The Ethics of Cloning and Embryonic Stem Cells as a Source of Tissue for Transplantation: Time to Take a Positive Approach to Law Reform in Australia

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ABSTRACT

Every day, people die because there are insufficient tissues available for transplantation. The development of cloning and embryonic stem cell line technologies offer real hope for developing better sources of tissues for transplantation. Moreover, these new technologies may mean that damaged tissue (after a stroke or heart attack, for example) can be replaced with normal functioning tissue rather than scar tissue. We have a moral duty to engage in this research. Recently, the Human Genetics Advisory Commission (HGAC) and the Human Fertilisation and Embryology Authority (HFEA) in the United Kingdom and the Human Genome Organisation (HUGO) endorsed "therapeutic cloning" as a source of tissue for transplantation. Research into "therapeutic cloning" and the development of embryonic stem cell lines is illegal in several states in Australia. It is time to review that legislation.

KEYWORDS: Cloning; transplantation; autonomy; embryonic stem cells; fetal tissue; embryo experimentation; abortion

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INTRODUCTION

There have been two recent scientific advances which hold great hope for producing new, abundant and better sources of human tissues and organs for transplantation. Moreover, these new advances may mean that injured tissue can replaced by properly functioning tissue, rather than scar tissue.

1. Establishment of Human Embryonic Stem Cell Lines

Stem cells are cells which are early in developmental lineage and have the ability to differentiate into several different mature cell types. Totipotent stem cells are cells with the potential to form a complete human being. Pluripotent stem cells are very immature stem cells with the potential to develop into any of the mature cell types in the adult (liver, lung, skin, blood, etc), but cannot form a complete human being on their own.

Recently, human embryonic stem (ES) cell lines have been established for the first time.[1] Embryonic stem cells are cells obtained from the inner cell mass of the blastocyst or preimplantation embryo (before 14 days). These cells are pluripotent. Embryonal gonadal cells, derived 5-9 week aborted fetuses[2], and embryonal carcinoma cells, derived from teratocarcinoma cells of the testis, have been cultured with similar properties.

These cells could be used to produced universal donor lines to produce any cell type. Embryonic stem cells from mice have been directed to differentiate into vascular endothelium, myocardial and skeletal tissue, haemopoietic precursors and neurons.[3] Clinical applications include haemopoietic repopulation and treatment of neurodegenerative disease, diabetes, spinal cord injury[4], as well as the screening of drugs.[5] Haemopoietic repopulation now has a role in treatment of haematological malignancy, storage disorders and rheumatoid arthritis. Embryonal carcinoma cells (EC cells) have recently been differentiated into neurons which are currently undergoing trials in the treatment of stroke.[6]. Animal research has suggested that such grafts can reverse cognitive and motor deficits.[7]

ES cells could be involved in a number of strategies to reduce immunological rejection: (i) banking of many ES cell lines representing the major histocompatibility complex (MHC) alleles to increase the chances of MHC matching; (ii) genetic alteration of MHC genes to reduce rejection; (iii) introducing the recipient's MHC genes through transgenesis and gene targetting.[8]

ES cells could also be vectors for gene therapy in the treatment of genetic disease. A gene could be inserted and tissue grown without genetic abnormality, which could be transferred to the patient.

2. Cloning

Cloning is the production of an identical or near-identical genetic copy.[9] Cloning can occur by fission or fusion. Fission is the division of a cell mass into two equal and identical parts, and the development of each into a separate but genetically identical or near-identical individual. This occurs in nature as identical twins.

Cloning by fusion involves taking the nucleus from one cell and transferring it to an egg which has had its nucleus removed. Placing the nucleus in the egg reprogrammes the DNA in the nucleus to replicate the whole individual from which the nucleus was derived: nuclear transfer (the sense of cloning employed in this paper). It differs from fission in that the offspring has only one genetic parent, whose genome is nearly identical to that of the offspring. (Cloning in mice is slightly different and involves injection rather than fusion.)

Human cloning could be used to produce cells, tissues or organs by producing a totipotent stem cell. This totipotent cell could be used to produce a blastocyst and the ES cell lines. Alternatively, it could be used to produce an mature embryo, fetus, child or adult from whom tissue could be removed. This second alternative will not be addressed in this paper.[10]

Thus, the recent advances in cloning technology[1112],offer scope to make ES cell technology an even more attractive source of tissue for transplantation, and also to increase the role of transplantation therapies in the treatment of degenerative and vascular disease. If the blastocyst from which the ES cells were derived was cloned from a mature (somatic) cell from the potential recipient of the transplanted tissue, there would be no tissue incompatibility because the cells would be the person's own. For example, a healthy skin cell could be removed from a person with leukemia. The nucleus of the skin cell would be removed and placed in the cytoplasm of an enucleated egg (nuclear transfer). The resulting clone would be allowed to divide to the blastocyst stage, and ES cells would then be removed to create cell lines for that particular individual. The great advantage of using cloning as the source of tissue is that the donor cell can be derived from the recipient, and so there are no problems with immunological rejection.

Research in Australia

ES cell technology has been described as the most significant development since recombinant DNA.[13] While both ES cell and cloning technology hold great promise for providing abundant sources of self-compatible tissue, and while Australia has the scientific capabilities to carry out this research, such research is illegal in many states of Australia.

The Infertility Treatment Act 1995 in Victoria, and the Human Reproductive Act 1991 in WA both prohibits destructive research on embryos (which harms the embryo or renders the embryo unfit for implantation or less likely to result in a pregnancy). This would imply that creating an embryonic stem cell line would be illegal in Victoria and Western Australia.

Victoria, WA and SA all have legislation prohibiting cloning. The NSW Minister for Health indicated in 1997 that he legislation would be introduced to ban cloning. The National Health and Medical Research Council (NHMRC) *Ethical guidelines on assisted reproduction*, produced in 1996,[14] state that destructive embryo research should only be approved in exceptional circumstances, and then only involving a restricted number of embryos. Cloning research would involve destructive embryo research and would thus be in contravention of these guidelines. It would also contravene other recommendations made in the NHMRC guidelines:

> "11.1 Developing embryos for purposes other than for their use in an approved ART treatment program.
>
> "11.3 Experimentation with the intent to produce two or more genetically identical individuals, including development of human embryonal stem cell lines with the aim of producing a clone of individuals."

Paragraph 11.1 also seems to prohibit the formation of embryonic stem cells. Indeed, paragraph 11.3 explicitly prohibits cloning with the aim of producing embryonic stem cell lines. These guidelines ban ES cell research, but this is understood in practice to refer to ES cell research for the purposes of cloning a human being.

In December 1998, the Australian Health Ethics Committee (AHEC) produced a report on cloning[15] which recommended

1. that all States and Territories enact complementary legislation on ART, "highlighting the need for legislation to prohibit the cloning of human beings."

2. that a two-tier approval process should be adopted for research that *involves* gametes and/or embryos. The first tier approval process requires assessment by a national panel of experts on the scientific merit and ethical acceptability of research involving gametes and/or embryos *before* the second tier approval of the research can be sought from a duly constituted institutional ethics committee.

The practical upshot of this is that producing ES cells and cloning are effectively prohibited by the NHMRC and by legislation in 3 states, and that other States may adopt the regressive and obstructive legislation as is in place in Victoria, South Australia and Western Australia.

AHEC recommend that the NHMRC allocate $3 million per year over the next 5 years to establish a primate research facility for the conduct of approved primate research related to cloning and stem cell biology. However, we know far more about the human genome (as a result of the human genome project) and mouse genome than we know of the monkey genome. This proposal would set back research in this field by years. There are also genetic differences and the results of this research may not be relevant to humans. Similar arguments were given when *in vitro* fertilisation was

proposed, but the technology was successfully developed without significant primate work preceding it. Lastly, this alternative may not avoid the ethical objections. Non-human primates have similar cognitive capacities to humans, in particular a capacity for self-consciousness, and cogent arguments have been given to extend the same moral protection to these animals as to humans.[16] Safety will most appropriately be evaluated in mice and then humans.

At least one centre in Australia, The Institute for Reproduction and Development in Melbourne, is currently engaging in research on embryonic stem cell lines created overseas. It is not clear whether embryonic stem cells are "embryos" for the purposes of the Infertility Treatment Act in Victoria. According to the Act, "embryo" means any stage of human embryonic development at and from syngamy (the point during fertilisation when there is fusion of the male and female pronuclei, and mixing of DNA from the egg and sperm, which is about 22 hours after the sperm first begins to penetrate the egg). At very least, it would be illegal to perform research into nuclear transfer as a source of embryonic stem cells or indeed to create any human embryonic stem cell line in Victoria.

Current legislation and guidelines limit the extent to which scientists in Australia can engage in research into realising the great potential of ES cell and cloning technologies. This situation is unlikely to change significantly and may even worsen if the AHEC recommendations are adopted. These restrictions have the following implications:

1. competition and diversity in biotechnology will be reduced as large biotechnology companies seek to patent and monopolise this new technology. Development and delivery will be dictated by commercial interests, making this technology unaffordable to many. The effects of monopoly have been well demonstrated in agriculture.

2. scientists in Australia have the capabilities to be participating in the development of these life-saving medical treatments.

3. Australian research must go off shore.

Most importantly, it is morally wrong not to promote this research.

The moral imperative to perform research into cloning and ES cells

There is significant need for more transplantable tissue, with as few as 5% of the organs needed ever becoming available [21], with the discrepancy between the number of potential recipients and donor organs increasing by approximately 10-15% each year in the US.[17] There also remain problems with the compatibility of tissue requiring immunosuppressive therapy with serious side effects.[18] [24]

A general principle guides medical practice: the duty of medical rescue. This principle states that when doctors could save a patient's life, and that life would be worth living, they should save that life. Consider the following hypothetical example.[19]

Lucas I Lucas is 22 year old man with leukaemia. The only effective treatment will be a bone marrow transplant. There is no compatible donor. However, there is a drug which selects a healthy bone marrow cell and causes it to multiply. A doctor would be negligent if he did not employ such a drug for the treatment of Lucas' leukaemia. Indeed, there is a moral imperative to develop such drugs if we can and use them.

Lucas II In this version of the example, the drug causes Lucas' healthy skin cells to turn into healthy bone marrow stem cells. There is no relevant moral difference between Lucas I and II. We should develop such drugs and doctors would be negligent if they did not use them.

If this is right, there is nothing problematic about cloning to produce cells or tissues for transplantation by controlling differentiation. All we would be doing is taking, say, a skin cell and turning on and off some components of the total genetic complement to cause the cell to divide as a bone marrow cell. We are causing a differentiated cell (skin cell) to turn directly into a pluripotent stem cell.

Lucas IIA In practice, it is most likely that skin cells will not be able to be turned directly into bone marrow cells: there will need to be a stage of totipotency in between. The most likely way of producing cells to treat Lucas II is via the cloning or embryonic stem cell route. In each case, a totipotent stem cell is produced, and this is induced to differentiate into blood cells. The production of a totipotent stem cell is the production of an embryo.

The Moral Status of the Embryo

Recent developments in science and ethics call into question the special respect given to the early human embryo by Australian legislation and guidelines. According to different moral views, the embryo or fetus has moral status or a right to life at different times:

1. Conception
2. Day 14
3. 6 weeks
4. Quickening (around 18 weeks)
5. Consciousness (not before 26 weeks)
6. Viability (currently around 22 weeks)
7. Birth
8. Sometime in the first year after birth

1. Conception

According to this view, from the point of **conception** on a person exists with a full right to life. This is the present view of Catholic Church.

There are a number of problems with this view. It implies that abortion is like the murder of an innocent person and that mass murder is occurring every day at abortion clinics. While many people are uneasy about abortion, they do not believe it is murder. This view also implies that post-coital contraception (such as the morning-after pill) is like murder. It implies that the destruction of a frozen embryo is like killing a person's life. Such destruction is requested regularly by couples and required by law in Victoria after five years if the embryo's parents cannot be contacted.

There are also problems extending this view to nuclear transfer. Conception involves the unification of two different entities, the sperm and the egg, to form a new entity, the totipotent stem cell. Cloning does not involve a sperm and or egg, and the resulting cell does not have a unique genetic identity. In the case of cloning, there is identity between the cell before and after nuclear transfer – it is the same cell. Something new and important does happen to the entity when it undergoes nuclear transfer, just as something new and important happens when a cell with a malignant potential becomes malignant. But it is the same cell.

Recent scientific research has revealed that sometimes two zygotes fuse after conception to produce one enduring entity (chimera).[2021] The resulting chimera cannot be identical with both zygotes from which it was formed, because this would imply that the two different zygotes were identical with each other (a logical impossibility). If this is so, the chimera must have come into existence at the time of embryo fusion, and not at conception.

The phenomenon of twinning also raises serious problems for the view that we begin to exist at conception. What happens when A divides into identical B and B* at day 2? When did B begin to exist? Was B identical with A? Both B and B* cannot be identical with A, because this would imply that the twins B and B* are identical to each other – that is, that they are both the same thing. This implies that B and B* came into existence when A divided on day 2, not at conception. Indeed, Dame Mary Warnock said: "the embryo hasn't decided how many people it is going to be." Thus the Warnock Committee concluded that embryo experimentation was justifiable until 14 days after conception. At that point, cells have committed themselves to producing the placenta or the embryo proper (including the brain). Soon after, at around day 18-20, twinning ceases to be possible (Siamese twins may be formed between day 14 and then).

2. 14 days

Because of the problems that twinning raises, some philosophers have claimed that when the initial single-celled zygote divides, there is nothing that continues to exist.[22] It is like an amoeba dividing. It ceases to exist and is replaced by two qualitatively identical amoebae. Similarly, when each of the daughter cells divides, it ceases to exist and is replaced by its own two qualitatively identical daughter cells. Again, there is nothing – no individual – that persists through these divisions. Only when the cells begin to be differentiated and to engage in co-ordinated activity do they together constitute a further individual.[23]

Jeff McMahan draws the following analogy. "Consider … an island on which there are people. Suppose these people are entirely unrelated: each came to the island independently of the others, each lives a solitary life with no communication or cooperation with the others, and each is even unaware of the existence of most of the others. In that case it seems clear that these individuals do not together constitute an individual of any substantial sort. If, by contrast, various relations obtain among them – if, for example, they are related genealogically, speak the same language, accept the same moral and religious beliefs, follow the same customs, cooperate together in complex ways, and so on – then it is plausible to suppose that they together constitute a distinct individual: a nation, for example."[24]

3. Consciousness – not before 24 weeks

The view that it is morally permissible to experiment on embryos up until 14 days after conception has gained some acceptance. It is the position in the England and Western and South Australia. There are a number of objections to this view. The problem with the 14 day view is that it identifies us, what is fundamentally us, with facts about our body or physical organism. Yet we seem to be more than physical entities – we are minds, or conscious minds to be more precise. Thus, there is an emerging view that permanent unconsciousness is a state as bad as being dead. When we are permanently unconscious, everything that matters in our lives is gone. Thus, in the case of Tony Bland, the young man rendered permanently unconscious by the Hillsborough football disaster, withdrawal of artificial feeding and hydration was justified on the grounds that Bland had no interest in remaining alive.[25] To put it another way, Tony Bland's mind was dead while his body lived.

Another example which supports the view that we are conscious minds is that of conjoined twins. No one doubts that these are two separate individuals with one body. They are not one person split in two, but two persons joined.[26]

A more extreme case is the hypothetical case of brain transplantation.[27] Imagine that you have an identical twin, A. You have disseminated cancer and will die in one week. However, your brain is intact. A suffers a massive stroke and is brain dead. Brain transplantation has been developed. Surgeons offer to transplant you brain into A's cranium. You accept. Most of us would consider that it is you who survives in A's body. Thus we cannot be identical with our body or organism.

If we are fundamentally conscious minds, we do not begin to exist at least until the structures are present which could support consciousness. The Royal College of Obstetricians and Gynaecologist's Working Party produced a report on Fetal Awareness in 1997. It concluded that the structural development for ability to be conscious of pain is not present in the fetus before 26 weeks. Thus, the fetus does not achieve a moral status before 26 weeks.

Potentiality

There is another objection to using cloned cells and embryos as a source of ES cells and tissue. These cells are potential persons. And it is wrong to kill a potential person or potential being like us. This objection is at the heart of public opposition to embryo research. It is subject to a well described objection: potential X's do not have the same rights as X's. For example, potential doctors do not have the same rights as doctors. Or Prince Charles is a potential king of England, yet he does not have the rights of the king.

Cloning, however, raises new problems with appeal to potentiality. Cloning shows us that somatic cells like skin cells have the potential to give rise to human beings too. But we do not hesitate to kill or excise skin cells. They are not like complete human beings. Hence, we are entitled to treat totipotent stem cells as we treat skin cells.

Mr Nicholas Tonti-Filippini, in a press release issued by the Catholic Archdiocese of Melbourne on Dec 1, 1998, sought to try to distinguish research involving cloning and embryonic stem cells, from other kinds of research in the following way:

"This is quite different from legitimate research involving ordinary human body cells. Such cells have no capacity to develop as a human being."

That claim is false. Ordinary human body cells would develop as a human being if subjected to the cloning procedure.

What happens when a skin cell turns into a totipotent stem cell is that a few of its genetic switches are turned on and others turned off. To say it doesn't have the potential to be a human being until its nucleus is placed in the egg cytoplasm is like saying that a car does not have the potential to get me from Melbourne to Sydney unless the key is turned in the ignition. Nuclear transfer is like a number of other conditions (such as adequate placental blood flow) which must be present if a skin cell is to become a person. There is no relevant moral difference between a skin cell sitting in the laboratory awaiting nuclear transfer and a fertilised egg sitting in a petri dish in an IVF clinic awaiting microsurgical transfer. In each case, the cell requires some technological intervention if it is to have a chance of developing into a person.

What matters morally is whether skin cells *can* become human beings with the application of technology, and whether they *should*. That is an important moral feature of nuclear transfer. Nuclear transfer is a technical intervention which it is necessary to employ if a skin cell is to become a person, just as microsurgical transfer of an embryo formed *in vitro* is necessary if the embryo is to become a person.

Cloning thus exposes new difficulties for those who appeal to the potential of embryos to become persons and the moral significance of conception as a basis for opposition to abortion. If all our cells could be persons, then we cannot appeal to the fact that an embryo could be a person to justify the special treatment we give it. Cloning forces us to abandon the old arguments supporting special treatment of fertilised eggs.

Indeed, this is fortunate. Every year, hundreds if not thousands of frozen embryos must be destroyed by law in Victoria because their parents cannot be contacted. If these embryos were "frozen people", this would be a great moral tragedy.

The Best Way Forward:Review Legislation

Every day, people die around the world because there are insufficient tissues available for transplantation. The development of cloning and embryonic stem cell line technologies offer real hope for developing new better sources of tissues for transplantation. We have a moral duty to engage in this research. In December 1998, after a major review and public consultation, the Human Genetics Advisory Commission and the Human Fertilisation and Embryology Authority in the UK distinguished between "reproductive cloning" (cloning to produce a complete individual) and therapeutic cloning (cloning to produce tissue for medical purposes. It endorsed research into embryonic stem cells during the first 14 days of development and took the brave step of endorsing "therapeutic cloning" as a source of tissue for transplantation. The HUGO Ethics Committee has followed by issuing a Statement on Cloning on March 29, 1999 in Brisbane that broadly supports "therapeutic cloning." Those states in Australia such as Victoria, South Australia and Western Australian which have legislation prohibiting cloning and embryonic stem cell research in humans should now review their legislation. The NHMRC should also adopt a more facilitatory position on cloning and ES cell research.

We need to revise our views about embryos. If we do not, we risk engaging in fetishism about cells, while real people die. Such fetishism is behind claims like those made by Mr Nicholas Tonti-Filippini in the recent Press Release by the Melbourne Catholic Church. He describes embryonic stem cells as "seriously disabled" and as being "friendless and defenceless." It is people, not cells, who are seriously disabled, and who are in need of friends and defence. He continues: 'If an … embryonic stem cell retains the capacity for development as a human embryo then, even if that capacity is damaged or incomplete, it *must be treated as a human embryo*."

Mr Tonti-Filippini believes we should treat an embryonic stem cell as if it were a human embryo, even if it would never develop into a person without technological assistance. The reality is that these are not little people, but cells. Embryos have the potential to become people. But so too does every cell in the body. While we debate about the status of embryos and ES cells, and our own morals, people die because they can't find an organ or tissue. We should put suffering people before cells.

Alternative Ways Forward

There are a number of alternatives to review of current legislation and guidelines.

1. Exempt research on ES cell lines from bans on embryo research

One way to go ahead with research into ES cells is to claim that they are not embryos for the purposes of legislation which prevents embryo research. The US Department of Health and Human Services (DHHS) has recently issued a legal opinion that embryonic stem cells are not "organisms" and so are not covered by the Federal ban on funding for embryo research in the US. This opinion is based on the observation that embryonic stem cells, although they can form any tissue in the body,

are unable to give rise to an embryo if implanted in the uterus[28] because they cannot form a placenta. The Australian Health Ethics Committee called them embryoid bodies rather than "embryos" because they lack the structural organisation of embryo. The HUGO Ethics Committee Statement on Cloning claimed that it is not clear whether totipotent stem cells created by nuclear transfer are embryos![29]

This strategy is less than perfect for several reasons. Firstly, it is unlikely to convince those who are opposed to embryo research and does not send the appropriate public signal that embryo research should be acceptable to the community. Indeed, 77 anti-abortion members of Congress have written two letters of objection to the Secretary of Health and Human Services in the US, claiming that such research violates "both the letter and the spirit" of the law banning Federal funding for embryo research.[30] Similar questions have arisen as to whether Victorian legislation regards ES cells as embryos.

Secondly, this attempt is a tendentious way of avoiding legislation prohibiting destructive embryo research After all, the source of ES cells is an embryo and involves embryo experimentation and destruction. Richard Doerflinger, a spokesman for the National Conference of the Catholic Bishops in the US said that "The reward for destroying [embryos] is an NIH grant to work on the stem cells thus produced." He said that destroying an embryo to obtain stem cells is morally equivalent to an abortion, and the new NIH policy contravenes the spirit of existing law.[31] Indeed, even if ES cells are not embryos, if the destruction of embryos was really morally wrong, it would be wrong to use cells from them. In a similar way, many countries now outlaw the use of commercially acquired organs[32], even if those organs were procured in another country. Forming ES cells is illegal but using cells lines imported from overseas occurs without objection. But if there were something seriously morally wrong with making ES cells, it would be wrong to make them anywhere and wrong to use them in Australia. We should conclude that either we should forbid that kind of research in Victoria, or revise our view that it is a serious moral wrong to form an ES cell.

2. Cow-human chimeras

Preliminary work has been done fusing human somatic DNA with enucleated cow eggs.[33] The resulting cell develops into a blastocyst but stop developing before organs start to form. That is, they will not form a mature organism. However, work has begun developing ES cell lines from these blastocyst cells. It is hard to see how such an entity could be seen as a human embryo, even a non-viable one. [3435]

This proposal may avoid some legal constraints. However, it would also offend the "moral sensitivities" of many people. Is there anything morally wrong with such research, if these cells are derived from somatic cells and never develop into embryos? We now produce human proteins from human DNA inserted into animals.[36] There does not seem anything objectionable about that. But if we can produce proteins in this way, why not blood cells?

3. Alter potential to form the trophoblast

Another theoretical possibility is to insert trophoblast inhibitor genes into or knock out genes from cloned somatic cells so that these cells will never form a placenta[37]. That is, they will be changed from totipotent to pluripotent stem cells. Preliminary animal research has not been done. While there is nothing morally objectionable about such a procedure, it does side step rather than address the fundamental issue: is a totipotent stem cell the kind of entity that has a right to life? However, if this is what is necessary in practice to allow the potentially life-saving research to go ahead, then so be it.

4. Dedifferentiation

It may be possible to research dedifferentiation or reverse differentiation of mature somatic cells to see if they can be made to turn directly into more immature stem cell forms without going all

the way back to totipotency. This would not raise any moral or legal objections. However, how possible it is remains to be seen. Cloning and ES cell technology seem at this point to offer more hope in the short term of yielding useful clinical treatments. And, because every day that the break throughs are delayed, someone else dies because the tissue they need is not available, that is a strong moral reason to support cloning and ES cell research.

5. By-pass totipotency

It may be possible to cause differentiated somatic cells to transform into pluripotent stem cells without a stage of totipotency.[38] Recently, neural stem cells have enticed to differentiate into blood cells in mice.[3940]

From the Present to Future

Cloning of course is not merely a future possibility. We could clone some humans now. Embryo splitting (artificial twinning) is possible now. It may increase the chances of some infertile couples or carriers of genetic diseases conceiving their own child[41][57]. At very least we should review all Australian legislation to:

1. Permit cloning and ES cell research for the purposes of developing tissues for transplantation.

2. Permit research into embryo splitting and nuclear transfer as ways of multiplying embryos for the treatment of infertility and avoidance of genetic disease.

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1 Thomson JA, Itskovitz-Eldor J, Shapiro SS et al. Embryonic stem cell lines derived from human blastocysts. *Science* 1998; 282: 1145-7.

2 Shamblott MJ, Axelman J, Wang S, et al. Derivation of pluripotent stem cells from cultured human primordial germ cells. *Proceedings of the National Academy of Sciences* 1998; 95: 13726-31.

3 Weiss MJ, Orkin SH. In vitro differentiation of murine embryonic stem cells: new approaches to old problems. *Journal of Clinical Investigation* 1996; 97: 591-5.

[4] Gaerhart J. New Potential for Human Embryonic Stem Cells. *Science* 1998; 282: 1061-2.

[5] Butler D. Breakthrough stirs US embryo debate. *Nature* 1998;396: 104.

[6] Doctors perform the first human brain cell transplant. CNN Interactive, July 1, 1998, <http://cnn.com/HEALTH/9807/01/braincell.transplant/index.html); Okie S. "Brain Repair: Doctors Implant Transformed Cancer Cells To Boost Recovery from Stroke," *Washington Post*, March 9, 1999, p Z12.

[7] Bonn D. First cell transplant aimed to reverse stroke damage. *Lancet* 1998; 352: 119.

[8] See Gaehart J, *Science*, 1998.

[9] Every cell division results in genetic differences between progeny which are not completely repaired by DNA repair mechanism. Though the vast majority of these differences have no functional implications, they are differences nonetheless, and cellular division does not normally produce an exactly identical copy of DNA (Pannos Iannou, personal communication).

[10] Savulescu J. Should we clone human beings? Cloning as a source of tissue for transplantation. *Journal of Medical Ethics* 199; 25: 87-95.

[11]] Campbell, KH, McWhir, J, Ritchie, WA, and I Wilmut. Sheep cloned by nuclear transfer from a cultured cell line. *Nature* 1994; 380: 64-66.

[12] Wilmut I, Schnieke AE, McWhir J, et al. Viable offspring derived from fetal and adult mammalian cells. *Nature* 1997; 385: 810-813.

[13] See Butler D, 1998.

[14] <http://www.health.gov.au/nhmrc/publicat/synopses/e28syn.htm>.

[15] The National Health and Medical Research Council Ausrtlian Health Ethics Committee. *Scientific, Ethical and Regulatory Considerations Relevant to Cloning of Human Beings.* Located at <http://www.health.gov.au/nhmrc/ethics/clone.pdf>

[16] Cavaleri P., Singer P. (eds) *The Great Ape Project: Equality Beyond Humanity*, London: Fourth Estate and New York: St Martin's Press, 1993

[17] Cooper DKC. Xenotransplantation – state of the art. *Frontiers of Bioscience* 1996; **1**: 248-65.

[18] It is not clear whether different patterns of X inactivation or the different mitochondrial complement of cloned cells will affect immunocompatibility.

[19] Savulescu, 1999.

[20] Strain, L, Dean JCS, Hamilton MP, Bonthron DT. Brief Report: A True Hermaphrodite Chimera Resulting from Embryo Amalgamation after In Vitro Fertilization. *The New England Journal of Medicine* 1998; 338: 166-9.

[21] Shigeki U, Masayuki N, Mikiko N, et al. Molecular biologic analyses of tetragametic chimerism in a true hermaphrodite with 46,XX/ 46, XY. *Fertility and Sterility* 1995; 63: 189-92.

[22] McMahan J. Cloning, killing and identity. *Journal of Medical Ethics* 1999; 25: 77-86.

[23] McMahan J. Cloning, killing and identity. *Journal of Medical Ethics* 1999; 25: 77-86.

[24] McMahan J. Cloning, killing and identity. *Journal of Medical Ethics* 1999;25:77-86.

[25] *Airedale NHS Trust v Bland* [1993] 1 All ER 821

[26] McMahan J. Cloning, killing and identity. *Journal of Medical Ethics* 1999;25:77-86.

[27] McMahan J. Cloning, killing and identity. *Journal of Medical Ethics* 1999;25:77-86.

[28] Wadman M. Embryonic stem-cell research exempt from ban, NIH told. *Nature* 1999; 397: 185-6.

[29] Human Genome Organisation (HUGO) Ethics Committee. Statement on cloning. 1999, Mar 29.

[30] Wadman M. Congress may block stem-cell research. *Nature* 1999; 397: 639.

[31] Wadman M. Embryonic stem-cell research exempt from ban, NIH told. *Nature* 1999; 397: 185-6.

[32] World Health Organisation. Guiding principles on human organ transplantation. *Lancet* 1991; 337: 1470-1.

[33] Cohen P. Organs without donors. *New Scientist* 1998, July 11, 4.

[34] Cohen P. Organs without donors, 1998.

[35] Marshall E. Claim of Human-Cow Embryo Greeted with Skepticism. *Science* 1998; 282: 1390-1.

[36] Trounson A. Cloning: potential benefits for human medicine. *MJA* 1997; 167: 568-9.

[37] Trounson A. and Gillam K. What does cloning offer human medicine? *Today's Life Science*. Mar/Apr 1999: 12-4.

[38] Vogel, G. Harnessing the Power of Stem Cells. *Science* 1999 March 5; 283: 1432-1434.

[39] Bjornson CRR, Rietze RL, Reynolds BA, et al. Turning Brain into Blood: A Hematopoietic Fate Adopted by Adult Neural Stem Cells in Vivo. *Science* 1999; 283: 534-537.

[40] Strauss E. Brain Stem Cells Show Their Potential. *Science* 1999; 283: 471.

[41] Trounson A. and Gillam K. What does cloning offer human medicine? *Today's Life Science* Mar/Apr 1999: 12-4.