Dimensions of Goodness

Edited by

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CHAPTER NINE

FINDING GOODNESS AMONG IS AND OUGHT DEBATES IN STEM-CELL RESEARCH

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1. Context

In 1997, the announcement of the birth of Dolly the cloned sheep stirred considerable public interest. Unfortunately, the noisy and sometimes hysterical discussion left an impression that the science was somehow suspect morally and that science was in conflict with ethics. The next year, the announcement of James Thomson's and John Gearhart's successful production of human stem cell lines fell on ground already conditioned by the cloning debates.[1] Many critics immediately assumed that they knew what was at issue and that this, too, was a matter of science in conflict with ethics.[2] The "ought" of ethical principles seemed to be at odds with the "is" of scientific innovation. The demands for applications of human embryonic stem-cell research to achieve highly anticipated clinical applications through what came to be called "regenerative medicine" muddied the waters considerably. Clinical applications seemed to offer clear ethical goodness, and yet seemed to be in conflict with other claims about purported goodness of respecting embryos.

A typical framing for such discussions includes insisting that the science and ethics are separate domains that intersect when applied to actual cases. Yes, science should be ethical. And yes, of course, ethical discussions should try to respect the workings and goals of science. But fundamentally, we should develop ethical frameworks independently. In particular, it is generally agreed that we should never try to derive "ought" claims from "is" claims. This formulation takes us to David Hume's well-

known insistence on the separation.[3] Epistemic claims about ethics have to look elsewhere then to science for grounding, while science must follow its own principles and methods so that "good science" is not necessary the same as "science doing good."

All successful introductory philosophy students know of Hume's warning. They know that we cannot get the ought from the is of nature. Here I take this admonition the other way around. It is equally problematic to begin from moral convictions and assertions about what must be right and attempt to reach conclusions about what must actually be the case. To put it another way: wishing something is so cannot make it so.

This may seem obvious, but it is precisely what many have done with human embryonic stem-cell research. With strong declarations about what they believe to be morally true, they then make statements about the nature of embryos. Yet those statements do not conform to scientific fact. Any attempt to derive what is from what is thought to be morally right cannot work. This paper examines the case at hand and begins with a demonstration of the biological knowledge about embryos to establish the "is" of embryo research. The first section lays out what is understood biologically about embryos. This is presented in historical context, to show the various competing ideas and how they have developed. The second section discusses current stem-cell research and lays out the issues involved there. Then we come back to the intersection of ethical and scientific claims to look at how we can negotiate reasonable intersections that respect all positions.

2. Biological Embryos

Historically, embryos were thought to begin as unformed matter. Aristotle presented the view of generation of animals that stood as the standard until the seventeenth and eighteenth centuries. On this interpretation of animal embryos (including humans), fluids from the male and female combine together. Over a period of "forty days," the fluids undergo a process whereby the final, formal, efficient, and material causes work together to bring about form out of the originally unformed. This process of gradual formation, known as epigenesis, was almost universally accepted by those who thought at all about how development occurs. Catholic, Muslim, and Jewish traditions embraced the same view.[4] And it makes sense, based on what one can experience and see: there does not seem to be any form there from the very beginning. Rather, form does seem to emerge gradually, whether one is judging by looking at something like a caterpillar or is experiencing the phenomenon as mothers do.[5]

Epigenetic understanding of embryos dominated until the seventeenth and eighteenth centuries. This view also generally involved some sort of vitalistic explanation of how that form emerged out of the unformed. Caspar Friedrich Wolff was one leading proponent of this view. Then metaphysical demands enticed some of the new natural philosophers of the Scientific Revolution toward an alternative account. In particular, they rejected vitalism. These metaphysical materialists, including Albrecht von Haller, Charles Bonnet, and Lazzaro Spallanzani, insisted that what exists in the world is only matter and motion, and any explanation must depend on only those two factors.[6] Since they could not imagine how form could arise from the unformed material without some vitalistic force or factor, they rejected vitalism and were thereby led to invoke preformationist ideas. Instead of beginning with truly unformed matter, they argued, the form must actually be there at the start.

The result was a period of rather vehement debate about principles, and also an intense period of observation and experimentation to try to see what is actually the case. Look inside the caterpillar to see whether there is a butterfly there, for example. Look at tadpoles to see if there are frogs already inside. Look at chicks to see whether there is a really a heart there from the beginning, and we only become able to see it later. Intense debates, intense observing, developing new ways to see better "inside" the organisms, and working to determine how to achieve well-founded evidence for scientific explanation: this was the heart of the period, with embryo research at the center of the action.

By the early nineteenth century, some preformationists continued to make their arguments, but the leading naturalists were following the same path as Karl Ernst von Baer. He looked at chicks and saw them clearly emerging from the unformed to defined form; he could see the moment the heart started to beat and the way parts moved around to form the chick. He looked at frogs and saw one big egg, which then divided into two and then four parts, and so on.[7] Von Baer studied these stages, and interpreted the way that cells divide in step after step of embryonic development.

This is not the place to rehearse the entire history of embryology, but it is important to note that the nineteenth century was a wonderfully active time. Cell theory provided a way to understand the divisions that occur gradually in development, and it seemed clear that some unit of life like cells provided a foundation for subsequent structure and function.[8] Studying details of cell action, along with details of the fertilization process and everything else they could observe fascinated a growing number of researchers. Epigenetic interpretations clearly dominated, with the focus on how to understand the steps in the developmental process.

The biological embryo was material that followed developmental processes through some combination of internal and external environmental forces. These embryological researchers assumed that they had an individual developing organism that became organized, and they did not make an effort to define any precise moment when life begins. Or when an individual life begins. Or what that means. The "is" discussions about embryos were not focused on identifying vitality or individuality, and indeed there was much discussion at the end of the nineteenth and the beginning of the twentieth century about how the "senescence" and death of one organism actually gives rise to "rejuvenescence" of another and therefore continuation of the germ line. The primary issue was identifying not some time when life began but rather what happened during the continuing processes of development.

That was the issue for biological researchers. In contrast, Pope Pius IX did find it useful to declare when an individual life begins. In the context of his pushing back to more traditional Church interpretations through what was eventually called Vatican I, Pius IX declared that an individual life begins at "conception," by which he clearly meant fertilization.[9]

This metaphysical view based on moral grounds was as good as any other in imposing a definition of life for religious purposes. Yet it carried with it something less benign. Pius IX used the interpretation to reinforce the view that abortion is illicit, as is birth control. The position was a metaphysical view grounded in ethical and religious interpretation. It was not fully consistent with the dominant epigenetic understanding of development that saw the individual living organism as coming into being only gradually. Yet at the time, the two could be made compatible with interpretation, something along the lines that what happens at conception is a sort of "ensoulment" that defines individuality, and what happens in development is the expression of that individuality in the context of its environment. On this sort of interpretation, the religious/ethical domain could remain largely separate from the material biological domain and might feel little need to intersect with it in ways that would demand deeper interpretation.

Yet the biological domain does exist, and by the end of the nineteenth century, researchers were learning a great deal more about it. They were documenting developmental stages in many organisms.[10] In humans, Wilhelm His collected all the human embryos he could find at all stages of development. He laid out the stages, which became rather hazy at the earliest points, since there was little to see and challenges in knowing even where to look. Franklin Paine Mall in the United States took up collecting human embryos and eventually the collection moved to Johns Hopkins with Mall, supported by Andrew Carnegie through what became the Carnegie Institution of Washington Embryology Department.[11] Through the public collection, publications, and eventually the website cited here, this provided a publicly visual representation of what an embryo is, and how it develops. It seemed clear from the very visible evidence that the embryo was not at all the same from the very earliest stages of "conception." Rather it changed quite considerably. And the embryo changed especially at eight weeks, when it is fully formed with all the essential parts and becomes known as a fetus (as noted in the very first edition of the *Encyclopedia Britannica* in 1771).

Meanwhile, in addition to this effort to observe and document human development, researchers who began to call themselves biologists looked at a wide variety of other organisms to see how they developed. They assumed that different types would develop differently, but that there were common patterns of development underlying each. Researchers, led in the United States by Charles Otis Whitman, carried out what they called cell lineage work, which traced the early stages in many organisms—from the moment of fertilization (which they showed is itself an extended and complex process) through each cell division, for as long as they could observe the results until the organism became too complex to observe directly inside it any more.[12]

Others wanted to see "inside" at least stages when the inside was not directly visible, and they turned to experimental embryology. Wilhelm Roux defined a program of *Entwicklungsmechanik*, which sought to discover the mechanics of developmental processes. With a hot needle, he poked one of the two cells of the frog's egg, after the first cell division. He assumed that this killed the cell, and that the remaining cell would develop as normal – ending up as one half a frog embryo with inert material stuck to it.[13] This is what seemed to happen, and for Roux it confirmed his idea that as the cells divide materially, they also divide up the hereditary units (which he believed resided with the chromosome in some way, though the details were not at all clear). Roux's experiments suggested a new sort of preformationism, or really a predeterminism.

Hans Driesch followed Roux's lead and carried out a similar experiment with sea urchins. He shook apart the two cells after the first division and watched them develop into two somewhat smaller and yet whole larval urchins.[14] In contrast to Roux's results, this showed quite clearly the capacity of each half to regulate development and to produce a new individual. One became two, or went through what seemed to be a sort of twinning process. Development happens epigenetically, and what counts as an individual is complex. The two distinct lives that emerged in

this case certainly did not begin as two immediately at fertilization—or not in any straightforward sense—but later.

Hans Spemann added another twist to the understanding of developing embryos with his "organizer" experiments. He discovered that a particular bit of an embryo, namely the dorsal lip of the blastopore stage, had the capacity to induce formation of a second embryo if it were placed inside a host embryo at the gastrulation stage. That is, what would normally have become one embryo actually had a second embryo attached to it and growing out of it.[15] Again, we see that the individuality is redefined much later than fertilization, and the embryo as a whole responds to changing conditions in complex ways.

The emphasis on genetics starting with the discovery of the double helix structure of DNA in 1953 by Watson and Crick led to much discussion about the interaction of genes and the developing embryo. Genetics suggested to some a sort of new predeterminism, wherein the genes carried the information that would direct development. This could be seen as reinforcing the idea that what defines the individual life does begin at fertilization—insofar as fertilization and genetics actually defines the individual life. The central questions about development nonetheless remained fundamentally the same.

Beatrice Mintz brought a new way of reorganizing embryos that should have raised many new questions about what we mean by an embryo and certainly what we mean by an individual. Working with mice, she showed that she could take individual cells from embryos at the two or four or even eight cell stage and combine them.[16] She could take them from different individuals, and even different strains of mice. The result was a mix of chimeras, made up of genetic material from different individuals but reformed into a new individual.

What is astonishing about this, in retrospect, is not that the work could be done. Rather, the fact that the embryo has the capacity to adjust to such changes and produce a complex new individual made up of different genetic information in different cells, but still make itself work as a functioning and apparently perfectly normal mouse—that is remarkable. Embryos have tremendous regulatory capacity, this work showed. And embryos are certainly not individual organisms that were defined and set in action at fertilization in the way that Pope Pius IX seems to have imagined. If we want our moral views to be consistent with the knowledge provided by the biology, we need to rethink this conclusion.

Another set of experiments in the 1970s by Leroy Stevens added yet another confirmation of the ability to regulate and adjust to changed circumstances, but in this case not always accurately. Funded by tobacco-

company money, Stevens was studying mouse tumor development in order to address the question whether it is the tobacco or the cigarette papers that cause cancer. Stevens discovered strain 129 which exhibited a strange behavior.[17] The testicles in many of these mice developed teratomas—that is, they generated a mix of hair, skin, teeth, and other tissues that (obviously) do not normally occur is the testicles. The cells differentiated into tissue, but in the wrong place. The developmental cues seemed to have gone wrong. And this raised questions about how the normal process of development is guided, and to what extent it can be redirected or "fixed" if there are "errors."

1978 brought the first successful *in vitro* fertilization. Robert Edwards and Patrick Steptoe tried and tried, and finally by accident discovered that the right timing of the egg cycle would allow them to fertilize the egg *in vitro*. Louise Brown, the first "test tube baby," seems to have developed completely normally, and she showed that even the fertilization process is very flexible and capable of regulation.[18] With pre-implantation genetic diagnosis, it became possible to take away one, or two, or even more of the cells of an eight-cell human embryo to test for genetic "disease." This is an extremely powerful tool, and it is again surprising to learn that at the eight-cell stage, each cell seems to be truly totipotent—or to have the capacity to become a whole individual organism. Or, it seems, any combination of cells from that eight-cell stage can recombine and develop into an individual, as Mintz had shown with mice.

The embryo is a highly flexible thing, with epigenetic development informed by genetics, but in ways that may be complex. Fertilization is a starting point, but development involves very complex processes with tremendous capacity for regulatory response to the changing environment. The individual organism is clearly an interactive whole, but it is not clear at what point should be said to "begin"—given the demonstrated capacity to remove or add cells or genes and change the process considerably. Furthermore, since most of the body cells die and are replaced many times during a life, it is not clear that the actual material individual organism conforms to the ethical view of it. Biology shows that we need a much more robust, dynamic, and complex idea of what life is. Stem-cell research provides a new perspective on what is. Then we can begin to think more wisely about the ethical implications that connect the biological and ethical domains.

3. Stem-Cell Research

As of today, there are three categories of stem cells: embryonic, adult, and induced pluripotent. All are defined in terms of their abilities to self-replicate, producing more like themselves, or to differentiate further.[19] Embryonic stem cells come, by definition, from embryos. Since, with our current technological capabilities, human embryos are only viable outside the mother's uterus up until the blastocyst stage and stem cells first develop at this stage, human embryonic stem cells come from blastocysts. Up to that stage cells are initially totipotent, up through the eight-cell stage in humans, which means that each cell can give rise to the total organism.

At that point, cells begin to divide differently and to develop into an inner cell mass surrounded by a single layer of cells, which becomes the placenta. Those cells inside the inner cell mass are called pluripotent, meaning that each of them has the ability to become any kind of cell in the body—but not all kinds. Up to the blastocyst stage, the embryo can grow in the laboratory dish, which has caused ethicists to ask "What's in the dish?"[20] For biologists, it is cells in the dish, and they make up an embryo. The embryo is not viable on its own past the blastocyst stage, and must either be frozen for later implantation or actually implanted in a mother at that point to continue living.

Stem cells of the second type are called "adult." In fact adult refers to any stage that is post-embryonic. There are embryonic stem cells that come from embryos, and adult stem cells that come from any stage including the fetus, its placenta, its umbilical-cord blood, and a developing or developed individual. Since some adult stem cells can come from aborted fetuses, for example, those who seek an ethical "clear bright line" to define "ethical stem cells," cannot look to the category of "adult" as providing that. The adult cells are undifferentiated but not totipotent, so that they can never become a whole organism. Nor are they pluripotent, so that they cannot become all of the different kinds of cells in the body; there are clearly limits, though researchers have not yet established exactly what those limits are.[21] Adult stem cells are harder to isolate in most cases, but once isolated they provide great clinical potential for those cases where the right kinds of cells are available. The limitations become important in the context of policy and regulation, as discussed later.

The third type of stem cell is newly discovered—or perhaps a better word would be newly "constructed," since there are not naturally occurring but are constructed in the laboratory. These induced pluripotent stem cells (iPSC) take advantage of the fact that pluripotency is a great asset. Being able to produce any kind of cell, just by selecting the medium

on which the cells are grown, which seems to be possible with pluripotent cells, allows research and potential clinical applications in areas and for types of conditions where adult stem cells are simply not available. Therefore, pluripotency is valuable. In addition, these cells begin as ordinary somatic cells (as cells taken from the body—the kinds that we give off all the time, like skin or hair cells). They are then programmed with the addition of particular genes, thereby being induced to become pluripotent. This research, carried out in mice in 2006 and humans in 2007, is tremendously exciting.[22] For many, such cells carry the scientific potential of pluripotent embryonic stem cells and also the "ethical" goodness of not being derived from embryos but rather from extra and expendable body cells. Unfortunately, biological and clinical research has suggested significant limitations in their use, but they nonetheless bring new possibilities into the discussions.

So, what are the realities in terms of applications? Starting in the 1950s, it has been clear that some cells have special clinical capacity to replicate themselves and differentiate into blood cells. Bone marrow in particular contains such stem cells, and researchers learned to treat leukemia and other blood diseases with bone marrow transplants. As has been discussed frequently, including through the NIIH website, this form of regenerative medicine has been advanced and improved for decades, and it relies on what are called adult stem cells.

For clinical trials, the National Institutes of Health provides a web service that tracks United States trials.[23] This provides public information about all trials and their status. Currently, there are many trials using adult stem cells, with some approved clinical results. As of mid-2011, two clinical trials were underway with human embryonic stem cells: one by Geron for treatment of severe spinal cord injury, and the other by Advanced Cell Technology for treatment of macular degeneration. For iPSC, researchers are largely still working out the biological issues of converting somatic cells to pluripotency, and carefully examining safety issues, though there are promises of therapeutic clinical trials soon in a few areas.

There is tremendous potential with all these types of stem cells, and the National Institutes of Health website reveals a dynamic field with many discoveries and innovations at the same time that those discoveries demonstrate that some hopes were not realistic. It will take time and considerably more research to explore the full range of stem-cell possibilities. In addition, it is important to note that much of what we are learning about adult and iPSC possibilities comes because of comparisons with embryonic stem cell development. Therefore, for now, the most

productive course of action is clearly to push ahead in all these areas and to foster as much communication, comparison, and open discussion as possible.

4. Policy and Regulatory Environment

In the United States, we have no federal stem cell policy. Or, rather, there are no restrictions at the federal level on what research can be done. What we have is a series of Executive Orders that have served as the grounding for policy and have set the regulatory climate for managing stem-cell research. As of 2011, Congress has passed no legislation directly related to stem-cell research, or rather the two bills that they did pass in 2006 and 2007 were vetoed by President George W. Bush and did not become law.

The push for regulation began in 1998, when Thomson first produced human embryonic stem cell lines. President Bill Clinton was in office. He called on the National Bioethics Advisory Committee (NBAC) for advice, and concluded that research with stem cells should be allowed. The question arose because of what seemed to be ambiguities in how the 1996 Dickey-Wicker "amendment" applied to stem-cell research. This legislation had been passed as a rider to the omnibus funding bill that included NIH and declared that the NIH was not allowed to use federal funds to support research

> in which human embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and 42 U.S.C. 289g(b).[24]

Moreover, the Amendment defined a human embryo as

> any organism, not protected as a human subject under 45 CFR 46 as of the date of enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes.[25]

This language has been included in every funding bill since.

The intention of the amendment was clearly to prohibit federal funding of research on embryos, while trying not to run afoul of the by-then already very large and lucrative *in vitro* fertilization business. Yet what was really prohibited? If federal funding was not actually used to destroy, discard, or knowingly subject embryos to injury or death, then was the research acceptable? Congress did not pass legislation explicitly governing stem-cell research in particular, and this left the matter either to open interpretation or to the president.

After considerable deliberation, the Clinton administration determined that research using human embryonic stem cells is, in fact, not prohibited and therefore is allowed. Producing a line of stem cells involves taking the embryo and destroying it in order to extract the mass of pluripotent stem cells from the inner cell mass. But as long as this process was carried out with private funding, then the Clinton administration declared that the research that followed had not been involved in the prohibited activity and was therefore allowed. The NIH Director at the time, Harold Varmus, sought a legal opinion from the Department of Health and Human Services general counsel Harriet Rabb. Rabb determined in 1999 that stem cells do not "meet the statutory definition of an embryo" and therefore that as long as the cell lines were derived with private funds, research would not violate Dickey-Wicker.[26]

Advisory Committees would lay out guidelines for the use of this research, and on August 25, 2000, NIH's "Guidelines for Research Using Human Pluripotent Stem Cells" were published. They established that stem cells must be derived with private funds from frozen embryos from fertility clinics, must have been created for fertility treatment purposes, be in excess of the donor's clinical need, and be obtained with donor consent.

When President George W. Bush ran for election, he promised to change that ruling. On August 9, 2011, in a speech delivered from the White House, he offered a nuanced order that prohibited using any federal funds for stem-cell research except for research on lines that had already been derived before he began his speech that evening. Bush established the President's Council on Bioethics, named Leon Kass as chair, and charged them to study the issues related to stem-cell research. As Bush learned of alternatives, he focused on research that replaced the need for any cells derived from embryos. In 2007, after the announcement of iPSC technology, he issued an Executive Order calling for a move toward alternative sources including renaming the Human Embryonic Stem Cell Registry as the Human Pluripotent Stem Cell Registry.

Congress passed legislation, but Bush vetoed it—twice. Then on March 9, 2009, President Barack Obama shifted federal policy again with an Executive Order that called for "Removing Barriers to Responsible Scientific Research Involving Human Stem Cells." He also called for the NIH to establish clear and ethical guidelines for research, which they did, along with National Research Council recommendations.

This is where matters stood until August 23, 2010, when Federal District Court Judge Royce Lamberth ruled that the plaintiffs in the case of Dr. James L. Sherley et al. versus Kathleen Sebelius et al. met the conditions for a preliminary injunction against the NIH and federal

funding of human embryonic stem-cell research. In a series of decisions that are clearly laid out in the case, it had been determined that James Sherley and Theresa Deischer had standing for their suit calling for "for declaratory and injunctive relief to prevent defendants' Guidelines for Human Stem Cell Research ('Guidelines') from taking effect."[27] Sherley and Deischer are involved with research on adult stem cells, and they claimed that they would be harmed if the Guidelines were in place and NIH funded embryonic stem-cell research. They would, they argued, be harmed by the competition. Furthermore, they maintained that adult stem-cell research and also iPSC research are both better science as well as ethically better. Judge Lamberth ruled in their favor, after an earlier finding that they did have standing in the case.

This brought an immediate uproar and shock to the research community, and the NIH halted funding. But only briefly, because an Appeals Court accepted the case and stopped the injunction. On April 29, 2011, Judge Douglas Ginsburg presented the majority decision, writing that

> We conclude the plaintiffs are unlikely to prevail because Dickey-Wicker is ambiguous and the NIH seems reasonably to have concluded that, although Dickey-Wicker bars funding for the destructive act of deriving an hESC from an embryo, it does not prohibit funding a research project in which an hESC will be used.[28]

The case was returned to Judge Lamberth, who reversed his earlier decision and accepted the Appeals Court ruling. A subsequent appeal took the case to Supreme Court, which on January 8, 2013 declined to hear the case.

Therefore, today we are again left with Executive Orders and legal interpretations that allow federal funding to continue and with no prohibitions or limitations on privately funded stem-cell research. This situation could change if Congress acts or through additional court challenges, and the situation is very likely to change as clinical and scientific advances change the facts of what is possible.

5. Is and Ought Intersecting

In the United States, we now have a mix of state regulations and federal guidelines that allow all forms of stem-cell research under certain conditions. Judging from public discussion, and especially from informal study of blogs and websites, a lot of the people who are very vocal about stem cells not very well informed—about the biological research, the

clinical applications, or reasoned grounding for ethical views. This leaves a bit of a muddle.

Some voices are not confused. The NIH is clear that it has the right to fund and intramurally support stem-cell research, including human embryonic stem-cell research following the now-established guidelines. Many call for human embryonic stem-cell research if it can help lead to therapies. Some argue that the research does not even raise ethical problems, on the grounds that the blastocyst stage of the embryo is not yet a fully formed human and is equivalent to a cluster of cells.

The Vatican is also quite clear about the Catholic view. The Pontifical Academy of Life lays out the argument very directly in its 2000 document "Declaration on the Production and the Scientific and Therapeutic Use of Human Embryonic Stem Cells." Within the document that includes a strong call for adult stem-cell research, we find the following. I quote the argument at length before then pointing out what is problematic about it:

> The ***first ethical problem***, which is fundamental, can be formulated thus: *Is it morally licit to produce and/or use living human embryos for the preparation of ES cells?*
>
> *The answer is negative*, for the following reasons:
>
> 1. On the basis of a complete biological analysis, the living human embryo is—from the moment of the union of the gametes—a *human subject* with a well defined identity, which from that point begins its own *coordinated, continuous and gradual development*, such that at no later stage can it be considered as a simple mass of cells.
>
> 2. From this it follows that as a "*human individual*" it has the right to its own life; and therefore every intervention which is not in favour of the embryo is an act which violates that right…
>
> 3. Therefore, the ablation of the inner cell mass (ICM) of the blastocyst, which critically and irremediably damages the human embryo, curtailing its development, is a *gravely immoral* act and consequently is *gravely illicit*.[29]

The problem here is with the first reason and its purported conclusion. The reasoning begins "on the basis of a complete biological analysis" and claims that "from the moment of the union of the gametes" (which is a "moment" that occurs over a period of time) the embryo is "a *human subject*" (which is not a matter for biological study but rather a social definition). Furthermore, it is false that the embryo "from that point begins its own *coordinated, continuous and gradual development*, such that at no

later stage can it be considered as a simple mass of cells." Biologically, we have seen that this is not accurate. In fact, it is possible to remove cells, as through pre-implantation genetic diagnosis, and thereby to cause a redirection of the "coordinated" development. Even more of a redirection is the addition or rearrangement of cells that we have seen is possible in production of chimeras. If, therefore, the supposedly "coordinated, continuous and gradual development" is highly malleable and responsive to changing conditions, then it is simply not true that the embryo has a "well defined identity." Or at least it is not true that it has the same well defined identity throughout all stages of its development if what was one can be split into two, or what were two can be combined into one. The first premise in the reasoning does not conform to biological fact.

Nobody ever assumed that religious interpretation does have to conform to biological fact, of course. And it is perfectly allowable for the Vatican—or anybody else for that matter—to issue ethical pronouncements completely independent of scientific fact. What is objectionable in this case is the attempt to make use of purported but inaccurate biological claims. My point is that the Vatican has in fact begun with reasons two and three, claiming that the embryo is a "human individual" from fertilization onward and that it is "gravely illicit" to interfere with it. The reasoning is really, then, to take that religious/ethical claim and on that basis to attempt to establish what the biological facts are. Since we know that the claim in reason one is not consistent with current biological science, it can derive only from either outdated understandings of science (but the Vatican has proven excellent at keeping up with the science in other cases) or from making assumptions about what is based on convictions about what ought to be.

As I have argued, that is not acceptable. We expect religious authorities to make ethical proclamations, and we expect scientists to do their scientific work. When the two intersect, we should ask that they each respect the other. There will be conflicts and even irresolvable differences at times. These should be worked out through respectful social discourse, and not by invoking false knowledge. Those scientists who have asserted that they know the embryo to be ethically neutral because it is not a "human person" are just as guilty in stepping outside their established knowledge as the Vatican is in asserting that the embryo is known to have one continuous biological "identity."

Notes

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[1] See M. J. Shamblott et al., "Derivation of Pluripotent Stem Cells from Cultured Human Primordial Germ Cells," *Proceedings of the National Academy of Sciences* 95 (1998): 13726–13731; John Gearhart, "New Potential for Human Embryonic Stem Cells," *Science* 282 (1998): 1061–1062; and James Thomson et al., "Embryonic Stem Cell Lines Derived from Human Blastocysts," *Science* 282 (1998): 1145–1147.

[2] See, for example, Nicholas Wade, "Embryo Cell Research: A Clash of Values," *New York Times*, July 2, 1999.

[3] See David Hume, *A Treatise of Human Nature* (London: Everyman's Library, 1977), III.1.2.

[4] See Aristotle, *Generation of Animals*, trans. A. L. Peck (Cambridge: Harvard University Press, 1979); and Shirley Roe, *Matter, Life, and Generation* (Cambridge: Cambridge University Press, 1981).

[5] See Peter Bowler, "Preformation and Pre-existence in the Seventeenth Century: A Brief Analysis," *Journal of the History of Biology* 4 (1971): 221–244; and Jane Maienschein, *Whose View of Life? Embryos, Cloning, and Stem Cells* (Cambridge: Harvard University Press, 2003).

[6] See Roe.

[7] See, for example, Karl Ernst von Baer, "Die Metamorphose des Eies der Batrachier vor der Erscheinung des Embryos," *Müllers Archiv für Anatomie, Physiologie und Wissenschaftliche Medizin* (1834): 481–509.

[8] On cell theory, see William Coleman, *Biology in the Nineteenth Century* (New York: John Wiley and Sons, 1971), 16–34.

[9] See Pope Pius IX, *Apostolicae Sedis moderationi* (Rome: The Holy See, 1869).

[10] See Nick Hopwood, "Producing Development: The Anatomy of Human Embryos and the Norms of Wilhelm His," *Bulletin of the History of Medicine* 74 (2000): 29–79.

[11] See Jane Maienschein, Marie Glitz, and Garland E. Allen, ed., *The Department of Embryology*, vol. 5 of *The Centennial History of the Carnegie Institution of Washington* (Cambridge: Cambridge University Press, 2005). See also the website of the Human Development Anatomy Center, accessed November 2012, http://www.medicalmuseum.mil/index.cfm?p=collections.hdac.index.

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[15] See Viktor Hamburger, *The Heritage of Experimental Embryology: Hans Spemann and the Organizer* (Oxford: Oxford University Press, 1988); and Hans Spemann, *Embryonic Development and Induction* (New Haven: Yale University Press, 1938).

[16] See Beatrice Mintz, "Formation of Genetically Mosaic Mouse Embryos," *American Zoologist* 2 (1962): 432.

[17] See Leroy Stevens, "The Development of Transplantable Teratocarcinomas from Intratesticular Grafts of Preand Postimplantation Mouse Embryos," *Developmental Biology* 21 (1970): 364–382.

[18] See Robert G. Edwards and Patrick Steptoe, *A Matter of Life: The Story of a Medical Breakthrough* (New York: Morrow, 1980).

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[20] See Glenn McGee and Arthur L. Caplan, "Human Primordial Stem Cells: What's in the Dish?" *The Hastings Center Report* 29 (1999): 36.

[21] See the National Institutes of Health Resource for Stem Cell Research.

[22] See Kazutoshi Takahashi, Koji Tanabe, Mari Ohnuki, Megumi Narita, Tomoko Ichisaka, Kiichiro Tomoda, and Shinya Yamanaka, "Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors," *Cell* 131, no. 5 (2007): 861–872, accessed November 2012, http://www.cell.com/fulltext/S0092-8674(07)01471-7.

[23] See the National Institutes of Health Clinical Trials Database, accessed November 2012, http://clinicaltrials.gov/ct/search?term=stem+cell&submit=Search.

[24] Dickey-Wicker Amendment, Public Law 104-99, 110 Statute 34 (1996).

[25] Dickey-Wicker Amendment.

[26] For discussion, see, for example, Kyla Dunn, "The Politics of Stem Cells," *NOVA ScienceNOW*, April 1, 2005, accessed November 2012, http://www.pbs.org/wgbh/nova/body/stem-cells-politics.html.

[27] Sherley v. Sebelius, 704 F.Supp.2d 63, 65 (D.C. Circuit 2010) (Judge Royce Lambeth).

[28] Sherley v. Sebelius, 644 F.3d 388, 390 (D.C. Circuit 2011) (Judge Douglas Ginsburg).

[29] Pontifical Academy for Life, *Declaration on the Production and the Scientific and Therapeutic Use of Human Embryonic Stem Cells* (Vatican City: The Holy See, 2000), accessed November 2012, http://www.vatican.va/roman_curia/pontifical_academies/acdlife/documents/rc_pa_acdlife_doc_20000824_cellule-staminali_en.html.