

Embryos and pseudoembryos: parthenotes, reprogrammed oocytes and headless clones

Helen Watt

Recent proposals for creating “pseudoembryos” by different techniques and moral status of such entities

What makes something (or someone) an embryo—as opposed to what is actually, and not just in biotech parlance, a collection of cells? This question has come to the fore in recent years with proposals for producing embryonic (or pseudoembryonic) stem cells for research. While some of those opposed to use of standard embryonic stem cells emphasise that adult (including umbilical) cells have a clinical track record, others argue that there may be further benefits obtainable from cells very like those of embryos, provided such cells can be derived in new ways. Rather than deriving them in ways that kill or otherwise endanger a living human embryo, they could be obtained from an entity that merely resembles a human embryo sufficiently closely for its cells to be of use. Such an entity might be created after introducing genetic changes to an ovum before it is activated by, for example, a cloning-type procedure, such that a gene essential to embryogenesis will be either absent, blocked in its expression, or over-expressed.^{1,2} The claim is that the ovum could be made to give rise to embryonic stem cells—mere living parts—without ever giving rise to a whole embryo, who is killed to obtain them. Whereas cloning “proper” winds back the specialisation of the cell nucleus to a point where a whole embryo is formed who has not yet specialised its cells, oocyte-assisted reprogramming (OAR), it is claimed, would wind back the specialisation merely to an intermediate point at which no embryo is created. Other methods proposed for deriving pseudoembryonic cells include parthenogenesis, in which an ovum is activated without a sperm, or even the insertion of an adult cell nucleus.¹

MORAL STATUS OF THE EMBRYO

In this paper, I assume that a genuine human embryo is a human organism, due to genetic and other factors, and therefore a human moral subject. It is not the purpose of this paper to argue in detail

for the view—admittedly counterintuitive to many—that the embryo has full human status. That said, it may be worth rehearsing some of the advantages of holding the position that the human person is simply the living human organism, at any stage of life. After all, this view provides us with a subject of a reassuringly bodily kind, who does not pass in and out of existence, or have its survival in any way attenuated, following changes in its mental states. (Embryos have, indeed, no mental states; however, they share this feature with older human beings at certain times in our lives.)

This position also avoids the peculiar dilemma of finding ourselves with two candidates for personhood occupying the same space: the organism which seems to acquire the supposed person-making feature and the entity supposedly created by that feature’s acquisition. It also avoids the unease we feel in saying that one and the same entity fluctuates in its moral status depending on whether a particular function has already been acquired and/or is currently possessed. It allows us to accept the common-sense view that immature humans have objective interests, and rights that those interests not be unjustly thwarted (eg, by experimental use).

So, assuming—if only for the purpose of this argument—that the embryo has full personal status, why might we think we can create pseudoembryos who lack this kind of status, but whose cells might still be experimentally useful? What kind of entity might a pseudoembryo be?

HYDATIFORM MOLES AND TERATOMAS

Here we might recall those naturally arising entities that are derived from human gametes but are not normally thought of as human organisms. One such entity is the (full) hydatiform mole, which produces not an organised body but merely placental material. Another such entity is the teratoma, a somewhat chaotic, if not entirely disorganised, cell mass, which produces skin, teeth and so on jumbled together, rather than body parts in due order.

PARTHENOTES AND PSEUDOCLONES

Already, scientists are experimenting with the deliberate production of various abnormal forms of cell division. Parthenogenesis, where an ovum is induced to start dividing without a sperm, has been carried out in mice, producing what is/resembles a small mouse embryo, but lacking a placenta. Further genetic interventions (the unblocking of one gene and blocking of another) result in a mouse pup that can go to term³—which does not, of course, show that a genuine mouse embryo can exist without such interventions.

Claims have been made to have produced human parthenotes, which the producers often describe as (non-viable) human embryos. While some commentators are understandably nervous about parthenogenesis in humans, others are more confident that a “human” parthenote, because of its limited potential, is not a genuine human embryo. Similar claims are made by those who call for an adaptation of cloning (eg, altered nuclear transfer including OAR^{1,2}) such that a genuine clone could not develop—or so it is maintained. Admittedly, the parthenote or pseudocloned would pass through some cell divisions before its cells are harvested; however, even an ovum with no nucleus can pass through a certain (lesser) number of cell divisions in a somewhat automatic way. The claim is that the parthenote or pseudocloned similarly does not have the potential to pass through human developmental stages: it is not on the developmental trajectory of a genuine human embryo.

UNBLOCKED RATIONAL POTENTIAL

What, then, might be a way of distinguishing pseudoembryos from embryos? Most would agree that the difference must relate to potential⁴ in some way—but in what way? Is there a link between a being’s interests in certain benefits and the potential which identifies that being as the kind of entity for whom such things are beneficial? Must the potential in question be immediate and/or unobstructed, or can it be long-term and/or blocked by a defect/disability?

Our first impulse might be to say that the embryo must have the potential for rationality. There are, however, serious problems with this suggestion, at least if potential is understood in the sense of unblocked (even if long-term) potential. After all, older human beings can be human beings without the unblocked potential for rationality—for example, when they are in a coma, reversible or otherwise. Such people are no less human beings/organisms—that is, continuing subjects of benefit or harm—for the fact that any potential they have for

rationality is currently blocked by their injury. Certainly, they would appear to have objective interests in regaining their (unblocked) rational powers, and rights that others assist, or at least do not deliberately prevent, their recovery. It would be odd to say that a patient has rights and interests concerning the retention of rational powers, but no rights or interests concerning their acquisition or reacquisition. (Here, we should remember the time-honoured principle that having an interest and taking an interest are two quite different things. The failed suicide who does not want to live has objective interests in physical and mental recovery, no less than the victim of accident or disease.)

To say that a genuine human embryo needs to have the unblocked potential for rationality leaves us, moreover, with problems similar to those mentioned earlier. Imagine a situation in which the embryo loses and acquires this long-term unblocked potential several times (eg, through genetic intervention). Are we to say that, contrary to this description, a new entity is created each time the potential is unblocked—and if so, what happens to the pre-existing entity which seems to acquire/reacquire that potential? Or, are we to say that one and the same entity loses all its status (including its morally significant interest in its own rational future) each time its potential is blocked—only to regain that status with the flick of a gene? Clearly, *some* genetic interventions, such as removing the nucleus from a one-cell embryo,ⁱⁱ will destroy the embryo's moral status—but only by destroying the embryo. By contrast, it is doubtful whether an intervention that merely blocks the expression of rational potential could destroy that embryonic being, much less any status it may have.

HUMAN ORGANISMIC POTENTIAL

If we are to identify a persisting subject of objective interests and rights, we must do so by finding some potential essential to the

ⁱNote that it is *active* potential—the power of an entity to *act*, while remaining the same entity⁴⁻⁶—which is in question here. The *passive* potential of a cell to be used to produce a different kind of entity is a separate phenomenon. True, embryonic cells are particularly plastic in terms of their ability to produce (or help produce) new organisms when isolated from and/or combined with other cells. We should, however, remember that adult cells can also be used to produce new living organisms, either by fertilisation or by cloning. Indeed, human adults, and even their gametes, have an active, not a mere passive potential to reproduce sexually—although they will forfeit their identity in the process in the case of gametes. Adult cells, like embryonic cells, can also be incorporated into existing organisms, as in stem cell research. The plasticity of a being's parts—that is, their ability to be put to new uses—does not change what those parts now constitute, or any moral claims that being may have.

subject, such that unless that potential is present, no organism exists of the kind we are considering. Bearing in mind that an organism is a self-organising living whole, we need to be clear that a living whole is present, not just a living part. Although necessary, this condition is certainly not sufficient; after all, the entity could be a living whole of some lower (non-rational) kind. Nor is it sufficient or, indeed, necessary that the entity be made from human gametes (sperm and egg), or contain 46 human chromosomes.

We should remember that human life is compatible with some fairly radical chromosomal errors: live-born babies who are tetraploid—that is, who have developed with double the correct number of chromosomes—have been reported. Conversely, some products of fertilisation have the right number of chromosomes, but chromosomes of the wrong origin—that is, hydatiform moles, all of whose chromosomes come from the male, and which only produce placental tissue.

Moreover, experimental interventions can blur the line between the human and the non-human. Already, cloning experiments have been performed where a human nucleus was transferred to an animal ovum. We can also imagine a human embryo being fused with a chimpanzee embryo, or otherwise subjected to a massive influx of genes from a non-human animal. Although the result may not be an embryo of any kind, let alone a human embryo, it would be good to establish some criteria for judging the results of such experiments, if only to prevent them from ever taking place.

HOLISTIC ACTIVITIES

What distinguishes normal (or indeed, disabled) embryos from mere collections of cells? Clearly, something to do with developmental potential—but what kind of developmental potential? After all, the embryo will sometimes be dying, like the human organism at a later stage—in which case, it will clearly not have the *unblocked* potential to develop as a fetus, infant and so on—let alone the unblocked potential for rationality that we mentioned earlier.

To be alive at all, the entity must have the potential for some future activity, however momentary. Life must be defined in relation to potential action, whether or not the entity is now acting. A frozen embryo is alive because of its tendency to act in a favourable environment, admittedly after “internal environmental” changes such as replacing the antifreeze with water before the embryo is thawed. The short-term

ⁱⁱTo say that the nuclear genes are necessary for the embryo's existence is not, however, to say they are sufficient, or that the human organism is reducible to its genes.

actions for which the embryo has the potential may superficially resemble those of (say) the hydatiform mole—for example, it may have the potential to go through one more cell division before death occurs. What makes the difference are the other tendencies which are present, albeit (since the embryo is dying) in blocked and thwarted form. In the embryo's case, these tendencies relate to the development of more mature self-organisation.

Self-organisation as a whole organism trivially involves holistic activities, as opposed to the local and/or random activities of mere living parts. Later in development, it is often claimed that such activities require a working brain; however, there is reason to doubt this. Individuals diagnosed as brain dead can heal wounds, fight infections, gestate babies and (in the case of children) grow up and pass through puberty. Some scepticism regarding the role of the brain as the body's essential organiser (as opposed to fine-tuner⁷) would appear to be in order.

ACEPHALICS

Whether or not the brain is required for holistic self-organisation in more mature (higher) organisms, it is very relevant to the question of what constitutes a *human* organism: an entity of the rational human kind. Consider the following example, which challenges the concept of “human organism”, and indeed that of “organism”. Many of us know of the existence of anencephalics: children born with working brain stems, but with massive damage to their upper brain. More rarely do we hear of acephalics, who (or which) lack a head altogether and are often supported by a baby to whom they are conjoined. If we were able to cause this condition genetically by a preconception intervention—for example, to produce a headless clone—what status would we ascribe to the entity damaged in this way from the outset? That would surely depend on the status we ascribed to the acephalic at a later stage.

Is an acephalic an organism in its own right, or merely an appendage of the twin, like the extra legs and so on sometimes found attached to a newborn baby? In the case of legs, we feel little temptation to say that a separate (although conjoined) organism is present. Legs alone do not seem to offer the self-controlling, holistic activities we require from organisms: for such local activity as they may engage in, the conjoined baby is an obvious suspect as the real controller.

By contrast, if the “appendage” is (or involves) a torso, we feel more tempted to call it an organism, as it may include some bodily systems of an apparently holistic nature. With acephalics—at least,

acephalics of a more complete kind—we are tempted to say that we know what the organism (if it is an organism) is *missing*. The structures they have (eg, the spinal cord structures) are geared, or partly geared, to support the human brain that they lack. In lacking the brain, they lack the structural precursors required for the development of rational thought—that is, they lack rational potential in its normal, unblocked form. Sympathy for their plight—as opposed to that of conjoined legs that do not “lack” such potential—seems, for that reason, morally appropriate. Such individuals would appear to have interests—including an interest in any future treatment, and rights—including the right not to be subjected to harmful experimentation.

So, where does all of this leave us in the case of parthenotes and pseudoclones? If the above analysis is correct, it is not sufficient to rule out human status to find that development (including rational development) is blocked, as this is the case for any dying embryo or indeed infant, who nonetheless has interests in the currently excluded rational future appropriate to a being of its kind. Note that it is not necessary for the damaged embryo to have specific genetic information for a working (rational) brain—any more than an adult with brain damage need have the more developed structures of a rational brain to be a being of a rational kind. If reconstructive surgery is needed to make a new brain (or part of a brain) grow where the old brain has been damaged, this is surely in the interests of an adult with brain damage. In the same way, if the injection of genes or cells would make the headless clone start constructing a head and brain in utero, this is surely in the health interests of the clone.

HEADLESS CLONES

What are we to say about the deliberate creation of damaged human embryos whose potential is blocked—or alternatively, about the deliberate creation of pseudoembryos? On the view of the embryo assumed in this paper, the question is easy to answer in the case of genuine (although damaged) embryos whose development is thwarted. In the words of Timothy Mosteller:

A headless clone, on Aristotle's view, just can't be happy. While she is the kind of being that could be happy, she is not happy because she cannot actualize her latent capacity to be happy. A headless clone can't move ahead towards happiness, because she can't actualize her head. But the question is how did she get that way? How did this human being

get into a state such that she could not become happy? Someone put her into that state. Someone made her unhappy. So, now what you have is one person (a scientist) who is intentionally making someone else (a headless human clone) unhappy.⁸

In some cases, it may be quite unclear whether a damaged human embryo will result from a genetic intervention. Caution is required before creating what may well be an embryo, bearing in mind that even a procedure which, if successful, would not create an embryo could produce a damaged embryo if it goes wrong—which is especially likely while the procedure is being developed.

This also applies to the creation of animal-human hybrids or chimaeras. Streiffer⁹ has pointed out the possible implications of such creations, on his own assumption that moral status can be increased incrementally in one and the same living being. Those of us who connect moral status to fulfilment as the kind of being one is—and who see a fundamental divide between rational-type and non-rational-type beings—still have reason to fear the creation of human (or at least, rational-type) beings for research purposes by combining human and animal cells. Any subsequent damage to the resultant being—including damage to its rational-type structures—would be no more defensible than similar damage to any human individual. Should such damage be done, a surviving chimaera would have—like any other damaged human/rational-type being—objective interests in recovering its health, so as to reach its rational fulfilment. (Whether the chimaera could survive the removal of *all* human cells and structures is a different question: this would seem to bring about its substitution by a truly subhuman entity.)

RESPECT FOR PARENTHOOD

In some cases of chimaerism, the resulting organism will be fairly clearly human—for example, when an animal trophoctoderm (producing the placenta) is combined with a human inner cell mass (producing the rest of the embryo). Perhaps one could be equally confident that (say) a given product of successful OAR is not a human being. However, even in cases where a genetic intervention produces what is clearly a mere pseudoembryo, there are moral considerations that might lead us to oppose its creation. It is worth recalling that in the case of fertilisation of human eggs with animal sperm or vice versa, no one expects a human embryo to be created (indeed, it is doubtful whether *any* embryo will be

created). Nonetheless, trans-species fertilisation is widely regarded as repugnant, perhaps because it is seen, however dimly, as disrespectful of human parenthood. To make a substantial contribution to what resembles, but is not, a human or animal embryo seems in some way a failure to respect the dignity of human procreation, which is partly rooted in the dignity of any human child. Even if we do not make use of human reproductive powers as such, but use a human nucleus, not a sperm, to activate an animal ovum, it is morally relevant that the human nucleus is substituting for the reproductive powers of two non-human animals. We fail to respect human parenthood, it seems, when we engage in an activity, which is both too close to—and also too remote from—achieving conception in a way befitting our kind.

ACKNOWLEDGEMENTS

I thank Anthony McCarthy, Patrick Carr, Kevin Flannery, Tadeusz Pacholczyk, Antoine Suarez, Ted Watt and two anonymous reviewers of the *Journal of Medical Ethics* for their comments on this paper.

J Med Ethics 2007;33:554–556.
doi: 10.1136/jme.2006.017426

Correspondence to: Dr H Watt, Linacre Centre for Healthcare Ethics, 38 Circus Road, London NW8 9SE, UK; h.watt@linacre.org

Received 16 May 2006
Revised 23 August 2006
Accepted 29 August 2006

Competing interests: None.

REFERENCES

- 1 **President's Council on Bioethics.** *White paper: alternative sources of pluripotent stem cells.* Washington, DC: President's Council on Bioethics, Section III, May 2005, http://www.bioethics.gov/reports/white_paper/index.html (accessed 16 March 2007).
- 2 **Arkes H, Austriaco N, Berg T, et al.** Joint statement on production of pluripotent stem cells by oocyte assisted reprogramming. http://www.bioethics.gov/reports/white_paper/text.html and http://www.cbhd.org/resources/stemcells/jointstatement_2005-06-20.htm (accessed 16 March 2007). For ongoing discussion of the proposal, see the *National Catholic Bioethics Quarterly*, <http://www.ncbcenter.org/ncbq.asp> and *Communio*, <http://www.communio-icr.com> (accessed 16 March 2007).
- 3 **Kono T, Obata Y, Wu Q, et al.** Birth of parthenogenetic mice that can develop to adulthood. *Nature* 2004;428:860–4.
- 4 **Wade FC.** Potentiality in the abortion discussion. *Rev Metaphys* 1975;29:239–55.
- 5 **Watt H.** Potential and the early human. *J Med Ethics* 1996;22:222–6.
- 6 **Watt H.** *Life and death in healthcare ethics: a short introduction.* London: Routledge, 2000:59–62.
- 7 **Shewmon DA.** The brain and somatic integration: insights into the standard biological rationale for equating “brain death” with death. *J Med Philos* 2001;26:457–78.
- 8 **Mosteller T.** Aristotle and headless clones. *Theor Med Bioeth* 2005;26:339–50.
- 9 **Streiffer R.** At the edge of humanity: human stem cells, chimeras, and moral status. *Kennedy Inst Ethics J* 2005;15:347–70.