CHAPTER I

Preliminaries

Is it ever morally permissible to use a human embryo solely as a means for benefit of others? One should think that this question would long ago have been posed if not decisively answered. Instead it was not until the late twentieth century that anyone created a human embryo outside a human body. Or so we assume. It was then that physicians devised a procedure by which to create embryos *in vitro*. That feat has since allowed many couples experiencing infertility to bring forth children. Following this procreative innovation, scientists began to ask whether embryos created outside the body could be used in research.

In the first instance, scientists imagined experiments that might augment our knowledge of human embryology. We collectively still know relatively little about early human development. For long it was believed that conception occurs by the mixing of semen and maternal blood. Aristotle and others so concluded upon observing that when pregnancy begins, menses ceases. Then entered the theory of preformation. In its most famous version, preformation portrayed a sperm head as containing a homunculus, a 'tiny human' that needs only to enlarge to develop. Not until 1827 was it observed that there exist oocytes released from human ovaries. An explanation for the penury of our ancestors' knowledge is not hard to find. Observational barriers constrained what they could discover.

Now that there exist embryos observable *in vitro*, scientists think of observing early development. They think of what they might learn that could amplify our understanding of fundamental biological processes, that could avail in facilitating reproduction, or that could lead to preventing or treating developmental abnormalities. They also think of derivatives of embryos. Here lies an avenue that has roused great hopes for curing dreadful maladies. Scientific ingenuity has devised ways in which experiments performed on derivatives of embryos might yield fundamental knowledge. Methods have also been envisioned in which embryonic derivatives would serve as vehicles by which physicians deliver therapies. The prospects for

such advances surged when, late in the twentieth century, biologists succeeded for the first time in deriving and culturing human embryonic stem cells. While these investigators did not wish to foster false hopes, they began to imagine a new era of regenerative medicine. They began to envision interventions that could constitute some of the most effective therapeutic advances in modern history.

1.1 EMBRYO USE

I shall employ 'embryo use' to denote the use of an embryo solely as a means. My use of 'embryo' will refer, except where otherwise indicated, to the human. On the permissibility of embryo use in research and therapy, the counsels of common sense are divided. Some people would condemn every instance of embryo use, regardless of expected benefit. In their view, hopes that medicine may succeed in a mission of mercy attach to means that we must abjure. Other people approve the use of donated embryos primarily by reason of the expected benefits. Still others approve use of all and only embryos left over from fertility care in the belief that otherwise those embryos would perish as waste.

Observers who have chronicled skirmishes over embryo use have often spoken of irreconcilable moral positions argued to a draw. The controversy about embryo use, they say, merely rehearses the controversy over abortion. Scratch an opponent of embryo use, they remark, and one will find an opponent of abortion. Serious thinkers have debated the use of various categories of embryo, among them the surplus embryo, the clone, the embryo formed in research, the parthenote. Thus far this discussion has been fragmented. As some commentators portray things, it probably does not lie within our ability to cobble together a consistent collective stance on embryo use and related practices such as abortion, assisted reproduction, and genetic intervention in reproduction. We would be well advised to forge some compromise. If thereby we collectively saddle ourselves with inconsistency, that should not unduly disappoint us, because on these matters, many of us are inconsistent separately.

I suggest that the foregoing gloss may stem from failure to recognize that in a philosophical controversy, narratives of battles do not substitute for the rigorous analysis of argument while sympathetically considering others' views. Narratives will tell us which and how many people espouse one view or another, or how people interact in groups and communities. The philosopher's contribution issues from hard thought trained on assembling a cohesive account sustained by compelling arguments responsive to

fundamental questions. Sometimes this work may remove seeming obstacles to agreement. 'One of the aims of moral philosophy,' as John Rawls taught us, 'is to look for possible bases of agreement where none seem to exist.'[1]

The present controversy presents compelling reasons to strive for a consensus. If the practice of embryo use were imposed as public policy by brute political machinery, that could leave a principled minority chafing under what it regards as immorality. If instead public policy thwarts the relief of suffering that a society has the ability to ameliorate, that will bring deep regret by and for all affected. Settling for either result without making a serious intellectual effort toward consensus would forsake the power of ideas.

The morality of embryo use is a question within normative ethics. Its analysis also raises questions about what we are. One prominent argument that we shall encounter beckons an understanding of what constitutes a human individual. Another line of reasoning evokes the question whether we should rest moral judgments on a particular teleology about body parts. Still another train of thought leads into the question of what ontological status a species holds, this insofar as the association of properties with species membership may be invoked as a ground for partiality. We shall also encounter the inchoate notion of developmental potential and the effect of discretion upon its extent. Within normative ethics, we shall have occasion to consider moral demands said to be placed upon us by such possible persons as it may make sense to posit in particular situations. We shall have to decide whether the duty to rescue, or any other duty, obliges a woman to undergo a transfer into her, or to allow a transfer into another, of an embryo formed outside her, this inquiry implicating the distinction between the duty to rescue and the duty of beneficence. Inasmuch as controversy over embryo use lies at the intersection of law, morals, and public policy, we shall also find reason to pause over what constraints should apply to the invocation of particular religious and moral views in the public arena. We shall as well find motivation to consider the sweep of moral views as if there were no such constraints.

I shall define a set of embryos that, so I shall argue, we may virtuously use in service of humanitarian ends. This set will consist of donated embryos that, by virtue of progenitor decisions, have permissibly been barred from entry into any natural or artificial uterus. These embryos have begun development, but they will not begin gestation. I shall argue that the use of these embryos for humanitarian ends is not only permissible and virtuous, but

[1] Rawls 1971a, p. 582.

that such use lies within the mandate of a collective duty. A distinguishing feature of my account will be the claim that its argument in chief commands assent even within the most prominent comprehensive views presumed to oppose embryo use. After probing to their roots the teachings of the leading presumptive opponent, we shall discover that a compelling case for donated embryo use resides there. We shall also learn that the principal argument for a contrary interpretation collapses after colliding with one of that view's bedrock beliefs.

From such lines of reasoning and their tributaries, a picture will emerge of a consensus awaiting recognition. In the work of laying the foundation for that consensus, we shall clear many conceptual brambles. Because a good case is not made better by overstatement, I shall disavow some arguments offered in support of embryo use that, according to my analysis, are unsound. Among these will be arguments asserting that twinnability precludes individuality, that imminent death is alone justificatory of embryo use, that embryo use is the utility-maximizing alternative, and that public appeals to comprehensive religious or philosophical doctrines are always out of bounds.

At various places within my discussion, embryonic stem cell research will serve as a point of entry. This field of research has brought embryo use to public prominence. But there seems no reason to assume that any one avenue of inquiry will exhaust the collective good achievable in research and therapy through use of donated embryos. In anticipation that multiple lines of fruitful inquiry may develop over time, I offer my account as a justification for the general case of embryo use in service of humanitarian ends.

1.2 THE BIOLOGICAL CONTEXT

'The student of Nature,' said the biologist T. H. Huxley, 'wonders the more and is astonished the less, the more conversant he becomes with her operations; but of all the perennial miracles she offers to his inspection, perhaps the most worthy of admiration is the development of a plant or of an animal from its embryo.'[2] The following sets forth the biological context for the discussion of embryo use that lies ahead.

Within a human ovary, the process of *oogenesis* culminates in the production of a *secondary oocyte*, one of which is released from an ovary at each ovulation. The exterior surface of each secondary oocyte is a protective

[2] Huxley 1894, p. 29.

shell, the *zona pellucida*. As and when a secondary oocyte is induced to begin dividing, *activation* is said to occur. In natural conception, activation occurs by fertilization, a process in which two *gametes*, a secondary oocyte and a single spermatozoon, fuse. Occurring in a fallopian tube connecting the ovary to the uterus, the process of fertilization lasts about a day. Entry of the sperm changes the oocyte into a single-cell *zygote*, which takes its name from the Greek ζυγωτοσ for 'yoke.' This name alludes to the two separated pronuclei in which at first the chromosomes from the oocyte and sperm respectively reside. Toward the end of fertilization, the pronuclei migrate together, touch, and exchange chromosomes. The ensuing merger of the paternal and maternal genomes is known as *syngamy*. The cell divides into two successor cells. After another day, the successor cells divide. Then the successors of the successors divide, and so on. This process of successive cell division is known as *cleavage* because as the number of cells increases geometrically, the average cell volume declines proportionately so that all the cells fit within the fixed volume enclosed by the zona pellucida. Each cell is a *blastomere*.

At about day 3, the whole structure compacts into a *morula*, a form that resembles a mulberry. By around day 5, the developing being has become a *blastocyst* (after βλαστο- for a bud or young growth and -κυστ for a bladder or pouch). The blastocyst consists of a spherical surface, the *trophoblast*, which will develop into the placenta, and a cluster of cells lying inside the surface, the *inner cell mass*, also known as the *embryoblast*. As cleavage continues, the blastocyst travels through the fallopian tube toward the uterus. The blastocyst hatches from the zona pellucida. The blastocyst will implant in the uterine wall, if ever, by day 7. Then follows development to the late blastocyst stage. At about day 14, there begins *gastrulation*, a process in which cells migrate and orient according to their future roles.

The foregoing postactivation events are the first steps in the human of *organismic development*. I understand organismic development as a process in which the genome, epigenetic systems, and external environment of a product of oocyte activation, or of a product of a plant propagule, interact so as to produce and transform an organism, or so as to transform a product originated as an organism, by means of phase changes occurring in a morphological sequence usual for organisms of its kind over the course of a life. A *phase change* in an individual of a given kind of substance is a change that things of that kind survive in accordance with the laws of nature.[3] When a flower blooms, a bear gains weight, or a child becomes an adolescent,

[3] Here I follow Lowe 1998, p. 186.

a phase change occurs. In the prenatal morphological sequence of human organismic development, the phase changes include the processes of cleavage, compaction, implantation, gastrulation, neurulation, mitotic cell division, regulated cell differentiation, and organogenesis.

To the Greeks after Homer, the fruit of the womb was known as an εμβρυον (*embruon*). The Latin term was *foetus*. Only in modern times have the extensions of these terms diverged. As I define the term, an *embryo* is a product of oocyte activation that is undergoing organismic development and that has not reached the ninth week of development. (The strict medical definition of 'embryo' demands attainment of the third week, but neither scientific usage nor common parlance imposes that condition.) A *fetus* is a prenatal product of oocyte activation that has attained the ninth week of organismic development. Moral concern would attach to an embryo insofar as it is undergoing organismic development even were it not yet an organism.

Assisted reproduction consists in a suite of procedures for initiating pregnancy by medical intervention. The techniques include *in vitro fertilization* ('IVF'), a procedure in which gametes are mixed outside the body. An IVF patient first receives daily subcutaneous injections of follicle-stimulating hormone, this to induce development of more than the usual one oocyte per month. She undergoes frequent blood tests and is otherwise followed closely by her physician. After weeks of such ovarian stimulation, the physician administers anesthesia, inserts a needle into an ovary, and extracts about a dozen follicles each containing a secondary oocyte. A laboratory technician then attempts fertilization of the oocytes by mixing them with sperm. After embryos form, the clinical embryologist examines the embryos under a microscope and, in consultation with the patient, selects several for intrauterine transfer. The physician performs the intrauterine embryo transfer within a few days after the embryos form. Then the patient waits to see whether she has become pregnant. There will commonly remain *surplus embryos*, embryos as to which intrauterine transfer has been declined. The clinic will freeze and store these embryos if the patient wishes. Patients regularly revisit the question whether to continue storing surplus embryos.[4] In the aggregate, assisted reproduction produces substantially more embryos than patients want babies.

In one technique of embryo creation that is useful in research, investigators induce asexual oocyte activation by organismic cloning. To clone is to

[4] In the UK, absent special pleading, an embryo must be discarded after five years (Human Fertilisation and Embryology Act 1990, c. 37, §14[1][c]). See also Brinsden 1999, pp. 215–216.

copy. 'Clone' derives from the Greek κλωʹν (*klon*) for 'twig.' A plant may be cloned by cutting and planting a shoot. In *somatic cell nuclear transfer*, an investigator activates an enucleated secondary oocyte as the investigator transfers into the oocyte a somatic cell's nucleus. The DNA of that nucleus is the *source DNA*. The result is a *clone embryo*. 'Clone embryo' is of the same form as 'mouse embryo' or 'clone adult.' (The journalistic label 'clone*d* embryo,' which reads 'copied embryo,' is a misnomer.) Somatic cell nuclear transfer is a method of organismic cloning inasmuch as it produces a product whose nuclear genome is a copy of the source's. That a somatic (nongerm) cell is the DNA source distinguishes the process from fertilization, which transfers the nucleus of a germ cell. The clone does not receive the DNA of the somatic cell's *mitochondria*, structures lying in the cytoplasm. The clone's mitochondrial genome will be that of the oocyte. *Reprocloning*, as I shall call it, consists in cloning by nuclear transfer followed by intrauterine transfer of the clone embryo. *Nonreprocloning* consists in cloning by nuclear transfer not followed by intrauterine transfer of the clone embryo. Reprocloning and nonreprocloning are mutually exclusive and jointly exhaustive of cloning by nuclear transfer. By reference to nonreprocloning and reprocloning, we may perspicuously describe research, distinguish practices for moral purposes, and express legal constraints. Stem cell research employs nonreprocloning but not reprocloning.

A product of sexual or asexual oocyte activation that is undergoing organismic development is a *conceptus*. I exclude from the extension of this term the extraembryonic supporting structures such as the placenta. (In strict medical parlance, 'conceptus' denotes a product of fertilization inclusive of supporting structures.) Some biologists have suggested that in moral debate, it avails to emphasize a distinction that I have just drawn, that between nonreprocloning and reprocloning, by ceasing altogether the use of 'cloning' for nonreprocloning, and using only the name 'nuclear transfer.' This suggestion travels in tandem with the proposal that we cease to use 'clone' and 'embryo' for a product of nonreprocloning.[5] 'Nuclear transfer' is informative so far as it goes. But it does not go far enough. According to the usage previously nourished in the scientific literature, cloning is a genetic event. That event concludes upon an oocyte's assimilation of source DNA, regardless whether there later occurs an intrauterine transfer of the clone. A clone does differ from a zygote: a clone begins with one nucleus, not two pronuclei, and a clone suffers from abnormalities in expression of imprinted genes and other defects. Even so, scientists routinely

[5] A fuller discussion of the response that follows is given in Guenin 2003a.

say that mature nonhuman clones (e.g., Dolly the sheep) have developed from embryos. Withholding 'clone' and 'embryo' from life forms heretofore called by those terms risks the appearance of legerdemain, of trying to smuggle in the creation of an embryo by not mentioning it, of switching labels in lieu of argument. If we did not already have 'embryo' to name a universe of moral concern, we would coin a term with like extension. It falls to the scientist and philosopher to root out misconceptions that ordinary language sometimes harbors, but in this case, it seems to me that ordinary language has got things right. In a convergence of scientific expository convenience and common parlance, 'embryo' is our generic term for a prefetal conceptus.

Parthenogenesis consists in organismic development begun upon activation of an oocyte without insertion of foreign DNA. Reptiles reproduce in such manner. Parthenogenesis does not naturally occur in mammals. Human parthenogenesis may be artificially initiated by electrochemical or mechanical stimulation of an oocyte. A human parthenote will not develop a functional placenta.

We may now sketch the role of embryos in stem cell biology. A *totipotent stem cell* is a cell capable of developing into an entire organism with placenta. *Nontotipotent stem cells* may be defined by two attributes, (a) self-renewal, the ability of populations thereof to perpetuate by cell division throughout the life of an organism, and (b) differentiability, the ability to issue in at least one type of highly differentiated descendant.[6] (This is a functional definition; in the laboratory, an investigator will apply an operational definition predicated on observables such as cell surface markers.) Stem cells are *unipotent* if they can issue in only one type of descendant (e.g., spermatogenic stem cells), *multipotent* if they can issue in a few cell types (e.g., hematopoietic stem cells), and *pluripotent* if they can issue in cells of all three *germ layers*, namely, the mesoderm, ectoderm, and endoderm, which is to say cells of all types except placental. Stem cells do not transform directly into specialized cells. Stem cells begin a differentiation sequence, a sequence in which each successive cell type is ever more differentiated. The sequence ends in specialized cells.

It is believed that most of the blastomeres produced during very early cleavage are totipotent stem cells, and that after about the eight-cell stage, totipotency has ceased. (To test for totipotency, an investigator would ascertain whether the subject can successfully implant in a uterus and develop. But we should be hard pressed to justify experimental intrauterine transfer

[6] Watt and Hogan 2000. A cluster of totipotent stem cells is not self-renewing.

of what an investigator believes may be a totipotent cell, i.e., a developing embryo.) At the blastocyst stage, the blastomeres of the inner cell mass are pluripotent. They cannot generate a trophoblast.

We may think of the early blastocyst stage, the period around day 5, as a brief pluripotency interlude that succeeds totipotency and precedes differentiation. One method of extracting blastomeres from an embryo during this interlude is *immunosurgery*. Originally perfected in mice,[7] this procedure strips away the trophoblast and separates the embryoblast from the trophoblast. The procedure unavoidably destroys the embryo. It was from blastomeres extracted during this interlude that investigators first grew populations of human *embryonic stem cells*, understood as indefinitely proliferating populations of pluripotent stem cells derived from embryos.[8] The investigators accomplished this feat by hitting upon growth media and conditions that, while nurturing cells so that they continue to divide, include ingredients that avert differentiation. Because blastomeres of the inner cell mass do not self-renew *in vivo*,[9] blastomeres are not themselves stem cells (unless, contrary to our definition, we demand for stem cells only differentiability). Thus 'embryonic stem cells' does not denote blastomeres but rather the cell culture derivatives of blastomeres. 'Embryonic' here denotes 'embryo-derived.'

While embryonic stem cells are derived from living embryos, pluripotent cells of another type, *embryonic germ cells*, are derived from abortuses at a late embryonic stage.[10] A consensus justification for use of abortal tissue arises in the case of a woman who undergoes an abortion without inducement by anyone and for reasons unrelated to research, and who thereafter donates the remains.[11] A donee scientist's use of such remains may be likened to a transplant patient's acceptance of the organ of someone recently deceased, or to the use of a donated cadaver in medical education, in each case on the condition that the donee is not complicit in the death of the source. The justification of such practices in virtue of such noncomplicity has gained recognition within the fount from which emanates the notion of complicity, the teachings of the Roman Catholic Church. These acknowledge the permissibility of 'experimentation carried out on embryos which are dead,' provided that 'there be no complicity in deliberate abortion and that the risk of scandal be avoided.'[12]

[7] Solter and Knowles 1975. [8] Thomson *et al.* 1998.
[9] van der Kooy and Weiss 2000. [10] Shamblott *et al.* 1998.
[11] It is feasible, as in 42 U.S.C. §§289g-1(b)(2)(A),(c), and 289g-2(b) (2000), to prohibit inducement.
[12] Sacred Congregation for the Doctrine of the Faith, *Donum Vitae* § I(4).

Many diseases and disabilities result from a deficiency in specialized cells of a single type. I refer here to maladies such as diabetes, Parkinson's, heart disease, muscular dystrophy, autoimmune diseases, multiple sclerosis, Lou Gehrig's disease, other degenerative diseases, and spinal cord injury. Type 1 diabetes results from insufficiency of insulin-producing pancreatic β cells, Parkinson's from insufficiency of dopaminergic neurons, and so on.

The discovery of how to grow human embryonic stem cells in culture immediately suggested the prospect of inducing such cells to issue in transplantable cells – whether fully specialized cells, precursors, or multipotent cells – with which to augment a patient's pool of cells of a given type. Even neurons might thus be generated. The birth of Dolly by cloning then suggested a strategy for obtaining immunocompatible cells for transplant: use a skin cell of a patient to produce a clone of the patient, derive an embryonic stem cell line, then induce differentiation into specialized cells. Another strategy consists in obtaining disease-specific pluripotent stem cells, observing how the diseases begin, designing drugs to combat the diseases, and testing the drugs on the exemplifying cells. Cloning compels attention because it puts on display cellular *reprogramming* (or *dedifferentiation*), an epigenetic process in which the transferred nucleus reverts to an undifferentiated state. Reprogramming involves cytoplasmic transcription factors observed in embryonic stem cells and clones. Through embryonic stem cell research in which these factors have been observed in action, investigators have devised ways to introduce or trigger the factors in somatic cells, thereby generating *induced pluripotent stem cells*. The embryonic stem cell is the gold standard of pluripotency to which all other cell types are experimentally compared, as well as the subject of studies through which investigators probe the most fundamental questions of stem cell biology. Studies of embryos and cells derived from them could also yield insights into cellular processes in general, including cancer. Other ingenious lines of inquiry may emerge in various fields of biomedical research as the fruit of further research. A vision has developed of research and therapy enabled by observing and reprising development at its earliest stages. Thus do we find our attention drawn to embryos that will never begin gestation.

1.3 AFFECTED BEINGS AND UTILITARIANISM

The word 'person' derives from the Latin *persona*, denoting a mask worn on stage. *Persona* correlates with the verb *personare*, to resound. An actor could speak more loudly by speaking through the cavity in his mask. The phrase '*dramatis personae*' eventually came to denote not masks, but roles.