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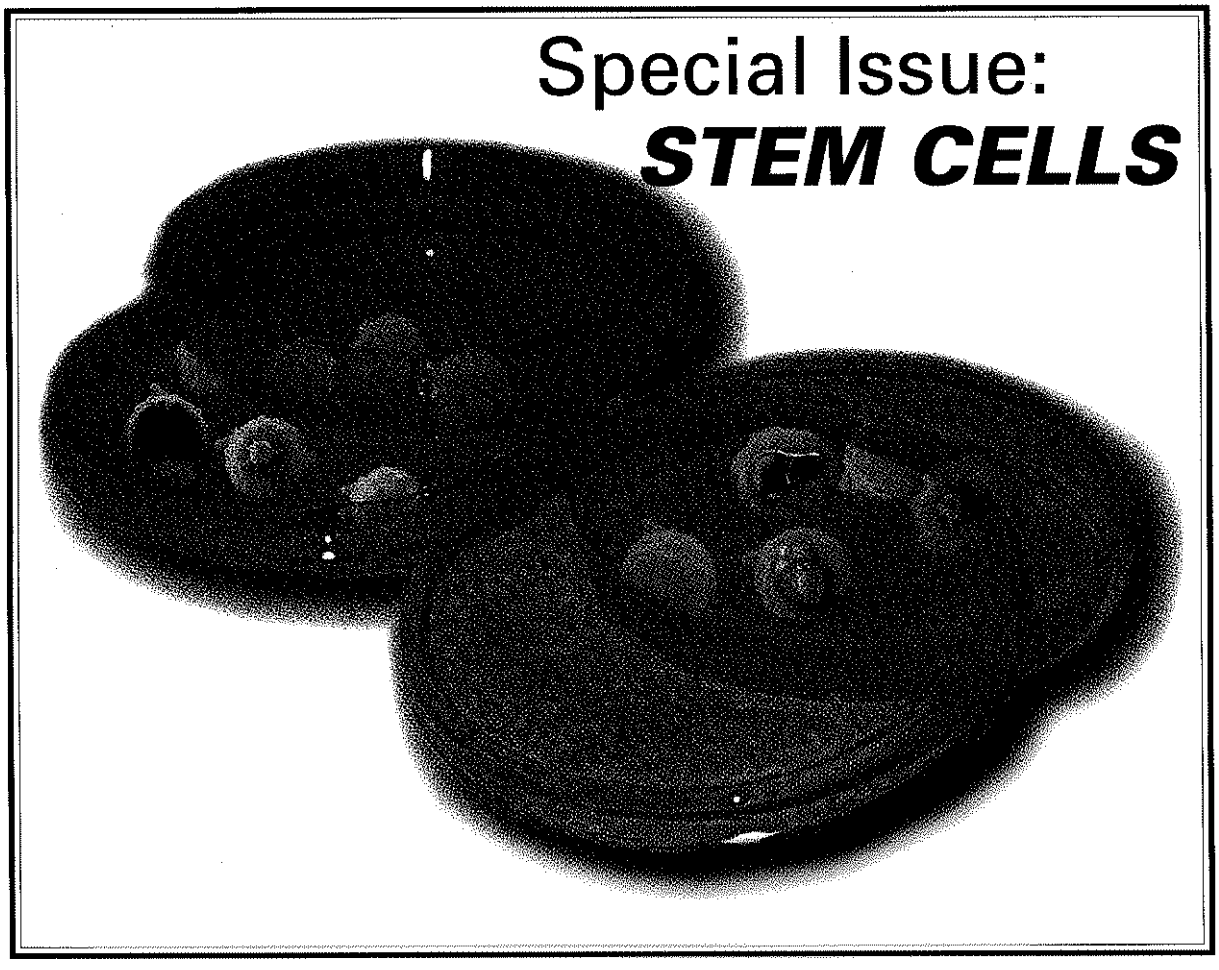

At Women's Expense: State Power and the Politics of Fetal Rights
Reviewed by Virginia Ashby Sharpe

Law and Bioethics: An Introduction
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Part II—What's in a Name: Embryos, Clones, and Stem Cells

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In 2001, the U.S. House of Representatives passed the "Human Cloning Prohibition Act" and President Bush announced his decision to allow only limited research on existing stem cell lines but not on "embryos." In contrast, the U.K. has explicitly authorized "therapeutic cloning." Much more will be said about bioethical, legal, and social implications, but subtleties of the science and careful definitions of terms have received much less consideration. Legislators and reporters struggle to discuss "cloning," "pluripotency," "stem cells," and "embryos," and whether "adult" are preferable to "embryonic" stem cells as research subjects. They profess to abhor "copying humans" or "killing embryos." Do they know what they are talking about? Do we? This paper explores the historical, philosophical, and scientific contexts that inform this heated discussion.

On 31 July 2001, the U.S. House of Representatives passed the Human Cloning Prohibition Act of 2001. On 9 August President George W. Bush announced his decision to allow limited research on existing stem cell lines but not on "embryos." In contrast, the United Kingdom has explicitly authorized "therapeutic cloning." In the blizzard of media attention, much has been said about the bioethical, legal, and social implications of these decisions and about whether and how to modify them. The Senate can decline to act on cloning, Congress can decide to override the president's executive order concerning federal funding, and the United Kingdom can take advantage of U.S. hesitations to ensure their lead in these areas of research. In the meantime, privately funded research and the work that goes on every day in fertility clinics can continue untouched by federal policy.

Throughout these discussions, and despite the excellent attempts of the National Institutes of Health (NIH) to provide information and education, subtleties of the science have received much less careful consideration (National Institutes of Health 2001). Legislators and reporters struggle with fundamental terms such as *cloning, pluripotency, stem cells,* and *embryos,* as well as whether "adult" are preferable to "embryonic" stem cells as research subjects. They profess to abhor "copying humans" and "killing embryos" but to see scientific research as an extremely important path to progress. Do we all know what we are talking about?

Scientists have largely resisted worrying about definitions not deemed scientifically important, and they have consequently allowed the public to define the central terms of discussion. As a television producer told geneticist Lee Silver, "Clones are not what you think they are." Silver (2001) concluded that "Science and scientists would be better served by choosing other words to explain advances in developmental biotechnology to the public." I disagree. Scientists should obviously choose terms that make scientific sense, then should provide clear definitions and be prepared to inform public debate. Without informed scientists' perspectives, we risk making bad policies, in some cases without even realizing that we are doing so, because we thought we were talking about something else. In addition, definitions change. They are a matter of convention among a relevant community, and can change either because what we know changes or because the community changes. This is the case for embryos, cloning, and stem cells—for each of which it matters very much what we mean, and for each of which the meanings have changed over times and in different communities. What follows here is a discussion of these terms in historical context.

Embryos

The first *Encyclopedia Britannica* (1771) defined an "embrio" as "the first rudiments of an animal in the womb, before the several members are distinctly formed; after which period it is denominated a foetus." The word is said to have come from a combination of *bryein* and *em,* for swelling inside. This fit a favorite late-eighteenth-century theory that organisms begin essentially as preformed encapsulated forms that swell and grow larger. It was also compatible with the alternative theory of epigenesis, or gradual emergence of form, typically thought to be guided by some vital force or directive agency in the Aristotelian sense of a becoming that actualizes preexisting potential. Both theories

regarded the embryo as an incipient organism, requiring time and nutrition to become an adult. It was also generally assumed that at some point in the process of development "quickening" occurs and indicates the beginning of life. The quickening seemed clearly to be the "real" starting point for individual development.

Several steps informed scientific understanding of embryos. In 1827 Karl Ernst von Baer discovered that mammals begin as eggs, as birds so manifestly do, and hence that mammals have continuity with previous generations through that material egg. Despite biologists' best efforts, they could see little about the development of those eggs hidden away inside the mammalian mother until the mid nineteenth century brought advances in microscopy and histological methods for fixing, staining, and microtoming. During the 1870s Wilhelm His developed a system for serially sectioning embryos that allowed study of internal structure and organization and led to his pioneering set of human developmental stages (His 1880). While biologists used the term *embryo* for all stages following fertilization, they saw the stages after formation of the germ layers as the important ones for development of individual organisms, and the earliest stages as largely a matter of cell division and nutrition. The fact that typically the dividing egg remains about the same size up through the blastocyst stage, despite cell divisions, reinforces this interpretation.

By the early twentieth century, biologists had modified both preformationism (now seen in terms of predetermined inherited material passed on from parents to offspring through inherited particles called genes) and epigenesis (the material unfolding of preorganized "organ-forming germ-regions" or the expression of relevant "fates" by cells and germ layers). Determining the balance of predirection and epigenetic emergence was, as Oskar Hertwig (1894) puts it, *The Biological Problem of Today.* Biologists prodded, sliced, and diced developing organisms from the germ cell stage through fertilization, morula, blastula, gastrula, and subsequent stages to uncover the processes and patterns of morphogenesis. Along the way it became much less important what they called an "embryo" or what the domain of "embryology" was thought to be. Usually, the terms referred loosely to all development from fertilization on, but the important stages were thought to be postgastrulation, which brings the formation of three germ layers.

Whereas leading morphologists, including His, Ernst Haeckel, and others, emphasized the significance of those germ layers as the starting point for differentiation and individuation, others began to look at the diversity of animals to push back discussions to fertilization and the very first cell division as also important for morphogenesis. Cell lineage, for example, involved tracing lineages of each cell from the unfertilized egg cell itself, though each division until the multiplication of cells made it impossible to follow the details any longer. With meticulous methods for preserving each stage (the egg itself, two cells, four cells, etc.), then observing and drawing or photographing the details, researchers discovered that from the beginning some species have very determinate cleavage patterns suggesting an early differentiation. In contrast, other species allow considerable regulation and demonstrate variability in developmental patterns.

Clearly, morphogenesis is a complex process, with variations across species and even within species depending on the details of an individual case. Throughout this period, morphogenesis, or genesis of form, remained the primary focus of research. The "embryo" receded into the background in importance as a sort of placeholder, while the series of defined stages and the patterns and processes of change gained importance.

One episode still appears in textbooks and class discussions, though we can learn new lessons from the case. Wilhelm Roux and Hans Driesch each experimented on the two-cell stage of an organism: Roux on frogs and Driesch on sea urchins. Roux killed one of the two cells with a hot needle and discovered that the remaining cell develops essentially as it would if it were part of the normal embryo. He concluded that development occurs in a mosaic manner, with individual cells adopting individual fates in the whole organism that follows. Driesch took the two-celled stage of his sea urchins and shook apart the two blastomeres, watching each grow into a larval form as if it were a reorganized whole and not just one half of a mosaic. Driesch concluded that each blastomere at the two- and even four-cell stage is "totipotent" and capable of considerable regulation in response to changing conditions surrounding the cell (Maienschein 1994).

This difference in their results raised fundamental questions about the nature of differentiation and led other biologists to take up parallel studies in other organisms for comparison. Some are more mosaic-like and others more regulative,

they discovered. In the period between 1880 and 1910, researchers made tremendous advances in understanding cells and development (Wilson 1896). Yet they soon reached the limits of those lines of research and had to set aside what they recognized were exciting questions about regulation and the limits of such totipotency and regulation.

Ross Harrison pursued new methods of exploration by culturing tissues outside the body for the first time; he cultured frog neuroblasts in a lymph medium and thereby carried out a first step toward current research on precursor and stem cells. Harrison and Hans Spemann also transplanted various parts of donor organisms onto other hosts to discover the relative contributions of each, and this led Spemann to his concept of the "organizer" at the gastrula stage (Hamburger 1988). During this time, deciding what was meant by an "embryo" or "organism" became less important than determining to what extent the stages were defined, predictable, and determined versus regulated in response to environmental conditions.

Around the same time, the ninth *Britannica* (1897) defined *embryology* as "somewhat vaguely applied to the product of generation of any plant or animal which is in process of formation." The term included all stages from fertilized eggs to birth, though a human embryo was seen as becoming a "fetus" at eight weeks, when it "has assumed the characteristic form and structure of the parent." Textbooks of human embryology outlined successive stages, focusing on appearance of organs and visible features such as limbs and face. Both because of what was possible with existing research approaches and because of what medicine deemed important, later fetal stages remained the primary focus.

We see this for humans in Keibel and Mall's edited classic 1910 *Manual of Human Embryology.* The authors admitted that they knew little of the early stages: "Nothing is known concerning the fertilization of the human ovum, but it may be presumed that it takes place in essentially the same manner as in other animals." "The segmentation stages of the human ovum have not yet been observed." And so on. They were restricted to what they could see with the few selected specimens they had, and these represented later stages, starting with the fourteen day "ovum," which itself revealed little. In later stages they could focus on recognizable organs and the sequence in which they arise (O'Rahilly and Müller 1987). Yet even here, the authors noted,

> It is clear that the normal fully developed organism cannot be produced without a certain regular succession in the development of the organs and a regular interdependence of the individual developmental processes, but it is open to question whether this interdependence is the result of the individual and independent development of each organ taking place in such a way that it fits into that of the others or whether it is due to the individual anlagen of an organism mutually influencing one another during the development so as to cause the formation of a normal organism. (Keibel and Mall, 980, xvi, 18)

These leading human embryologists used the terms *ovum* and *organism,* while focusing on the succession of parts and organ. They largely yielded the term *embryo* to nonscientific usage. Biologists instead considered "morphogenesis," "organogenesis," "growth," "differentiation," and such processes. By the 1960s "embryology" had largely disappeared along with discussion of embryos, giving way to "developmental biology." Encyclopedia definitions also became looser, so that the *Britannica's* current "embryo" is

> the early developmental stage of an animal while it is in the egg or within the uterus of the mother. In humans the term is applied to the unborn child until the end of the seventh week following conception; from the eighth week the unborn child is called a fetus.

This looseness of terminology began to matter a great deal more for political, legal, and social reasons after 1978, when Patrick Steptoe's team demonstrated the astonishing efficacy of in vitro fertilization. They could fertilize human eggs in the laboratory, implant them, and watch mothers bring them to term. They learned to nurture the eggs in glass dishes, select the most viable, freeze and save them, and to manipulate these eggs in many ways. Because of the evident therapeutic benefits to otherwise infertile patients, and perhaps because Steptoe did not announce his efforts until they had been successful, the public accepted this innovation as a medical advance.

The Vatican was not happy, seeing such manipulation of even early developmental stages as morally illicit, since Pope Pius IX had in 1869 declared that "ensoulment" and hence life begins at conception. As Karen Dawson noted rather understatedly in the 1990 volume *Embryo Experimentation,* "The debate about embryo research is far from finished and will continue to occur whether governments seek to regulate this rapidly developing area of science" (Singer et al. 1990, xvi). None-

theless, public opinion in the Western world has accepted in vitro medical therapies to allow more people to bear children. Jewish and Muslim scholars, for example, regard life as starting later (40 days is the most commonly accepted time). Typically, the term *embryo* has applied to the stages from fertilization through the eighth week in humans, but there is clearly an important qualitative biological difference between the blastula and gastrula stages.

The U.S. Congress has passed legislation to protect human embryos, the most recent laws prohibiting use of federal funds for "the creation of a human embryo for research purposes or for research in which a human embryo is destroyed." In the fiscal year 1998 Appropriations Act, they explicitly defined human embryos to

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

Fertilization was clearly thought to be key. Yet it is difficult to discover any clearly reasoned argument leading to this decision or any biologically informed discussion of whether subtle distinctions ought to be allowed. Instead, wrapping this decision into omnibus appropriations acts seems to have allowed it to slide through without significant debate. There is room for more careful consideration of what we mean, why, and with what implications.

Up through the blastocyst stage, it is possible to culture the human egg in a glass dish, outside the body. After gastrulation, at least with current technology, it is not. Up until that stage, the blastocyst cells remain largely "plastic" and at least multi or pluripotent (capable of becoming more than one or all cell types). In mice, for example, it has proven possible to combine pairs or small clusters of cells from different organisms and have them join and develop together normally, as a sort of hybrid or chimeric new organism. By gastrulation this regulative response is no longer possible, at least with present technologies and understanding. The cells have by then begun to differentiate and to become channeled into their respective fate paths.

There is a difference between the blastula and gastrula stages then, and it is important. Yet we have not developed conventionally accepted terms for these differences. The NIH refers to the entire process as the embryo, while Bush followed many others in referring to the preimplantation blastula as a "pre-embryo." Clearly, it was important to him to make the distinction. The pre-embryo is different from an embryo: perhaps it is not "alive" in the same way, perhaps it is not an "individual," or conceptually not yet a "potential human" in the same way that an implanted and differentiated post-gastrula embryo is. As R. J. Blandon put it in 1971, summarizing Reichert's 1873 studies, the blastocyst is that "structure existing during the period between the end of cleavage and the attachment of the embryo to the uterine wall." It is not itself "the embryo, [Reichert] declaims, but only the developmental stage of a new creature, which is the embryo" (19).

Clearly there are biological differences, and much hinges politically on our definitions. Defining a pregastrulation embryo as something different may be the most useful approach. This is certainly the line taken by the British parliament in 1990 when they agreed to allow some research on the grounds that "such embryos have not progressed to the point that they can be considered as individuals" (*Nature* 2001). We could follow Lee Silver's suggestion and seek different terms altogether, but those will not inform the public discussion that relies on familiar and conventionally accepted language. Therefore, we need to work harder to clarify our definitions, to recognize that these will change over time as we learn more, and to develop clearer and scientifically defensible connections between the biological and public language usage. Historians, philosophers, and bioethicists can help with that process.

Cloning

When Ian Wilmut and the Roslin Institute team announced that they had cloned a sheep using a new technique, people around the world scrambled to understand what somatic cell nuclear transfer really means (Wilmut et al. 1997). The image of babies as miniature copies of parents or as time-delayed twins disturbed many people. After all, the child is not supposed to be the brother of the man—or woman. The collective, if sometimes fascinated, "yuck" suggested that people were not ready for this. And so, as many governments worked to determine whether and what regulations should be imposed, and as Ian Wilmut himself took a lead in speaking out against cloning humans, the U.S. Congress began to generate its own proposed legislation.

Congressman Vernon Ehlers, himself a Ph.D. physicist and one of the few in Congress with any significant scientific training, proposed a very clean and simple bill that would have outlawed the use of federal funds to clone humans for the purposes of creating a human being. Numerous other bills also appeared, in various stages of development, and a few made their way to committees. I was working as science advisor to my congressman at the time, and was astonished that some of the early bills were so vaguely worded that they would have outlawed gene cloning or even, in the most extreme case, much of agriculture and even identical twins—one early draft bill proposed to prohibit all genetic replication. Fortunately, in the course of a series of hearings and staff briefings, it became clear that the representatives did not sufficiently know what they were talking about to take action. When the Food and Drug Administration declared that they would exercise control over any possible cloning and therefore that no special law was needed, there was a sigh of relief. This held off the perceived need to rush to action. It also helped that Wilmut kept reminding people how difficult the cloning process was, and how many failures occurred before achieving that initial success.

What became very clear very quickly was the importance of words and of perspective. The concept of cloning was not new. "Cloning" actually first appeared in agriculture, when Herbert John Webber wrote in 1903 of "clons" that were "groups of plants that are propagated by the use of any form of vegetative parts such as bulbs, tubers, cuttings, grafts etc. and are simply parts of the same individual" (Webber 1903). By the 1920s cloning covered a variety of asexually reproducing genetic copies, including tree runners, regenerating worms, bacterial divisions, and cell copying in cultures.

In the 1950s Robert Briggs and Thomas J. King successfully transplanted nuclei from donor *Xenopus laevis* into host frogs. This was cloning through nuclear transplantation, but they could not achieve success with nuclei taken from post-gastrula stages (Briggs and King 1952). In the 1960s John Gurdon significantly expanded the range of techniques and cells, including differentiated frog somatic cells, that could be cloned this way. The work was technically challenging, yielding a low success rate, and attempts to transfer the techniques to mammals failed. The successes showed that there were no natural barriers to such hybrids, but the prospects for human cloning seemed very remote. A brief media blitz gave way to skepticism; the public probably assumed that such cloning would not happen, and relatively few scientists continued to pursue the possibilities.

Textbooks suggested that there was no evidence that it was impossible to do such cloning in mammals and even humans. James Watson, John Tooze, and David Jurtz wrote in their *Recombinant DNA: A Short Course* (1983) that "in the immediate future there is little likelihood of nuclear transplantation being attempted with any other mammalian species" or even much beyond frogs.

> If the efficiency and reproducibility can be improved, the method may, however, find a place in animal breeding. In theory it could be attempted with human eggs and embryonic cells, but for what reason? There is no practical application. (207–208)

That was 1983, and only two years after the first American human in vitro fertilization, so the enormous possibilities in terms of enhancing human fertility were not yet apparent.

The 1950s and 1960s brought cloning of cell lines, with the recognition that there is tremendous advantage in having a large collection of genetically identical cells: both to control experimental variables and to have sufficient material should therapeutic uses be developed. This cell-culturing research built on the earlier tissue-culture studies that had begun decades earlier in developmental biology. The 1960s brought gene cloning, with the same advantages of genetic duplication. Progressively faster, more accurate, and more efficient laboratory techniques and microbial "factories" have made gene cloning a familiar activity for undergraduate scientists today. The advances have carried us far beyond what Briggs and King could have imagined, but the concepts remain the same. Cloning consistently refers to the full range of types of genetic copying, whatever way that is carried out and on whatever organisms.

Notwithstanding the many efforts to explain that genetic replication does not mean that the expressed offspring cells, tissues, or organisms will be exact copies of the original, the popular perception still sees it that way. As Silver noted, cloning escaped the biologists because of Dolly and the subsequent furor and took on its own public meaning. This does not mean that biologists should give cloning up to the popular press, however. Rather scientists need to continue informing discussions

and helping public figures make the distinctions necessary to ground sound policy and legal rulings.

House bill H.R. 2505, *Human Cloning Prohibition Act of 2001,* defines human cloning as

> human asexual reproduction, accomplished by introducing nuclear material from one or more human somatic cells into a fertilized or unfertilized oocyte whose nuclear material has been removed or inactivated so as to produce a living organism (at any stage of development) that is genetically virtually identical to an existing or previously existing human organism.

Somatic cell "means a diploid cell (having a complete set of chromosomes) obtained or derived from a living or deceased human body at any stage of development." With those definitions, the proposed law states that

> It shall be unlawful for any person or entity, public or private, in or affecting interstate commerce, knowingly (1) to perform or attempt to perform human cloning; (2) to participate in an attempt to perform human cloning; or (3) to ship or receive for any purpose an embryo produced by human cloning or any produce derived from such embryo."

This bill was passed by the House in part to set the boundaries for decisions about stem cell research and to make it clear that even if such research were allowed, human cloning for the purpose of reproducing humans would be prohibited. To date, the Senate has not enacted any similar bill and seems unlikely to do so without further provocation.

What is important is the boundary constraints that Congress is trying to establish. Far from that initial frightened reaction to the idea of runaway Frankenstein-like scientists copying people in their labs, a more reflective consideration has led to an idea of cloning in terms of somatic cell nuclear transfer. Either the Congress is not aware of the possibility or does not find worrisome that a researcher might transfer a nucleus (or even an entire cell) from, for example, a blastocyst into another oocyte from which the nucleus had been removed. This would involve nuclear transfer, but not technically somatic cell nuclear transfer. It could be cloning in the biological sense, since the goal would be genetic copying by the resultant cells. But it is not cloning in the sense of H.R. 2505. Perhaps the Congress and Congressional staffs meant to cover this contingency with the definition that somatic cells are derived from the human body during any stage of development. But technically, the blastocyst is not yet a "body," so that still leaves ambiguity.

Cloning clearly includes a range of activities, and that range is likely to expand as we learn more. It is important not to rush to judgment to ban all possible currently foreseeable activities, since we will surely predict imperfectly, nor to allow everything just because we cannot develop crisp definitions. It is also important that scientists not give up the discussions because they are difficult and not central to carrying out the work of each individual scientist. In the long run, it does matter. If legislators are going to make decisions that will restrict some scientific research, then scientists had best be involved in informing those decisions. Historians, philosophers, and bioethicists can help provide perspective, demonstrate what is and is not new, what is and is not good scientific research, and what ethical, legal, and social implications are likely to result.

Stem Cells

As with embryos and cloning, the term *stem cells* has taken on public meaning. Yet here, perhaps since there is no immediate intuitive sense of the term, the public discussion has been more closely informed by scientific explanation. The primary association is with embryos, since "embryonic stem cells" have moved into the forefront of public debate quite recently.

Also as with embryos and cloning, stem cells and research on them are not new. Yet as with cloning, technical innovations in recent years have excited public imagination. With cloning, Dolly evoked images of sheep-like genetically copied humans. With embryonic stem cell research, the images are of killed embryos on the one hand or of magical laboratory-generated miracle cures on the other. Neither is realistic nor even close to the whole story.

When Driesch discovered that each of two or even four separated blastomeres could develop into a whole sea urchin larva, he demonstrated that each cell retains a totipotency or ability to make the whole. As early-twentieth-century research placed the material of inheritance in genes, arranged in chromosomes, and passed along through cell and nuclear division to each daughter cell, this raised what Thomas Hunt Morgan called a paradox of development. If all the cells within an organism have the same genetic constitution, what causes them to differentiate? And to what extent is the differentiation determined, or flexible in response to differ-

ent environmental conditions? This set of questions, essentially a new form of the preformation-epigenesis debates, has dominated developmental biology. Exploration of this set of issues lies at the root of stem cell research.

Some cells are able to give rise to an entire, normal, healthy organism. These are totipotent cells, and the fertilized egg is the most obvious example. In human beings, under some conditions, all of the blastomeres up to the eight-cell stage can do the same, yielding identical octuplets. Again focusing on humans, until the blastocyst stage there is no reason to believe that any cells are fully differentiated into different cell types. Indeed, the form *blasto,* as in *blastomere, blastocyst,* or *blastoderm,* was used widely by the late nineteenth century for stems, sprouts, or germs, in the sense of *able to give rise to form.* During the blastocyst stage, it begins to be the case that each cell can no longer give rise to the whole organism by itself. Instead of totipotency, therefore, some of these cells are pluripotent or multipotent, and in later developmental stages following gastrulation they become differentiated as unipotent, or precursor cells for some particular cell type. Distinctions in these terms are important, and much political ferment hinges on them.

Pluripotent or stem cells are those capable of becoming many, some would say all, of the different cell types of the normal body. This does not mean, however, that any one stem cell can become all the types. Indeed, it cannot. There is no evidence of the capacity and no actual cases in which stem cells give rise to entire organisms. Stem cells, therefore, are not tiny embryos in the rough, nor can they become embryos. They are not "alive" in the sense of giving rise to entire living organisms, though they are capable of reproducing themselves. True pluripotent stem cells can replicate and can give rise to lines of future stem cells as well as to differentiated cells of a variety of types. Current definitions hold pluripotent stem cells as able to give rise to "most" or "every" cell type, and at least to some types of cells from each of the three germ layers. In practice, however, it is very difficult to prove that any line of stem cells can, in fact, actually give rise to *every* type of cell. Theoretically, however, that is believed possible.

In the 1950s F. C. Stewart showed that he could generate a whole carrot from single root cells, thereby demonstrating totipotency and raising once again the question of just how flexible the most "plastic" cells are. Nuclear transplantation demonstrated a great deal of adaptability in frogs. And, following the discovery in the 1960s that bone marrow transplants allowed patients to produce healthy blood cells to treat anemia and leukemia, the 1960s brought major advances in understanding the multipotent hematopoietic stem cells. These cells carry out two functions: they differentiate into normal blood cells, and they also maintain and renew the population of stem cells. J. P. Lewis and F. R. Trobaugh (1964) argued that they therefore satisfied the definition of stem cells. These cells both self-renewed and differentiated into blood cells; hence they gave rise to two cell types. They were therefore multipotent and considered true stem cells. From the 1960s until recently, such multipotent bone marrow cell lines have provided our best known example of stem cells. They later also proved to differentiate into other cells useful to the immune system and therefore to have considerable therapeutic potential, in addition to demonstrating wider multipotency than originally thought.

Discussions of such stem cells formed a basis for discussion of regeneration. How is it that some organisms, some of the time, and for only some cells, are capable of regenerating injured parts? Crabs can regenerate a claw, but humans cannot regenerate a hand. Worms can regenerate most of their segmented bodies, and snakes regularly regenerate their skins. Why, how, when, under what conditions, and can we use an understanding of such processes to develop medically useful applications, researchers asked. Biologists, who had previously assumed that differentiation works in only one direction, since daughter cells cannot go back to a more general state, occasionally questioned that assumption. As Elizabeth Hays wrote in 1974, "Until better experimental evidence is forthcoming, it no longer is useful, however, to think of differentiation as an irreversible condition, even though we know that somatic cell differentiation is very stable." She acknowledged that

> this is difficult to do because our concepts so overlap that we almost invariably think of differentiation as a restriction of developmental potency, even though we know that cells like the ovum that are truly totipotent actually are differentiated, highly specialized cells. (405)

This was a period of trying to sort out what was meant by stem cells, precursor cells, differentiated and undifferentiated cells, and the extent to which the normal condition could be overruled by experi-

mental manipulation. It is the time when the groundwork for our current discussions began. Unfortunately, it was also a time when some of the definitions remained murky. Whether a stem cell must be multipotent or pluripotent and what difference that makes were such core questions. What has changed in recent decades is, first, the discovery that stem cells seem to have far wider capabilities than previously thought and, second, that embryonic stem cells appear to have the greatest capacities—and there are vast collections of embryos in storage in fertility clinics.

In 1994 the NIH Human Embryo Research Panel recognized the potential in human embryo research, but nonetheless called for moral caution in pursuing this study. The debates might have stalled there, but for the independent publications by James Thomson and John Gearhart in 1998 (Thomson et al. 1998; and Gearhart 1998). They showed that stem cell lines could be cultured and could be caused to differentiate into a variety of cell types. As reporter Gretchen Vogel (2000) summarized in a special stem cell issue of *Science,*

> Conventional wisdom has assumed that once a cell has been programmed to produce a particular tissue, its fate was sealed, and it could not reprogram itself to make another tissue. But in the last year, a number of studies have surprised scientists by showing that stem cells from one tissue, such as brain, could change into another, such as blood. (1418)

These discoveries served to "signal the unexpected power of stem cells." As leading stem cell researchers hasten to point out, even as they argue for federal funding of their research, many open questions remain, including how much stem cells can be made to do and whether the most controversial stem cells derived from embryos will prove sufficiently more efficacious to overrule the moral concerns. That we will never learn if we do not ask remains very clear. And that we will not be certain what we have learned unless we are very careful to define our terms and to develop a shared accumulation of knowledge is equally clear.

Conclusions

Suddenly in the past few years, cloning and stem cell discoveries have heated political discussions about when and what to regulate and where to draw lines on what procedures scientists should be allowed to pursue. As seen in the preceding discussion, it very much matters what the underlying terms mean. If the public decides to protect embryos, we had better know whether we mean by that fertilized eggs, blastocysts, gastrulas, or only postimplantation stages. Bush and his advisors refer to "pre-embryos," "frozen embryos" stored in fertility clinics, and researchable cell lines from embryos already "destroyed." Bush's 9 August 2001 televised speech suggested that he sees cell lines as derived from "destroyed embryos," as already nonliving, and therefore as legitimate research subjects, whereas frozen fertilized eggs have a different status, as live embryos. Others would disagree, but in diverse ways. We see considerable reliance on fuzzy definitions to make biologically questionable distinctions that then have tremendous political force.

Clearly it matters what we count as an embryo, what it means to destroy one, and what capacities each developmental stage holds. It matters what we mean by cloning and how we distinguish embryonic and adult stem cells and whether they must be pluripotent or multipotent to have therapeutic value. If world leaders and legislators place restrictions on the pursuit of scientific knowledge, the scientific community must work hard to ensure the best possible understanding of the science involved. Historians, philosophers, and bioethicists must also work hard and must avoid being seduced by facile distinctions and false hopes growing out of uncorrected misunderstandings and misinterpretations. It is vitally important to define terms clearly and carefully, and for at least a representative set of experts to engage effectively in public discussion not just of the details of their own science but of the words used and the implications of the choices made. ■