Cells4Life

the experts in stem cell processing

Clinical Update 2014

Bringing you up-to-date on the latest research into stem cell therapies.

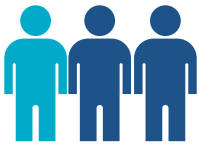
Cells4Life
the experts in stem cell processing

Welcome to the future of medicine...

Despite an early focus on blood stem cell transplant therapies, there has been a clear shift towards regenerative medicine over the last five years. It is now currently estimated that 1 in 3 people will benefit from therapy using family-banked cord blood stem cells in their lifetime.

Cells4Life continues to champion the collection and storage of cord blood due to the overwhelming advantages it offers in stem cell therapy.

(Expert Opin Biol Ther. 2007 Sep;1311-22. The potential of cord blood stem cells for use in regenerative medicine. Harris DT, Badowski M, Ahmad N, Gaballa MA)



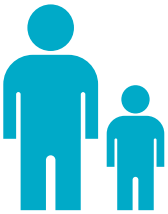
"1 in 3 people will use their own stem cells in their lifetime"

Ref: Harris, 2007

Cord Blood Banking

4,300+

Over 4,300 Clinical Trials using stem cells [1]



Perfect match
1:1 child
1:4 sibling

Over 80+ Diseases treated

Public & Private Banking

Public

Available if there is a matched sample, used for transplant only

- 1:5,000 lifetime chance of needing a stem cell transplant from a donor[2]
- Sample can be used by anybody who is a match

Private

Always a perfect matched sample, access to emerging regenerative therapies

- 1:3 chance of your child using their own stem cells in their lifetime[3]
- Sample can only be used by the child or their family

(1) www.clinicaltrials.gov
(2) Nietfel, JJ et al., Biol. Blood and Marrow Trans. 2008; 14:316-322
(3) Expert Opin Biol Ther. 2007 Sep;1311-22. Harris DT, Badowski M, Ahmad N, Gaballa MA.

Clinical Update 2014

Contents

Autism

Neurological | Umbilical Cord Blood

Autism is a spectrum disorder known to be caused by certain gene factors involved in brain development and early life environment. It is more common in boys than girls, with signs and symptoms appearing from age 2 to 3 years. It can be frequently associated with intellectual issues.

Over 500,000 people in the UK have an autism spectrum disorder, costing £27.7 billion each year for services and support. £2.7 billion is support for children, while £25 billion is for adult care. Figures from the London School of Economics shows the lifetime costs are £1.23 million for a person with a combination of autism and intellectual problems, and £800,000 for a person with autism only.

Clinical trials

So far, patient data from Georgia Health Sciences University in Augusta has yet to show dramatic differences in patients treated with stem cells. A proposed clinical trial is now underway at the Sutter Neuroscience Institute California. Using autologous cord blood, the study aims to try and reverse the effects of this disease where it is not attributable to other factors such as genetic disorders, head injury or prematurity.

The premise of this treatment is that mesenchymal stem cells may positively impact the immune and neural dysregulation. The ability of these cells to migrate to sites of damage and limit pro-inflammatory responses combined with an immunosuppressive capacity is unique and provides the possibility to pass the blood-brain barrier. We await results.

Animal studies

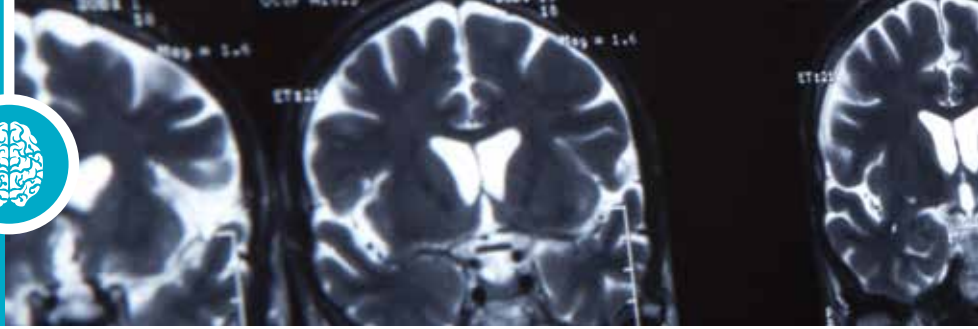
So far, there have been animal models developed with brain lesions, genetic mutations affecting neurotransmitters, or hormonal changes affecting sociability. These are currently being used to understand the biochemical process of this disease.

Summary

At this time there is insufficient data to indicate if this approach will be of benefit, but the early results do seem to show efficacy.

Related links

http://bjp.rcpsych.org/content/194/6/500.abstract
http://aut.sagepub.com/content/13/3/317.abstract
http://www.ncbi.nlm.nih.gov/pubmed/23142422
Neurosci Res. 2012 Dec;74(3-4):184-94. doi: 10.1016/j.neures.2012.10.004. Epub 2012 Nov 6. Animal models of autism with a particular focus on the neural basis of changes in social behaviour: An update article. Olexová L, Talarovicová A, Lewis-Evans B, Borbélyová V, Kršková L.
http://www.checksutterfirst.org/neuro/autism



Cerebral Injury

Neurological | Umbilical Cord Blood

Cerebral injury reduces or limits supply of blood and thus oxygen to the brain, resulting in the death of brain tissue. The effects can be severe, life-long or fatal. 1 million people in the UK attend A&E with head injury every year, at an annual cost of over £4.1 billion. Road traffic accidents account for 50% of all cerebral injuries, with young men between their late twenties and mid-thirties being the largest patient population. Meanwhile, patients over 65 years of age most commonly suffer cerebral injury as a result of a fall. Cerebral injury can also be associated with birth, with an incidence rate of between 1.7 and 3 per 1,000 live births. Litigation of birth-related cerebral injury cases in the UK is estimated at £20 million per annum.

Clinical trials

There are currently five clinical trials investigating the use of cord blood as a treatment for cerebral injury in newborn or young children. Some are focusing on the use of allogeneic cord blood to address the fact few children have their own cord blood saved at time of birth. One study is investigating the possible protein changes that occur in brain damage, with a view to understanding the mechanisms and therefore the nature of the damage. This has yet to report.

Other studies are currently in progress and no interim results are available as of yet. The timing and cell dose is part of this investigation.

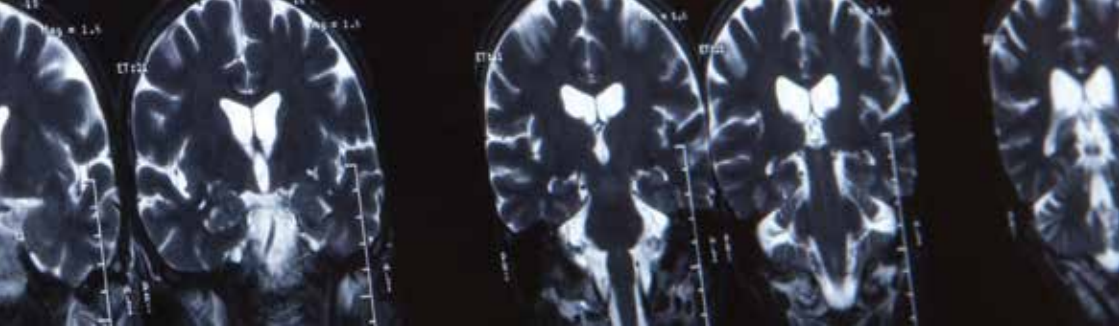
There is a concern that cells implanted to the brain may not be controllable and could therefore cause further problems. As it is difficult to remove matter from the brain, being able to correct such an issue needs to be avoided. As a result, there is no current work where cells or tissue are directly implanted into the brain.

Cell line

Lund University has developed a mechanism for producing brain cells in the lab. This has helped to understand how brain cells are formed from stem cells.

Animal studies

The clinical trials mentioned are based on strong animal model data, in which the intravenous transfusion of cord blood to rats shows significant improvement in motor and neurological skills. This study also showed the cells migrated to the area of injury and expressed specific neurological markers. There was evidence of the cells integrating to the vascular network at the injury site.



Summary

Cerebral injury research has many parallels with stroke research as the causes are lack of oxygen to the brain resulting in damage. There is a lot of funding and work in this broader area that promises to bring good results in the near future.

Related links

http://www.ukabif.org.uk/information/data

http://www.ukabif.org.uk/index.php?option=com_chronocontact&chronoformname=support

https://www.headway.org.uk/key-facts-and-statistics.aspx

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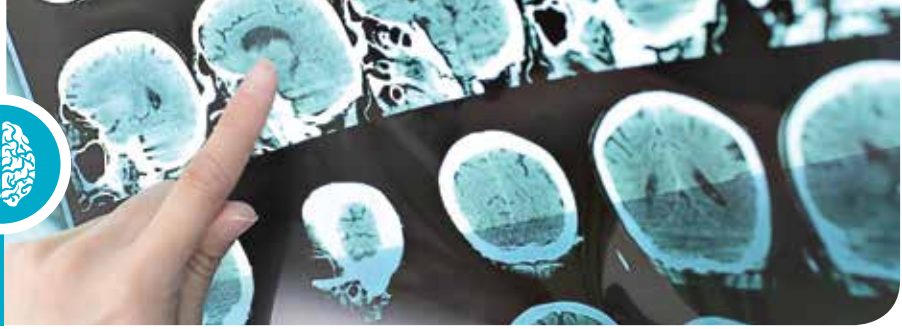

Stroke

Neurological | Umbilical Cord Blood

There are two primary causes of stroke – bleeding on the brain and a clot in the artery supplying blood to the brain. Both result in the loss of oxygen to brain tissue. Prevention is the most effective and common treatment, including medicine and lifestyle changes to reduce risk factors associated with stroke.

120,000 people experience a primary stroke in the UK every year, and a further 30,000 have a subsequent stroke. In total, it is estimated that there are 1 million stroke sufferers in the UK, 50% of whom rely on other people for day-to-day living activities. With most sufferers over the age of 65, it is the third most common cause of death in the UK and the largest cause of disability. Severity of the disease varies and depends on the extent of damage suffered by the brain.

The average cost is £15,000 to £30,000 per patient per annum for the first 5 years post stroke. Long-term costs can exceed £135,000 depending on the longevity of the stroke victim. The overall cost to the UK per year is £7 billion.

Cell line

ReNeuron have developed a cell line to treat stroke victims that is currently being used in the UK. Presently no adverse effects have been seen, but the full data is not yet available.

Animal studies

Much work has been done in rats as a model of the disease to look at the effects of implanting neural-derived cells into the affected brain. This shows that direct injection of cultured cells to the lesion can be effective.

Summary

A meta-analysis of the animal model data available shows that early treatment with autologous cells is beneficial for structural outcomes. However, functional outcomes are not time-dependent and allogeneic cells can be more effective.

Related links

http://www.ninds.nih.gov/disorders/stroke/stroke.htm

http://clinicaltrials.gov/ct2/show/NCT01151124
Pilot Investigation of Stem Cells in Stroke (PISCES).

http://www.ninds.nih.gov/research/stem_cell/index.htm

http://www.ncbi.nlm.nih.gov/pubmed/22213183
Stem Cells. 2012 Apr;30(4):785-96. doi: 10.1002/stem.1024. Implantation site and lesion topology determine efficacy of a human neural stem cell line in a rat model of chronic stroke. Smith EJ, Stroemer RP, Gorenkova N, Nakajima M, Crum WR, Tang E, Stevanato L, Sinden JD, Modo M.

http://www.nao.org.uk/idoc.ashx?docId=11ED54B8-BABF-4C0E-AEFC-2A09B55DE4AE&version=-1
Economic burden of stroke in England Division of health and social care research Saka et al.

Cerebral Palsy

Neurological | Umbilical Cord Blood

Cerebral palsy is a chronic long-term condition whereby muscle control is affected due to brain cerebrum damage as a result of asphyxia (lack of oxygen). This can occur prior to the birth as a result of:

- Reduction in the blood supply to the white matter as a consequence of infection, maternal low blood pressure, premature birth and cocaine use.
- Abnormal brain development due to a genetic abnormality, infection or trauma.
- Intracranial haemorrhage due to stroke, maternal high blood pressure or infection.
- Blood supply interruptions during birth such as the cord being around the neck.

Cerebral palsy can also occur after birth, usually as a result of infection or traumatic injury.

Cerebral palsy affects 1 in 500 babies in the UK annually, and is usually associated with other compounding medical conditions such as epilepsy. There are currently 110,000 sufferers in the UK, costing the NHS £4 billion per year to treat and care for. There is also the cost of lost income for carers, out of pocket expenses, psychological effects and the impact on productivity.

Clinical trials

There are currently nine clinical trials listed using cord blood for treatment of cerebral palsy. Two of the most prestigious research institutes – Duke University and Georgia Health Sciences Institute – are working on clinical trials in this area (NCT01072370 and NCT01147653). A very good summary paper has been written by Titomanlio et al (see below), which indicates from preliminary data that this may be effective, but a long-term follow up is needed.

Summary

Although stem cell treatment is still very experimental, cord blood appears to offer advantages over other stem cell sources, with autologous sources of stem cells proving to be the best. It is also worth noting that these are still in the clinical trial phase and so are not yet widely available.

Related links

http://www.nhs.uk/Conditions/Cerebral-palsy/Pages/Causes.aspx

www.nice.org.uk/nicemedia/live/13803/60879/60879.doc

http://www.publications.parliament.uk/pa/ld200809/ldhansrd/text/91104-gc0003.htm#091104114000035

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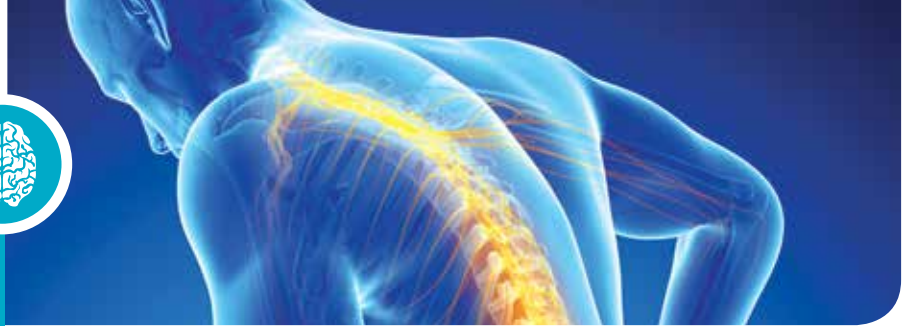
Ann Neurol. 2011 Nov;70(5):698-712 Stem cell therapy for neonatal brain injury: Perspectives and Challenges. Titomanlio L, Kavelaars A, Dalous J, Mani S, El Ghouzzi V, Heijnen C, Baud O, Gressens P.



Spinal Cord repair

Neurological | Umbilical Cord Blood

There are an estimated 13,500,000 neurons in the human spine, with 31 pairs of nerves covering a 70cm spinal column. A spinal cord length of 43cm to 45cm (sex dependent) has 318 cervical segments. Injury to any part of this can cause motor impairment and disruption to normal bodily functions. In the UK, £500 million is spent on caring for people with spinal cord injury every year. 40,000 people in the UK live with paralysis.

Falls and road traffic accidents account for over 78% of spinal injury. The age range for sufferers has historically been predominantly males aged between 15 and 40, but is now being skewed towards older people. This may be due to higher survival rates after accidents or differences in reporting injuries.

Due to the age at which these accidents occur, the morbidity and economic impact is substantial. Over 21% of sufferers are unable to return to their own home, and are housed in institutionalised accommodation. Only 1% of people suffering spinal injury experience complete neurological recovery.

Clinical trials

To date, single patient treatments have shown success in repairing injury to tissue at a specific site using cord blood or bone marrow-derived haematopoietic stem cells. The efficacy of the treatment in these individual cases has not been curative, but has promoted neurological transmission to tissue that was previously deprived of sensation or motion. In some clinical and animal work it has been shown that the shorter the time between injury and treatment, the better the outcome.

Currently, there are three clinical trials underway to investigate the use of cord blood as a treatment option for patients with spinal injuries. Some of these are aimed at understanding how the repair is affected, while others are looking at dose and mechanism.

Patient studies

There is one published case of cord blood being transfused to a patient with spinal injury that resulted in improved sensory perception and mobility in the hip and thigh regions. This was supported by MRI and CT data showing regeneration at the injury site.

Related links

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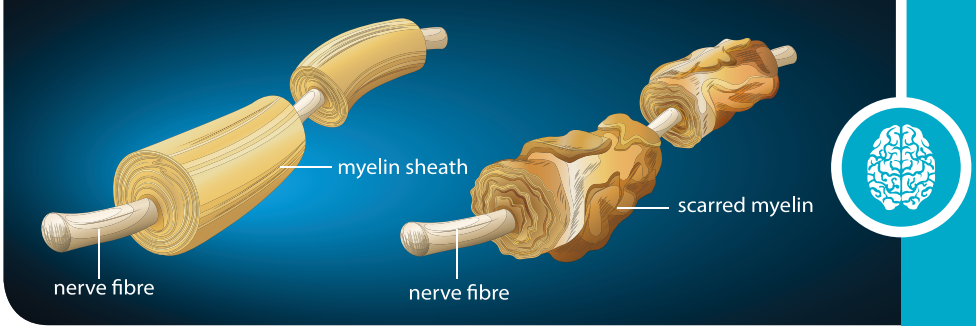


Multiple Sclerosis

Neurological | Umbilical Cord Blood

Multiple sclerosis (MS) is an autoimmune response that destroys the myelin sheath that protects the nerves in the brain and spinal cord. The resulting nerve damage leads to sensory disturbances and an inability to control muscles.

A progressive disease, the associated consequences of MS can be partial paralysis in addition to complications with communication and feeding – all of which has a negative impact on patient quality of life. Current research indicates a possible genetic predisposition coupled with environmental triggers as the cause.

MS affects approximately 1 in 1,000 people, with a familial history reducing these odds to 1 in 50. It can be associated with other illnesses and disease such as type 1 diabetes, leukodystrophies and osteoporosis. There are currently 100,000 people in the UK with MS, costing £1.34 billion per year to treat.

Clinical trials

A phase IIa study was performed on a small patient cohort. This showed some improvement in vision, but limited impact on disease progression, measured by disability worsening.

Animal studies

Research using mice models of the disease have shown that mesenchymal stem cells (MSC) can inhibit the pathogenic immune response. This response was not mediated by stem cells being incorporated into the central nervous system, but by the MSCs triggering an anti-inflammatory response.

Patient studies

There are four reported patient trials, all using autologous MSCs isolated from bone marrow. The methods of administration were intrathecally, intravenously plus intrathecally or just intravenously. The most efficacious route was intravenously only, which resulted in peripheral tolerance of myelin antigens, axon formation and remyelination. This is also the least invasive route of administration with fewest possible adverse side effects. A mean dose of 1-2 x106 cells per kg bodyweight was used. These are all phase I open label safety studies.

Future clinical trials

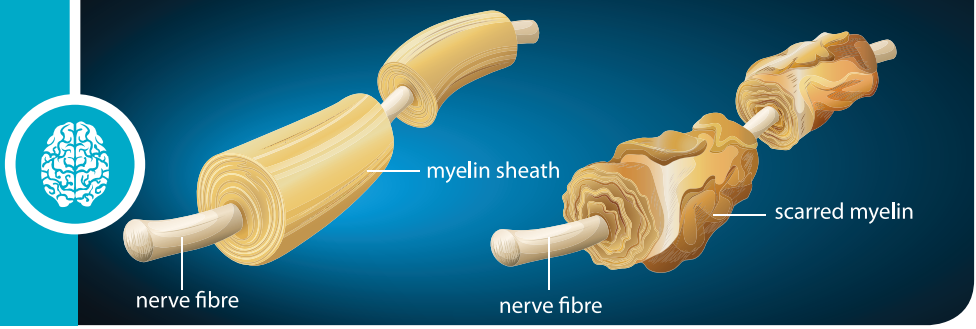
A further study using a randomised cross-over placebo-controlled design is scheduled for 2013 under the acronym MESEMS. Again using autologous bone marrow-derived MSCs, the studies will be carried out in multiple countries and the results pooled to provide a larger patient cohort. There are 10 centres already in the EU, with USA and Canadian centres currently obtaining funding and local permission to participate.

Summary

Currently there is no cure for MS, and existing results of stem cell work indicate that MSCs may possibly provide an alternative treatment option. The aim is to understand how tissue repair can be mediated, although replacing damaged neuronal tissue with functioning tissue is some way off.

Related links

http://www.msrc.co.uk/index.cfm/fuseaction/show/pageid/746



Multiple Sclerosis

Neurological | Umbilical Cord Blood

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Huntington's Disease

Neurological | Umbilical Cord Blood

Huntington's disease is a progressive brain disorder resulting in the slow loss of brain cells. Mutation results in a longer than normal protein, which accumulates in the brain cells, specifically those controlling motor function. Cognition and mental disease issues may also be involved. Onset usually occurs in middle age and reduces expected lifespan, with an average time from disease onset to death of 15 to 25 years. However, the earlier the onset of disease, the shorter the life expectancy. Death is usually due to infection, injuries relating to a fall or other complications.

Between 6,500 and 8,000 people in the UK are affected, costing £12 million per year for treatment and support. It appears to be more common in European ancestry populations.

Cell line

A stem cell line with the genetic defect has been created to help model the disease and test possible treatments. Genes that combat the effects of the disease could be introduced to cell lines to stimulate production of brain cells, or stem cells may be introduced to repair the damaged brain cells in situ.

Animal studies

Present treatments slow the disease progression, and some symptomatic treatments are available. Stem cell-based therapies are currently in animal model phase only. This includes formation of GABA neurons that can be implanted into the brain to effect a restoration of function. This has been successfully undertaken in mice, but the GABA neurons were created from embryonic stem cells, which are ethically difficult.

Future work

Future work may include transplantation of specific cell types such as neurons into the damaged area. All of these are possible avenues that are being investigated. It is anticipated that cell-based therapies may be available in 5 to 15 years.

Summary

A stem cell-based treatment for Huntington's disease is many years away, yet current research aims to use stem cell technologies to understand and work on gene therapy and symptomatic treatment.

Related links

http://www.nhs.uk/Conditions/Huntingtons-disease/Pages/Causes.aspx

http://jnnp.bmj.com/content/63/suppl_1/S19.full#xref-ref-16-1

http://jrsm.rsmjournals.com/content/98/12/550.full

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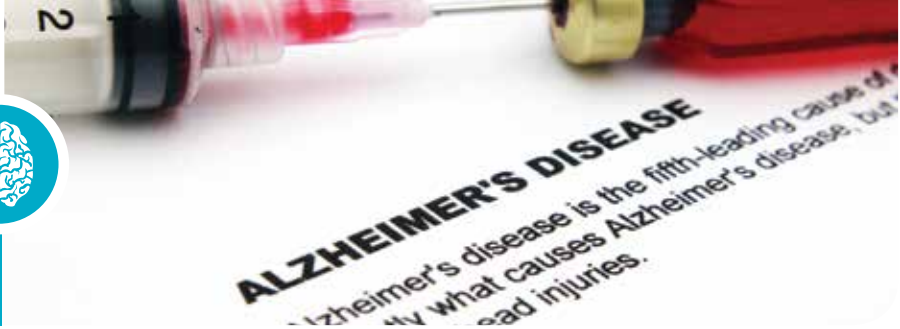

Alzheimer's

Neurological | Bone Marrow

Thought to be caused by a combination of genetic predisposition and environmental factors, Alzheimer's disease results in the loss of brain cells and the development of plaques created by the protein beta amyloid. It also results in tangles caused by the protein tau within the brain tissue.

This disease is estimated to affect 820,000 people in the UK, costing £23 billion to the UK every year. 17,000 of those sufferers are younger people, and two-thirds are female. 670,000 people are carers for suffers of dementia, and there are 60,000 deaths per annum attributable to it.

Clinical trials

There are two current clinical trials using stem cell treatments to either slow the progression of, or ameliorate Alzheimer's disease. Research at Kings College London is using stem cells to test new drugs, while research at Nottingham University seeks to understand the biology of transforming bone marrow-derived haematopoietic cells into nerve cells with a view to being able to transplant these.

Cell line

Work has been published showing the positive effect of mesenchymal stem cell (MSC) populations on the plaques produced by this disease.

Animal studies

In addition, the anti-inflammatory effect of cord blood MSCs in mouse models has been shown to be effective. Mice were shown to regain learning and memory functions when treated with cord blood.

Patient studies

One US company has worked on the use of adipose cells to provide a treatment, although no data has been published yet. It has been indicated in marketing material that this slows the progression of the disease.

Future research

Both of these avenues of investigation indicate cord blood as a possible therapeutic candidate in the near future. However, there are no plans to initiate trials of stem cell-based therapies in current published resources.

Summary

Currently the use of stem cells to treat this disease is limited to understanding its pathology.

Related links

http://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=99

http://www.eurostemcell.org/story/stem-cells-therapy-alzheimers-disease-part-2-2

http://www.alzheimersresearchuk.org/research/

Parkinson's Disease

Neurological | Umbilical Cord Blood, Bone Marrow, Adipose

Parkinson's disease is caused by a lack of dopamine due to nerve cell death in the brain. The cells are constantly sending signals, resulting in a higher than normal concentration of calcium in the cells, possibly increasing the metabolic rate of the cells and leading to cell death. Death of these cells affects the motor function of the muscles, and has a cumulative effect, with the outward effects usually only apparent when 70% or more of the cells have been lost. The most common physical complications are associated with dysphagia or swallowing. Emotional complications arising from changing hormone balance, vision, sleep and mental acuity decline are also symptomatic – all of which can lead to increased care needs.

Parkinson's disease is not fatal, but reduces longevity and can lead to severe incapacity. The older the person at the onset of Parkinson's, the quicker the disease progression. It has been estimated that 1 in 20 people with Parkinson's has a genetic cause for the disease. It usually affects those over 50 years of age, but 1 in 20 are under 40.

127,000 people in the UK have this condition, costing between £25,630 and £62,147 per person per annum. 93% of this cost is non-medical professional care and indirect informal care costs.

Cell line

Currently, all stem cell work is focused on understanding and modelling the disease, with a view to being able to pinpoint treatments and assess their efficacy. The ability to produce dopamine-producing cells and transplant these to the brain seems to be the most promising avenue of research.

The exact mechanism to ensure these cells are retained and successfully integrated into the brain is still being worked on, alongside technical mechanisms for operating on the brain without creating unwanted side effects.

Future work

Some reports indicate that clinical trials for the transplantation of such cell cultures may be starting in 2014 or 2015.

Summary

At present no treatments are available for this disease. It is hoped that the cell line work in modelling this disease will lead to therapies in the future.

Related links

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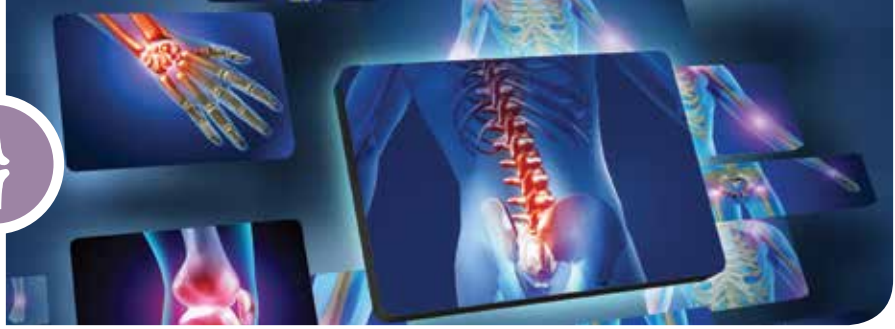

Osteoarthritis

Skeletal Disease/Injury | Bone Marrow, Adipose

Osteoarthritis is degeneration of the cartilage, which is a tough flexible tissue that covers the ends of joints and forms structures such as ears, nose and the windpipe. Cartilage permits bones to glide over each other and prevents bones rubbing together. Injury, inflammation or damage of the cartilage due to sport, genetic factors or autoimmune activity leads to pain and lack of mobility in the affected joints. It can therefore be acute, with sudden onset due to injury, or it can manifest as chronic long-term degradation.

The exact number of osteoarthritis sufferers is unknown due to the milder symptomatic sufferers not seeking medical assistance or relying on over-the-counter medication to control the pain and inflammation. Nevertheless, an estimated 8 million people are affected by osteoarthritis in the UK, and its cost is thought to amount to 1% of annual UK GNP. Over 10,000 people per annum require medical treatment for damage.

Osteoarthritis is most common in women over 50 years of age, while accidental damage occurs most frequently in those under 35.

Clinical trials

The anti-inflammatory effect of mesenchymal stem cells (MSC) is of particular interest. So far, clinical trials all focus on MSCs from various sources and in combination with a variety of other media to mediate an anti-inflammatory response.
Most trials require follow up for many years due to the progressive and degenerative nature of the disease, so most have yet to conclude and provide finalised results.

Presently there are 20 clinical trials listed on www.clinicaltrials.gov using stem cells to investigate alternative treatment options for cartilage damage. Most are sourced from adipose or from bone marrow as an autologous source of stem cells (e.g. NCT01159899, NCT00891501 and NCT01399749). Some are also assessing bioscaffolds combined with both autologous and allogeneic stem cells to effect a better repair with greater longevity (e.g. NCT00850187).

There is also work assessing the benefits of autologous versus allogeneic sources of MSCs. However, there are currently no clinical trials using cord blood, although this is likely to be a function of the availability of sufferers with cord blood samples.

Related links

http://www.cartilagehealth.com/acr.html

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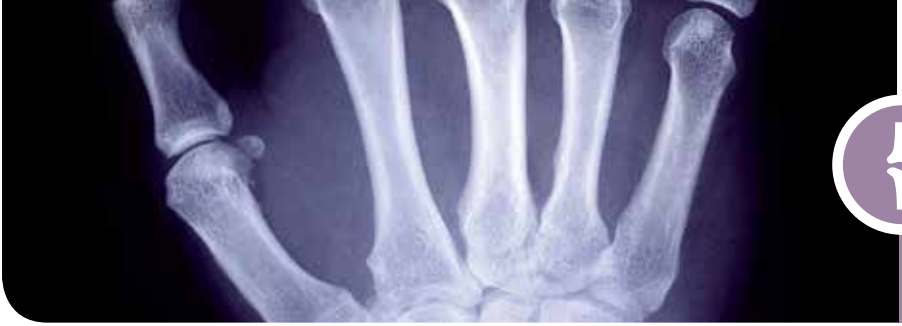

Rheumatism

Skeletal Disease/Injury | Umbilical Cord Blood, Adipose

Rheumatism is caused by the immune system attacking the lining of the joints, which causes pain, inflammation, swelling, permanent joint damage and deformity. The triggers for this are thought to be a combination of genetics and environmental factors. Oestrogen is also thought to be involved. An estimated 690,000 people in the UK live with rheumatism, frequently women between 40 and 70 years of age. It costs the UK £8 billion per year in productivity losses.

Clinical trials

There are currently 15 registered trials using stem cells to treat rheumatoid arthritis. NCT01547091 is looking to use umbilical cord-derived stem cells to treat this. NCT00282412 uses allogeneic haematopoietic stem cells from a matched sibling to restore the immune system after ablative therapy, with results due in 2014. NCT01663116 uses adipose-derived stem cells for treatment, with results collection still ongoing.

Animal studies

A significant study showed that treatment using umbilical cord-derived stem cells was successful in mice, and was the basis of future human clinical trials referenced above.

Patient studies

Small patient studies have been reported, which gave rise to the above clinical trials.

Summary

The outcomes of the above trials will assist with the development of treatment strategies to provide a long-term repair mechanism, in addition to possible disease avoidance mechanisms.

Related links

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http://www.nras.org.uk/includes/documents/cm_docs/2010/e/1_economic_burden_of_ra_final_30_3_10.pdf

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3046518/ 2010 November 16. Therapeutic potential of human umbilical cord mesenchymal stem cells in the treatment of rheumatoid arthritis. Yanying Liu, Rong Mu, Shiyao Wang, Li Long, Xia Liu, Ru Li, Jian Sun, Jianping Guo, Xiaoping Zhang, Jing Guo, Ping Yu, Chunlei Li, Xiangyuan Liu, Zhenyu Huang, Dapeng Wang, Hu Li, Zhifeng Gu, Bing Liu and Zhanguo Li.

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Bone Formation

Skeletal Disease/Injury | Bone Marrow

Breaks in bone can result in an inability to repair normally after 3-6 months, particularly if complex, repeated or as a result of disease. This inability to repair normally occurs in 1% of all fractures, but is disproportionate in lower leg fractures (19%) or where there is movement at the fraction site. 343,536 people in the UK are admitted to hospital with fractures every year, with £2 billion alone spent annually on approximately 70,000 to 75,000 hip fracture cases.

Mesenchymal stem cells (MSC) are found in cord blood, bone marrow and peripheral blood, and it has been widely demonstrated that such cells exhibit the same cell surface markers as those found on bone cells. Therefore, they can be induced to create cells with the same characteristics as bone cells.

Clinical trials

The NCT01206179 clinical trial looked at the use of bone marrow-derived MSCs to promote bone formation in non-union fractures. A further study (NCT01435434) looks to use autologous bone marrow cells with a bioscaffold to repair non-union fractures. This is scheduled to start patient recruitment in 2014.

Animal studies

In mice it has been shown that the addition of bone morphogenetic protein 2 (BMP-2) to human cord blood improves the formation of bone in such injuries. It is thought that this may form part of a clinical trial in the near future. A comparison of embryonic-derived stem cells to cord blood stem cells shows that the latter produces better bone formation in rats when seeded to a bone matrix.

Patient studies

A small-scale study with children suffering from osteogenesis imperfecta in 1999 demonstrated the safety and efficacy of bone marrow-derived MSC.

Summary

Further work has been done in the repair of non-union bone fractures using stem cells and bioscaffolds, as well as using donor material such as bone grafts.

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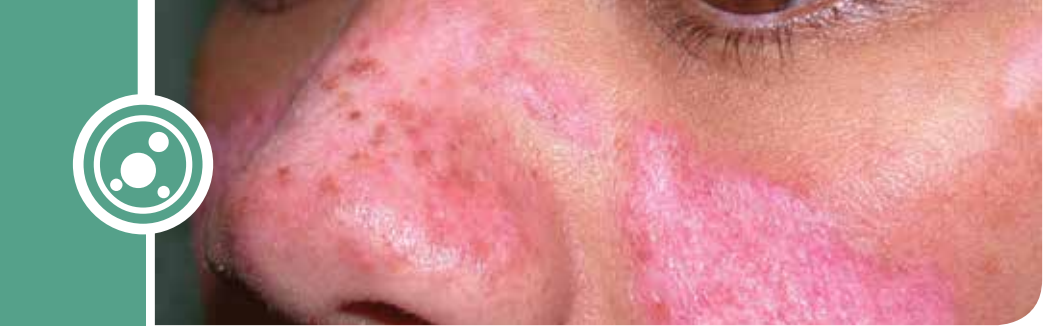

Lupus

Autoimmune/Inflammatory | Allogeneic Stem Cell transplantation

Lupus is a chronic disorder of the immune system that results in too many antibodies being produced. This causes inflammation that may affect multiple organs of the body. It is thought lupus may be inherited, although hormone activity and viral infections have also been implicated as causative agents. It is neither infectious nor contagious.

Lupus predominantly affects Afro-Caribbean, Chinese and Asian origin females at an incidence rate of 50 to 100 per 100,000. It is most commonly associated with hormonal changes such as pregnancy, menopause and puberty. Most lupus sufferers are unable to work full time or are considered disabled. Currently, 50,000 people may have lupus in the UK, costing £7,913 per patient per annum.

Current research

Current treatments focus on the reduction of antibodies and symptomatic relief of pain associated with the disease.

Clinical trials

There is one current clinical trial (NCT00278590) recruiting patients to look at the use of allogeneic stem cell transplant. This is not due to complete until July 2014.

Cell line

Current work using mesenchymal stem cells (MSC) elucidating the immune-modulatory effect of MSCs in the body – particularly in pro-inflammatory disease models – shows some promise for a more effective treatment.

Animal studies

Mice work shows that transplantation of mesenchymal stem cells (MSC) would induce repair of the immune system, possibly by T cell regulation.

Patient studies

A patient study was undertaken using allogeneic MSCs in four sufferers. At 12 to 18 months follow up, there was evidence of disease remission, shown by improvement in serological markers and renal function.

Summary

The use of cord blood, bone marrow and peripheral blood-derived stem cells of haematopoietic lineage have been shown to be effective, but follow up and long-term progression has yet to be confirmed.

Related links

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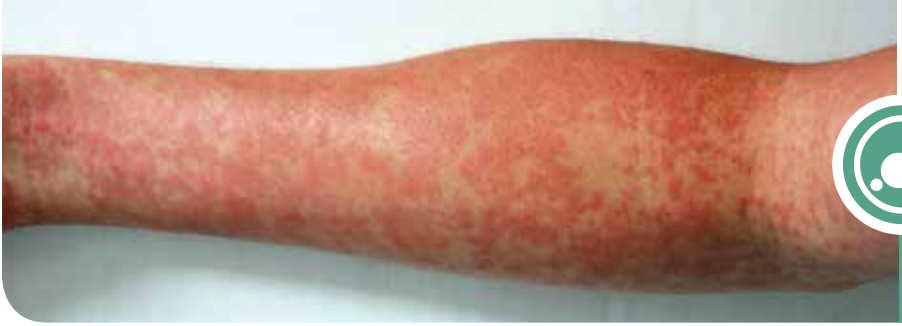

Graft versus Host Disease (GVHD)

Autoimmune/Inflammatory | Umbilical Cord Blood

Graft versus host disease (GVHD) occurs when a transplant of human tissue such as blood or organs from a donor to a recipient is attacked by the recipient's immune system. The results can be chronic, acute or even fatal.

20% to 80% of patients having a donor transplant will develop some degree of graft versus host disease, which typically occurs 21 to 25 days post-transplantation. In acute cases this is 26% to 34% for fully matched grafts and 42% to 52% for partially matched grafts. In chronic cases, this is approximately 30% for fully matched grafts and 60% to 70% for partially matched grafts.

Clinical trials

A phase II study at the Karolinska Institute is now being followed up in a European randomised study. No results are available as yet.

There is also a small study published looking at the co-transplantation of mesenchymal stem cells (MSC) with the donor haematopoietic cells that showed some beneficial effect, but the dose and the handling of the MSCs were flagged as critical parameters.

Patient studies

MSCs are currently being assessed for treating chronic GVHD. A 19-patient study showed 14 patients in complete or partial remission with no adverse effects, with 5 of these patients able to stop immune suppressive treatments.

Summary

Initial results using MSCs to treat this are promising, more work is planned to further clarify this.

Related links

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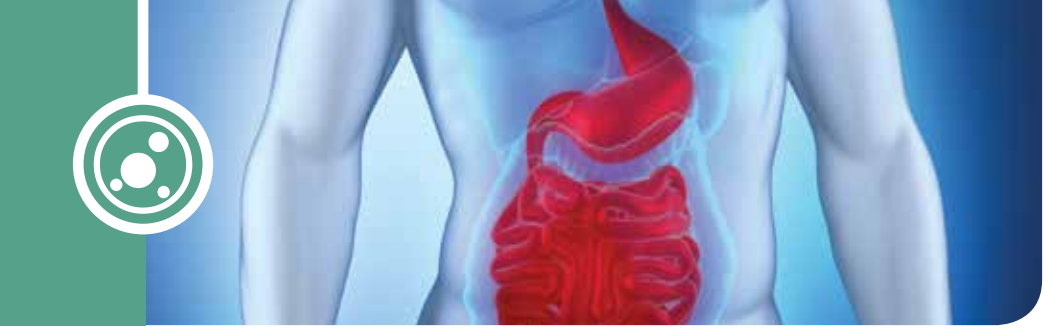

Crohn's Disease

Autoimmune/Inflammatory | Bone Marrow, Peripheral

The exact cause of Crohn's disease remains unclear, but a genetic predisposition and environmental factors including possible microbiological infection are considered the most likely combination. The result is an excessive quantity of Tumour Necrosis Factor (TNF) produced that indiscriminately kills all gut floras. Without the normal gut flora, food digestion is compromised.

New cases of Crohn's disease are diagnosed at a rate of 7 per 100,000 people. It usually arises in those aged between 16 and 30 years of age, or between 60 and 80 years of age. It is more prevalent in women than men, in white than black or Asian people, and is most common in people of European Jewish descent. Currently 90,000 people are living with Crohn's disease in the UK at a cost of £1,652 per patient per 6-month period.

Clinical trials

A clinical trial at Nottingham is underway, which completed recruitment in June 2012. This uses stem cells mobilised from bone marrow. There are four further clinical trials, one using peripheral blood stem cells, two using cultured stem cell lines and a third using allogeneic stem cell transplantation.

There has also been further work using adipose-derived stem cells to treat fistula complications arising due to Crohn's disease. This reported a 69.2% reduction in fistula draining events and 56.3% complete closure rate, with 30% complete closure of all existing fistulas.

Patient studies

One study has been undertaken using autologous bone marrow-derived mesenchymal stem cells (MSC) at a dose of 1-2 x 10^6 cells per kg bodyweight. A French study used peripheral blood-derived MSCs to treat patients, with some success but numbers were small. These led to the current clinical trial being proposed.

Future work

Due to the inflammation caused by the autoimmune response, the role of MSCs could be critical in the moderation of the immune response in this disease.

Summary

The proposed clinical trial will provide more data understanding about this disease and the potential to treat it with haematopoietic stem cells.

Related links

http://www.nhs.uk/Conditions/Crohns-disease/Pages/Causes.aspx

http://europepmc.org/articles/PMC1774248

http://www.nottingham.ac.uk/scs/divisions/nddc/astic/astictrial.aspx/

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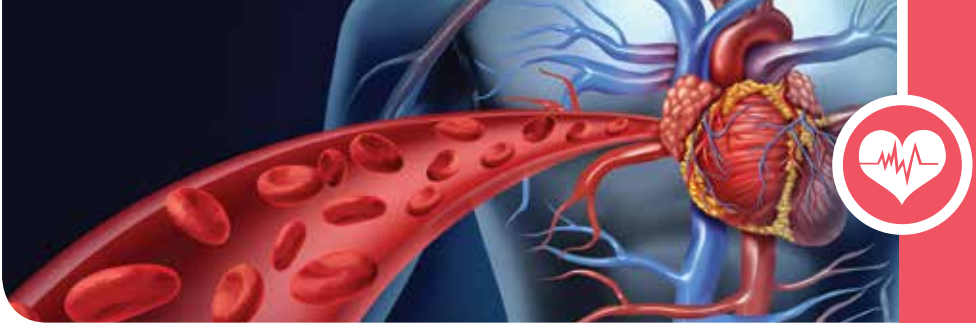


Myocardial Infarction

Heart and Vascular Disease | Bone Marrow

Myocardial infarction is usually caused by a blood clot that prevents flow to part of the heart muscle. The lack of oxygen causes tissue death, which leads to scar tissue formation that ultimately weakens and reduces heart functionality.

Blood clots are usually formed due to fatty patches developing within the arteries, although other causes are possible. 146,000 people in the UK have a myocardial infarction every year, with the estimated annual economic burden of post acute myocardial infarction heart failure estimated at between £125 and £453 million. Cost per patient depends on the severity of disablement and the increased risk of heart failure, which in turn increases the required incapacity treatment and help. There is also the considerable cost to the economy of reduced productivity, time off work and premature retirement for those under the age of 65.

Current treatment focuses on dissolving the clot, unblocking the artery, controlling the heart rate and provision of oxygen.

Clinical trials

Bone marrow-derived stem cells have been used to treat patients by repairing the damage to the muscle. There have been 13 trials to date using this stem cell source. One clinical trial has also been completed using autologous cells derived from heart biopsies.

These trials are all in adult patients who do not have cord blood stored (NCT01467232). Results published after a 2-year follow up show a sustained positive effect, with 9 out of 20 patients showing new heart tissue replacing scar tissue. There is one current clinical trial using cord blood-derived mesenchymal stem cells (MSC), but data has yet to be published.

There is also a European-funded project (EU FP7-BAMI) assessing the efficacy of stem cell therapies versus other treatments. This is assessing 33 trials comprising 1,700 patients, with follow up for several years.

Cell line

Work has been ongoing to try and create new cardiac parts such as heart valves from autologous stem cell sources. Whilst this is possible in theory, it has not yet surpassed the need for bioscaffolds and biomaterials.

Current research at the University of East Anglia is looking into the development of a heart in utero, and hopes to understand how different heart cells form. Other research has looked into the prevention of scar tissue formation. This is linked to the ability of haematopoietic cells to produce blood-carrying structures.

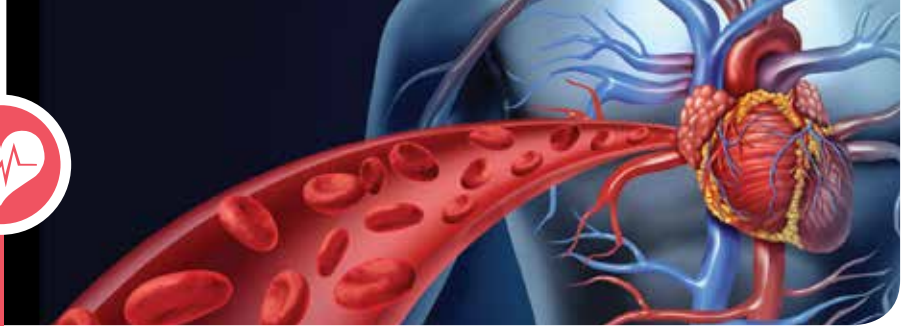
Under the leadership of Mark Sussman in San Diego, a new Integrated Regenerative Research Institute has been set up with the aim of "trying to turn back the aging clock of your heart".

Animal studies

Both mice and rats have been used as models to assess cord blood-derived stem cell therapies for myocardial infarction. This shows a positive effect, but has yet to show the mechanism of that effect.

Summary

Myocardial infarction is the leading cause of death in the developed world. It is both a disease in its own right and a secondary complication of other diseases. Currently, the use of stem cells is seen as key to providing novel treatments and to understanding the mechanisms of repair.



Myocardial Infarction

Heart and Vascular Disease | Bone Marrow

Related links

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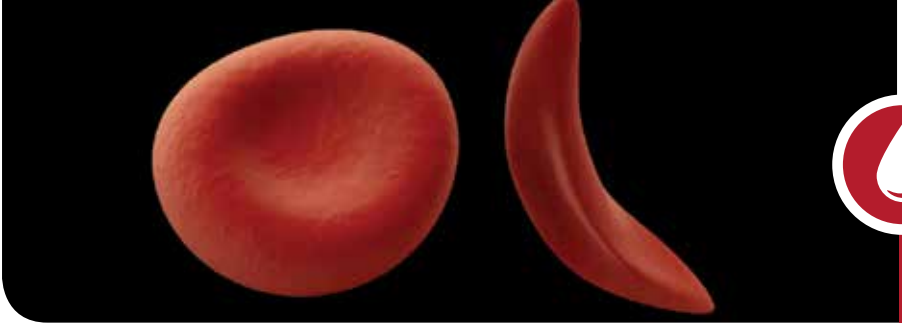

Sickle Cell Disease

Blood Disorder | Umbilical Cord Blood

Sickle cell disease is a form of anaemia resulting from a genetic abnormality in the haemoglobin-producing genes, and is usually inherited. It is a recessive disease, meaning that two copies are needed for the disease to be symptomatic. If contracted, the haemoglobin-containing red blood cells form a sickle or crescent shape, which limits the amount of oxygen these cells are able to carry. The red blood cells are also more prone to breakage and to form blockages in smaller blood vessels. Complications of the disease include infections, crises of pain episodes, eye problems, predisposition to strokes and other ischemic events.

Sickle cell disease is more common in people of African and Mediterranean descent, with a single copy being found in 25% of people and between 1% to 2% of all babies born with this disease. It is also seen in people of South and Central America, Caribbean and Middle Eastern descent. It is common for sufferers to die between 20 and 40 years of age. Currently, 12,500 people have sickle cell disease in the UK, with a lifetime cost of between £92,323 to £185,614 per patient.

Clinical trials

It is known that transplantation of haematopoietic stem cells can treat sickle cell disease successfully. Clinical trial NCT00029380 demonstrates this, with results to be confirmed after follow up. A trial with expanded cells is being planned.

Cell line

Work has been done to alter the haematopoietic cells from the individual, which in the lab has been shown to be effective. However, these have not been tested in humans, and the expectation is that this is a long way away from clinical trial.

Future work

Most research is focusing on the symptomatic treatment of the disease and controlling its expression to reduce the severity of the effects in individuals.

Summary

For individuals who are of a high-risk ethnic background, it is acknowledged that storage of cord blood to assist with future transplantations of either themselves or family members should be considered as routine.

Related links

http://www.umm.edu/ency/article/000527.htm

http://www.patient.co.uk/health/Sickle-Cell-Disease-and-Sickle-Cell-Anaemia.htm

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Diabetes

Type 1 Diabetes | Umbilical Cord Blood

Type 1 diabetes is an autoimmune disease that causes the beta cells of the pancreas to be destroyed. This results in insufficient insulin being produced, and therefore uncontrolled sugar levels in the blood.

The cause of type 1 diabetes may be related to genetic predisposition and environmental triggers. Currently, 3.8 million people in the UK have been diagnosed with diabetes. £9.8 billion a year is spent on it, which accounts for around 10 percent of the NHS budget. £1 billion is spent on treating type 1 diabetes, while the remaining £8.8 billion is spent on treating type 2 diabetes. 79% of these costs relate to treating complications of diabetes rather than the disease itself.

Diabetes increases the risk of heart disease, stroke, limb amputation, blindness, kidney failure, dental disease, neuropathy and premature death. It usually precludes being able to obtain private medical insurance due to the high risk of future health issues, and can also impact on employment opportunities.

The focus of current treatments is insulin replacement and lifestyle management. To address the root cause of the disease, insulin-producing cells must be tolerated by and thrive in the affected body. Pancreas and islet transplantation has been successful, but requires immune modulation of the recipient to prevent the autoimmune reaction. This can have long-term consequences.

Clinical trials

Currently, the clinical trials registry notes 47 trials investigating treatments of type 1 diabetes. Seven of these have, or are recruiting patients to investigate treatments using cord blood stem cells. The results are positive, but the long-term benefits are still under investigation.

A stem cell educator trial (NCT01415726) has been conducted where T cells from the diabetic patient are co-cultured with cord blood from healthy donors. 15 type 2 diabetic patients were treated, with long-term follow up results to be published. This study has now been extended, and is currently recruiting for type 1 diabetic patients. There is also a study using cord blood derived mesenchymal stem cells, which is due to report soon.

Cell line

Production of a stable cell line of insulin-producing beta cells has been achieved at the University of Pittsburgh to study immune response and help test possible therapies for it.

Patient studies

Some smaller patient studies have been conducted and published. 11 children were treated with their own cord blood at the University of Florida and followed up for 3 to 13 months. The study showed that immediately after treatment the requirement for insulin was lower than before treatment. This has not been shown to be a long-term solution, as the reduced insulin requirement was not seen at a post 12-month follow up.

A 57-patient randomised study reported by Hu et al shows a stem cell preparation from human umbilical cord Wharton's Jelly can reduce or ameliorate the need for insulin in patients under 25 years of age who had stable glucose and insulin levels for at least one month prior to treatment. This provides a baseline of efficacy and treatment dose, but requires more detailed work. The follow up term for

this study was 24 months, but a much longer-term follow up is required.

Future research

Immune modulation by mesenchymal stem cells (MSC) is a phenomenon that is poorly understood, but has huge implications for most diseases and injuries. MSCs are known to act in several ways in the immune system, and the overall result is the release of pro-inflammatory substances.

Summary

The incidence of type 1 diabetes and its associated morbidity and mortality are a global concern. While the exact mechanism of the disease is not clearly understood, improvements in the understanding of how certain stem cells affect the immune system, and how the specific cells affected can be protected, are the focus of current research efforts.

Relevant links

http://www.diabetes.co.uk/type1-diabetes.html

http://www.diabetes.org.uk/About_us/News_Landing_Page/NHS-spending-on-diabetes-to-reach-169-billion-by-2035

http://www.diabetes.org.uk/Documents/Reports/Diabetes_in_the_UK_2010.pdf

http://www.pittmag.pitt.edu/?p=880

http://www.medicalnewstoday.com/articles/240160.php

http://www.clinicaltrials.gov

http://www.biomedcentral.com/1741-7015/10/3/abstract
"Reversal of type 1 diabetes via islet beta cell regeneration following immune modulation by cord blood-derived multipotent stem cells"; Yong Zhao, Zhaoshun Jiang, Tingbao Zhao, Mingliang Ye, Chengjin Hu, Zhaohui Yin, Heng Li, Ye Zhang, Yalin Diao, Yunxiang Li, Yingjian Chen, Xiaoming Sun, Mary Beth Fisk, Randal Skidgel, Mark Holterman, Bellur Prabhakar and Theodore Mazzone; BMC Medicine 2012, 10:3, published online 10 January 2012; DOI:10.1186/1741- 7015-10-3.

http://www.reuters.com/article/2007/06/25/us-diabetes-cordblood-idUSN2528805620070625

http://care.diabetesjournals.org/content/32/11/2138.full
Diabetes Care. 2009.

http://care.diabetesjournals.org/content/32/11/2138
November 2009; 32(11): 2138-2139. doi: 10.2337/dc09-1456.

http://www.ncbi.nlm.nih.gov/pubmed?cmd=search&db=PubMed&term=+Bleich+D%255Bauth%255D
PMCID: PMC2768207 Umbilical Cord Blood and Type 1 Diabetes A road ahead or dead end? David Bleich, MD.

http://www.nature.com/nri/journal/v8/n9/abs/nri2395.html

http://www.ncbi.nlm.nih.gov/pubmed/23154532
Long-term effects of the implantation of Wharton's jelly-derived mesenchymal stem cells from the umbilical cord for newly-onset type 1 diabetes mellitus. Hu J, Yu X, Wang Z et al Endocrj Nov 2012 doi: 10.1507/endocrj. EJ12-0343.

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