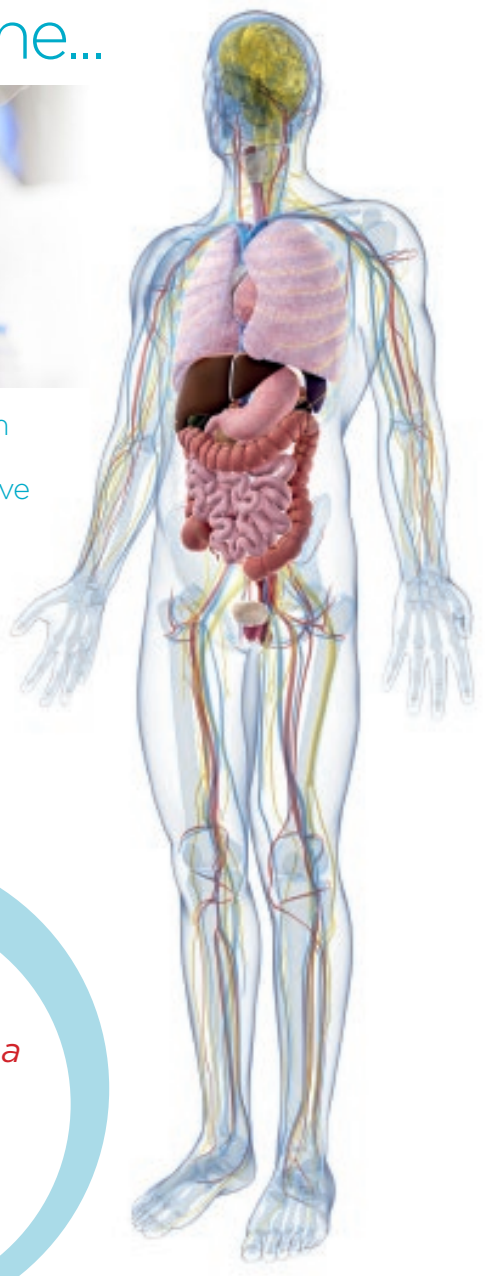
Cells4Life
the experts in stem cell processing

Clinical update

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

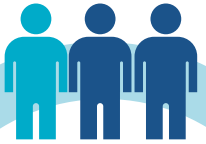
Welcome to the future of medicine...



Despite an early focus on blood stem cell transplant therapies, there has been a clear shift towards regenerative medicine in recent years.

It is now currently estimated that 1 in 3 people will benefit from a regenerative therapy 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.

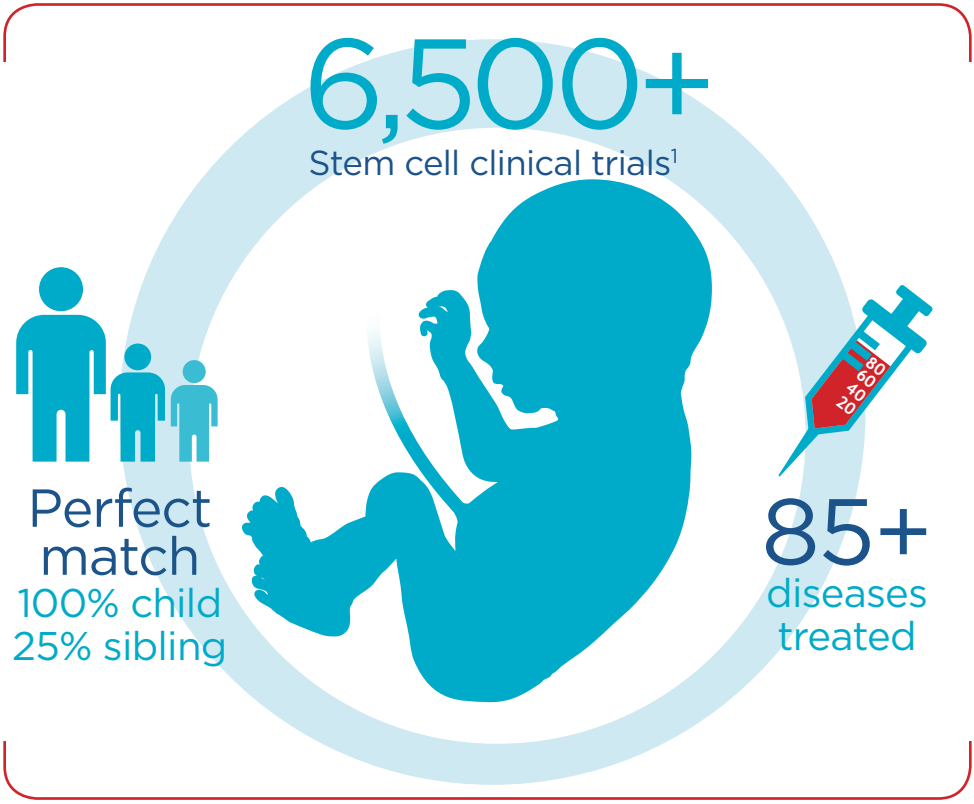
(Expert Opin Biol Ther. 2007 Sep;1311-22. The potential of cord blood stem cells for use in regenerative medicine. Harris DT, Badowski M, Ahmad N, Gaballa MA)



"1 in 3 people will benefit from a regenerative therapy in their lifetime"

Ref: Harris, 2007

Cord Blood Banking



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 needing a regenerative therapy in a lifetime[3]
- Sample can only be used by the child or their family

(1) www.clinicaltrials.gov

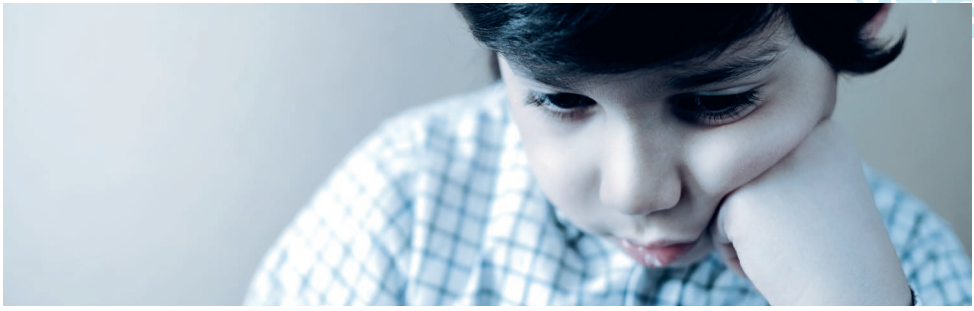
(2) Nietfel, JJ et al., Biol. Blood and Marrow Trans. 2008; 14:316-322

(3) Expert Opin Biol Ther. 2007 Sep;1311-22. Harris DT, Badowski M, Ahmad N, Gaballa MA.

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 affects a person's social interaction, communication skills, interests and behaviour.

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

There is currently no cure for autism. A trial by the Sutter Neuroscience Institute in Sacramento, California staged a small-scale trial based on the idea that autism is linked with a dysfunctional immune system, which may delay – or damage – the nervous system.

Researchers reported improvements in children's socialization and language skills, as stem cells had modulated inflammatory responses in the brain.

Another cord blood trial at Duke University, North Carolina noted 'significant improvements' in patients' vocabulary, social communication skills and eye tracking.

Releases

Cells4Life has released three stem cell samples for the treatment of autism since 2017.

Summary

Cord blood stem cells can, and have, been used to successfully treat and improve the symptoms of autistic children, further data is required to determine the levels of improvement that can be achieved.

Related links

http://bjp.rcpsych.org/content/194/6/500.abstract

http://aut.sagepub.com/content/13/3/317.abstract

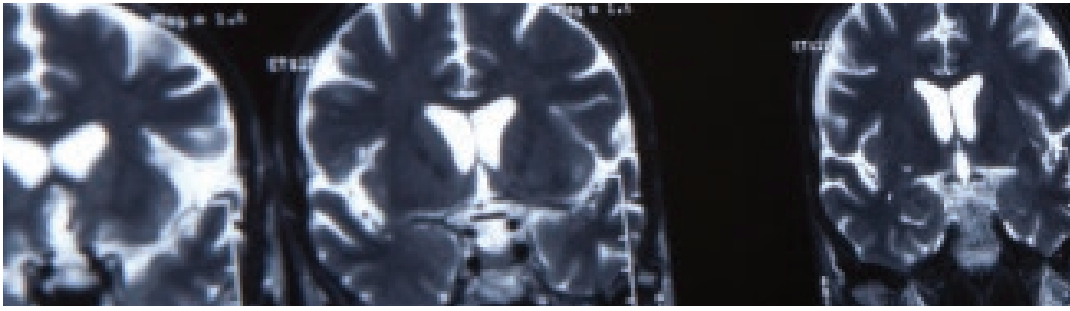
http://www.checksutterfirst.org/neuro/autism

https://news.sutterhealth.org/2018/02/07/cord-blood-stem-cell-study-shows-promise-autism/

https://edition.cnn.com/2017/04/05/health/autism-cord-blood-stem-cells-duke-study/index.html

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.

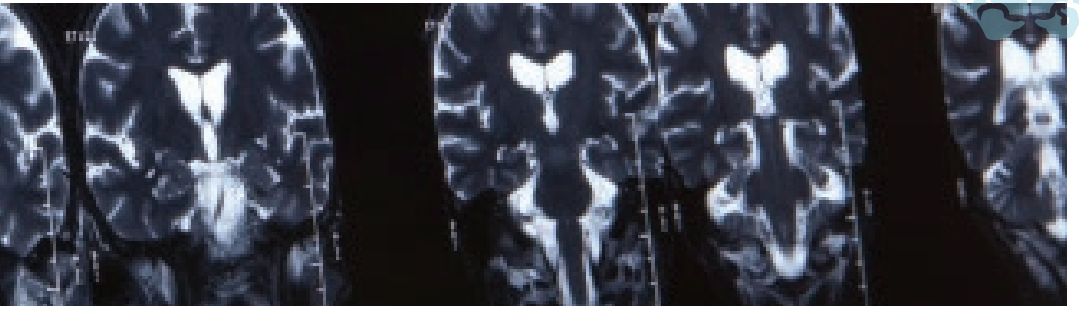
Clinical trials

There are currently 34 clinical trials investigating the use of cord blood as a treatment for cerebral injury, and 55 investigating stem cell uses.

Some focus on the use of allogeneic cord blood to address the fact that few children have their own cord blood saved at 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.

Research increasingly suggests that cord blood stem cells have the ability to pass through the brain's protective barriers. Once in the brain, they appear to promote healing thanks to their anti-inflammatory properties, growth factors and circulation boosters. They home directly to the damaged area and work to improve blood flow, and regrow blood vessels.

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

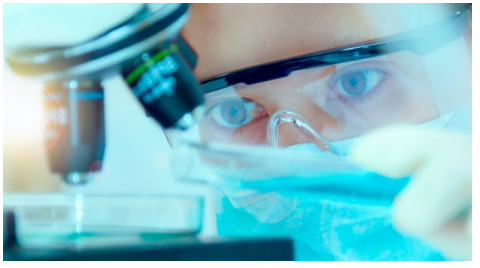
The clinical trials mentioned are based on strong animal model data, in which the intravenous transfusion of cord blood to rats shows significant improvement in motor and neurological skills. This study also showed the cells migrated to the area of injury and expressed specific neurological markers.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

Releases

Cells4Life has released four samples since 2012 for the treatment of cerebral injuries.

Summary

Cerebral injury research has many parallels with stroke research, as the causes are lack of oxygen to the brain which results 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

http://clinicaltrials.gov/ct2results?term=cord+blood+brain+injury&Search=Search

http://www.ncbi.nlm.nih.gov/pubmed/12075993

Cell Transplant. 2002;11(3):275-81. Intravenous administration of human umbilical cord blood reduces neurological deficit in the rat after traumatic brain injury. Lu D, Sanberg PR, Mahmood A, Li Y, Wang L, Sanchez-Ramos J, Chopp M.

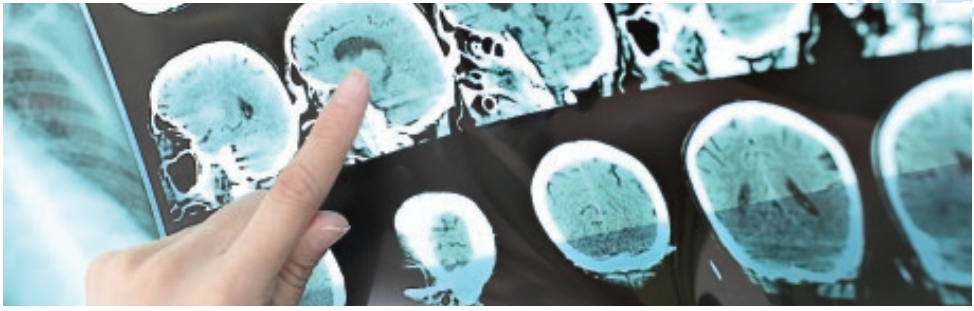
http://www.ncbi.nlm.nih.gov/pubmed/22964590

Bone Marrow Transplant. 2012 Sep 10. doi: 10.1038/bmt.2012.169. Rescuing the neonatal brain from hypoxic injury with autologous cord blood. Liao Y, Cotten M, Tan S, Kurtzberg J, Cairo MS.

http://www.sciencedaily.com releases/2012/05/120524092220.htm

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.

Clinical trials

Scientists at Duke University, North Carolina are testing the effect of cord blood on sufferers of adult ischemic stroke. 1000 patients between 18-90 will undergo transfusions within 3-10 days of stroke. Limited early results show that patients recovered motor function and speech ability.
A 2016 study at Stanford University School of Medicine previously studied the impact of injecting stem cells into the brain. Patients all reported improved motor function, and some even regained the ability to talk and walk again.

Summary

Cord blood treatments are promising for sufferers of adult stroke. Mesenchymal stem cells have been show to aid recovery on a small scale, with more trials in the pipeline.

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

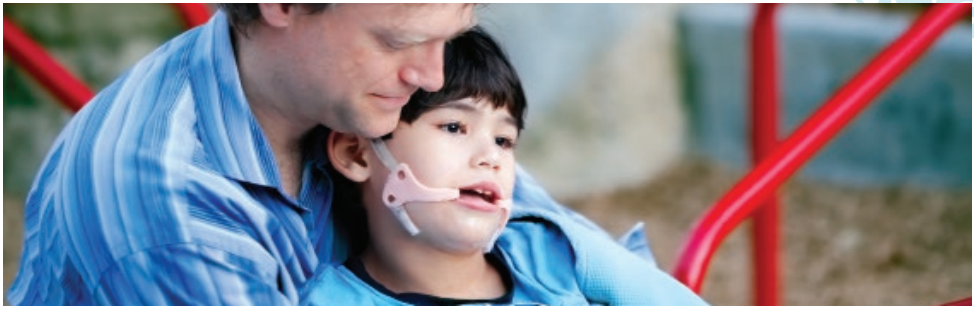
Economic burden of stroke in England Division of health and social care research Saka et al.

https://www.ncbi.nlm.nih.gov/pubmed/29752869

https://med.stanford.edu/neurology/divisions/stroke/recovery.html

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 19 clinical trials listed using cord blood for the treatment of cerebral palsy.

One of the most prominent stem cell trials is taking place at Duke University, North Carolina under the guidance of Dr. Joanne Kurtzberg. Patients with cerebral palsy receive several cord blood transfusions and so far, results show key improvements in their cognitive function, behavior and social skills.

Releases

In 2018, Cells4Life released our first cord blood sample for the treatment of cerebral palsy.

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

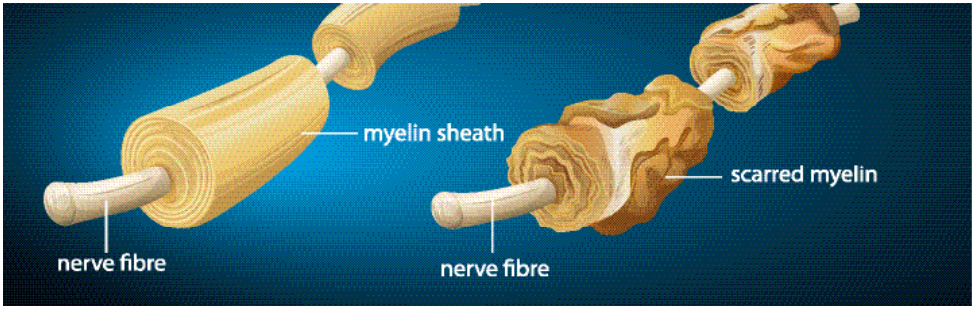
http://www.publications.parliament.uk/pa/ld200809/ldhansrd/text/91104-gc0003.htm#091104114000035

http://onlinelibrary.wiley.com/doi/10.1002/ana.22518/abstract

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.

Multiple Sclerosis

Neurological | Umbilical Cord Blood



Multiple sclerosis (MS) is an autoimmune response that destroys the myelin sheath, which 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

There are currently 193 clinical trials investigating stem cell applications for MS.

A recent international study suggested that stem cells could halt MS. Doctors depleted patients' immune systems using chemotherapy, before rebuilding them with a stem cell transplant. In a test of 50 people, the transplant failed in just 6% of patients.

A similar preliminary study in the Journal of American Medical Association took haematopoietic stem cells and replaced patients' immune systems. Results showed 80% of patients remained free of symptom flare-ups.

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 that may halt or reverse the condition.

Related links

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

http://www.nhs.uk/conditions/Multiple-sclerosis/Pages/Introduction.aspx

http://www.nice.org.uk/nicemedia/live/10930/46699/46699.pdf

http://www.ncbi.nlm.nih.gov/pubmed/15905186

Blood. 2005 Sep 1;106(5):1755-61. Epub 2005 May 19. Mesenchymal stem cells ameliorate experimental autoimmune encephalomyelitis inducing T-cell anergy. Zappia E, Casazza S, Pedemonte E, Benvenuto F, Bonanni I, Gerdoni E, Giunti D, Ceravolo A, Cazzanti F, Frassoni F, Mancardi G, Uccelli A.

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Lancet Neurol. 2011 Jul;10(7):649-56. Mesenchymal stem cells for the treatment of multiple sclerosis and other neurological diseases. Uccelli A, Laroni A, Freedman MS.

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Exp Neurol. 2005 Sep;195(1):16-26. Human bone marrow stromal cell treatment improves neurological functional recovery in EAE mice. Zhang J, Li Y, Chen J, Cui Y, Lu M, Elias SB, Mitchell JB, Hammill L, Vanguri P, Chopp M.

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Arch Neurol. 2008 Jun;65(6):753-61. Neuroprotection and immunomodulation with mesenchymal stem cells in chronic experimental autoimmune encephalomyelitis. Kassis I, Grigoriadis N, Gowda-Kurkalli B, Mizrachi-Kol R, Ben-Hur T, Slavin S, Abramsky O, Karussis D.

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Nat Neurosci. 2012 Jun;15(6):862-70. Hepatocyte growth factor mediates mesenchymal stem cell-induced recovery in multiple sclerosis models. Bai L, Lennon DP, Caplan AI, DeChant A, Hecker J, Kranso J, Zaremba A, Miller RH.

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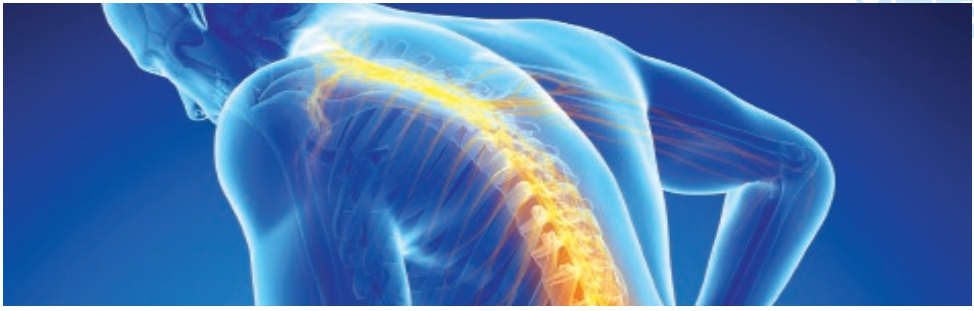
Stem Cells. 2006 Feb;24(2):386-98. Role for interferon-gamma in the immunomodulatory activity of human bone marrow mesenchymal stem cells. Krampera M, Cosmi L, Angeli R, Pasini A, Liotta F, Andreini A, Santarlasci V, Mazzinghi B, Pizzolo G, Vinante F, Romagnani P, Maggi E, Romagnani S, Annunziato F.

http://www.ncbi.nlm.nih.gov/pubmed/22236384

Lancet Neurol. 2012 Feb;11(2):150-6. Autologous mesenchymal stem cells for the treatment of secondary progressive multiple sclerosis: an open-label phase 2a proof-of-concept study. Connick P, Kolappan M, Crawley C, Webber DJ, Patani R, Michell AW, Du MQ, Luan SL, Altmann DR, Thompson AJ, Compston A, Scott MA, Miller DH, Chandran S.

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

Clinical trials focus on three main approaches; first, to bridge the injury so that axons, which are part of nerve cells, can regenerate; second, to replace lost myelin, which is a protein that helps communicate nerve cell impulses; and third, to protect the cord from spreading damage after injury.

There are 31 clinical trials using mesenchymal stem cells to treat spinal cord injuries. The hope is that they can re-establish some circuitries within the nervous system.

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.

Related links

http://www.ncbi.nlm.nih.gov/pubmed/16162459
Cytotherapy. 2005;7(4):368-73.

A 37-year-old spinal cord-injured female patient, transplanted of multipotent stem cells from human UC blood, with improved sensory perception and mobility, both functionally and morphologically: a case study. Kang KS, Kim SW, Oh YH, Yu JW, Kim KY, Park HK, Song CH, Han H.

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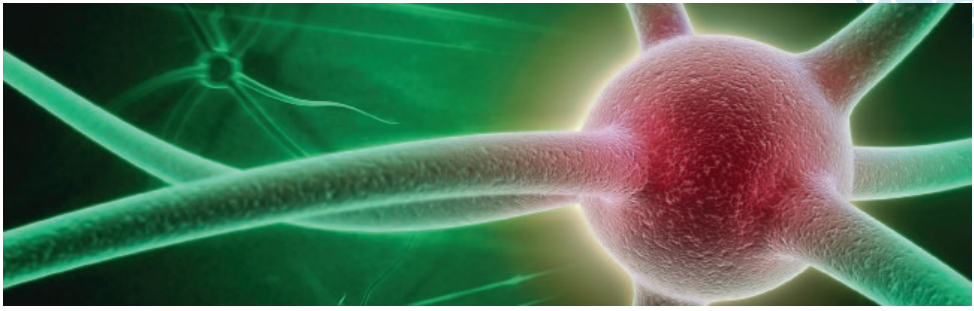
Huntington's Disease

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.

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.

A small-scale study showed that human umbilical cord cells could increase the life span of mice with Huntington's disease. They also reduced the rate of weight loss in subjects.

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

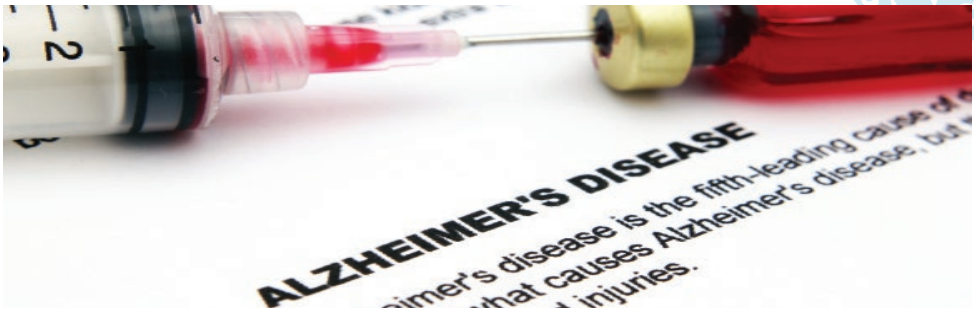
http://jrsm.rsmjournals.com/content/98/12/550.full

http://www.news.wisc.edu/20451

http://www.hdsa.org/research/stemcells/stemcelloverview.html

Alzheimer's

Neurological | Umbilical Cord Blood, 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. It is the leading cause of death in England & Wales (11.6% of deaths).

Clinical trials

There are four current clinical trials using cord blood treatments for Alzheimer's disease.

Scientists in Japan are treating the condition in trial stages by transplanting mesenchymal stem cells from patients' fat tissue to the blood stream. Results offer hope of an eventual cure.

Induced pluripotent stem cells (iPS) are playing a crucial role in research. Doctors are reprogramming the stem cells of patients with Alzheimer's, and then creating neurons to study the disease and how it forms.

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

Summary

Cord blood could be a viable and potent candidate for therapies and treatments for Alzheimer's patients in the near future. The work done by scientists in Japan offers real hope of a cure.

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.

Clinical trials

Previously, stem cell research for Parkinson's was limited to understanding the disease. Now, however, it represents a promising treatment option.

In Kyoto, induced pluripotent stem cells are being used to create dopaminergic progenitors. These are injected into a region of the brain called the putamen, which is linked with the neural degeneration typical of patients with the condition. The progenitors develop into neurons, and the neurons release new dopamine.

The exact mechanism to ensure these cells are retained and successfully integrated into the brain is still being investigated.

Summary

At present no treatments are available for this disease and stem cells do not offer a cure. They do, however, represent the possibility of a more effective therapy than is currently available.

Related links

http://www.ncbi.nlm.nih.gov/pubmed/21235405.

J Med Econ. 2011;14(1):130-9. The economic burden of advanced Parkinson's disease: an analysis of a UK patient dataset. Findley LJ, Wood E, Lowin J, Roeder C, Bergman A, Schifflers M.

http://www.nhs.uk/conditions/Parkinsons-disease/Pages/Introduction.aspx

http://www.parkinsons.org.uk/research/current_research/life_with_parkinsons.aspx

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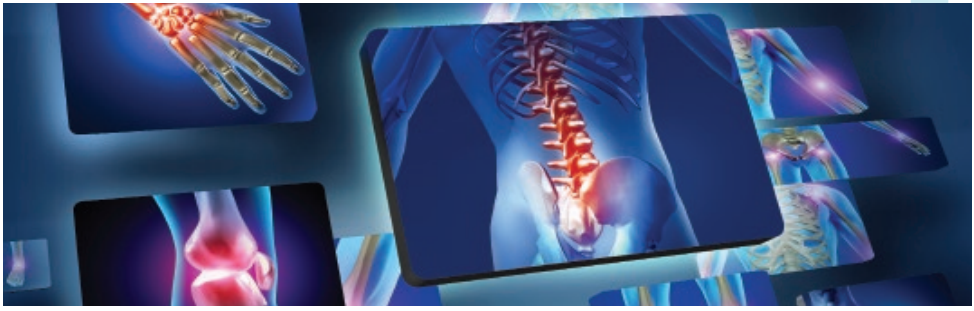
Osteoarthritis

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.

8.75 million people suffer from osteoarthritis in the UK; one third of people over 45 suffer from the condition.

Clinical trials

There are 104 clinical trials exploring stem cells and osteoarthritis. Most of these focus on the anti-inflammatory effect of mesenchymal stem cells MSC. There are also three trials exploring cord blood uses in osteoarthritis cases and in China, a study at Peking University People's Hospital showed that stem cell injections in lab mice reduced inflammation and improved arthritic symptoms.

Summary

It seems highly possible that stem cells offer the opportunity to reverse some of the most serious symptoms of osteoarthritis and even cure the condition.

Related links

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

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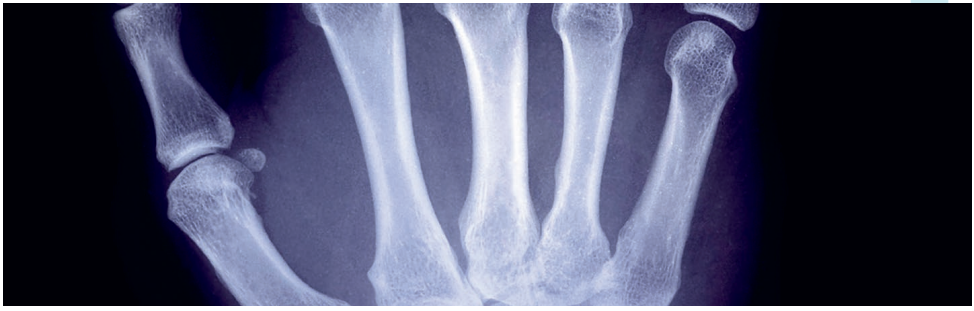
Rheumatoid arthritis

Skeletal Disease/Injury | Umbilical Cord Blood, Adipose



Rheumatoid arthritis is an autoimmune condition affecting the joints and caused by inflammation. Patients with rheumatoid arthritis suffer from cartilage degradation because their immune system generates a faulty response.

This response affects various parts of the body, such as the collagen that keeps cartilage healthy. The triggers for this are thought to be a combination of genetics and environmental factors. Oestrogen is also thought to be involved.An estimated 400,000 people in the UK live with rheumatoid arthritis.

Clinical trials

There are currently 23 registered trials using stem cells to treat rheumatoid arthritis.

In Panama, rheumatoid arthritis is treated with local injections direct to the site of the affected joint. Case studies suggest that stem cells have completely restored joints to full health.

Animal studies

A significant study showed that treatment using umbilical cord-derived stem cells was successful in mice.

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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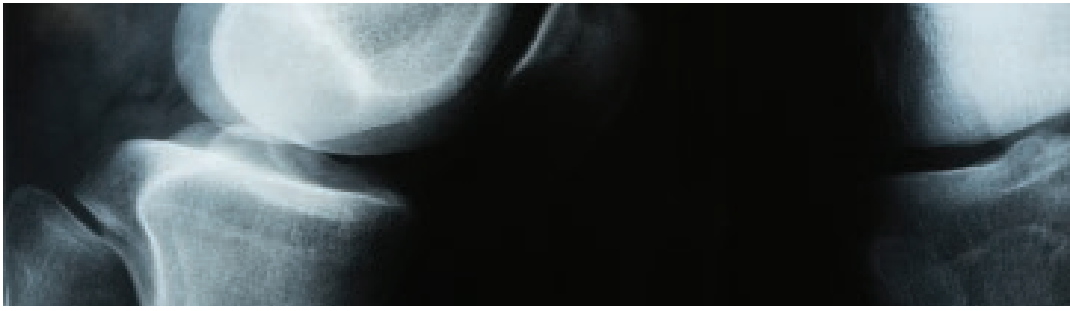
Bone Formation

Skeletal Disease/Injury | Bone Marrow



Breaks in bone can result in an inability to repair normally after 3-6 months, particularly if they are 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 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

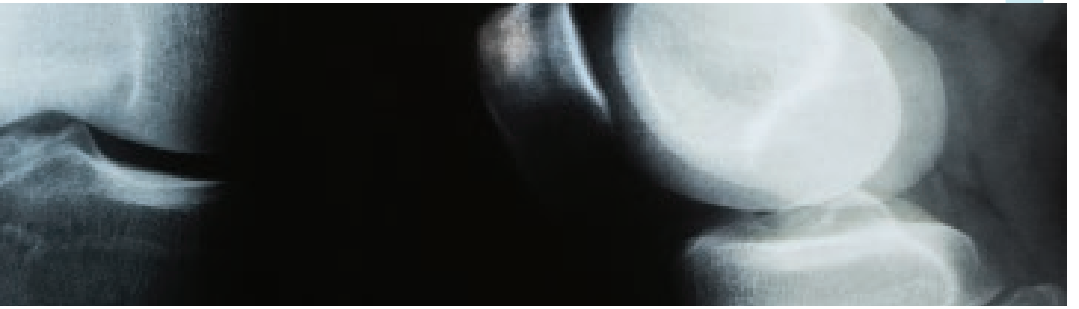
In mice, it has been shown that the addition of bone morphogenetic protein 2 (BMP-2) to human cord blood improves the formation of bone in such injuries. It is thought that this may form part of a clinical trial in the near future. A comparison of embryonic-derived stem cells to cord blood stem cells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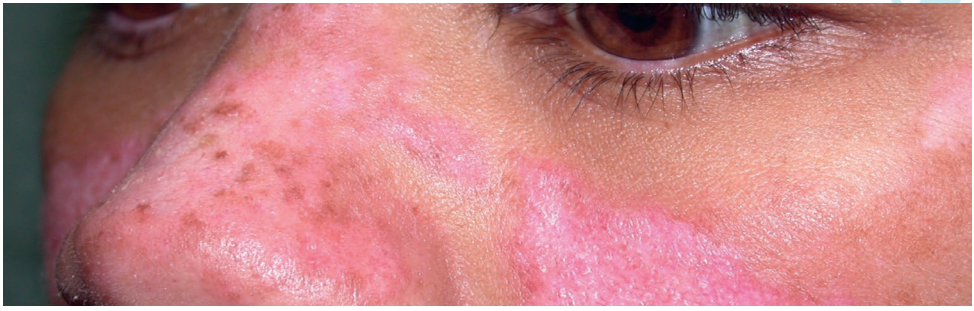
Lupus

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.

Clinical trials

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

However, a recent clinical trial in China suggested that stem cells could dramatically improve quality of life for sufferers of Lupus. 16 patients received umbilical cord stem cell infusions, which caused disease activity to fall significantly after three months. Six patients also saw improvements in associated kidney damage.

Current work investigating the immune-modulatory effect of MSCs in the body – particularly in pro-inflammatory disease models – shows promise for more effective treatment.

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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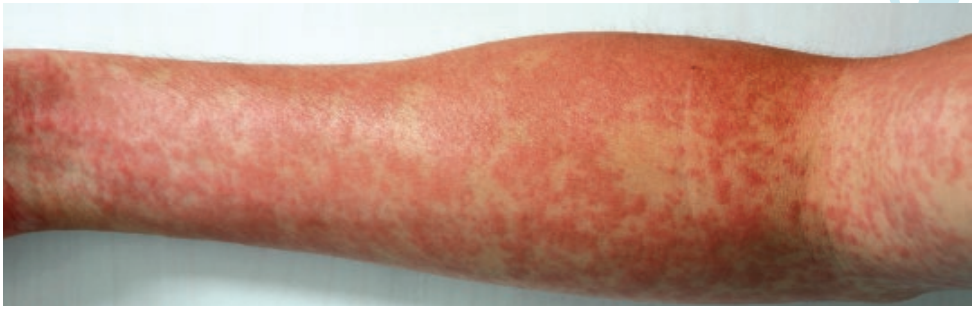
Graft versus Host Disease (GVHD)

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

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. Significantly, transplants of umbilical cord blood come with a very low risk of graft versus host disease. This is because cord blood stem cells are a donor's perfect genetic match.

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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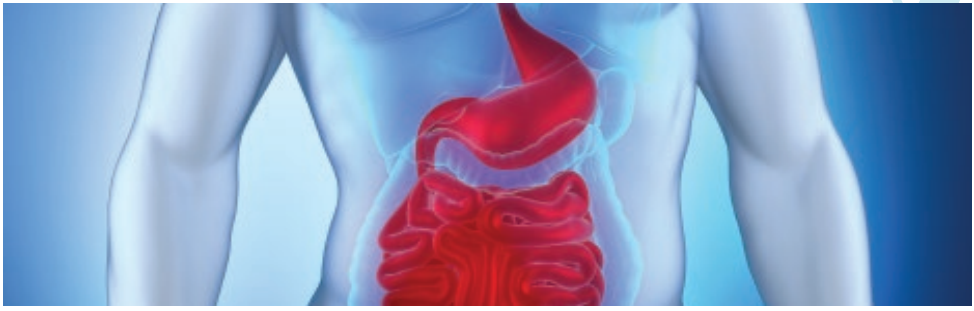
Crohn's Disease

Autoimmune/Inflammatory | Bone Marrow, Peripheral, UCB



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 the prodution of an excessive quantity of Tumour Necrosis Factor (TNF) 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

Currently there is no cure for Crohn's disease but there are 47 studies investigating the application of stem cells. 5 of these include cord blood or tissue.

A trial using adipose-derived stem cells to treat fistulae formed due to Crohn's disease. Cord blood infusions successfully reduced fistulae in 69.2% of patients and for 30% of patients, completely closed them.
Another trial is using stem cells to 'reboot' patients' immune systems. Doctors administer chemotherapy, collect stem cells, and then reintroduce them to create a new immune system.

Finally, in China, a completed trial at Shaanxi Provincial People's Hospital concluded that umbilical cord mesenchymal stem cells are effective for treating Crohn's disease, although there were some mild side effects.

Summary

Several trials have pointed towards stem cells as a key way of significantly reducing the symptoms of Crohn's disease in future.

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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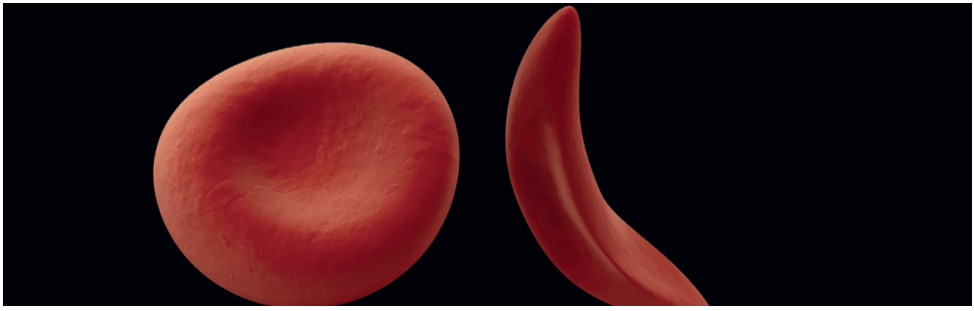
Sickle Cell Disease

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.

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

http://jpubhealth.oxfordjournals.org/content/22/4/500.full.pdf

http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001554/

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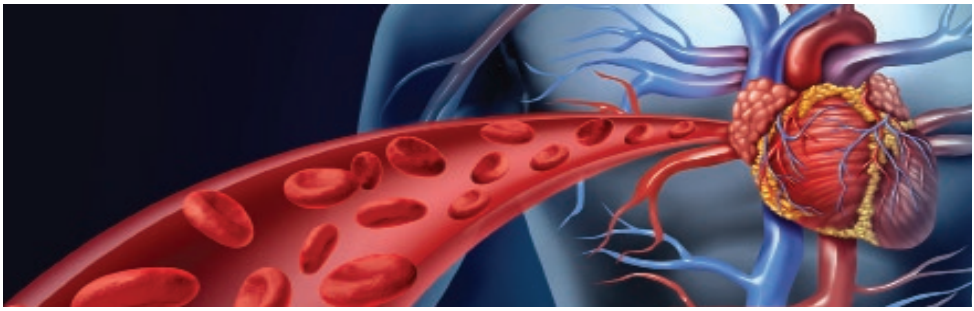
Myocardial Infarction

Heart and Vascular Disease | Bone Marrow, UCB



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

There have been 13 trials to date using cord blood to treat heart disease.

The American Heart Association published results of a study where patients received intravenous infusions of umbilical cord stem cells. Doctors reported a fourfold improvement in the hearts' ability to pump blood, improved quality of life, and no adverse side effects.

At the Children's Hospital Los Angeles, a team injected umbilical cord stem cells into the hearts of babies born with a birth defect called Hypoplastic left heart syndrome (HLHS). The syndrome occurs when babies are born with a defect in the form of the left side of their heart. It is thought that cord blood stem cells could encourage the heart tissue to regrow.

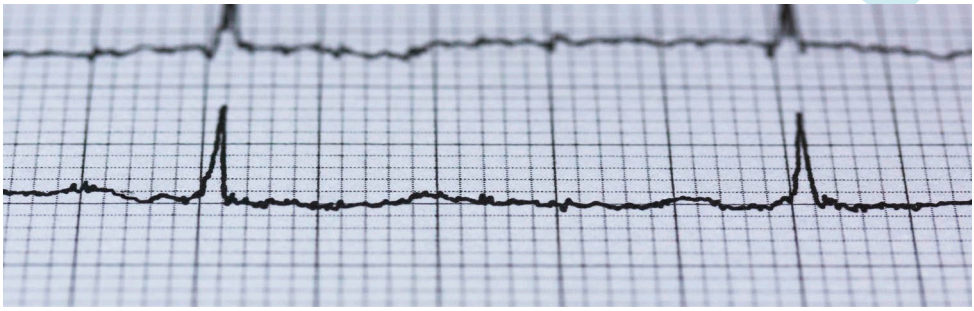
There is also a European-funded project (EU FP7-BAMI) assessing the efficacy of stem cell therapies versus other treatments. This is assessing 33 trials comprising 1,700 patients, with follow up for several years.

Latest developments

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". At the University of Texas, scientists grew an entire heart from stem cells.



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.

Related links

http://www.patient.co.uk/health/myocardial-infarction-heart-attack

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Epidemiology of neonatal encephalopathy and hypoxic–ischaemic encephalopathy Jennifer J. Kurinczuk, Melanie White-Koning, Nadia Badawi.

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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 48 stem cell 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.

Researchers at Harvard have had success with using stem cells to treat type 1 diabetes in mice. The researchers were unable to inject stem cells directly into pancreatic islets because of the fragility of the pancreas; additionally the pancreas releases highly toxic enzymes when manipulated. The team created the HCELL homing molecule to guide the stem cells to the inflamed pancreatic islets in the preclinical trials. The injections were found to create a sustained reversal of diabetes and take away the need to administer insulin for up to two years.

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.

Another trial found that daily insulin injections could be delayed for two-and-a-half years thanks to a stem cell transfusion.

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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