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by

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The recent report of the cloning of human beings has reignited the debate surrounding the nature of the pre-implantation embryo.[1] For many, the line of argument most threatening to the position which accords the pre-implantation embryo the moral status of a person from the moment of fertilization is the proposal that scientists have shown that the early embryo is not an individual. Theologian Norman Ford has formulated the challenge this way: "(W)hen the zygote divides during normal development to form two cells, do we have a *two-celled individual*, or simply two individual cells? (Original emphasis)."[2] In response, he and others have asserted that the totipotency of the cells of the early embryo, that is their ability to give rise to several individual adult organisms, suggests that no individual is present early in development.[3] Individuality, the argument continues, is a characteristic that only arises with the appearance of the primitive streak when the embryo no longer has the potential for twinning. This conclusion has been widely used in support of proposals that would lead to the destruction of early human embryos since the lack of individuality would suggest that no single entity is present which would merit moral status.[4]

New empirical data has now undermined this position. Two recent cellular studies on axial development in the mouse embryo have clarified the developmental events which occur immediately after fertilization providing compelling evidence that the embryo, even during its earliest stages of development, is an integral whole. Though these experiments

were done in mouse embryos, human embryos would be expected to develop in a parallel fashion. In answer to Ford's question, we can now say with scientific certainty that the two-celled mammalian embryo is indeed a two-celled individual.

Early studies of mammalian embryonic development suggested that the pattern of the embryo was not formed immediately at fertilization but arose through a process of cell interaction and communication.[5] Two landmark studies have challenged this orthodoxy. In the first study, Piotrowska and Zernicka-Goetz showed that the sperm entry point (SEP) predicts the plane of initial cleavage of the mouse egg.[6] Using fluorescent beads to mark the SEP, the authors were able to show that the SEP defined the plane of cleavage dividing the embryo into distinct halves. Furthermore, in 75% of 92 two-celled embryos, the cell which contained the SEP divided first. This is significant because earlier dividing cells become preferentially incorporated into the inner cell mass which will later develop into the adult organism. In other words, division in the early embryo is not at random – at fertilization, the sperm already patterns the zygote so that it divides in a specific way. Positional information exists from the very first moment of the zygote's existence and the embryo is never an unorganized mass of cells. As the authors of the study state: "We conclude that two axes of the blastocyst (the coordinate system which positions the cells in a later stage of development characterized by the appearance of a cavity, the blastocoel, within the embryo) become specified in the single-cell embryo."[7] In the second study, Richard Gardner confirmed this conclusion in his own work where he injected small oil drops into the zona pellucida, the outer shell of the zygote, in order to observe the establishment of the embryonic axes.[8] Significantly, the axes of the blastocyst have been implicated in establishing the axes of the fetus suggesting that continuity exists between the one-cell embryo, the blastocyst, the fetus, and therefore, the newborn.[9]

Both these scientific papers clearly demonstrate that the early mammalian pre-implantation embryo manifests an integrity characteristic of intact organisms – the two-celled embryo is a two-celled individual and not two individual cells. Each cell of the two cells is already specified such that each will give rise to particular cell lineages within the embryo.[10] Note that the specification of positional information in the embryo by the sperm entry point suggests that its existence as a new organism, which is defined here as a discrete unit of living matter which follows a self-driven, robust developmental pathway[11], can be traced back to fertilization. This would counter any other suggestion that could be made that the new individual comes to be either when its own intact genome first comes into being with the fusion of both the sperm and the egg pro-nuclei or when its own genes are first expressed, events which do not occur until some hours or even

days after fertilization.[12] In sum, the empirical data, by pointing to the unity and uniqueness of the pre-implantation embryo, has confirmed the assertion that fertilization properly marks the beginning of the mammalian and thus human individual.

Two objections can be made to the position described above. Both deal with the metaphysics of individuality. First, it can be argued that continuity of development does not ensure that the two-celled embryo is the same individual as the mature organism. Consider the following scenario: If I take a rotten old rowboat and gradually replace its worn out components, piece by piece, until I end up with a lacquered, gleaming runabout with a Mercury outboard motor, do I still have the same boat? There is a continuity of development, after all. Could the process of human embryonic and fetal development not simply be an example of this type of process? In response one can point out that an underlying presupposition for the argument presented in this essay is that biological individuals which are integral wholes are radically different from non-biological individuals which are simply organized collections of parts. Individual living organisms manifest an integrity that allows them to maintain their identity through billions of sequential changes involving their parts. In contrast, individual galaxies made up of billions stars or individual herds of dozens of elephants do not. But is this a reasonable distinction? The answer is clear, I think, when one considers the alternative. Decades of kinetic and metabolic studies using a variety of experimental techniques suggest that 98% of the atoms of the adult human body, including those found in the brain and nervous system, are replaced in about two years.[13] In light of this, it would seem that anyone who rejects the distinction between living substances and non-living aggregates would have to conclude that he or she can only exist and be identified as a distinct and unique human individual for a maximum of two years, a point which, I believe, is obviously ludicrous. The embryo is not a rowboat.

Second, if a two-celled embryo is in fact an organism, how then do we explain twinning? What happens to the individual here? In response one can demonstrate that developmental plasticity does not necessarily preclude individuality. The planaria and the hydra are two simple organisms that can give rise to identical clones if they are dissected in the appropriate manner.[14] Each half has the potential to generate an intact organism and yet no one would doubt the individuality of the original intact invertebrate. In the same way, the early embryo, though already an individual, still manifests a developmental plasticity which allows each totipotent cell to give rise to an intact organism if the embryo is disrupted. Note, however, that this would interrupt the normal developmental process of the embryo and would involve a reprogramming of the cells and the respecification of the embryonic axes first specified at fertilization. It is significant that

twinning is associated with an increased incidence of birth defects in humans.[15] This is just another reminder that twinning is the exception and not the rule in mammalian embryonic development.

References

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http://www.liebertpub.com/EBI/default1.asp

2. Norman Ford, "The Early Human Embryo as Person in Catholic Teaching," *National Catholic Bioethics Quarterly* 1 (2001): 155-160, p. 160.

3. For representative formulations of this proposal, see N. Ford, *When Did I Begin?* (Cambridge: Cambridge University Press, 1988), pp. 116-131, and H. Kuhse and P Singer, "Individuals, Humans and Persons: The Issue of Moral Status," in P. Singer, H. Kuhse, S. Buckle, K. Dawson, P. Kasimba, Eds., *Embryo Experimentation* (Cambridge: Cambridge University Press, 1990), pp. 65-75.

4. For example, this position was endorsed in an unsigned opinion piece in the prestigious scientific journal *Nature* as one reason for the licitness of embryonic stem cell research. In fact, as the essay points out, the British Parliament in 1990 was persuaded to permit experimentation on pre-gastrulation embryos precisely by this argument. See "The Meaning of Life," *Nature* 412 (2001): 255.

5. For details and citations to the relevant literature, see Martin H. Johnson, "Mammalian Development: Axes in the Egg?," *Current Biology* 11 (2001): R281-R284.

6. Karolina Piotrowska and Magdalena Zernicka-Goetz, "Role for Sperm in Spatial Patterning of the Early Mouse Embryo," *Nature* 409 (2001): 517-521.

7. Ibid., p. 521.

8. R.L. Gardner, "Specification of Embryonic Axes Begins Before Cleavage in Normal Mouse Development," *Development*, 128 (2001): 839-847.

9. For details, see M.A. Ciemerych, D. Mesnard, M. Zernicka-Goetz, "Animal and Vegetal Poles of the Mouse Egg Predict the Polarity of the Embryonic Axis, Yet are Nonessential for Development," *Development* 127 (2000): 3467-3474.

10. Even more recent lineage tracing studies have confirmed this discovery. See K. Piotrowska, F. Wianny, R.A. Pederson, and M. Zernicka-Goetz, "Blastomeres Arising from the First Cleavage Division have Distinguishable Fates in Normal Mouse Development," *Development* 128 (2001): 3739-3748.

11. B. Goodwin, "Development as a Robust Natural Process," in W. Stein and F.J. Varela, eds., *Thinking About Biology* (Reading, MA: Addison Wesley Publishing Co., 1993), pp. 123-149.

12. For instance, theologian Lisa Sowle Cahill suggests that since scientists have shown that fertilization is a process, it cannot be the moment when individuality is specified. See her "Abortion, Sex and Gender: The Church's Public Voice," *America* 168 (1993): 6-11. A similar argument is made by T.A. Shannon and A.B. Wolter in their "Reflections on the Moral Status of the Pre-Embryo," *Theological Studies*, 51 (1990): 603-626, pp. 606-608.

13. No one single study reports this result. The calculation for this is as follows. Studies of body composition show that the human body is made up primarily of eleven elements. However, 99% of the total atoms are H, O, C, and N. Further, nearly all of these atoms are found as water, protein, fat and carbohydrates which are the four largest categories of molecular components of the human body. Approximate replacement rates for these components (assuming for simplicity that there is no weight gain or loss) can be calculated for the 70-kg reference man.

Water: In the reference man, 42 kg is water with a replacement rate of approximately 10% per day. Consequently, 99% of the total water in the human body will be replaced *de novo* in approximately 60 days.

Protein: In the reference man, 10.5 kg is protein with a replacement rate of approximately 1% per day (Turnover rate: 250g/day with absorption rate of 184 g/d.). Consequently, 99% of the total protein in the human body will be replaced *de novo* in approximately 450 days.

Fat: In the reference man, 12 kg is fat with a replacement rate of approximately 0.71% per day(Turnover rate: 210g/day with absorption rate of 142 g/d). Consequently, 99% of the total fat in the human body will be replaced *de novo* in approximately 650 days.

Carbohydrates: In the reference man, 0.5 kg is glycogen (carbohydrates) with a replacement rate of approximately 35% per day (Turnover rate: 220g/day with absorption rate of 800 g/d). Consequently, 99% of the total carbohydrates in the human body will be replaced *de novo* in approximately 11 days.

In sum, the component with the limiting replacement rate is fat. We can conclude therefore that 99% of 99% (that is, 98%) of the total atoms of the human body are replaced in approximately 650 days, which is less than two years. In fact, this would

be an overestimate, given the higher turnover rates of the other bodily components. Note that less than 1% of the total atoms in the body (composed primarily of minerals and rare elements) have a negligible replacement rate. If one held the non-substantial view of the human body, could one claim that conservation of these few atoms is responsible for maintaining personal identity? In response, I return to the rowboat analogy. Would the conservation of a few nails in the transformation of the rowboat into the speedster be sufficient to maintain that the original boat remains? I think not. Finally, it is noteworthy that atomic replacement also occurs throughout the neural system which for many materialists is responsible for maintaining personal identity in the human being. This replacement of atoms takes place during normal metabolism within cells and occurs even in the absence of cellular replacement or replication.

Body composition data was obtained from *Report of the Task Group on Reference Man*, International Commission on Radiological Protection (New York: Oxford University Press, 1975). Absorption/digestion rates were taken from R.M. Berne and M.N. Levy, eds. *Physiology*, 4th edition (St. Louis: Mosby, 1998) cited in "Digestion and Absorption: Lecture 61," presented by Prof. Wechsler at: http://www.mmi.mcgill.ca/Unit4/Wechsler/lect61digestionabsorption.htm, accessed on November 8, 2001. Maximum values of the indicated range were used in the calculation. Turnover rates were communicated to me by (water) P. Spanel and D. Smith [See their paper with S. Davies, "Rapid Measurement of Deuterium Content of Breath Following Oral Ingestion to Determine Body Water," *Physiol. Meas.* 22 (2001): 651-659]; (protein) D. Matthews [See his paper, "Proteins and Amino Acids," in *Modern Nutrition and Disease*, 9th edition. M.E. Shils, J.A. Olson, M. Shike, and A.C. Ross, eds. (Baltimore: William & Wilkins, 1999), pp. 11-48]; and (carbohydrates and fats) R. Wolfe [See his book, *Radioactive and Stable Isotope Tracers in Biomedicine: Principles and Practice of Kinetic Analysis*, (New York, Wiley-Liss, 1992)]. I thank these individuals for their assistance.

14. For details, see K. Agata and K. Watanabe, "Molecular and Cellular Aspects of Planarian Regeneration," *Semin. Cell Dev. Biol.* 10 (1999): 377-383, and W.A. Muller, "Pattern Formation in the Immortal Hydra," *Trends. Gen.* 12 (1996): 91-96.

15. For details, see P.M. Layde, J.D. Erickson, A. Falek, and B.J. McCarthy, "Congenital Malformation in Twins," *Am. J. Hum Genet.* 32 (1980): 69-78, and B. Luke and L.G. Keith, "Monozygotic Twinning as a Congenital Defect and Congenital Defects in Monozygotic twins," *Fetal Diagn Ther* 5 (1990): 61-69.