HUMAN CLONING AND STEM CELLS: unravelling the issues

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In 1997, scientists in Scotland announced that the previous year they had produced Dolly the sheep, cloned from the cell of an adult sheep's mammary gland. In 1998, US scientists cultured the first stem cell lines taken from human embryos. Together, these developments raised the fear of human cloning, a new market in human eggs and the promise of personalised body tissues to treat people with serious diseases such as Parkinson's disease and diabetes.

Scientists in the UK and South Korea, which are two of only seven countries worldwide that allow this type of research, have now produced cloned human embryos. This briefing explains the science and techniques behind human cloning and the laboratory culture of stem cells. It considers the claims made for these techniques and the problems faced by the research and its potential applications, together with the intertwined social, ethical and legal issues.

Cloning and stem cells – new knowledge, difficult questions

Although every cell in the body contains a complete complement of genes, only certain genes in each are operational depending on the type of cell (e.g. whether it is a blood, brain, muscle or stem cell). Until 1997, scientists believed that once a cell, other than a stem cell, had developed to carry out a specific function in the body – for instance, it had specialised into becoming a skin or liver cell – the genes which were switched on and off in that cell were 'fixed'. However, this assumption was dramatically overturned when Dolly, the cloned sheep, was created from the nucleus (the part of the cell that contains the chromosomes) of a mammary gland cell taken from an adult sheep and placed inside a sheep's egg cell, the nucleus of which had been removed (an enucleated egg).[1] To clone a sheep, the nucleus from the adult cell is first fused with the enucleated egg often by using an electrical 'shock' and then, in the environment of the egg, the nucleus is able to code for the development of *all* the cell types of a sheep's body.

Shortly after Dolly was born in 1996, another breakthrough occurred when stem cells from human embryos were first cultured in the laboratory.[2] Stem cells have the ability to self-renew and to generate specialised, differentiated cells – a property known as 'pluripotency'. While other specialised cells can divide, they cannot form other types of cell. Before 1998, scientists had cultured stem cells taken from mouse embryos, but not from humans or other species. Theoretically, this development means that long-term cultures of embryonic stem cells isolated from a human embryo could be maintained in the laboratory and then stimulated in some way to become different body tissues, such as liver or heart muscle.

Scientists want to try to use personalised stem cells to overcome problems of organ rejection. Although organ and bone marrow transplants from healthy donors are used as treatments for people with conditions such as kidney failure or leukemia, a good genetic 'tissue match' and drugs to suppress the patient's immune system are required for success. The significance of cloning and embryonic stem cell culture is that together they raise the prospect of being able to establish embryonic stem cell lines that are genetically identical to an individual patient. These stem cells would be cultured in the laboratory by inserting a nucleus from a patient's cell into an egg taken from a woman (not necessarily related to the sick person) and creating a cloned embryo. Theoretically, stem cells from this personalised embryonic cell line could then be stimulated into producing whatever type of specialised cells (e.g. nerve or muscle) is

required to treat that individual, without encountering the previous problems of organ rejection. Using the cloning technique to develop genetically identical replacement body tissues in culture is usually called 'therapeutic cloning' to distinguish it from 'reproductive cloning', which would involve transferring the cloned embryo into a woman's womb, to develop into a baby.

In the last decade, knowledge about adult stem cells also started to increase

In the last decade, knowledge about *adult* stem cells also started to increase. Adult stem cells are found in small numbers throughout the body among specialised cells, such as in the brain and kidney, and can assist in repair of tissues following injury. Stem cells derived from bone marrow and umbilical cord blood have been used for some years to treat diseases such as leukemia and some inherited diseases of the blood (e.g severe combined immunodefficiency syndrome, SCID, and sickle cell disease), but stem cells from other body
tissues have not been investigated so much. Ground-breaking research in 1998 showed that bone marrow stem cells from mice could develop into muscle cells, not just blood cells.[3] Subsequent work has confirmed that adult stem cells can be isolated from many parts of the body, cultured in the laboratory and, like embryonic stem cells, induced to develop into specialised cells.[4] This 'plasticity' raises the prospect of 'reprogramming' an individual's own adult stem cells to provide new tissues when needed. Its potential questions the need for cloning and embryonic stem cells.

Cloning – the technique and its problems

'… it is questionable whether there are any clones that are entirely normal.'
Ian Wilmut, 'creator' of Dolly, 2002.[5]

The success rate of cloning is very low: there is less than a 5% chance of a live birth and a range of developmental abnormalities are seen

The technique of cloning human cells is outlined in Box 1. A whole range of animal species has now been cloned, including mice, sheep, cattle, pigs, goats, cats, rats and horses, and using nuclei from a variety of adult cells.[6] The success rate is very low: there is less than a 5% chance of a live birth and a range of developmental abnormalities are seen including abnormal placental development, oversize at birth, and disorders of the muscles, skeleton, heart and lungs.[7,8] However, offspring of cloned mice and cloned cattle conceived naturally appear to have been largely normal,[8,9] suggesting that developmental problems seen in cloned animals do not arise through gene abnormalities, but because the mechanisms controlling foetal development are not operating properly.

Research now suggests that, in cloning, errors can occur in the 'reprogramming' of adult cell DNA, affecting subsequent development. Programming of DNA (the systems which determine which genes are active in a cell at a particular time) is controlled by inherited, but non-genetic, factors known as epigenetic factors.[6,10,11] This highly complex control system includes the amount of certain chemical (methyl or histone) groups that are attached to the DNA and how tightly folded the DNA is in a cell.

The abnormalities seen in cloned animals have revealed a lot about normal development and the role of these epigenetic factors. Nonetheless, these abnormalities also raise questions about whether cloned embryonic stem cell lines and any body tissues derived from them would develop normally.
It can take very many embryos to produce a human embryonic stem (hES) cell line. Although there are now many hES cell lines developed from normal embryos, to date there have been only two reports of successful hES cell lines derived from human embryos produced by cloning.

The first cloned hES cell line was produced by scientists in South Korea[12] who have now produced 11 cloned hES cell lines from different individuals.[13] In May 2005, scientists at Newcastle University in the UK announced that they had managed to clone human embryos from adult cells, but had not yet established cell lines.[14] There have also been reports of cloned bovine[15] and murine[16] embryonic stem cell lines being produced, but the technique appears to be far from routine.

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Inevitably, by improving the cloning technique to develop cloned human embryonic stem cells lines, knowledge and experience is gained that could be used to improve the likelihood of creating cloned humans if cloned embryos were implanted in a woman's womb.

Box 1: The cloning technique

Cloning means creating an exact copy of something. In genetics, this means a genetic copy of a cell or a whole organism or animal including a human being. To create a copy of a whole organism, cloning, or **somatic cell nuclear transfer (SCNT)** as it is called in the scientific literature, involves:

⇒ extracting eggs from a woman and removing their nuclei. The eggs may come from women in IVF programmes or be sourced in other ways including by paying women or seeking voluntary egg donation;

⇒ extracting the nucleus from a cell taken from an adult. This could be any cell because the same genes are found in virtually every cell in the body;

⇒ injecting the adult nucleus into the enucleated egg. Although the nucleus has been removed from the egg, some genetic material does remain in the mitochondria, which are the tiny energy-generating organs of the cell. This means that any clone resulting from the procedure is not actually an exact copy of the adult cell, as some of the genetic material will have come from the egg. Because mitochondria are in the egg but not the sperm, this genetic material is always passed on to offspring via the mother, never the father;

⇒ the enucleated egg and nucleus are fused using an electrical or chemical shock and the cell starts to divide and form an embryo; a cloned embryo could then be used in one of two ways:

- It could be implanted in a woman's womb with the intention of her carrying the baby to term. This has been called **reproductive cloning** and is banned in the UK. In the UK, embryos in the laboratory cannot be allowed to develop beyond 14 days – the time limit for experimentation on embryos laid down in the Human Fertilisation and Embryology Act 1990.
- Cells could be extracted from the embryo and cultured in the laboratory into **embryonic stem cell lines,** which may be immortal (kept growing permanently). Scientists hope it will be possible to stimulate these embryonic stem cells to differentiate into a variety of cell types, such as muscle, nerve or skin, but this has not yet been achieved.

Stem cells – comparing embryo and adult stem cell potential

'Predicting the future of stem cell applications is impossible, particularly given the early stage of the science of stem cell biology.'

R Kirschstein and LR Skirboll, 2001[17]

There are four types of stem cell that could be used in therapies: adult, embryonic, foetal (a developing baby is known as a foetus when the embryo is more than seven–eight weeks old) and cloned embryonic. There are some differences between foetal and embryonic stem cells, such as in their ability to differentiate, but they have many broad similarities and are considered together here. The properties of adult, embryonic and cloned embryonic stem cells are compared in Table 1. Whichever type of cell is used, the differentiation of the stem cell into a specialised type of cell, such as muscle or skin, will have to be controlled in the laboratory, by altering the culture conditions, but this is by no means a well established technique.[17]

Currently, there are no established treatments using cloned or naturally derived hES lines, and it is not clear how successful any treatment would ultimately be – or indeed whether it will be possible at all

Research with hES cell lines derived from IVF embryos is at an early stage, but it has been possible to stimulate these cells to develop in an uncontrolled way and show characteristics of nervous and pancreatic tissue. Cartilage, muscle, nerve and pancreatic cells have been derived from mouse embryonic stem cells, suggesting that such potential should exist for human cells.[17,18] The potential of hES lines from cloned embryos to differentiate into specialised cells has not yet been studied, however. Research shows that adult human stem cells can
differentiate into a range of cell types and those isolated from blood and bone marrow have produced various cell types including nerve, liver and fat cells,[19,20,21] while those from the brain have yielded a range of blood, nerve and muscle cells.[22]

Currently, there are no established treatments using cloned or naturally derived hES lines, and it is not clear how successful any treatment would ultimately be – or indeed whether it will be possible at all. But scientists have proposed that stem cells could be used to treat a range of degenerative diseases and traumatic injuries by replacing the destroyed or dysfunctional tissue, including:[17,23]

- Parkinson's disease;
- diabetes;
- kidney and liver disease;
- heart muscle following heart attacks;
- spinal cord injuries;
- burns.

Most stem cell research is still focused on understanding how stem cells function and develop. The therapies that are being pursued are very much at the experimental stage. There have been some reported successes in laboratory animals. For example, embryonic stem cells have been shown to develop into neurones and improve the condition of rats with a form of Parkinson's disease,[24] and cloned foetal liver stem cells have been used to regenerate damaged heart muscle in mice.[25] In one trial involving people with Parkinson's disease, cells taken from the brain tissue of seven–eight week aborted embryos were injected into their brains. This gave some improvement in younger patients, but 15% of patients had uncontrollable muscle movements because of over-activity of the transferred cells.[26]

In contrast to embryonic stem cells, adult stem cells are at a more advanced stage of investigation and are showing therapeutic potential. In the laboratory, bone marrow stem cells have been used to repair heart damage and begin to reverse conditions such as heart disease, and the use of bone marrow stem

to treat patients with myocardial infarctions has been reported to have reduced the size of the infarct and improved heart function.[28,29]

For some stem cell therapies to be successful, the cells may also have to be genetically modified. For example, to use stem cells to treat a person with Type I diabetes, a disease in which the person's immune system destroys the islet cells that produce insulin, any cloned or adult stem cells inserted into that person would have to be modified so they are not destroyed as well. This genetic modification would introduce additional risks and has not yet been researched in human cells.

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Table 1: Comparison of the properties of different types of stem cells[17,30,31,32]

Characteristic	Adult stem cells	Embryonic stem cells	Cloned embryonic stem cells
Ability to differentiate into different cell types	Uncertain whether adult stem cells are truly pluripotent, but evidence of 'plasticity' is now well established. Bone marrow stem cells from mice shown to be truly pluripotent.	Can differentiate into all cell types but process not controlled yet.	Not known.
Host acceptance or rejection after transfer	If into same adult from which the cells were cultured should not be rejected.	Embryonic stem cells may escape immune rejection in some cases - but will still need tissue matching and some immunosuppressive drugs. Some cell lines are cultured on 'feeder cell layers' derived from animals which may trigger an immune reaction. New techniques have been developed to avoid this.	No immune rejection expected if transfer is into the same person from whom the nucleus for the cloned cell was taken. There is a possibility that proteins produced from the mitochondrial genes remaining in the egg could cause an immune reaction.
Potential to meet demand for treatment	Adult stem cells are relatively few in number and are difficult to isolate from some sites. However, relatively small numbers of cells are likely to be needed as they can be multiplied in culture.	The development of embryonic stem cell lines is restricted by the availability of embryos. If a large range of embryonic stem cell lines is developed, it may be possible to use conventional tissue typing to find a suitable match.	Because each patient would need their own cloned cell line, the need for a huge number of eggs and the practical difficulties in obtaining them is likely to seriously restrict availability.
Requirement for genetic modification to give therapeutic success	Would depend on the nature of the disease.	Should not be required if 'healthy' embryonic stem cells are used.	Would depend on the nature of the disease.
Potential for adverse side effects	Recent reports suggest that cells may become cancerous if they divide many times over long periods. This may not be significant for individual treatments, but could be for stem cell banking.	Undifferentiated embryonic stem cells can divide in an uncontrolled way and form tumours known as teratomas.	The cloning technique may affect cell differentiation. Teratomas may form as with embryonic stem cells.

Building businesses around 'regenerative' medicine

The majority of all types of stem cell research is conducted in, and funded by, the public sector because of the considerable uncertainties about the potential for therapies to be developed and used commercially. However, Europe's investment in stem cell research, such as the 11.9 million euros for the EuroStemCell project,[33] usually includes biotechnology companies and provides one way that companies can reduce their research costs. The UK's Stem Cell Initiative (UKSCI),[34] announced in the 2005 budget and jointly supported by the Departments of Health and Trade and Industry, will be a collaboration between the Wellcome Trust, research councils, government departments and the
proposed private-sector-led UK Stem Cell Foundation. Economic, not just health, interests shape the stem cell research agenda.

Several biotechnology companies have already been formed to exploit future commercial opportunities

Several biotechnology companies have already been formed to exploit future commercial opportunities. All the major companies are based in the USA, with the exception of ReNeuron in the UK. There is also interest in stem cell treatments in small companies based in Singapore, India and Australia; several spin-out companies from UK universities have been established, including Nova Thera from Imperial College, Cell Centric from Cambridge and ReInnervate from Durham. The US companies Geron and Advanced Cell Technologies are likely to remain significant players because of the key patents they own on fundamental aspects of the technology. The Wisconsin Alumni Research
Foundation (WARF) also patented the 1998 research that developed human embryonic stem cells culture techniques in the USA. It has granted only seven licences and Geron, which funded much of the work, has exclusive licences for heart, nerve and pancreatic insulin-producing embryonic stem cell lines. Patent licence fees are said to be deterring progress in the USA.[35]

No large pharmaceutical corporations have a significant interest in stem cell research except for their potential use in areas such as drug safety testing.[36] One company, the Institute for Regenerative Medicine based in Barbados, is offering stem cell therapies (probably of dubious value as there seems to be no research data to support the claims) for a range of disorders. It accesses embryonic stem cells from the Ukraine,[37,38] raising the disturbing prospect of an international trade in eggs and aborted foetal material.

A major objection to research on embryos centres on the potential of an embryo to develop into a human being and the view that an embryo should have the same rights and moral status as a person

Contested morality

Debates about the desirability or otherwise of cloning and embryonic stem cell research are inevitably intertwined because both require experimentation upon, and the use of, embryos. Adult stem cells are often promoted as an alternative to avoid the ethical objections associated with experimenting on embryos or using embryos as a source of treatments.[39]

A major objection to research on embryos centres on the potential of an embryo to develop into a human being and the view that an embryo should have the same rights and moral status as a person.[40] Some take an absolute position in relation to the embryo – that it has a right to life – and so are opposed to embryo research. Others qualify the status of the embryo and the foetus, depending on, among other considerations, how many days, weeks or months old it is. This position allows for research on embryos in certain circumstances, depending on the potential benefits, justification for research and alternatives. Within this latter position there are differences as to whether an embryo should be *created* expressly for experimentation and, if the research progresses, to provide personalised stem cell therapies, or whether research should be restricted to eggs and embryos that have been retrieved

and created as part of the IVF process but will not be used for this. Others argue that tissues from aborted foetuses and eggs that have not been fertilised in IVF procedures would otherwise simply 'go to waste'; that the majority of embryos do not become babies during natural reproduction because they do not implant in a woman's uterus or because the woman has a miscarriage; and that the huge potential benefits create a moral imperative to do the research.[14] Specific objections to cloning and the use of embryos arise from the belief that the practice further commodifies and instrumentalises life and living beings, including humans. This belief is often expressed in law as the 'undermining of human dignity'. These concerns are exacerbated and exemplified in issues relating to the large numbers of women's eggs that would be needed both in cloning research and to obtain just one 'personalised' (cloned) treatment, and to global and social inequalities. The issues surrounding the use of eggs are detailed in Box 2.

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Box 2: Issues in human egg collection

Cloning requires a large number of eggs. To create Dolly the sheep, 277 eggs were used to produce 29 cloned embryos which were implanted in 13 ewes, but only one pregnancy went to full term. To produce the first human embryonic stem cell line, 242 eggs from 16 women were used, although the latest results from South Korea have improved success to one in 20.[13] Therefore, the development of personalised embryonic stem cell lines will require large numbers of eggs, raising the questions of where they will come from and at what cost?

Opening an egg market

Women having IVF treatment and undergoing sterilisation may come under increased pressure to 'donate' some of their eggs for research. If cloning research proceeds these two sources are unlikely to provide enough eggs, thus adding to calls for women to be paid, or to be paid more than current rates, to give their eggs. This pressure would be greatest for poorer women with fewer economic opportunities, either in countries where the research is being conducted, or in other less affluent countries with an adequate medical infrastructure and in which 'IVF tourism' is already developing. Romania is one country where the selling of eggs is increasing,[42] and there are concerns that an international trade in women's eggs could develop, as it has for human organs and body parts. The Human Fertilisation and Embryology Authority in the UK is considering whether it should start to allow payment for eggs – currently only expenses can be paid.

Women's health

The egg retrieval process is potentially hazardous to a woman's health in the short and long term, largely because of the hormone treatment she receives, first to close down her ovaries, and then start them up again to produce more than the usual single egg. In rare cases, women experience ovarian hyperstimulation syndrome, a painful swelling of the ovaries in which fluid can spread to the lungs and which is potentially fatal. Other more commonly recorded side-effects include hot flushes, feelings of depression, headaches, sleeplessness, nausea, vomiting, abdominal pain and shortness of breath.[43]

Whose benefit?

Cloning research is largely directed at the market for new treatments for richer people in developed countries because the individualised approach of this type of treatment, if it ever works, will be particularly expensive.

There is also a concern that by allowing therapeutic cloning, reproductive cloning will inevitably take place at some point in the future, even if it is not carried out by the same researchers. Human reproductive cloning involves several safety issues. Because cloning is so unsuccessful in other animals, it is likely that, even if the techniques are improved, some attempts to clone

humans would involve suffering and harm to the pregnant women and to any resulting babies. While many bioethicists oppose cloning on principle, some believe that if these safety questions could be overcome, then there is no objection to producing cloned babies,[44] and, indeed, that it would be unethical to oppose it if it allowed some infertile couples to have a child genetically related to at least one parent.

Public attitudes

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Most research on public attitudes has shown that people usually immediately reject the notion of reproductive cloning. Depending on the country, people may be more sympathetic to embryo stem cell research because of its claimed future benefits, although they may be uncertain about creating embryos for such purposes.[45] In the UK, qualitative research carried out for the Medical Research Council, when it was considering establishing a stem cell bank, showed that women and couples who have experienced IVF treatment tend to regard embryos as potential babies; those who have not are much more hesitant about research uses of embryos.[46] There was little support among those taking part in this research for the creation of embryos for research by cloning. People also tended to regard therapeutic cloning simply as part of the cloning process as a whole, including reproductive cloning. Other UK research has shown that, while people may find therapeutic cloning acceptable, the types of research and its purposes and possible alternatives are crucial in making such a judgement.[47]

Regulating cloning and embryo stem cell research

The various approaches taken to regulate cloning and embryonic stem cell research mirror the ethical debates. Despite worldwide rejection of reproductive cloning, less that one-quarter of the world's nations have formally banned it.[49] However, no country explicitly allows reproductive cloning and regulation would probably be quickly introduced if the prospect arose. [50]

In relation to therapeutic cloning, some countries do not allow the creation of embryos for research (allowing only research on IVF embryos) or do not allow any research on embryos at all, and thereby implicitly do not allow the production of a cloned embryo. The most liberal nations, including the UK, allow experimentation on embryos up to a certain number of days, including both those created through IVF and through cloning or other artificial means. Table 2 examines current international responses, and Table 3 examines selected national legislation to illustrate the spectrum of regulatory approaches.

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However, national legislation is still evolving and some countries, such as Israel, New Zealand and Russia, have specific provisions to review their position against therapeutic cloning in the future.

In the UK, the Human Fertilisation and Embryology Authority (HFEA) considers applications to conduct research on embryos. Research is now allowed to:[57]

- promote advances in the treatment of infertility;
- increase knowledge about the causes of congenital diseases;
- increase knowledge about the causes of miscarriage ;
- enhance knowledge in the development of more effective contraception;
- detect genetic or chromosomal abnormalities before implantation;
- increase knowledge about the development of embryos;
- increase knowledge about serious disease;

  or
- enable any such knowledge to be applied in developing treatment for serious disease.

Following peer review, an HFEA committee assesses a research application to determine whether the use or creation of embryos is necessary for the research purpose.[58] Only a short paragraph about the application is made available to the public until after the decision is made when more information may be released.

Two applications to produce cloned human embryos for research have now been approved in the U.K.

Two applications to produce cloned human embryos for research have now been approved. The first was granted in August 2004 to Newcastle University to understand embryo development and develop treatments for diseases such as diabetes and which has succeeded in producing cloned embryos.[59,14] The second was granted in February 2005 to Ian Wilmut, one of the scientists who created Dolly the cloned sheep, at the Roslin Institute in Scotland, to study motor neuron disease.

Table 2: International organisations' positions on cloning[51-53]

International Body	Current Status
United Nations	In 2001, an 'International Convention Against the Reproductive Cloning of Human Beings' was submitted to the 56th session of the General Assembly at the request of France and Germany, [51] and the proposal was debated at the UN several times (57th, 58th and 59th sessions of the Sixth Committee). Two positions emerged: the first, supported notably by the USA, called for a ban on all forms of cloning; the other, supported by the UK and Japan, advocated a ban on reproductive cloning but to allow therapeutic cloning. The UN remained in deadlock for some considerable time but, on 8 March 2005, the General Assembly adopted resolution 59/280, containing in its annex the text of a United Nations Declaration on Human Cloning, by a vote of 84 to 34, with 37 abstentions. This non-binding agreement bans all forms of cloning, but is not expected to be observed by those countries that support therapeutic cloning.
Council of Europe	In 1997, the Council of Europe agreed the 'Convention on Human Rights and Biomedicine', with an additional protocol on cloning added in 1998. [52]Article 1 of the cloning protocol addresses reproductive cloning: 'Any intervention seeking to create a human being genetically identical to another human being, whether living or dead, is prohibited.' To date, 31 member states have signed the Convention and 29 the additional protocol, showing agreement in principle. However, only 18 signatories have ratified the Convention and 14 signatories the additional protocol, the UK not being among them.
European Union	The Charter of Fundamental Rights of the European Union (2000) prohibits the reproductive cloning of human beings (Article 3). Within EU member states, there is a great divide in views on the ethics of therapeutic cloning. This split falls predominantly along state-religious lines with more Catholic countries generally opposing all cloning while Protestant countries are more open to therapeutic cloning.As a result of this difference in opinion, there is no EU-wide cloning law and attention has focused on EU research funding.There remains much disagreement and the position continues to evolve: [53] · In 2002, a one-year moratorium on EU funding of embryo research protocols was established. · In July 2003, the EU paved the way to funding research into therapeutic cloning but only if the stem cells were derived from IVF embryos provided for research before July 2002. · A vote in the European Parliament in November 2003 agreed to widen this definition to allow public funding for stem cell research while prohibiting funding for the creation of embryos specifically to obtain stem cells. There was no final agreement in the Council of Ministers and research proposals are assessed on a case-by-case basis.

Table 3: Regulations adopted in different counties to illustrate the range of regulatory responses.[49,50,53,54,56]

Country	Allows therapeutic cloning to create embryos	Allows production of embryonic stem cell lines from IVF embryos	Further information
UK	**Yes**	**Yes**	The 1990 Human Fertilisation and Embryo Act was amended in 2001 to include embryo research for non-fertility based reasons, implicitly encompassing embryo stem cell research. The HFEA is responsible for regulating all embryonic stem cell research in the UK. Both embryos from IVF treatments and embryos produced using cloning can be used in research. Reproductive cloning is prohibited.
USA	**Yes & No**	**Yes & No**	The cloning debate is highly politicised and polarised in the USA, with the Bush administration ideologically opposed to embryo research. In February 2003, a Human Cloning Prohibition Act, which sought to criminalise cloning, stalled in the Senate. Currently, federal funds cannot be used for embryo research, although research on existing human embryonic stem cell lines is allowed. Private companies can produce cloned human embryos. California has introduced a law supporting stem cell research and providing state funds. Its decision to invest $350 million a year in embryo stem cell research for a decade gained strong public support.
Austria **Germany** **Ireland** **Italy**	**No**	**No**	No interventions in embryos are allowed that are not for the benefit of the embryo. Thus, in effect, no embryo research is permitted. In Germany and Austria, research can be conducted on imported embryo stem cell lines.
Australia **Canada** **Denmark** **France** **Netherlands** **Japan** **Spain** **Switzerland**	**No**	**Yes**	Research is permitted using IVF embryos to isolate embryonic stem cells. The creation of embryos for research purposes is prohibited. Australia is to reconsider its position on therapeutic cloning in 2005.
Finland **Greece** **Israel**	**?**	**Yes**	Position on therapeutic cloning is not clear.
Belgium **China** **Japan** **Singapore** **South Korea** **Sweden**	**Yes**	**Yes**	Like the UK, it is possible to create an embryo through therapeutic cloning or other means for research.

Conclusions

Although the idea of cloning to produce a baby has been met with widespread revulsion and condemnation, it is not banned in all countries. The efforts of some bioethicists to argue against a ban if safety concerns can be addressed are worrying. The safety issues are unlikely ever to be fully resolved. Allowing people to reproduce themselves through cloning would be a significant further step in regarding babies as accessories designed to meet parents' wishes. This is likely to be presented as 'choice', further reducing human lives and citizenship to nothing more than a
sophisticated shopping trip. There is an urgent need to find new ways of expressing and giving importance to the unease that this creates and the values it reflects before such practices and techniques are normalised by bioethicists and scientists.

Allowing people to reproduce themselves through cloning would be a significant further step in regarding babies as accessories designed to meet parents' wishes

The prospects for any stem cells, whether cloned, embryonic or adult, to produce new treatments and cures are far from clear. The extravagant claims made more often reflect the desire of scientists and companies to secure funding and support than reality. Politicians seem easily swayed by the excitement and appear to forget that, as with other medical innovations, progress is usually slow and only a small proportion of original expectations are met. There is a risk that excessive hype will eventually lead to cynicism among the public.

There is a very real practical constraint on the potential for cloned and normal embryonic stem cells: the availability of human eggs. While some may be obtained from IVF treatments, the supply is very limited. A market and international trade in human eggs could evolve with some women suffering side effects from the medical interventions, possibly threatening their own fertility and even their lives. It is likely to be poor and disadvantaged women who will be most vulnerable to such exploitation.

In many ways, adult stem cells appear to hold much better prospects for developing treatments for some conditions judged by both ethical and efficacy criteria. The use of adult stem cells in clinical trials is already showing some promise and issues about supply of eggs and the use of embryos do not exist.

Careful regulation is needed if societies are to gain this knowledge and use it wisely without creating an exploitative market in eggs, embryos

Perhaps the most important contribution that cloned and normal embryonic stem cells are likely to make is to improve understanding of cell differentiation. But careful regulation is needed if societies are to gain this knowledge and use it wisely without creating an exploitative market in eggs, embryos, foetuses and treatments – treatments that would be the preserve of the wealthy. An extremely important ethical question that is rarely asked is whether the money spent on such research and applications might provide better improvements in health care if invested elsewhere.

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