

# Is there a scientific basis to distinguish the moral status of biological entities? The example of parthenotes

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## Abstract

The fact that upon implantation in a properly functioning uterus a biological entity does not implant or dies soon after implantation is not a sufficient condition for concluding that such an organism is not an embryo and a person. Indeed, it could be a human person with a severe congenital defect, who could be rescued through an appropriate therapy. We need, therefore, a method for distinguishing between a biological entity, which is a sick embryo and a human person, and one, which is an embryo-like organism without personhood (pseudo-embryo). In this essay we argue that the *epigenetic information* granting the potentiality to develop the *neural activity responsible for spontaneous motility* can be considered a scientific basis for determining the moral status and achieving such a distinction.

## The developmental potentiality of a cell also depends on its *epigenetic information*

In sexual reproduction, each individual inherits one set of chromosomes from each parent. Normally there are two copies of each gene: one copy in a maternal chromosome and another copy in the corresponding paternal one. The maternal and paternal genomes are not exactly equivalent, but are endowed with different *imprints*, regulating the expression of a number of genes during embryonic development. The *imprints* or 'epigenetic modifications' consist in chemical changes in the DNA or in the chromosomal proteins that may mark any gene without changing the DNA sequence, and are transmitted through cell divisions (Loebel and Tam 2004).

In order for normal development to take place, the epigenetic inactivation of one gene from a gamete needs to be counterbalanced by the presence of the corresponding active gene from the other gamete. In certain cases, development fails if there are two active copies of the same gene (one copy in the maternal-derived and another in the paternal-derived chromosome). In such a case, it would be necessary to knockout or inactivate one of the copies to enhance normal development.

This demonstrates that the *developmental program* depends not only on the genetic sequence but also on the epigenetic state of the cell. Epigenetic activation or inactivation of genes can dramatically change the developmental potentiality.

## In defining death we assume that the human soul is intrinsically united to the neural activity responsible for breathing and other spontaneous movements.

Deciding about the moral status of an organism requires observable biological criteria. The definition of death as brain death, for instance, clearly establishes a transition point at which moral status of a person disappears on the basis of objective observable standards. Theoretically, one defines brain death as the complete, irreversible loss of all brain and brain stem functions. However, it is likely that some neural activity and integrative functions may continue even after brain death. In the clinical praxis, one declares a body brain dead when it has lost the *potential* to perform determined *spontaneous* movements, as for

instance breathing, eyes and legs movements. This requires in particular the disappearance of the neural activity responsible for such movements.

By *spontaneous* movements we mean movements of the human body like arm, leg, and lip movements, head flexion and rotation, eye and breathing movements (Huarte and Suarez 2004). Even if they are often unconscious and even intentionless, they are potentially will-directed movements, i.e., they can always be directed by the will when chosen. In contrast to these movements of the lips, tongue, eyes, fingers, etc., it is not possible to use “heart beating” to communicate messages. Movements, which are not caused by some stimulus external to the body, but which are strongly programmed by biology and cannot be brought under the immediate control of the will, we call *autonomous* movements. Another kind of movement that escapes the control of the will is a nerve *reflex* reaction that has an external cause. Neither autonomous movements nor reflexive ones are meant to be connoted by our term “spontaneous.”

By assuming that a brain dead organism is not a human person, we *immediately* associate personhood (or in philosophical terms, the activity of a human soul) with the *potentiality* for unfolding spontaneous motility. In particular, we correlate the activity of a human soul with neural activity as this reveals capability for spontaneous movements. By contrast, we do not associate the activity of the human soul directly with the activity of the heart, liver or kidneys, even if a lethal injury to these organs will ultimately also cause the loss of spontaneous movements. Consequently, transplantation e.g. of the heart cannot be considered equal to “transplanting” the human soul from one body to another.

### **Each human cell or organism with the *epigenetic information* granting potentiality to develop the neural activity responsible for *spontaneous fetal motility* deserves the moral status of a human person**

Spontaneous fetal motility appears in humans from the seventh pregnancy week (De Vries, Visser and Prechtl 1982), and is considered the sign of neural activity. However the fact that an embryo exhibits neural activity (responsible for breathing and other spontaneous movements) and *not only* heart beating depends exclusively on *embryonic information*, already well established before implantation, just like the sex of the fetus depends exclusively on *embryonic information*, and not on any information coming from the maternal organism.

Consequently, in accord with the definition of death, a biological entity or organism carrying an *epigenetic information* that makes it possible to unfold spontaneous fetal motility is animated by a human soul, and deserves the moral status of human person.

### **Principles for distinguishing between sick human embryos and pseudo-embryos**

The embryonic developmental path is richly branched and shows several bifurcations. The first one is the differentiation of the outer cell layer of the blastocyst (trophectoderm), which after implantation gives rise to placenta and extraembryonic tissues, and of the inner cell mass (ICM). The second main bifurcation consists in the differentiation of the ICM into further extraembryonic tissues and the primitive ectoderm. The next main bifurcation consists in the differentiation of the primitive ectoderm into ectoderm (external layer), mesoderm (middle layer), endoderm (internal layer), germ cells and extraembryonic mesoderm. The three embryonic germ layers are the source of all tissues of the body. In particular, the mesoderm differentiates mainly into bone marrow (blood), lymphatic tissue, connective tissues (bone, cartilage), vascular system, urogenital system, skeletal, smooth and cardiac muscles; the ectoderm into skin, neural tissue, eyes, pigment cells (The National Institute of Health, 2006).

For discussing the moral status of biological entities, we consider first the case of *androgenotes*, which are sometimes produced in nature, if during gamete fusion, the female nucleus is expelled from the oocyte. Androgenotes carry faulty epigenetic information due to a lack of maternal genes. Though exhibiting at the beginning an embryo-like development, androgenotes give rise to a blastocyst with well-developed outer layer (trophectoderm) but lacking the inner cell mass (ICM). After implantation, androgenotes produces in the uterus an entity called a “complete hydatidiform mole,” having the appearance of a bunch of grapes, and whose cells remain undifferentiated. A type of tumor called *chorion-epithelioma*

can arise from these entities. An epigenetic defect inhibiting the differentiation of the proper embryonic tissues and inducing only the differentiation of extra-embryonic ones *directly* excludes the potentiality for unfolding neural activity, and makes an organism intrinsically incapable of being animated by a human soul.

The opposite case would be an epigenetic alteration leading to a defective trophectoderm but a well-formed ICM. In this case the blastocyst would not be able to implant, and therefore would die. Notwithstanding, the organism has the epigenetic information directly responsible for the emergence of neural activity. Indeed, if one would inject the ICM into a healthy trophectoderm, one can expect that the so reconstituted blastocyst would be able to implant and develop to birth. This epigenetic alteration does not frustrate directly the development of neural activity, and could be compared to an intervention thwarting the implantation of a normal embryo into the uterus. We consider the organism carrying such an alteration a sick embryo and a human person.

Consider now the case of *parthenotes*. One can trick human oocytes into dividing, for instance by injecting an RNA molecule encoding for an enzyme produced by sperm (this RNA molecule allows the oocyte to synthesize the specific enzyme) (Rogers et al. 2004). Human oocytes contain two sets of chromosomes, one of which is normally discarded within two hours of fertilization. Using a chemical treatment to prevent this, one produces diploid *parthenotes* with both sets of chromosomes coming from the mother. They carry faulty epigenetic information due to a lack of paternal *imprinting*. These parthenotes appear to undergo the same changes as naturally fertilized eggs: They undergo cell-cleavages for four or five days, and some form blastocysts. Observations in mouse models show that parthenotes are capable of undergoing early post-implantation development; combining parthenogenetic primitive ectoderm with fertilization-derived trophectoderm and primitive endoderm (triple tissue blastocyst reconstitution) one can obtain parthenotes, which reach the stage of having vigorous heart beat and visceral yolk sac circulation, though they do not appear to go beyond this (Gardner et al. 1990; Kono et al. 1996; Surani 2002). However, observations with chimeras show that parthenogenetic stem cells have a differentiation potential comparable with heterozygous stem cells: they participate in normal embryonic development of chimeric animals following injection into blastocysts, and appear most likely to be incorporated in the brain (Strain et al. 1995; Boediono et al. 1999). These results support the conclusion that parthenotes fail to reach fetal motility not because a defective placenta or heart, but because defects in the brain itself: the parthenogenetic cells develop potential for contributing to brain centers only together with fertilization-derived cells. Parthenotes are organisms that develop heart beating and blood circulation but do not unfold the neural activity required for spontaneous fetal motility. *We assume that from a moral point of view such organisms share the same status as brain dead adults (i.e. after irreversible breakdown of the cortex and the brain stem), and should not be considered persons.* In more philosophical terms one could say that a parthenote lacks the biological conditions required for animation through a human soul, in much the same way as a brain dead adult.

Consider finally the case of an epigenetic defect that after gastrulation would inhibit the healthy differentiation of the cardiac muscle cells. As a consequence, the organism would die at mid-gestation, but not because direct inhibition of the emergence of neural activity: The epigenetic alteration does not directly prevent the neural activity but only *indirectly*. This mid-gestation lethality could be rescued by the injection of a low number of wild-type embryonic stem cells into the faulty blastocysts. We think that such a defect is easily comparable to a heart lethal injury, and their restoration to heart transplantation. Accordingly, *we think that in this case the comparison with a brain dead body does not hold, and assume that such an organism shares the same status as an adult with a healthy brain but with lethal injuries to other vital organs.* Therefore, from a moral point of view, the biological entity is also a sick embryo and deserves the moral status of a person.

We introduce now the abbreviation *DIANA* (Directly Inhibiting the Appearance of Neural Activity) to denote epigenetic alterations that frustrate the embryonic development on the path leading *directly* from the zygote to the emergence of the neural centers triggering fetal motility. Alterations frustrating the development on branches that do not differentiate into brain cells are *not DIANA* alterations, even if they may be lethal and lead *indirectly* to the failure of the brain development, as a consequence for instance of a defective heart or placenta. We sum up our view with the following three principles:

1. Any abnormality of the developmental program including one or several *DIANA* defects renders an organism inadequate to be animated by a human soul.
2. In absence of any *DIANA* defect, then one must conclude to the presence of a human soul, and consider the organism as a person with possibly some severe congenital illness.
3. If there is doubt about whether an organism contains a *DIANA* defect, one cannot exclude the presence of a human soul.

### Some definitions

According to the preceding three principles we introduce the following definitions:

An *embryo* is an organism that either is capable of reaching spontaneous fetal motility or has no *DIANA* defect. Human embryos are persons. An alteration of the *gene expression program* inducing disorganized growth *before* emergence of heart beating and blood circulation is not a sufficient condition to exclude a human person. An organism incapable of reaching spontaneous fetal motility but without any *DIANA* defect is a 'disabled' or sick embryo, and a sick human person.

A *pseudo-embryo* is an organism carrying at least one *DIANA* defect. Organisms that *additionally* carry other defects are also pseudo-embryos. Pseudo-embryos carrying exclusively *DIANA* alterations could be compared to a body without brain but with the other organs working well.

Against this view one could object that a *DIANA* alteration may be *reversible* (for instance, one could remove it through appropriate epigenetic modifications of the cells in an early developmental stage), whereas brain death follows from an *irreversible* damage. However, this objection does not invalidate our principles. We assume that a human soul is present, if the cell or organism owns the intrinsic potentiality to unfold the neural activity responsible for spontaneous movements. In case of a brain dead we have to deal with a body, which before exhibited such movements. Therefore to declare the person dead we have to be sure that his body no longer has potentiality for spontaneous motility, and for this reason we test whether it has irreversibly lost the capacity of performing such movements. By contrast, a human cell that has a *DIANA* alteration from the very beginning has no potentiality for spontaneous motility, and we assume that it is not a person. If one removes the alteration at a later moment and produces an organism capable of reaching spontaneous fetal motility, then we assume that a new person appears at the very moment the alteration disappears, the same way as we assume that a new person appears after fertilization.

Notice further that it is the *minimal developmental potentiality* (i.e. the inherent capability for unfolding spontaneous fetal motility), and not viability (i.e. the capability of reaching birth), what is decisive for determining the moral status.

### Conclusion

We have argued that as far as one accepts the clinical criteria of brain death as a *scientific basis* for defining death, one should reasonably accept that there is also a well-defined scientific basis for resolving the issue of the moral status of early developmental stages: a human cell with an *epigenetic information* bestowing potentiality to reach the stage at which *spontaneous fetal motility* appears should be considered a person; alterations of the developmental program that directly inhibit the appearance of neural activity (*DIANA* defects) are incompatible with personhood; organisms with defects other than *DIANA* are 'disabled' embryos, i.e. sick persons.

Admittedly, clearly establishing whether a particular defect is a *DIANA* one or not, may require substantial experimental work. But establishing cut-off clinical tests allowing us to have an appropriate definition of death also required substantial effort. For the time being, only epigenetic alterations present in androgenotes and standard parthenotes can be considered *DIANA* defects on the basis of available observations.

The issue of determining the moral status of human cells or biological entities is far of being closed. We hope that our proposal may contribute to explore it more in depth.

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