**Abstract**
At Vetsix, December 2005, we were given an introduction to the potential of stem cell research. While initial research has led to the establishment of stem cell therapies such as bone marrow transplants to form tendon tissue, the ultimate goal now for researchers is whether stem cells could provide living, natural replacements for diseased tissues and organs. The possibilities this aspect opens up include cures for many diseases such as Alzheimer’s, Parkinson’s and diabetes. However my research focus is on the possibility for a long-term cure for patients with spinal cord injuries. Spinal cord injuries are commonplace although some animal species/breeds are more vulnerable such as horses and daschunds. Although treatment exists for patients with spinal injuries, stem cells could provide an effective way to restore and accelerate movement and sensation recovery by repairing the actual cell causing the injury at cellular level.

**Introduction**
Since Rudolf Virchow announced over 200 years ago, that disease starts at a cellular level, people have been investigating diseases. Cells form the initial building blocks of all living organisms, whether it is a fish, a daffodil or human being. Later discoveries have found that the first cells to take part in the formation of an organism are embryonic stem cells. Stem cells are undifferentiated cells that have the ability to multiply and develop into any type of cell in the body through a process called pluripotency. In theory, stem cells hold the ability of allowing researchers to ‘grow’ specialized cells or tissue, which could be used to treat injuries or disease currently incurable. The best source of stem cells for use in research is from embryo’s created in in-vitro fertilization (IVF). Harvesting these stem cells however destroys the embryo, which many see as unethical. I will consider the ethical problems later.

**How are embryonic stem cells harvested?**
Therapeutic cloning is used to obtain embryonic stem cells. This refers to the creation of cloned embryo from which the stem cells are then gathered.

**FIGURE 1**
Therapeutic cloning involves removing the nucleus from an unfertilized egg and fusing this egg with another body cell. The nucleus of this body cell now forms the new nucleus of the egg. This process is called ‘cell nuclear transfer’ (CNT) or ‘somatic cell nuclear transfer’ (SCNT). The egg with the inserted nucleus is then shocked using an electrical charge to provoke cell division. The cell then divides to form a blastocyst. As DNA from a living organism forms the genetic material of the egg, an embryo with identical DNA to the donor is produced i.e. a clone. Likewise embryos donated from in-vitro fertilization are used. At this point the inner cell mass that contains the stems cells is removed and transferred into a culture dish lined with feeder cells. Here the cells are allowed to divide and multiply into millions of immature, undifferentiated cells.
The practice of therapeutic cloning is currently licensed in the UK through the Human Fertilisation and Embryo Authority (HFEA). This allows researchers to potentially create a stem cell line and produce blastocysts. The blastocyst is allowed to develop for a maximum of 14 days before it is considered for reproductive cloning. Reproductive cloning is identical to therapeutic cloning apart from the fact that the blastocyst is allowed to develop into an embryo and is implanted into a female. In the UK it is illegal to practice reproductive cloning on humans. However it has been used on many animals such as sheep e.g. Dolly the sheep - 1997.

The establishment of millions of cells in therapeutic cloning leads to the creation of an embryonic stem cell line. The UK currently has 3 stem cell lines although this may soon rise as new world leaders with interest and support into stem cell therapies are seeing that the increased funding, facilities and finest scientists are available for such research. Simpler forms of stem cell therapy have been around for years such as bone marrow transplants for leukemia victims and other techniques such as grafting new skin cells to treat burn victims. The majority of therapy conducted to date however has been adult stem cells as opposed to embryonic stem cells. Adult stem cells, found in adult bodies, are limited in the fact that they can only become the cell type of their original tissue. For instance, adult stem cells found in the fat can only become a fat cell and likewise for adult stem cells found in the cornea, heart, brain, skin or bone marrow.

One area that remains though is it the potential for embryonic stem cells to provide a treatment or cure for spinal cord injuries. The spinal cord is a vital part of the central nervous system consisting of nerve cells (Figure 3) that send signals to the brain. If any of these nerves are damaged they are, at present, impossible to regenerate.

**FIGURE 2**

**FIGURE 3**

Nerve Cell

Spinal cord injuries can be classified as either complete or incomplete:
Complete – total loss of control below site of injury
Incomplete – part loss of control below site of injury
Both however, involve some degree of sensation or motor function loss.
The possibility of restoring these damaged nerve cells has been brought forward with the findings of several studies that have shown that stem cells injected into animals can repair damaged spines, moreover the myelin. Myelin is a fatty protective layer that surrounds the nerve axons and keeps the nervous impulse within the axon. Axons are long nerve fibres that run from the CNS to the receptors. As a result of these electrical transmissions the body can perform its conscious and reflex actions. A conscious action is an action with is ‘thought about’ whereas reflex actions occur automatically without thought by bypassing the brain. Therefore without this electrical transmission the body cannot more i.e. paralysis. For instance, John Hopkins University in Baltimore, Maryland successfully injected embryonic stem cells into rats with injured spinal cords. In just 24 weeks these rats could support their own weight. Despite this, many teams such as Hans Keirstead at the University of California, Irvine, have identified a problem – undifferentiated embryonic stem cells can lead to tumor formation or rejection.

Assuming that it is possible to make the embryonic stem cell develop into the desired cell – whether before placed in the organism to be treated or after, this would enable vets to cure many animals which otherwise would unfortunately result in a previously perfectly healthy animal being put to sleep.

**Discussion**

Embryonic stem cells may be the end to many fatal diseases if existing understanding of their functioning is correct, allowing specially made cells, tissues and organs to replace/repair damaged or destroyed ones. This would ultimately allow any fault in the mammalian body to be cured. Although scientists have not yet been able to produce complete organs, they have been able to manipulate the production of specialized cells from undifferentiated embryonic stem cells through pluripotency. For instance, Dr Lior Gerstein and others managed to coax stem cells into becoming beating heart cells which indicates the potential treatments for numerous heart conditions. The outcome of these possibilities is enormous; it means the patients would be able to acquire brand new, living body parts as opposed to insulin pumps, titanium joints or plastic blood vessels and other artificial implants. By transplanting cells into patients, damaged tissues could be repaired and hence result in a cure for diseases such as multiple sclerosis, sickle cell anemia and cancer. Stem cells have been identified to play huge roles for instance in tumors and cancers where they are believed to carry the malignant tissue, possibly through mutation or changes in the DNA sequences. Replication and maturation of these ‘tainted’ stem cells then allow the tumor or cancer to return after the treatment. Stem cells were first identified to be connected with leukemia in 1997 by John Dick and others at the University of Toronto. Similarly, in 2003, Michael Clarke of Stanford found stem cells in cancerous breast tissue. By understanding that stem cells are able to maintain the cancerous element, researchers can clearly now see why past treatments have not been able to totally eradicate some cancers; for instance – the treatment only attacks the cancerous cells while allowing the cancerous stem cells to secretly carry their cancerous element and remain in the body before they replicate and mature.
However, imagine a spinal cord injury where a tumor is not involved. Damage to the spinal cord, which is highly concentrated with nerve cells, can lead to paralysis below the site of injury or loss of sensation. Although one would expect the adult stem cells found in the spinal cord to be capable of developing into and replacing the damaged nerve cells naturally, this is not the case. Adult stem cells are able to make new connections of neural cells, but not enough are naturally available to fully restore the spinal cord which makes their practicality for such large use a problem. This implies that the larger and more destructive the injury the smaller the chance of recovery. This statement appears to coincide with common sense.

One aspect of my research therefore focuses on the possibility of overcoming this availability factor that has stopped the natural healing of many spinal injuries. Every year, thousands of unwanted embryo’s, composed entirely of embryonic stem cells, are destined for disposal at fertility clinics. Imagine if from these embryos; the embryonic stem cells within them could be cultivated in order to become nerve cells. These newly cultivated nerve cells could then be injected into the spinal cord. In theory the injected nerve cells should make neurons and repair the spinal cords insulating myelin. The myelin sheath is important to keep the impulse inside the axon. Therefore without the myelin, the impulse is lost. Promising evidence that this injection of stem cells heals paralysis comes from Anderson who injected mice treated with human embryonic stem cells with diphtheria toxin, which killed the human cells. As expected the movement improvements disappeared suggesting strongly that the human cells were solely responsible for the recovery. Despite this, the immune systems of these mice had been immobilized. In reality, to immobilise the immune system of a patient could potentially place the patient under more risk from infections and disease. The other option however, allowing the immune system to remain, runs risks of rejection.

The normal treatment available now at Veterinary Practices throughout the UK for animals with paralysing spinal injuries is euthanasia. Animals that have suffered less critical injuries are sometimes operated on if the owner so wishes. These methods all appear crude when the idea of a straightforward injection would deliver treatment straight to the site of injury.

Using an injection as opposed to surgery would relieve the animal of any further stress, complications and discomfort. Surgery is often a lengthy, risky route which also requires ongoing after treatment. Many clients find this an immensely stressful and emotional option and with the high possibility of death, often opt for euthanasia. Injecting embryonic stem cells to the injury would allow the spinal cord to rejuvenate itself with natural cells. The embryonic stem cells would be able to replace the damaged nerve cells and restore the insulating sheath (myelin) that had been destroyed. This would mean a cure for spinal cord injuries where the disability is caused by the destruction of the myelin.

Although no embryonic stem cell treatments have yet been released to treat spinal injuries the release of such treatment is credible. When such a treatment is released however, as with all new treatments, I suspect it will be costly - animal drugs are much more expensive than human drugs. Despite this I highly suspect that many owners would
be willing to pay these costs, if they can save the life of their family pet or even improve the quality of its life.

One factor though that I strongly believe will have an impact on the popularity of such a product would be the ethical issues surrounding embryonic stem cells which has generated much interest and public debate. Extracting the embryonic stem cells in the harvesting procedure destroys the unborn child – a potential person. Many people believe that it is wrong to destroy a human being, not matter how small they are. The conflicting argument however is that these embryos are fated to be thrown away. It can therefore be argued that these embryos have shown no signs of life at such early development and that by throwing them away is simply a waste when they could provide such medical advances. An ethical dilemma is unavoidable. Another ethical barrier is that there is no alternative to embryonic stem cells. As Professor Harry Moore, Centre for Stem Cell Biology at the University of Sheffield quotes, “Only embryonic stem cells have the true capacity to develop into all the different cell types of the body”. Therefore one has to consider which is the lesser of two evils – to destroy an embryo or to allow diseases and injuries that cause so much suffering and death to continue when they could be been cured.

Conclusion
Spinal cord injuries are fatal for many animals. However I believe that an embryonic stem cell injection would greatly reduce the number of fatalities. Lately there have been reports on how vets currently hold the highest suicidal rate which has been linked with their roles in euthanatising animals. This therefore may benefit many vets that work for instance with race horses which suffer many spinal injuries.

A problem however with embryonic stem cell injections is the risk of tumor formation or tissue rejection. Tumor formation can occur when undifferentiated stem cells from a different organism are injected into the body. However if through therapeutic cloning the DNA to be transferred into the new nucleus came from the patient, this would overcome this problem. Although this overcomes the problem of tissue rejection, it may take too long and prove too complicated to produce separate stem cell lines for individual patients. This is when cord blood may be relevant. Cord blood is the blood left in the umbilical cord and placenta after birth. These stem cells are immature and have not yet learned to attack foreign bodies, which makes them less likely to be rejected. The norm is to discard cord blood after birth but recent knowledge and awareness of its benefits have led to the formation of cord blood banks.

Although it may be many years before embryonic stem cell treatment is available to treat spinal cored injuries, I believe that one day it will be possible to rejuvenate the nerve cells with the spinal cord after injury. This is clear by the fact that researchers have been able to manipulate cells into forming new nerve cells that produce new connecting branches and restore the insulating myelin. This allows internal injuries to be cured by cell rejuvenation as opposed to mechanical mending by vets with tools.
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