

A
Research
Paper
from
No Less Human

Ethical
stem cell treatment

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What are stem cells?

Each individual human life normally begins at the point when the father's sperm fertilises the mother's egg, and this is the case for all naturally conceived human beings. Fertilisation by in-vitro fertilisation (IVF) occurs in the same way, but is done in a test-tube rather than within the mother's body.

The life of a person cloned from another human being would also begin with a single cell. However, in this case the reproduction is non-sexual and does not involve sperm at all. In this case the single cell which is the start of life is produced by fusing a cell from the person to be cloned with an unfertilised egg. (For a detailed explanation of this, see *Questions and Answers on Human Cloning* produced by No Less Human.)

This single cell from which every human life begins then develops and gives rise to more than 200 cell types (eg blood cells, brain cells, heart cells etc.) which make up the adult human body. New cells with unique characteristics are therefore constantly being generated and integrated into the overall structure of the developing embryo.

Early embryos contain stem cells, which can give rise to all cell types in the body. A stem cell is an un specialised cell that has the capacity to give rise to many different types of specialised cells. When a stem cell divides, it generates two progeny or 'daughter' cells. These cells may both remain as stem cells or one of them may become committed to differentiate and form more specialised cells. The term "stem" thus means that these cells are the source or origin of other, more specialised, cells. However, stem cells are also found in the placenta and umbilical cord, and in many (perhaps all) adult body tissues, such as fat, bone marrow, blood, skin, muscle etc.

In the process of obtaining stem cells from an embryo, the embryo has to be destroyed. However, no human life has to be destroyed to obtain adult stem cells, or stem cells from umbilical cords or placentas.

Why are stem cells useful?

In recent years it has been suggested that stem cells could be used to replace tissue destroyed by disabling conditions, for instance Parkinson's disease, heart disease, spinal cord injury, diabetes, Alzheimer's disease, stroke and bone disorders. To make the cells as compatible as possible with the patients receiving them, adult stem cells may be taken from the patient's own body. Otherwise, an embryo can be produced which is a clone of the person to be treated. This has been promoted as providing a

“twin” to the person who wants to be cloned, though in fact even cloned embryos are not completely identical. (See *Questions and Answers on Human Cloning*, produced by No Less Human.) Embryonic stem cells may also be derived from artificially fertilised IVF embryos, although they would then not be a genetic match to the patient.

Stem cell banks have now been set up both in the UK and in the USA. The world’s first stem cell bank was opened in Hertfordshire in May 2004, to “improve access to high quality stem cells for research.” The stem cells stored there come from embryonic, fetal and adult tissues.¹ In addition to this a private stem cell bank including 18 colonies of embryonic stem cells with rare genetic defects that trigger congenital disabilities as well as more than a hundred “lines” of normal human embryonic stem cells has been opened at the Reproductive Genetics Institute in Chicago.²

It is entirely ethical to take cells from a patient’s own body to treat disease or disability. It is completely unethical to create either an artificially fertilised IVF embryo or a cloned embryo, only to destroy it in order to harvest its stem cells.

Some scientists argue that embryonic stem cells have a greater ability than adult cells to treat disabling conditions. They base this claim on the fact that early embryonic stem cells give rise to all the tissues in the body, and are thus “totipotent” or capable of generating all cell types.³

However, over the last few years, much research has demonstrated that adult stem cells and other ethical sources of stem cells such as umbilical cord blood and placenta have a remarkable degree of “pluripotency” meaning that they can give rise to more than one type of tissue. There has been an attempt to dismiss these results as being a result of cell fusion, where cells fuse together and it appears that one cell has taken on the characteristic of the other without true differentiation (the ability to develop into a particular cell type.) However, although this may occur in some cases, numerous articles have demonstrated genuine adult stem cell multipotency (the ability to give rise to many different cell types) without cell fusion.^{4 5 6 7 8 9 10 11}

¹ “First stem cell bank in the world is opened in UK” by Susan Mayor. *BMJ* 29 May 2004

² “Human stem cell bank doubles its lines” by Shaoni Bhattacharya. *New Scientist* 15 February 2005

³ “The Basics about stem cells” by Maureen L. Condit. *First Things*. January 2002

⁴ Badorff, C. et al. (2003). *Circulation* **107**:1024-1032. “Transdifferentiation of Blood-Derived Human Adult Endothelial Progenitor Cells Into Functionally Active Cardiomyocytes”

⁵ D’Ippolito, G. et al. (2004). *J. Cell Sci.* **117**(Pt 14):2971-2981. “Marrow-isolated adult multilineage inducible (MIAMI) cells, a unique population of postnatal young and old human cells with extensive expansion and differentiation potential.”

⁶ Hermann, A. et al. (2004). *J. Cell Sci.* **117**:4411-4422. “Efficient generation of neural stem cell-like cells from adult human bone marrow stromal cells”

Even more significantly, numerous studies have demonstrated the very real ability of these ethically-derived stem cells to treat a wide range of serious diseases, some examples of which are provided in later sections of this booklet.

There are also very serious medical risks involved in using embryonic stem cells – far greater risks than those with adult stem cells.^{12 13 14 15} There is therefore an urgent need to also consider such risks when examining whether embryonic stem cells should be used or not. This is especially urgent considering that the results could be fatal in patients receiving embryonic stem cell transplants.

Embryonic stem cell research might lead to new therapies. Can this ever be wrong?

Biomedical research can take a variety of forms. For instance, research may be designed, commonly in animals, to test a model that closely resembles a possible form of therapy for a human disease or disabling condition. In this case it is hoped that the procedures that have been developed in the experimental animals can be directly translated to human treatment. In research of this type, the likelihood that the therapy will successfully translate to human treatment will depend both on the accuracy with which the experimental animal model mimics the human disease and on the extent to which the human clinical response to the new therapy resembles that of the animal.

In the specific instance of the use of embryonic stem cells to treat human diseases, scientists originally envisaged that these cells could be directly transferred into patients in the same way that was being tested in animals. However, in the course of the last few years, substantial practical obstacles

⁷ Jiang, Y. et al. (2002). *Nature* **418**:41-49. “Pluripotency of Mesenchymal Stem Cells Derived from Adult Marrow.”

⁸ Kodama, S. et al. (2003). *Science* **302**:1223-1227. “Islet Regeneration During the Reversal of Autoimmune Diabetes in NOD Mice”

⁹ Muller-Borer, B.J. et al. (2004). *Am J Path* **165**:135-45. “Adult-Derived Liver Stem Cells Acquire a Cardiomyocyte Structural and Functional Phenotype ex Vivo”

¹⁰ Oh, S-H. et al. (2004). *Lab Invest.* **84**:607-617. “Adult bone marrow-derived cells trans-differentiating into insulin-producing cells for the treatment of type 1 diabetes”

¹¹ Zuk, P.A. et al. (2002). *Mol. Biol. Cell.* **13**:4279-4295. “Human adipose tissue is a source of multipotent stem cells.

¹² Erdo, F. et al. (2003). *J. Cereb. Food Flow Metab.* **23**:780-785. “Host-dependent tumorigenesis of embryonic stem cell transplantation in experimental stroke”

¹³ Cervantes, R.B. et al. (2002). *Proc. Natl. Acad. Sci. USA* **99**:358603590. “Embryonic stem cells and somatic cells differ in mutation frequency and type.”

¹⁴ Humpherys, D. et al. (2001.) *Science* **293**:95-97. “Epigenetic Instability in ES Cells and Cloned Mice.”

¹⁵ Humpherys, D. et al. (2002.) *Proc. Natl. Acad. Sci. USA* **99**:12889-12894. “Abnormal Gene Expression in Cloned Mice Derived from Embryonic Stem Cell and Cumulus Cell Nuclei”

to many of the proposed forms of therapy (as summarized elsewhere in this booklet) have arisen such as the formation of aggressive tumours by embryonic stem cells, when used to treat diseases in animal models.

Practical obstacles to “therapeutic” cloning (cloning embryos with the intention that their stem cells be used for research or therapy, which will entail the destruction of the embryos) include the inability to obtain the vast numbers of human eggs that would be required, and the risks that egg donors undergo, such as the risk of severe ovarian hyperstimulation syndrome.

In contrast to biomedical research which depends on establishing a “treatment model” in an animal, much so-called “basic” research is directed to gaining new knowledge that may ultimately enable new forms of treatment to be developed. Those who advocate the use of embryos and stem cells derived from them in this variety of research commonly say that to oppose the accumulation of any new knowledge is itself immoral. It seems reasonable, before accepting this argument as endorsing the use of embryonic stem cells, to think about the general proposition that the pursuit of knowledge is always good.

There have been many instances in which “potentially valuable” research which may have added to human knowledge was not done because to do so would have infringed values held in higher regard. There are plenty of examples of research which many or most people oppose on ethical grounds. Many people oppose the use of higher primates for AIDS research. No doubt this could be of great benefit to humans but many nevertheless oppose it. Yet how can we know what valuable knowledge we may be forgoing if we do not do this research?

There has been a growing revulsion in many people about research using some classes of human subjects, particularly those who are especially vulnerable. The most vulnerable people need the greatest protection from harm. And there are no more vulnerable human individuals than embryos.

What possible problems could arise?

In addition to the unethical nature of embryonic stem cell research, there are also profound medical reasons for preferring stem cells from these ethical sources. Even in very small numbers it has been found that embryonic stem cells, including those derived from embryos produced for “therapeutic” cloning, generate tumours called teratomas or

teratocarcinomas which develop quickly and are potentially lethal.^{16 17}

¹⁸Indeed, according to Professor Alan Trounson (See footnote 20) it is a requirement for these cells that they generate tumours, in order to demonstrate that they are genuine embryonic stem cells, however they are derived.^{19 20}

A paper in *The Lancet* has also given a strong warning about the dangers of the risk of an additional type of tumour formation in embryonic stem cells and therapeutic cloning as a result of epigenetic flaws, which are a particular problem with embryonic stem cells and cloned embryos.²¹ There could be problems if these flaws, which occurred in animal studies, are also found to occur with human embryos.²² There are also unpredictable defects in gene expression with embryonic stem cells and cloned embryos.²³

Even some scientists who are in favour of embryonic stem cell research and treatments have admitted that **“large hurdles still need to be overcome to ensure safety and efficacy of embryonic stem cells.”** They go on to say that **“a single embryonic stem cell line could be used for many hundreds, if not thousands of patients, exponentially amplifying the potential risk of disease transmission...”**²⁴

By contrast to all these difficulties with embryonic stem cells, there is no evidence of teratoma or teratocarcinoma formation with adult stem cells.

Recently it has been found that extensive multiplication of stem cells from fat can cause these cells to become cancer forming.²⁵ However, this would not be relevant for the vast majority of adult stem cell therapies, since most of these would involve either immediate autologous transplantation (using the patient’s own cells) or short term multiplication rather than the greatly extended periods of growth observed in this study on stem cells from fat.

¹⁶ Erdo, F. et al. (2003). *J. Cereb Blood Flow Metab.* **23**:780-785. “Host-dependent tumorigenesis of embryonic stem cell transplantation in experimental stroke”

¹⁷ Bjorklund, L.M. et al. (2002). *Proc. Natl. Acad. Sci. USA* **99**:2344-2349. “Embryonic Stem Cells Develop into Functional Dopaminergic Neurons after Transplantation in a Parkinson Rat Model.”

¹⁸ Wakitani, S. (2003). *Rheumatology* **42**:162-165. “Embryonic stem cells injected into the mouse knee joint form teratomas and subsequently destroy the joint.”

¹⁹ Hwang, W.S. et al., (2004). *Science*. **303**:1669-1674. “Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst.”

²⁰ “Double triumph in stem cell quest” by Michael Le Page & Rowan Hooper. *New Scientist*. 25 May 2005

²¹ Humpherys, D. et al. (2001). *Science* **293**:95-97. “Epigenetic Instability in ES Cells and Cloned Mice.”

²² Allegrucci c, Denning C, Priddle H, Young L.(2004). *The Lancet* **364**(9429):206-208 “Stem cell consequences of embryo epigenetic defects”

²³ Humpherys, D. et al. (2002). *Proc. Natl. Acad. Sci. USA* **99**:12889-12894. “Abnormal Gene Expression in Cloned Mice Derived from Embryonic Stem Cell and Cumulus Cell Nuclei.”

²⁴ Braude, P., Minger, S., Warwick, Ruth M. “Stem cell therapy: hope or hype?” *BMJ* 21 May 2005

²⁵ “Old stem cells can turn cancerous” by Andy Coghlan. *New Scientist*. 21 April 2005

This is confirmed by countless bone marrow transplants over the decades, which have not caused cancer.

In any case, embryonic stem cells appear to have a far greater risk of tumour formation, since, unlike adult stem cells, they do not require extensive periods of growth to become tumour-causing.

It should be noted that many references are made to the fact that many years of research will be necessary to provide treatments using embryonic stem cells, if indeed they ever do become available.²⁶ Meanwhile ethical sources of stem cells are already being used in treatments, as the sections below clearly show.

The role of ethical stem cell research in treating and curing disabling conditions.

In general, as cells become more specialized, the number of cell types to which they give rise becomes more restricted. This has caused many scientists to believe that adult stem cells are less useful than those derived from embryos. However, in January 2002, the announcement was made that stem cells from the bone marrow of adults could turn into “**most, if not all**” tissues in the body. This suggested that stem cells from alternative sources could have the same “totipotent” properties as embryonic stem cells, an extremely important finding.²⁷ ²⁸ Other adult and post-natal stem cells have also been found to be multipotent.

In recent years, extensive research into ethically derived stem cells has demonstrated that their potential to heal damage to the body is far greater than previously thought. The rapidity of this progress has been truly extraordinary, and there has been much success in treating disabling conditions. Scientists working with ethically derived stem cells are finding that they have huge potential to treat or in some cases even to cure disability and disease.

This leaflet focuses on seven common disabling conditions; Parkinson’s disease, heart disease, spinal cord injury, diabetes, Alzheimer’s disease, stroke and bone disorder, and shows how adult stem cell research is already reversing or treating them, or has the potential to do so.

²⁶ Keirstead H.S., Nistor G, Bernal G et al. 11 May 2005. *Journal of Neuroscience* **25**(19):4694-4705. “Human Embryonic Stem Cell-Derived Oligodendrocyte Progenitor Cell Transplants Remyelinate and Restore Locomotion after Spinal Cord Injury.” *Journal of Neuroscience*.

²⁷ “Ultimate stem cell discovered” by Sylvia Pagan Westphal. *New Scientist* 23 January 2002

²⁸ Jiang Y et al. (2002) *Nature* **481**:41-49. “Pluripotency of mesenchymal stem cells derived from adult marrow”

Parkinson's Disease

Parkinson's Disease is a condition in which there is a disturbance in a chemical called dopamine in the brain. The disease can have a variety of causes. The limbs of people with the disease are affected by tremor, and, as the disease progresses, the face develops a rigidity leading to a "mask-like" expression. In addition the person walks in a shuffling way and may have repeated and involuntary movements of the fingers.

From the year 2000, there have been a number of reports that stem cells taken from human bone marrow^{29 30} or umbilical cord blood³¹ can be transformed into brain cells. These are readily available sources of stem cells - umbilical cords are usually thrown away as hospital waste and bone marrow is also relatively easy to obtain. These cells offer good possibilities for the treatment of Parkinson's disease.

Following these discoveries, it was shown in 2001 that transplanting stem cells from bone marrow into the brain promotes a significant degree of recovery in a mouse model of Parkinson's disease.³² Another study has shown that bone marrow stem cells can be differentiated *in vitro* (in the laboratory) into neurons which secrete dopamine to treat a rat model of Parkinson's Disease. When transplanted, the rats showed improvement in stepping and limb reaching.³³

Very promising work has also been carried out using stem cells derived from the olfactory bulb (a structure connected to the nose which is involved in the sense of smell) to generate dopamine neuron cells. When transplanted back into the mice from which the cells were derived, they produced a very marked functional recovery.^{34 35}

²⁹ "New hope of giving sight to the blind" by Mark Henderson. *The Times* 12 November 2001

³⁰ Sanchez-Ramos, J. et al. (2000) *Exp. Neurol.* **164**:247-256. "Adult Bone Marrow Stromal Cells Differentiate into Neural Cells *in vitro*"; Woodbury, D. et al. (2000). *J. Neurosci. Res.* **61**: 364-370. "Adult Rat and Human Bone Marrow Stromal Cells Differentiate into Neurons"; Reyes, M. and Verfaillie, C.M. (2001) *Ann. New York Acad. Sci.* **938**:231-233. "Characterization of Multipotent Adult Progenitor Cells, a Subpopulation of Mesenchymal Stem Cells."

³¹ Sanchez-Ramos, J. et al. (2001) *Neurology* **56** (suppl.3): S03.001. "Molecular and Cellular Evidence for Neural Progenitors in Human Umbilical Cord Blood."

³² Li, Y. et al. (2001). *Neurosci. Lett.* **315**:67-70. "Intracerebral Transplantation of Bone Marrow Stromal Cells in a 1-methyl-4-phenyl-1,2,3,6-Tetrahydropyridine Mouse Model of Parkinson's Disease."

³³ Dezawa M, Kanno H, Hoshino M, Cho H, et al. June 2004 *Journal of Clinical Investigation* **113**(12):1701-10 "Specific induction of neuronal cells from bone marrow stromal cells and application for autologous transplantation."

³⁴ Impagnatiello, F. et al. (2001) *Soc. for Neurosci. Abs.* **26**(1):554. Abs. 209.4. "Neuronal Stem Cell Transplantation Elicits a Long Lasting Functional Recovery in 6OHDA Lesioned Mice."

³⁵ Pagano, S.F. et al. (2000) *Functional Neurology* **15**(20):125-156. "Neural Stem Cells Deriving from Olfactory Bulb, A Possible Therapeutic Approach in Parkinson's Disease."

Most interesting of all has been the successful treatment of the disease using the patient's own stem cells.³⁶ Mr. Dennis Turner, of San Clemente, California USA had Parkinson's disease for five years, and was affected by increasing rigidity and tremor. In an operation, neural stem cells were removed from his brain while he was still awake. The doctors grew the cells in the laboratory and after several months they had about six million cells, which were then injected back into Mr. Turner's brain in March 1999.

Almost immediately there was a reduction in his symptoms, and after a year, total clinical scores for his physical ability improved by 83%. His scores improved by 88% when he was not taking medication, with significant improvement in muscle rigidity and control of tremor. Three years after the treatment he was **“essentially free of almost all symptoms of Parkinson's disease.”**³⁷ Dr. Levesque, who performed the treatment, noted that he would like to try a similar technique on patients with motor neuron disease, multiple sclerosis, stroke-related disabilities, Alzheimer's Disease and possibly lower spinal cord injuries.³⁸ Dr. Levesque is now planning to use the same technique to treat a dozen people with Parkinson's Disease.

Part of the long-term treatment of Parkinson's disease may require prevention of dopaminergic neurons (those which produce dopamine) dying off. It is therefore very encouraging that research using rodents has shown that it may be possible to treat the disease by transplantation of cells from the patient's own carotid body, a chemical receptor in the neck.^{39 40}

Heart disease

As with Parkinson's disease, it is often suggested that embryonic stem cell research offers hope of treating or even curing heart disease.⁴¹ The truth is that stem cells from alternative, ethical sources are already being successfully used.

³⁶ Levesque M.F, Neuman T. “Autologous Transplantation of Adult Human Neural Stem Cells and Differentiated Dopaminergic Neurons for Parkinson Disease: 1 Year Postoperative Clinical and Functional Metabolic Result” Abstract of paper given at the 70th Annual Meeting of the American Association of Neurological Surgeons. 8 April 2002

³⁷ Interview with Dr. Michel F. Levesque on “Autologous Adult Stem Cell Transplantation” *Grassroots Connection* 4 December 2002

³⁸ Interview with Dr. Michel F. Levesque. *Grassroots Connection*. November 2002

^{39,39} Benner E.J. et al (2004). *Proc. Natl Acad. Sci. USA* **101**:9435-9440. “Therapeutic immunization protects dopaminergic neurons in a mouse model for Parkinson's disease.

⁴⁰ Toldeo-Aral J.J, Mendez-Ferrer, S. Pardal R, Echevarria M. Lopez-Barneo J. 1 January 2003. *Journal of Neuroscience* **23**(1):141-148. “Trophic Restoration of the Nigrostriatal Dopaminergic Pathway in Long-Term Carotid Body-Grafted Parkinsonian Rats.”

⁴¹ “Hope of repair for damaged hearts” by Nigel Hawkes. *The Times* 2 August 2001

Stem cells from bone marrow can turn into all the cell types found in the heart, and this is a readily available source of cells. Experiments using stem cells from bone marrow to treat heart attack in rodents have demonstrated a great improvement in recovery from heart attack, and a greatly reduced mortality rate.⁴²

The case of Ian Rosenberg shows what can be achieved using an ethical source of stem cells. He had a massive heart attack 25 years ago, and by the age of 67, the cocktail of tablets he had been taking started to lose their effectiveness. He says **“I only had months to live. I couldn’t even walk up two steps – not two flights, two steps.”** He had his own stem cells taken from his bone marrow and injected into a vessel feeding his heart in 2004 at the Johann Wolfgang Goethe University Hospital in Frankfurt, and over the next couple of months he began to recover. He returned to playing golf, and took a trip to Venice, the first time for many years that he had not needed to use a wheelchair at the airport.⁴³

In a study undertaken by Dr. Amit Patel of the University of Pittsburgh McGowan Institute for Regenerative Medicine, 15 patients who had exhausted all other treatment options showed markedly improved heart function after receiving injections of their own bone marrow stem cells. All of them had some degree of improvement, some with dramatic results, while the conditions essentially remained unchanged in the 15 patients randomized to be a control group.⁴⁴

Professor Neil Scolding, Professor of Neurosciences at the University of Bristol has written many times on the success and future potential of stem cells from adult sources. He noted that:

...heart attack patients have already received injections of bone marrow cells into the heart, apparently with benefit. [Adult stem cells] cannot now be considered of inferior medical potential. There is no evidence that anyone will suffer if embryonic research is discouraged.^{45 46}

⁴² Kocher, A.A. et al. (2001) *Nature Medicine* 7: 430-436. “Neovascularization of Ischemic Myocardium by Human Bone Marrow-Derived Angioblasts Prevents Cardiomyocyte Apoptosis, Reduced Remodeling and Improves Cardiac Function.”; Orlic, D. et al. (2001a) *Nature* 410:701-705. “Bone Marrow Cells Regenerate Infarcted Myocardium.”; Orlic, D. et al. (2001b) *Proc.Natl. Acad. Sci. USA* 98:10344-10349 “Mobilized Bone Marrow Cells Repair the Infarcted Heart, Improving Function and Survival.”

⁴³ “Don’t go breaking my heart” by Lisa Melton. *New Scientist* 25 September 2004

⁴⁴ “Stem cells given in minimally invasive procedure improve heart function.” *Medical News Today* 26 January 2005

⁴⁵ “Key distinctions in stem cell research” Letter by Prof. Neil Scolding. *The Daily Telegraph*. 15 November 2001

⁴⁶ “Use of stem cells in creation of embryos” by Prof. Neil Scolding. *The Lancet*. Letters. 15 December 2002

Bone marrow cells have now been used to treat acute heart attack in nine clinical trials involving more than 100 patients. Various aspects of heart function have been improved in each.⁴⁷

Spinal Cord Injury

Injury to the spinal cord can cause varying degrees of paralysis, depending on the site of the injury. It may also result in incontinence of bladder and bowel. It is another disabling condition which is often cited as justifying embryonic stem cell research. However, there have been extremely interesting developments in treating spinal cord injury with alternative sources of stem cells.

A Korean team of researchers led by Prof. Song Chang-hun of Chosun University reported in November 2004 that they had transplanted multi-potent stem cells from umbilical cord blood to a 37 year old woman named Hwang Mi-Soon who sustained a spinal cord injury in 1985 which damaged her lower back and hips, and who had been unable to stand up or walk. The scientists isolated stem cells from umbilical cord blood and then injected them into the damaged part of her spinal cord. The sensory and motor nerves started to improve 15 days after the operation and she could move her hips. After 25 days, her feet responded to stimulation. She says **“This is already a miracle for me. I never dreamed of getting to my feet again.”** A photograph shows her standing with calipers and a walking frame – smiling broadly!^{48 49}

The following month it was reported that Kim Gould, a British woman who was paralysed in a riding accident, had regained some movement after taking part in a pioneering trial in which stem cells were transplanted from her nose into her spine. Following the treatment, undertaken by Dr. Carlos Lima of the Egaz Moniz Hospital in Lisbon, Portugal, Dr. Lima said **“All of our patients have some kind of recovery. We have no doubts about sensory recovery and some voluntary motor recovery. They move and feel below the lesions [area of injury] as never before. And there is even some bladder and bowel control recovery.”**

⁴⁷ Keating A. Biol Blood Marrow Transplant. 11.2. (2005) quoted in Quesenberry P.J, Dooner G, Dooner M, Abedi M. “Igoratio Elenchi. *Science* 20 May 2005 “Red Herrings in Stem Cell Research”

⁴⁸ “Korean Scientists Succeed in Stem Cell Therapy” by Kim Tae-gyu. *The Korea Times*. 26 November 2004

⁴⁹ “Umbilical cord cells ‘allow paralysed woman to walk’ By Roger Highfield. *The Daily Telegraph* 30 November 2004

Mrs. Gould can now crawl and lift each leg to move it forwards. She has regained some sensation in her legs, and can stand and make some progress with calipers and a walking frame.⁵⁰

American scientists at Griffith University Eskitis Institute for Cell and Molecular Therapies have shown that adult stem cells from a region in the nasal cavity contain nerve fibres which are in a continuous state of growth throughout adult life. These cells can give rise to many different types of cells, such as nerve, liver, heart and muscle cells. They do not seem to form tumours or teratomas as embryonic stem cells tend to do.⁵¹

Similarly, Prof. Geoffrey Raisman, Director of the Spinal Repair Unit at University College London has also discovered that there is a region in the nasal cavity in which nerve fibres are in a state of continuous growth throughout adult life. This team transplanted cells from this region into the injured spinal cord of laboratory rats and found that the cells had a remarkable capacity to integrate into damaged pathways, laying a kind of “bridge” over the gap in the nerve fibres caused by injury. Human trials will begin within 3 years.

If the animal research transfers successfully to humans, as with Dr. Lima’s work, the patient could be his or her own cell donor. Paralysed rats used in their studies regained the ability to reach and climb, and also to breathe independently.⁵² There are “very promising” ongoing studies investigating whether this approach can also restore bladder, bowel and sexual functions.⁵³ Similar, researchers in Massachusetts found that rats that had been paralysed by severing the spinal cord, could swim and walk after transplantation with another type of adult cell. Professor Vacanti, who carried out this work, noted that it should be possible to use cells from the patient for transplantation.⁵⁴

⁵⁰ “Stem cells help paralysed woman to move” by Roger Highfield. *The Daily Telegraph*. 6 December 2004

⁵¹ Murrell W. et al. (2005) *Developmental Dynamics* **233**:496-515 “Multipotent stem cells from adult olfactory mucosa”

⁵² Li, Y. et al. (2003). *J. Neurosci.* **23**:727-731. “Transplantation of olfactory ensheathing cells into spinal cord lesions restores breathing and climbing”

⁵³ “Spinal repair pioneer to speak in NY on 20th January” *Medical News Today* 19 January 2005

⁵⁴ Vacanti, M.P. et al. (2001). *Transplantation Proceedings* **33**:592-598. “Tissue-engineered Spinal Cord.”

Professor Raisman says, **“This is what will get people out of wheelchairs. This is what will make stroke patients get better. This is what will restore the optic nerve in blindness, and the auditory nerve in deafness... This will be revolutionary if we’re successful.”** Significantly, he also says, **“There’s no need to use other stem cells.”**⁵⁵

Stroke

In February 2001 it was reported that American scientists had succeeded in transplanting stem cells from umbilical cords into rats with damage caused by stroke, with dramatic improvements in recovery. Human trials were expected to follow this success, and the scientists noted that the technique offered hope of improvement of people with a wide range of other disabling conditions.⁵⁶

A lot of work has been done on animal models demonstrating that stem cells from bone marrow or umbilical cord blood can significantly improve recovery from a stroke.^{57 58 59} For example, in February 2001 it was reported that American scientists had succeeded in transplanting stem cells from umbilical cords into rats with damage caused by stroke, with dramatic improvements in recovery. Human trials were expected to follow this success, and the scientists noted that the technique offered hope of improvement of people with a wide range of other disabling conditions.⁶⁰

In November 2004, Brazilian doctors transplanted the patient’s own bone marrow stem cells into a 54 year old woman who had had a stroke. She had lost movement on the right side of her body and could not understand other people or communicate with them. 17 days after the transplant she was discharged from hospital, having recovered movement, comprehension and some speech, and further improvements were reported in the following months.⁶¹

⁵⁵ “UK Scientists Open the door to Repairing Spinal Cord Injuries.” Official UK Government website. British Embassy in the USA 21 January 2005

⁵⁶ “Victims of stroke could be helped by babies” *The Times* 20 February 2001

⁵⁷ Li, Y. et al. (2002). *Neurology* **59**:514-523 “Human Marrow Stromal Cell Therapy for Stroke in Rat: Neurotrophins and Functional Recovery”

⁵⁸ Vendrane, M. et al. (2004) *Stroke*. **35**:2390-5 “Infusion of human umbilical cord blood cells in a rat model of stroke dose-dependently rescues behavioural deficits and reduces infarct volume”

⁵⁹ Willing, A.E. et al. (2003) *Cell Transplantation* **12**:449-454. “Mobilized peripheral blood cells administered intravenously produce functional recovery in stroke.”

⁶⁰ “Victims of stroke could be helped by babies” *The Times* 20 February 2001

⁶¹ “Brazilians to widen stem cell study in strokes” by Andrei Khalip. *Reuters* 19 November 2004

Most recently a clinical trial has been carried out on 5 stroke patients, using the patients' own mesenchymal stem cells from bone marrow. The results are very promising, and trials are now going on to determine the optimum conditions for dosage and timing of administering the stem cells.⁶²

Diabetes

Diabetes is a condition in which carbohydrates such as sugar and starch are not correctly handled ("metabolized") by the tissues of the body. It can lead to heart and circulatory disease, kidney failure and blindness, and it is caused either by a shortage of insulin, a hormone that regulates blood sugar levels, or by the body's failure to respond to insulin, a hormone found in the pancreas.

There are two types of diabetes. In type 1, the body's immune system mistakenly destroys beta cells in the insulin-making parts of the pancreas. Those who have this type of diabetes, mostly children and young adults, lack insulin and need to inject it every day. Type 2 diabetes is more common, and occurs when the body becomes resistant to insulin, sometimes as a result of obesity.

As with other disabling conditions, it is frequently suggested that embryonic stem cells provide the only realistic possibility of treating diabetes.⁶³

However, it was reported in May 2005 that Dr Sarah Ferber and her colleagues at the Endocrine Institute in Tel-Hashomer Israel had been able to persuade adult liver cells to produce insulin, which is normally produced by the islet cells in the pancreas. Another team led by Professor Ammon Peck have coaxed liver stem cells to become insulin-secreting pancreatic islet-like cells.^{64 65 66}

A team led by Dr. Simon Smukler at Toronto University, Canada, have also found immature cells in the pancreas of adult mice that were able to develop into cells that produce insulin. If the same precursor cells are present in humans, it may be possible to cure people with Type 1 diabetes.⁶⁷

⁶² Bang, O.Y. et al. (2005) *Ann. Neurol.* **57**:874-82. "Autologous mesenchymal stem cell transplantation in stroke patients."

⁶³ "Scientists identify 'the spark of life'" by Mark Henderson. *The Times* 18 July 2002

⁶⁴ Sapir, T. et al. (2005). *Proc. Natl Acad. Sci. USA* **102**:7964-7969. "Cell-replacement therapy for diabetes: Generating functional insulin-producing tissue from adult human liver cells"

⁶⁵ Yang, L. et al. (2002). *Proc. Natl. Acad. Sci. USA* **99**:8078-8083. "In vitro Trans-Differentiation of Adult Hepatic Stem cells into Pancreatic Endocrine Hormone-Producing Cells"

⁶⁶ Reuters May 2005 quoted at <http://www.medicinenet.com/script/main/art.asp?articlekey=47205>

⁶⁷ Seaberg, R.M. et al. (2004). *Nat. Biotechnol.* **22**:1115-1124 "Clonal Identification of Multipotent Precursors from Adult Mouse Pancrease that Generate Neural and Pancreatic Lineages"

Adult stem cells have already been demonstrated to reverse diabetes in mice, and several types of adult stem cells have been shown to do this, including stem cells from bone marrow.⁶⁸

One way of doing this is by creating insulin-secreting islet-like cells from adult stem cells. These are collections of special cells scattered throughout the pancreas that secrete insulin, which is then poured directly into the blood stream. The scientists then transplant these cells into insulin-dependent diabetic mice. The mice that do not receive implants generally die within two or three weeks following withdrawal of insulin, or become seriously ill with excessive sugar in the blood. However there is a reversal of diabetes in the animals that receive the implants.^{69 70 71 72 73}

Other scientists have succeeded in killing off the cells that attack the pancreatic beta cells in diabetics. This appears to permit the existing pancreatic beta cells and stem cells to recover, and allow the stem cells to form new insulin-secreting beta cells.⁷⁴ Follow-up work by this team from Harvard appears to have achieved permanent reversal of diabetes in mice.⁷⁵

All this work provides very strong evidence that adult stem cells are likely to lead to a highly effective treatment, or even a cure for diabetes.

On the other hand insulin-producing cells derived from embryonic stem cells have so far been demonstrated either to be largely ineffective or dangerous when applied to diabetic animals. For example, it was claimed that embryonic stem cells were induced to differentiate into insulin-secreting pancreatic islet-like cells. However, these cells had only 2% of the insulin required to treat diabetic mice. There was a short-lived effect on the mice and they eventually died.⁷⁶

⁶⁸ Oh, S-H. et al. (2004). *Laboratory Investigation* **84**:607-617. "Adult bone marrow-derived cells transdifferentiating into insulin-producing cells for the treatment of type I diabetes."

⁶⁹ Ramiya, V.K. et al (2000). *Nat. Med.* **6**:278-282 "Reversal of Insulin Dependent Diabetes Using Islets Generated in vitro from Pancreatic Stem Cells"

⁷⁰ Seaberg, R. M. et al. (2004). *Ibid.*

⁷¹ Yang, L. et al. (2002). *Proc Natl. Acad. Sci. USA* **99**:8078-8083. "In vitro Trans-Differentiation of Adult Hepatic Stem Cells into Pancreatic Endocrine Hormone-Producing Cells"

⁷² Sapir, T. et al. (2005). *Ibid.*

⁷³ Oh, S-H. et al. (2004). *Laboratory Investigation* **84**:607-617. "Adult bone marrow-derived cells transdifferentiating into insulin-producing cells for the treatment of type-1 diabetes"

⁷⁴ Ryu, S. et al. (2001) *J. Clin. Invest.* **108**:63-72. "Reversal of Established Autoimmune Diabetes by Restoration of Endogenous Beta Cell Function."

⁷⁵ Kodama et al. (2003). *Science* **302**:1223-1227. "Islet Regeneration During the Reversal of Autoimmune Diabetes in NOD Mice."

⁷⁶ Lumelsky, N. et al. (2003). *Science* **292**: 1389-1394. "Differentiation of Embryonic Stem Cells to Insulin-Secreting Structures Similar to Pancreatic Islets"

When investigated more thoroughly it was discovered that the embryonic stem cells were not making insulin at all! Rather, they were simply accumulating it from the culture medium (the “bed” on which the embryonic cells were grown), where it was present in very low concentrations.⁷⁷ It is thus apparent that the original work which has been claimed to demonstrate that embryonic stem cells could produce insulin and treat diabetes in mice was profoundly flawed, and did not in fact demonstrate insulin production. Work by other groups using the same protocol has confirmed this.^{78 79}

An apparent improvement was reported in this protocol, in which the cells appeared to produce and release insulin in far greater amounts.⁸⁰ However, subsequent research again strongly indicated that the insulin release was not in fact the result of production of insulin, but was connected with release from dying cells which appeared to have accumulated insulin from the culture medium, so the cells would not be suitable for transplantation for the treatment of diabetes in humans.⁸¹

Despite the failure of these embryonic stem cells to make insulin-secreting pancreatic beta cells and the discovery that the cells did not make insulin at all but accumulated it from the medium, and that the insulin is associated particularly with dying cells and neuronal cells rather than pancreatic beta cells,^{82 83} the original article has been frequently quoted as demonstrating that embryonic stem cells can make insulin-secreting cells which could treat diabetes.

Yet another research group found a temporary reversal of diabetes for up to 3 weeks with embryonic stem cells, but the cells subsequently failed, and the mice all died. On post-mortem examination, the majority of the mice were found to be developing teratomas.⁸⁴

It is worth remembering that things are not always what they seem in the reporting of stem cell work, and that those promoting embryonic stem cell treatments sometimes exaggerate or misrepresent the efficacy of the research...

⁷⁷ Ragagopal, J. et al (2003). *Science* 299:363. “Insulin Staining of ES Cell Progeny from Insulin Uptake”

⁷⁸ Sipione, S. et al. (2004.) *Diabetologia* 47:499-508. “Insulin expressing cells from differentiated embryonic stem cells are not beta cells”

⁷⁹ Hansson, M. et al. (2004). *Diabetes* 53:2603-2609. “Artifactual Insulin Release From Differentiated Embryonic Stem Cells”

⁸⁰ Hori et al. (2002). *Proc. Natl. Acad. Sci. USA* 99:16105-16110. “Growth inhibitors promote differentiation of insulin-producing tissue from embryonic stem cells.”

⁸¹ Hansson, M. et al. (2004) (Ibid)

⁸² Hansson, M. et al. (2004) (Ibid)

⁸³ Sipione, S. et al. (2004) (Ibid)

⁸⁴ Fujikawa, T. et al., 2005. *American Journal of Pathology* 166:1781-1791. “Teratoma Formation Leads to Failure of Treatment for Type I Diabetes Using Embryonic Stem Cell-Derived Insulin-Producing Cells”

Alzheimer's Disease

Alzheimer's disease is a form of presenile dementia, which is caused by atrophy of the pre-frontal areas of the brain. As with other disabling conditions, the development of stem cell treatments in animals using umbilical cord blood and adult sources have shown that it is possible to treat Alzheimer's disease, despite the fact that many reports suggest that only embryonic stem cells have this potential.^{85 86}

In March 2005 it was reported that stem cells could offer promise in treating neurodegenerative diseases such as Alzheimer's disease in another way. Stem cells are present throughout the brain and, if doctors knew the signals, stem cells already in the brain could be activated to repair injury due to Alzheimer's, according to Mark Mehler, Chair of the Neurology Department at Albert Einstein College of Medicine in New York.⁸⁷ This approach has already proven to be effective with the treatment of Parkinson's disease in animals.⁸⁸

In July 2005, an article in *Science* reported a surprising degree of recovery from memory loss in a neurodegenerative mouse model similar to Alzheimer's disease, by suppression of a specific protein in the brain which may be involved in causing the disease.⁸⁹ This indicates that recovery of a significant degree of memory loss in Alzheimer's disease may be possible, not just cessation of memory loss. If therapy of this nature were to be combined with stem cell therapy, whether by transplantation or stimulation of the stem cells already in the brain, it could be very effective.

Another interesting development has been the revelation by Prof. Mark Tuszynski, Professor of Neurosciences at the University of California in San Diego that transplants of a patient's own genetically engineered skin cells can slow the progress of Alzheimer's disease. This therapy involves genetically modifying the skin cells to make a protein called nerve growth factor, which prevents nerve death and stimulated activity. It was the injected deep into patients' brains, and it has been shown to increase neural activity and substantially reduce the rate of mental decline.⁹⁰

⁸⁵ The Genetic Spark of Life : *Science Forum* 18th July 2002

⁸⁶ Ende, N. et al. (2001), *Journal of Medicine* **32**:241-247. "Human Umbilical Cord Blood Cells Ameliorate Alzheimer's Disease in Transgenic Mice"

⁸⁷ "Activating stem cells may treat Alzheimer's" by Janice Hopkins Tanne. *BMJ* 19 March 2005

⁸⁸ Fallon, J. et al. (2000). *Proc. Natl. Acad. Sci USA* **97**:14686-14691. "In vivo induction of massive proliferation, directed migration, and differentiation of neural cells in the adult mammalian brain"

⁸⁹ SantaCruz et al. (2005). *Science* **309**:476-481. "Tau Suppression in a Neurodegenerative Mouse Model Improves Memory Function."

⁹⁰ "GM skin cells help treat Alzheimers?: Neural transplants may rein in mental decline" by Helen R. Pilcher. *Nature Neuroscience*. 28 April 2004

Interestingly, Michael Shelanski, co-director of the Taub Institute for Research on Alzheimer's Disease and the Aging Brain at the Columbia University Medical Center in New York has said that of all the diseases that may someday be cured by embryonic stem cells treatments, Alzheimer's is among the least likely to benefit. He says, **"I personally think we're going to get other therapies for Alzheimer's a lot sooner."**⁹¹

In the meantime it appears that ethical sources of stem cells may provide significant benefits, and are both safer, and likely to produce quicker and more certain treatments for disabling conditions.

Bone disorders

Osteogenesis Imperfecta is a genetic disorder in which bones break easily and frequently, often from little or no apparent cause. Some people with this condition will have several hundred fractures in a lifetime.

Remarkable results in the treatment of children with this condition have been obtained using bone marrow stem cells.^{92 93}

Osteoporosis ("porous bone") is a disease in which bones become fragile and more likely to break. 1 in 2 women and 1 in 5 men over the age of 50 in the UK have osteoporosis (3 million people in the UK.)

Professor Michael Longaker, Professor of Surgery at Stanford University Medical Center in California has demonstrated for the first time that certain types of stem cell (called adipose-derived adult stromal cells) from fat tissue can be coaxed to repair large holes in the skulls of mice which would otherwise fail to heal.⁹⁴ These cells exist in adults in pockets of fat under the skin, making them abundant and easy to get to. These cells worked just as well as bone marrow stem cells at repairing the holes in the bone, and did it seven times faster. By 12 weeks the holes had been completely bridged. Professor Longaker says this work has **"tremendous potential to become a new therapy and could help in the fields of joint replacement, spinal fusion and osteoporosis."**

⁹¹ "Stem Cells An Unlikely Therapy for Alzheimer's" by Rick Weiss. *Washington Post* 10 June 2004

⁹² Horwitz, E.M. et al. (1999). *Nat. Med.* **5**: 309-313. "Transplantability and therapeutic effects of bone marrow-derived mesenchymal cells in children with osteogenesis imperfecta"

⁹³ Horwitz, E.M. et al. (2002). *Proc. Natl. Acad. Sci. USA* **99**:8932-8937. "Isolated allogeneic bone marrow-derived mesenchymal cells engraft and stimulate growth in children with osteogenesis imperfecta: implications for cell therapy of bone.

⁹⁴ Longaker, M.T. et al. (11 April 2004). *Nature Biotechnology*. "Adipose-derived adult stromal cells heal critical-size mouse calvarial defects.

A Personal Concern

I have a very personal reason for being particularly interested in these issues. I am National Coordinator of No Less Human, a group within SPUC which campaigns to protect the lives of all disabled people, from conception to natural death. I am a full-time wheelchair user, as I was born with spina bifida, and I have several other disabling conditions including osteoporosis. Both spina bifida and osteoporosis are potentially treatable with both embryonic and ethically-derived stem cells⁹⁵ and the ethically-derived work holds the prospect of improving life for many people with conditions like mine.

However, I am totally appalled at the suggestion (made both by scientists and by the British Government) that unethical stem cell research using human embryos is somehow justified because it might “help” people like me.⁹⁶ I cannot think of anything more reprehensible than to suggest that it is acceptable to research upon and kill the most vulnerable of human individuals because there may be something in it for me.

Conclusion

It is clear that using human embryos which are considered surplus to the requirements of IVF treatment, or creating human embryos (whether by IVF or by cloning) only to deliberately destroy them in order to harvest their stem cells is completely unethical. There are no such ethical problems with stem cells obtained from adult sources. In addition to these ethical considerations, there are also very strong scientific reasons why all available resources should be put into developing research from stem cells derived from adult sources.

Dr. Michael Antoniou, a molecular geneticist and Senior Lecturer at Guy’s Hospital has said:

What is evident from studies conducted to date is that adult stem (AS) cells show as much therapeutic potential as embryonic stem (ES) cells. Indeed as Dr. Philip Jones (University of Oxford) told the [House of] Lords [Select Committee on Stem Cell Research], AS cells offer far greater potential for cures than ES cells ...

⁹⁵ Zuk, P.A. et al. (2001). *Tissue Engineering* 7:211-228. “Multilineage Cells from Human Adipose Tissue: Implications for Cell-Based Therapies.”

⁹⁶ House of Commons debate on the Human Fertilisation and Embryology (Research Purposes) Regulations. 19 December 2000, *Hansard*, Col. 260.

Governments around the world should back major initiatives in AS cell research which could harbour the same if not a greater and safer therapeutic potential, and avoid the problems of working with ES cells/therapeutic cloning.⁹⁷

In similar vein, Professor Neil Scolding warns that embryonic stem cell therapy carries a risk of creating tumours, in addition to the huge ethical problems involved in using and destroying human embryos. However he speaks of the **“very exciting prospects”** of adult stem cell therapy for curing neurological and degenerative diseases as well as heart disease.⁹⁸

The only ethical and sensible conclusion is that embryonic stem cell therapy is both totally unethical and potentially dangerous. It is ethical sources of stem cells which are already providing treatments, and which will be the key to great advancements in the treatment of a very wide range of disabling conditions.

ALISON DAVIS JULY 2005

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⁹⁷ Antoniou, M (2001). *Nature Medicine* 7:397-399. “Embryonic stem cell research. The Case Against.”

⁹⁸ “Exaggerated claims of cures threaten stem cell research” by Kaye McIntosh. *BMJ*. 4 June 2005