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SUBMISSION

to the

HOUSE INQUIRY INTO SCIENTIFIC, ETHICAL AND REGULATORY ASPECTS OF HUMAN CLONING

THE STANDING COMMITTEE ON LEGAL AND CONSTITUTIONAL AFFAIRS

HOUSE OF REPRESENTATIVES

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INTRODUCTION

The biological development of a human being is remarkable. From the beginning of the fertilization process a sophisticated self-directed process is set in motion. Intrinsic to this first cell is the inherent capacity to manage the blindingly complex protocol of human design. The continuum that is human life has begun, and once initiated, if all goes well, will result in the birth of that human being. From the first moment, the genetic code in concert with the cellular environment, orchestrates the myriad of messages necessary to assemble the human form.

Different terminology is used to describe each phase of the process, such as embryo and foetus, each step unveiling a variety of features. However, these features emerge along a continuum of change, new landmarks of genetic expression, with a precision in time and space. Throughout, there is no stage or characteristic that allows for a definitive assignment of greater or lesser value or worth. The distinction between embryo and foetus, for example, is arbitrarily set at 8 weeks. Indeed, even when it comes to birth, which is no doubt the most notable juncture in the course of development, the change, though highly significant, nevertheless entails minimal changes in the nature of the person, and may perhaps best be described as ‘changing address’.

HUMAN EMBRYOS

Some people deny moral status to the human embryo on philosophical grounds. There is, however, no agreement among philosophers as to when personhood begins or ends because there is no agreement on how to define personhood. Personhood is, therefore, an unsafe basis upon which to make public policy. Others have denied moral status to the embryo on scientific grounds. The early embryo has been described as ‘simply’ a collection of cells or even an undifferentiated mass, largely formless until the appearance of the primitive streak around 14 days. Scientists’ limited understanding of what is occurring within these cells during this time has been extrapolated to imply a lack of meaning or significance. The jump from biological facts to dogmatically certain philosophical conclusions is not persuasive when there are significant gaps in human knowledge. Such jumps, however, have not been an uncommon occurrence in the history of science.

The limited understanding of what is occurring within the embryo at the earliest stage of its development has been reinforced by the use of the term ‘pre-embryo’ to describe the embryo during this early developmental phase. By using the power of semantics in this manner, the moral status of the early embryo was denied, conveniently justifying embryos to be treated as research objects.

In the UK, embryo experimentation up to 14 days is allowed under license. At the recent Australian Academy of Science forum on cloning[1], Professor Martin Evans from the UK clearly stated that the choice of 14 days had more to do with *expedience* than anything else. In reality, given the technology at the time, 14 days was about the maximum time that embryos could be maintained *in vitro* and hence remain available for experimentation. Fourteen days was an arbitrary choice, and the appearance of the 'primitive streak' was a convenient marker, held up as having a significance beyond what embryology dictated. It is important to note that the use of the term 'pre-embryo' is in the process of being discarded, in recognition of the fact that its use ascribes a diminished or non-existent value to the early embryo.[2]

It is clearly important then that the terminology used in this debate is true to the biological facts and gives a fair account of what is known, even if that knowledge is limited.

EMBRYONIC STEM CELLS

The cells that constitute the early embryo, particularly those that make up the inner cell mass (ICM) of the blastocyst, have recently been isolated and grown in culture.[3,4] This scientific advance has been greeted with great enthusiasm and fanfare, and the manipulation of these embryonic stem cells (ES) cells has been ascribed the potential to usher in a new age of medical treatment with the hope of treating some of humanity's most distressing and intractable diseases.

ES cells may be pluripotent or totipotent, that is with the capacity for differentiation to become many or all of the 200 or so cell types constituting the human body, perhaps even one day open to manipulation with biochemical signals under the direction of researchers. The ability to

[1] One of the authors of this submission, Dr Gregory K Pike, was present at that meeting by invitation of the Academy.
[2] Richard M. Doerflinger (The Ethics of Funding Embryonic Stem Cell Research: A Catholic Viewpoint. *Kennedy Institute of Ethics Journal* Vol. 9 No. 2, 137-150, 1999) notes that "Some textbooks that once used 'pre-embryo' have quietly dropped the term from new editions, now describing the newly fertilized zygote simply as an embryo." Furthermore, the National Bioethics Advisory Commission (NBAC) defines an "embryo" as "the developing organism from the time of fertilization" (NBAC 1997, P. appendix-2). Langman's Medical Embryology Sixth Edition does not use the term "pre-embryo". The comparative lawyer Albin Eser has suggested that "the naïve (speaking from a normative-theoretical perspective) and rather simplistic efforts to get rid of the basic value problem through terminological 'degradation' of the pre-implantation embryo to the status of 'pre-embryo' or even to simple 'seed' or 'germ' should be abandoned. Rather than prejudicing the value questions involved through conceptual-terminological game-playing it would be better to concentrate on the question that is lastly decisive: To what extent does or should a species-specific human (since originating from human gametes) new entity of life – i.e., at least genetically capable of achieving the full potential of a human being – possess sufficient value to make us unwilling to allow for total freedom of choice with respect to maintaining or destroying this life?" A. Eser, "Experiments with embryos: legal aspects in comparative perspective", UK National Committee of Comparative Law 1987 Colloquium Legal Regulation of Reproductive Medicine (Cambridge) cited in Anthony Fisher, IVF The Critical Issues, (Melbourne: Collins Dove, 1989), 173-174.
[3] Thompson, J.A. *et al*., Embryonic stem cell lines derived from human blastocysts. *Science* **282**:1145-1147, 1998.
[4] Shamblott, M.J. *et al*., Derivation of pluripotent stem cells from cultured human primordial germ cells. *Proc. Natl. Acad. Sci. USA* **95**:13726-31, 1998.

differentiate into a plethora of cell types should come as no surprise since that is exactly what ES cells will eventually do if allowed to stay put in the ICM, except that in the ICM they will direct their own differentiation into the fully formed human. The hope is that in an isolated and cultured form, they can be coaxed into becoming cardiac cells, glandular cells or nerve cells at the will of the operator. The fact that these cells have been isolated from viable embryos, subsequently destroyed, or from the gonads of aborted foetuses, in a slightly different procedure, raises serious ethical concerns in its own right, which we will not address here.

The hope invested in stem cell research is closely tied to the prospect of human cloning. If it were possible to clone adult human differentiated cells in a manner similar to that used to clone Dolly, and then the developing embryo divulged of its ES cells, these cells may be able to be directed to become immunologically compatible tissues or even organs[5] for the treatment of the individual from whom they were derived. In the process, an embryonic human being would have been created for the sole purpose of being destroyed for the benefit of another, an act we consider unconscionable. Lord Alton captured the real meaning behind the benign sounding 'therapeutic cloning' when he said:

> The process involves a form of technological cannibalism according to which your tiny twin and triplet siblings must pay with their lives on the altar of your 'medical' treatment. This vampiric transfusion of life from the cloned sibling to the original sick patient is the paradigmatic example of using others as a means to an end. It is simply revolting and ethically beyond the pale.[6]

The use of the term 'therapeutic cloning' to describe this process is an example, as outlined earlier, of semantic gymnastics intended to create an artificial distinction between cloning which allows a cloned individual to be born, so-called 'reproductive cloning', and that which destroys an embryonic human being. Both are reproductive cloning. To allow any distinction to be made immediately implies a different status for the embryo that could be used to legitimise its destruction. Indeed the choice of the word 'therapeutic' is laden with positive meaning, and serves to weaken opposition to the real meaning of the procedure. In the Australian Academy of Science position statement, recommendation 1[7] states that 'reproductive cloning' to produce human foetuses is considered unethical and unsafe, but that research on cells derived from cloning techniques should

[5] The hope of developing human organs *in vitro* has not yet been realised. The construction of an organ in this way may fairly be described as an exercise in science fiction, but even if it were possible there can be little doubt of its extreme technical complexity, and probable enormous cost.

[6] For Lord Alton's full address, go to http://www.match.org.uk

[7] The full text of Recommendation 1 is as follows: Council considers that reproductive cloning to produce human fetuses is unethical and unsafe and should be prohibited. This is in accord with international opinion (Annex 5). However human cells derived from cloning techniques, from ES cell lines, or from primordial germ cells should not be precluded from use in approved research activities in cellular and developmental biology.

not be precluded from research. The clear implication here is that the production of embryos by cloning techniques, and their subsequent destruction prior to becoming foetuses, is acceptable. By all definitions, including the Academy's, an embryo becomes a foetus at 8 weeks. Hence research on the developing human up to 8 weeks is recommended by the Australian Academy of Science.

Moreover, it might well be thought that if cloning embryos is acceptable for 'therapeutic purposes' involving their destruction, why could not other embryos be formed for destructive experimental purposes. That is, so-called 'therapeutic cloning' may well be seen as a stalking horse to get a broad acceptance of the creation and use of embryos for destructive experimental purposes thereby undermining State laws which already prohibit this way of treating embryonic human beings.

Since we consider there to be no merit in the artificial distinction between 'therapeutic cloning' and 'reproductive cloning', it is our recommendation that 'reproductive cloning' be the only term used to describe the asexual reproduction of a human being by cloning.

SLIPPERY SLOPE CLONING

If the terms 'therapeutic cloning' and 'reproductive cloning' are taken up and formalised in various position statements, and perhaps law, there is every reason to expect an expansion of the context of therapeutic cloning to include foetuses, particularly given the fact that it would be much easier to allow organs to develop 'naturally' in the cloned foetus before harvesting, rather than attempt the extremely difficult technical process of organogenesis *in vitro* from ES cell directed differentiation. In this vein, there have already been calls for the harvesting of organs from embryos and foetuses.[8]

If cloned foetuses were allowed to develop, the next 'natural' consequence would be to allow cloned embryos to be implanted and develop till birth. Even if 'therapeutic cloning' was permitted and 'reproductive cloning' banned, it is hard to imagine that once our IVF clinics and research facilities are replete with cloned embryos, someone will not try implantation and full pregnancy cloning. For those who consider allowing the birth of a cloned individual to be acceptable or even in some cases ethically demanded, this would be a small and relatively easy step to take. Furthermore, without legal parity from one country to the next, a supply of cloned embryos from one country could easily be transported to another where full pregnancy cloning might be allowed, or at the very least be minimally restricted.

[8] Savulescu, Julian. Should we clone human beings? Cloning as a source of tissue for transplantation. *Journal of Medical Ethics* **25**:87-95, 1999.

There are a host of ethical difficulties that would arise in the event that cloning for the production of a born human being were allowed, and since very few people would contest the insurmountable nature of these ethical problems we will not detail that discussion here.[9]

ADULT STEM CELLS

The use of ES cells to achieve the medical therapeutic aims alluded to earlier may not be the only avenue open to researchers. There has been some interesting work in recent years on the use of stem cells from other tissues in the adult human body. The use of these cells may not be ethically problematic. Studies at Harvard Medical School have shown that mouse neural stem cells can be injected into the brains of mice with a degenerative disorder, and the abnormal cells replaced by a large number of normal cells.[10] In an interesting twist, neural stem cells could be coerced into becoming blood cells, including cells carrying out an immune function such as B and T lymphocytes.[11] As Malcolm Moore from the Memorial Sloan-Kettering Cancer Center in New York states:

> Lineage-defined progenitor cells in adult tissues may be more plastic than hitherto thought. They might have the capacity to de-differentiate, or be reprogrammed, becoming totipotent stem cells.[12]

Perhaps the seemingly obvious outcomes of ES cell research could be supplanted by more effective and morally acceptable research using adult stem cells. In the serendipitous world of scientific research, it would not be the first time that less conspicuous research turns out to be the most fruitful approach for medical therapeutic application.

When it comes to alternatives, there is an ethical imperative to first pursue those avenues that are morally less problematic. As Doerflinger notes:

> Even among those who do not recognize the human embryo as having the rights of a person, it is widely held that harmful experiments must not be performed on

[9] The Australian Academy of Science, for example, has strongly recommended against the cloning of born human beings.
[10] Reported by Abi Berger, Neural stem cells successfully transplanted. *British Medical Journal*, 12 June 1999, **318**:1575.
[11] Bjorson *et al*., Turning brain into blood: a hematopoietic fate adopted by adult neural stem cells *in vivo*. *Science* **283**:534-7, 1999.
[12] Malcolm Moore, "Turning Brain into Blood" – Clinical Applications of Stem-Cell Research in Neurobiology and Hematology. *The New England Journal of Medicine*, August 19, 1999, **341(8)**:605-607.

> the embryo unless they are the only feasible means for obtaining vitally important medical benefits.[13]

Furthermore, the United States National Bioethics Advisory Commission (NBAC) likewise concluded:

> Because of ethical and moral concerns raised by the use of embryos for research purposes it would be far more desirable to explore the direct use of human cells of adult origin to produce specialized cells or tissues for transplantation into patients.[14]

Some say that it is first necessary to conduct research using human ES cells so that the basic science can be determined on these pliable cells before proceeding to manipulate adult stem cells. However, it may be possible for de-differentiation and re-differentiation to proceed without the use of ES cells. Clearly, as evidenced by the making of Dolly, fully differentiated adult somatic cells are malleable enough to be de-differentiated to an embryonic state, so perhaps partial de-differentiation to an intermediate cell without the production of an embryo would be possible. In that event the option for re-differentiation to a variety of tissue types may still exist. Furthermore, much foundational work is yet to be done using animal ES cells, before proceeding to manipulating human cells. Professor Peter Rathjen from Adelaide University, speaking at the Australian Academy of Science cloning forum, recently described work using mice that identified some of the factors responsible for directed differentiation. The science is so much in its infancy that it is our opinion that to launch into work on human ES cells is premature, as well as being morally problematic.

HUMAN/ANIMAL FUSION

A further recent development needs consideration. Dr Michael West, head of Advanced Cell Technology (ACT) in Worcester, Massachusetts, USA, recently reported an experiment conducted by one of ACTs researchers in which a human nucleus was placed in an enucleated cows egg. The cell began to divide, approaching the 16-32 cell stage. It has been argued that this type of experiment avoids certain ethical dilemmas by obviating the need for human eggs. Dorothy Wertz states that:

[13] Robert M. Doerflinger, The Ethics of Funding Embryonic Stem Cell Research: A Catholic Viewpoint. *Kennedy Institute of Ethics Journal* **9(2)**:137-150, 1999.
[14] NBAC 1997, pp.30-31.

> … use of cows eggs to jump-start human cells for possible organ transplantation may actually be the most ethical approach to date.[15]

To reduce such a serious ethical issue to 'jump-starting' human cells is to miss the import of combining human genetic material with animal cells, which themselves, although enucleated in this case, will also include a component of bovine genetic material. Wertz likens this process to the hamster egg test in which the viability of human sperm is tested by their injection into hamster eggs. The suggestion that this test raised "few, if any ethical criticisms"[16] is remarkable given the strong objections voiced by many bioethicists at the time.

There are reasons behind the immediate "yuk" factor experienced by many about the mixing of human and animal cells or gametes. It is not just the concern, however valid, about the nature of the developing embryo, and what it could be, confounding as it does our defining sense of what is animal and what is human, but more deeply it is an affront to human dignity. And dignity may perhaps best be understood in terms of the value or worth of human life and its distinction from the rest of the animal kingdom. Reductionist notions of human life as mere molecules or biochemical machinery have little to say about the deeply held respect for human life that is the hallmark of most of humanity's highest endeavours and achievements. When at times in history that respect has been lost, we witness some of humanity's most appalling behaviour. The centrality of that respect in the understanding of human nature is paramount, and ought not be traded for anything inferior.

RECOMMENDATIONS

1. That there be no distinction made between 'therapeutic cloning' and 'reproductive cloning'.
2. That the cloning of all members of the human family, embryos, foetuses and the born, be defined as 'reproductive cloning'.
3. That reproductive cloning be banned.
4. That human embryos not be created for the purpose of experimentation or destruction.
5. That the human genome not be mixed with cells of animal origin for the purpose of creating embryos or embryo-like structures.
6. That research on human adult stem cells be encouraged.

[15] Dorothy C. Wertz, Human Cells in Cows' Eggs: Another Source of Organs for Transplant, *The Gene Letter* **3(2)**: 4-6.
[16] *Ibid.*