expected to allow them to move their development into needed direction. For example, if someone suffers from heart failure, embryo stem cells being inserted in the lesion can differentiate into cardiac muscle cells³. Now researchers are doing trials in treating Stargardt's macular dystrophy, type I diabetes mellitus, Parkinson's disease, heart failure, spinal cord injury⁴. They hope stem cells can help to cure these disorders.

But the easiest way to derive embryo stem cells is to destroy embryos⁵. Researchers consider such a way of obtaining stem cell to be permissible because they move the line of beginning a human life to the point before which they look at the embryo as a biomass. We need here to distinguish the border line which defines the moment of human's advent to life.

Gene editing and gene therapy

We view these problems together because they have a lot in common in the light of the topic discussed. Both gene editing and gene therapy influence the developing of embryo by editing its genes.

Now the gene alteration is possible with the use of the molecular system of CRISP-Cas9. The system can be compared with gene scissors. It finds the specific

³ Menasche Ph. et al., Human embryonic stem cell-derived cardiac progenitors for severe heart failure treatment: first clinical case report, *European Heart Journal* (2015) 36, 2011–2017. doi:10.1093/eurheartj/ehv189. Available at <https://academic.oup.com/eurheartj/article/36/30/2011/2398140> [accessed 13.02.19]

⁴ Trounson A, McDonald C., Stem Cell Therapies in Clinical Trials: Progress and Challenges. *Cell Stem Cell* 17, July 2, 2015 – Available at <https://www.cell.com/action/showPdf?pii=S1934-5909%2815%2900267-2> [accessed 12.02.19]

⁵ Thomson, J. A. et al., Embryonic stem cell lines derived from human blastocysts, *Science* 282, 1145–1147 (1998);

Cowan, C. A. et al. Derivation of embryonic stem-cell lines from human blastocysts, *N. Engl. J. Med.* 350, 1353–1356 (2004)

region in DNA structure, cuts it and inserts the gene fragment needed⁶. This can result in changing 'sick'/damaged gene (in case of gene therapy) or acquirement of new features (in case of gene editing). The example of the first is the correction of β -thalassemia gene⁷ (associated with the blood disease) and the gene, deficiency of which may lead to the emergence of favism⁸ (disease of blood, a hemolytic response to the consumption of fava beans). The example of second is the correction of genes to give an embryo a new feature. It was reported that the scientist from China, He Jiankui claimed two twins to be born with gene modification for an ability to resist possible future infection with HIV, the AIDS virus⁹. There is no official report of that but if it is true, his experiment is the first case of gene editing children's birth.

Still there is a lot of concerns on ethical permissibility of such experiments. Because CRISP-Cas9 is reported to be very efficient for editing the gene needed, but there is no evidence that such gene scissors will not cut other similar genes unexpectedly¹⁰, so called 'off-target events'. And there is another concern with possibility of CRISP-Cas9 modified cells to generate tumor cells¹¹. There is no evidence of this, but such a presumption based on available data¹² has to be checked precisely and proven to be absent.

In respect that embryo gene editing can threaten him with damage and death, every gene intervention should be used with proven safety to embryo's life after the

⁶ Ma Y. et al., Genome modification by CRISPR/Cas9. *FEBS Journal* 281 (2014) 5186–5193. doi:10.1111/febs.13110

⁷ Liang P, Ding C, Sun H, et al., Correction of β -thalassemia mutant by base editor in human embryos, *Protein & Cell* 8 (2017) (11): 811–22.

⁸ Tang, L, Zeng Y, Du H, et al., *Mol Genet Genomics* (2017) 292: 525. <https://doi.org/10.1007/s00438-017-1299-z> available at <https://link.springer.com/article/10.1007%2Fs00438-017-1299-z> [accessed 16.02.19]

⁹ 'Chinese researcher claims first gene-edited babies. Interview of He Jiankui by Marilyn Marchione/ Associated Press, November 26, 2018 – Available at <https://apnews.com/4997bb7aa36c45449b488e19ac83e86d> [accessed 16.02.19]

¹⁰ Schaefer KA, Wu W-H, Colgan DF, et al. (2017) Unexpected mutations after CRISPR-Cas9 editing in vivo, *Nature Methods* 14(16): 547–8 available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5796662/> [accessed 17.02.19]

¹¹ Nuffield Council on Bioethics (2018) *Genome Editing and Human Reproduction: social and ethical issues* (London: Nuffield Council on Bioethics) available at <http://nuffieldbioethics.org/project/genome-editing-human-reproduction> [accessed 17.02.19]

¹² Haapaniemi E, Botla S, Persson J, et al. (2018) CRISPR-Cas9 genome editing induces a p53-mediated DNA damage response, *Nature Medicine*, published online 11 June, available at: <https://www.ncbi.nlm.nih.gov/pubmed/29892067>; Ihry RJ, Worringer KA, Salick MR, et al. (2018) p53 inhibits CRISPR-Cas9 engineering in human pluripotent stem cells, *Nature Medicine*, published online 11 June, available at: <https://www.ncbi.nlm.nih.gov/pubmed/29892062>

border line when he is considered to be a human. The necessity of such a border line appears to be much stronger if we realize that researchers can do the gene alteration experiments on the healthy embryos. So where is the line allowing to view the embryo as an object for the experiment but not a subject of inter-human relationships?

Different Views on the origin of a human in embryo development

In contemporary science there is no consensus in definition of the moment demarcating an embryo as a biological object allowed to be used and an embryo as ethical subject which demands the relation equal to every human.

Some researchers claim that we ought to recognize a human in an embryo only after his brain formed and begun its functioning. For example, Goldering (1985) writes '*medically the term a 'human being' should be defined by the presence of an active human brain. The brain is the only unique and irreplaceable organ in the human body, as the orchestrator of all organ systems and the seat of personality. Thus, the presence or absence of brain life truly defines the presence or absence of human life in the medical sense*'¹³.

The existence of brain functioning for recognition as a human seems to be rare amongst scientists. But the appearance of the nervous system became the wide-spread criterion of earlier recognition of humanity in an embryo. Such a criterion is concerned with the Committee of Inquiry into Human Fertilization and Embryology, commonly called the Warnock's Committee after the chair of the committee Mary Warnock. The need to do embryo research forced UK government to entrust making the report to the Committee, which was published in 1984 and became the important directives in regulation of embryo research¹⁴.

The report looks at an embryo as an accumulation of cells and allow every research to happen until 14th day¹⁵, when the primitive streak, the antecedent of the nervous system, appears¹⁶. In accordance with that report an embryo must be recognized as a human being after 14 day of his development.

¹³ Goldering J. M. The brain-life theory: towards a consistent biological definition of humaneness, *Journal of Medical Ethics*, 1985, No. 11, pp. 198-204 doi:10.1136/jme.11.4.198

¹⁴ LaTourelle, Jonathon J. The Report of the Committee of Inquiry into Human Fertilisation and Embryology (1984), by Mary Warnock and the Committee of Inquiry into Human Fertilisation and Embryology. *Embryo Project Encyclopedia* (2014-10-02). ISSN: 1940-5030 <http://embryo.asu.edu/handle/10776/8208>

¹⁵ Warnock M. The Warnock Report, *British Medical Journal*. Volume 291, 20 July 1985, p. 187

¹⁶ Gaffin J. The discussion (after Baroness Warnock's paper). *British Medical Journal*. Volume 291, 20 July 1985, p. 189

Despite of Warnock's Committee statement, some scientists draw the line demarcating biomass and humanity in an embryo much earlier. Perspectives on that are as follows. 1) In the third day when an embryo consists of eight cells, not tightly attached each other and so the embryo looks like a colony. But in the late third day it ceases to be a gentle formation; its cells become bound tightly together and resemble a mulberry (morula stage), they cannot be individually removed without destroying the others and so exactly in this time an embryo is thought to cease being a colony and to form a human¹⁷. 2) In the stage of one-cell embryo, called a zygote, there is a period of time for about 15 hours after penetration of a sperm cell into an egg when the father's nucleus is moving towards the mother's one but not combined yet. The process of their fusion got the name of syngamy, because their separate genetic material combines in the whole formation – zygote's nucleus. Some researchers do not regard a zygote as a human before such combination occurred¹⁸. 3) But there is the point of view considering an embryo to be a human from the moment of conception just after a sperm cell penetrated an oocyte¹⁹.

So, we have totally different views on the moment of becoming of human. On the one hand an embryo is thought to be a human from the very beginning. On the other hand, it is considered to be a human at his further development (after 15 hours, 3 days, 14 days or after his brain starts functioning).

Orthodox perspective on the moment of human's origin

Despite of abundance of scientific views on the time of a human emergence in life in a stage of embryo development there is no consent among them. One of the most serious disagreements concerns with materialistic desire to base the concept of 'human' purely on scientific foundations. But 'human' is a complex notion. To understand what a human is and moreover when he comes into existence we ought to use other fields of knowledge in order to analyse data from Biology and Medicine.

We find important arguments in Christian Revelation. Firstly, we have the Evangelical episode about the Theotokos and Elizabeth's meeting (Luke 1:39-40). It

¹⁷ Gerard J. Towards a Hierarchical Definition of Life, the Organism, and Death, *Foundations of Science*, 2010, No. 15, pp. 245–262 - Springer. DOI 10.1007/s10699-010-9177-8.

¹⁸ Golichenkov V. A. (chairman of Embryology department of Moscow State University) in Dukhovich V. priest, Molchanov A. Yu. (in Russian) *The beginning of life and prenatal human development: from biology toward bioethics*. Moscow: Lepta-kniga, 2013, p. 111; "Fertilization is a complex sequence of coordinated events that begins with contact between a sperm and an oocyte...and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote" in *Keith L. Moore and T.V.N. Persaud, The Developing Human*, 7th ed. (Philadelphia: Saunders-Elsevier, 2003), p. 31.

¹⁹ *Condic M. L. When Does Human Life Begin?*, Westchester Institute for Ethics & the Human Person. White paper, 2009, Vol 1, no. 1.

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happened just after Angel Gabriel had annunciated to Mary that She will give the birth to the Lord. Then *'Mary, rising up, traveled quickly into the hill country to a city of Judah and she entered into the house of Zechariah, and She greeted Elizabeth'* (Luke 1:39-40). After Mary greeted Elizabeth, the child, who was John the Baptist, was fulfilled with Holy Spirit because he got to know his Lord in the Mary's womb. But the time of Mary's pregnancy was about two or three days (that is to come from Nazareth to the city Judah, where Zechariah's house was). Thus, in time of 2 days (notice the implantation process of the embryo didn't occur yet in such amount of time!) the organism in Mary's womb was the human-Lord Jesus Christ.

But in the Holy Tradition we celebrate the incarnation of our God not after two days but even earlier – from the very beginning, from the moment of Annunciation, just after Mary agreed with Angel's offer *'Behold, I am the handmaid of the Lord. Let it be done to me in according to your word'* (Luke 1:38).

The Orthodox perspective on the moment of a human emergence in life is just after the sperm penetrated the egg. After that we must recognize the developing organism to be a human. In addition, in Church's Canons we find the prove of such a statement. In the second rule st. Basil the Great writes *'The woman purposely destroys her unborn child is guilty of murder. With us there is no nice enquiry as to its being formed or unformed'*²⁰.

Thus, every practice such as an abortion, the use of contraceptive pills or devices, embryo experiments, getting embryo stem cells, concerned with destroying or burdening of an embryo must be avoided. Other procedures should be studied carefully on which of them harms embryos and which is not. And this is the most important criterion to define appropriate methods of IVF, gene editing and others dealt with embryos. For instance, if a variant of IVF does not produce excess embryos and leads to formation only one transferred into wife's womb it can be accepted from Orthodox point of view.

The Orthodox perspective gives the new solution for Bioethical issues concerned with the beginning of human life. That is why the discussion in the society on these problems resulted in social policy and laws has to take account of Christian views as one of the different sides of the concept 'human'.

²⁰ St. Basil of Caesarea. *The letter 188 to Amphilochius*, concerning the Canons, in the Complete works of Saint Basil.