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Stem cells: ethics, legislation and regulation

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1. Introduction

I shall speak briefly about some of the ethical issues arising out of stem cell research, and about some ways in which legislation and regulation in the UK has responded to ethical requirements across the last decade. In doing so, I shall draw on experience as a member of the *Human Genetics Advisory Commission*, which combined with the *Human Fertilisation and Embryology Authority* [HFEA] to report on these issues soon after the cloning of Dolly the sheep, and also of the House of Lords Select Committee on Stem Cell Research, which reported to Parliament in February 2002. The Human Embryology and Fertilisation Authority [HFEA] is a statutory body established under the Human Fertilisation and Embryology Act of 1990 (c.37), which has responsibility of all regulation of all fertility clinics in the UK. *Cloning Issues in Reproduction, Science and Medicine*, Joint Report of the Human Fertilisation and Embryology Authority and the Human Genetics Advisory Commission; published Department of Trade and Industry, December 1998; Report *of the House of Lords Select Committee on Stem Cell Research*, [HL 83(i)] February, available at http://www.parliament.the-stationery-office.co.uk/pa/ld/ldstem.htm.

Broadly speaking, I think there are three distinct clusters of ethical issues that arise in the area of stem cell research. The first arises simply, because this is research using human tissue, so raises issues about consent, restriction to acceptable purposes and avoidance of inappropriate commercialisation. The second group of issues arises, because some stem cell research may be done neither on animal stem cells nor on adult stem cells, but on human embryonic stem cells, so requires the use and destruction of human embryos, usually but not necessarily of embryos surplus to IVF requirements (which must otherwise be destroyed). The third set of issues arises if embryos for research are created by Cell Nuclear Replacement: if we permit use of CNR to create human embryos for research purposes, will we end up with reproductive cloning?

2. The permissibility of embryo research

For our purposes today, I believe that it is the second group of issues that is the most important. However, it may be that this judgement reflects a particular UK view, developed in a context in which there has for more than 10 years been effective and detailed control of IVF. It may perhaps surprise you that I speak of effective and detailed control in the UK, given that it is commonly said that the UK has more liberal – in some views too liberal – legislation in this area. However, it is interesting to note that some criticisms of the supposedly lax regulation in the UK come from jurisdictions in which there is much less effective legislation or regulation to

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control reproductive technologies, or even to prevent reproductive cloning.

So let me briefly describe the legislation and regulation in the UK, and then set out what I regard as a profound moral change arising from advances in biomedicine. In the HFEA was established by Act of Parliament with powers to regulate all use of human gametes and all IVF. The system requires meticulous control in all IVF Centres: each successful fertilisation of a human egg creates an embryo that is recorded and afforded certain legal protections (e.g., may not be exported, may not be mixed with non-human material, may not be kept beyond 14 days when the primitive streak first emerges). The 1990 Act permits a highly regulated use of embryos for research in reproductive medicine, if such research can be done in no other way. In the 1990 Act the permitted purposes for embryo research were (a) promoting advances in the treatment of infertility, (b) increasing knowledge about the causes of congenital disease, (c) increasing knowledge about the causes of miscarriages, (d) developing more effective techniques for contraception, (e) developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation. Up to 1999 the Authority had issued licenses for research use of 53,497 spare embryos donated for the purpose. The Act also provides that where research for the permitted purposes can be achieved *only* by specific creation of an embryo, this may be licensed: up to 1999 the Authority issued licenses for the creation of 118 embryos. *Report of Select Committee on Stem Cell Research*, [HL 83(i)] 4.26. The statistics cover the period from the establishment of HFEA to 31 March 1999.

There are those who believe that all embryo research must be wrong. However, it is worth reminding ourselves that without such research there would be no IVF, and that IVF is not possible without some destruction of embryos. I personally regard the idea that freezing embryos while the process of fertilisation is incomplete avoids destruction as an illusion – the more so because the very demonstration of the safety of freezing and thawing itself required such experiments. The only consistent opponents of embryo research are those who also oppose all IVF, not to mention all abortion. In the UK, as in many other European countries, there are circumstances in which abortion and IVF are permitted. Those who are not opposed to these practices cannot consistently oppose embryo research for ethically serious purposes, provided it is well regulated.

I personally believe that the revolution in molecular biology that lies behind the possibility of stem cell research provides a profound moral challenge to the arguments most commonly used to oppose embryo research. The most frequently heard argument against embryo research, and so against embryonic stem cell research, is that the embryo is a potential person, that persons have a right to life, and so that the embryo has a right to life. As a matter of fact, the usual formulations of this argument are not sound: for we do generally accord rights on the basis of potentiality. For example, we do not think that because a child of 10 has the potential to become medically qualified, she already has the right to practise as a physician. So the argument would have to be amended to claim that from the very earliest stages of embryonic life – the zygote, the blastocyst – we are dealing with actual persons. Such claims have not been backed with evidence, or indeed with argument. To make the argument convincing it would be necessary to show that the fertilised egg has the rights of a human being.

Moreover, any argument from potentiality is now in deep trouble. The revolution in biology that has led to the possibility of stem cell research has played havoc with our views of potentiality. Until recently it was assumed that cells could differentiate but not dedifferentiate. The undifferentiated cells of the blastocyst could develop into the numerous differentiated cells of the mature human body. The creation of Dolly the sheep demonstrated that dedifferentiation of cells is possible. It is this fact that has given rise to hopes that research on adult stem cells may lead to tissue based therapies. If adult stem cells have the potential to dedifferentiate, we may be able to dedifferentiate them and to derive stem cells, and so other cells, of any required type from adult stem cells, and so to avoid using embryos. For example we might be able to derive neural stem cells, and so nerve cells, from haematopoietic (blood) stem cells found in bone marrow. This is surely worth investigation, and provides good reason for research into the potentialities of adult stem cells. However I believe that if this hope is realised the supposed *moral* distinction between adult and embryonic stem cell research may vanish. Let me explain.

The hopes pinned on adult stem cell research are based on the thought that it may prove possible to ded-

ifferentiate these cells – and then to differentiate them in a different direction. The process of dedifferentiation would return a cell to or towards pluripotentiality (or totipotentiality: the use of these terms has not yet stabilised) – in short to the condition in which it has the potential to develop into any and all of the cell types that comprise the human body (see HL 83(i) 2.4 for a discussion of the terms of debate). Now, it may be the case that such dedifferentiation would not return an adult stem cell to the totipotency of the zygote, since it may be the case that no precursor cells for the placenta emerge, and so that no implantation and no development into a foetus, an infant, a child or an adult would be possible. Nevertheless if a fully dedifferentiated adult stem cell could form any and all the cell types in the human body, it would in effect be an embryonic stem cell. I therefore fail to see that its moral status would be different from that of an embryonic stem cell derived from an embryo: what makes the embryo worthy of respect surely cannot be exclusively the cells which will make up the placenta! My conclusion is that we have reason to support research into stem cells – adult and embryo – because such research is likely to be scientifically and ultimately therapeutically significant, and that there may be no deep moral distinction to be drawn between adult and embryonic stem cells. Either adult stem cells cannot be dedifferentiated, and so have limited therapeutic potential or, if they can be dedifferentiated, the moral arguments for adult and embryonic stem cell research will stand or fall together. If all adult stem cell plasticity were based on a potentiality to transdifferentiate but not to dedifferentiate we might reach a different conclusion: but we know from the case of Dolly the sheep that the potentiality to dedifferentiate exists *in adult cells* and presumably also in adult stem cells. I should add that this argument was not used by the Select Committee, and that the report is more concerned to evaluate the evidence for the possibility of advancing by research on adult stem cells alone: we did not find convincing evidence.

3. The control of embryo research

Let me turn away from this ethical argument and offer some comments on the interplay between recent legislative, legal and ethical concerns in the UK. Following reports by expert committees in 1997–2000, new Regulations were passed in 2001 permitting the granting of licenses for embryo research for additional purposes, including obtaining knowledge of serious disease and of therapies. As before, a license can be granted only if there is no other avenue of research that could achieve the same results. The new purposes were (a) increasing knowledge about the development of embryos, (b) increasing knowledge about serious disease, and (c) enabling any such knowledge to be applied in developing treatments for serious disease. Both Houses of Parliament accepted these extended purposes with large majorities.

However, there was then a legal challenge to the 1990 Act from the Pro Life Alliance. They contested the assumption that the Act covered embryos created by CNR, and so the claim that the HFEA could use its powers to regulate the use of such embryos to prevent reproductive cloning. Since the 1990 Act had been passed before CNR was developed it was not explicit on this issue. The received view was that the Act would apply to CNR embryos, but this had not been tested in the courts. On 15 November 2001 The High Court upheld the Pro-Life Alliance claim, with the result that the HFEA no longer had the power to regulate the use of CNR embryos, and so to prevent attempts at reproductive cloning. At this juncture a well-known advocate of reproductive cloning from another EU country announced that he would seek to clone a human being in the UK. This was a puzzling and perhaps irresponsible announcement. First, there are many other jurisdictions without legislation against reproductive cloning, and even if reproductive cloning appeared legal in the UK, nevertheless all fertility treatment remained strictly under the control of the HFEA who have made it clear that they will not permit attempts at reproductive cloning. Second, animal work shows that reproductive cloning is neither simple nor safe.

Parliament immediately passed legislation criminalising any attempt at reproductive cloning: The Human Reproductive Cloning Bill became law on 4 December 2001 (*Human Reproductive Cloning Act*, 2001, HL 57. http://www.hmso.gov.uk/cgi-bin/htm_hl3). The Government also appealed against the High Court verdict, and the Court of Appeal reversed the High Court's discussion in favour of the Pro Life Alliance on 18 January, thereby confirming that the HFEA

would have control over any embryo created by CNR. The window of opportunity for adventurers was very brief, and in my opinion the detailed controls meant that the window was never really open. The UK now has double protection against attempts at reproductive cloning: it is illegal with severe penalties, and the HFEA have full control of all use of embryos. Furthermore they are know to be effective regulators, who have refused to permit a range of adventurous forms of fertility treatment that have been permitted in some other jurisdictions. Somewhere in the world somebody may try to clone a human being: but they will very stupid if they choose to do so in the UK.

You may think that I am too confident about the effectiveness of legislation: of course, there are no guarantees in this life. However, I have come to have great respect for the drafters on the 1990 Human Fertilisation and Embryology Act. What they produced was a system of regulation of embryo research with a clear default structure. No embryo research could be done without licences from HFEA. HFEA could issue no license unless the research was for a permitted purpose, and necessary for that purpose. Further they could issue no licence for the creation of an embryo specifically for research purposes, unless the proposed research was for a permitted purpose, and necessary for that purpose, i.e. could not be done without the creation of an embryo. As the statistics show, licenses have been sparingly granted. The Select Committee report has recommended that the same default structure covers the creation of embryos for research by CNR, and the Report recommends *that CNR embryos should not be created for research purposes unless there is a demonstrable and exceptional need which cannot be met by the use of surplus embryos* (Recommendation 11).

Where have we ended up in the UK? I think that at this stage we have a strong consensus that reproductive cloning of humans must be banned. We have acceptance of the use of IVF, and of strictly controlled embryo research. We have extended those controls to cover research into Embryonic Stem Cells, but only when research on animal or adult stem cells cannot serve as an alternative. Broadly speaking, I believe, the current structure of UK legislation and regulation provides that if the hopes expressed by those who think that all research can be done on adult stem cells are borne out, then it will not be open to the HFEA to issue licenses for embryonic stem cell research.

Of course, many further issues lie ahead, including the creation of a stem cell line bank, which the Select Committee sees as a necessary adjunct of the commitment to minimise the use of embryos in research. This is currently a matter for discussion by expert committees, and may call for the creation of separate banks for research and for the development of therapies, both with high standards for identifying provenance, for ethical consents and for maintaining cell lines in culture. However these I believe are topics for another day.