Health-MS

Information for patients

Treatment of Multiple Sclerosis with autologous stem cells derived from bone marrow

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General information

The company

Head office Cells4health is located in a business center among other companies in this historical building.

The history of Cells4Health

Cells4health (C4H) a Dutch company was founded by clinical pharmacologist Dr. C. Kleinbloesem about 2 years ago. During the first year the company started collection and storage of adult stem cells. That included cord blood and bone marrow stem cells. That was for possible use in the future. Just about a year ago C4H expanded its activities by starting to deliver stem cell treatments to patients. This started with treatment of patients with myocardial infarction, peripheral circulation disturbances, neurotrauma like spinal cord injury and neuro degenerative diseases like MS and ALS. In these indications either clinical trials are being conducted, or therapies are already available now.
Nowadays C4H also deliver treatments for MS and ALS patients.

Mission statement of Cells4health

Cells4Health's one major mission is to develop and apply regenerative treatments utilizing the wonderful self healing autologous stem cells already available within the human body, to cure diseases that are not curable by any other means; in this way meeting unfulfilled medical needs.

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic neurological disorder that affects the **central nervous system** (brain and spinal cord). The disease process results in inflammation and damage to **myelin** (insulation for nerve fibers) and other cells within the nervous system. Because myelin aids the conduction of nerve signals, damage to myelin results in impaired nerve signaling and may impair normal sensation, movement, and thinking. This damage occurs in patches that appear as distinct lesions on **magnetic resonance imaging** (**MRI**). The patches cause different symptoms, depending on their location within the nervous system.

Multiple sclerosis primarily affects adults, with an age of onset typically between 20 and 50 years, and is more common in women than in men. The cause of this disorder is not known, but environmental, viral, and genetic factors are thought to play a role.

Symptoms

- Visual disturbances, which may include eye pain, distortion or loss of vision in one eye, or impairment of color perception
- Difficulty walking or performing tasks that require coordination
- Loss of sensation
- Fatigue and/or weakness
- Loss of bowel or bladder control

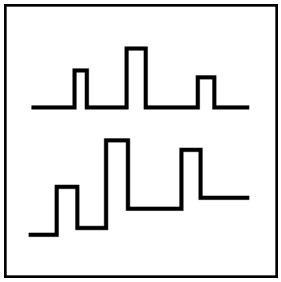
Diagnosis

In addition to a complete medical history and physical examination including a detailed neurological examination, your doctor may order blood tests and refer you to a **neurologist** (a doctor with specialized training in diseases of the nervous system). Your doctor may also order an MRI scan of your head and/or spinal cord to look for the characteristic patches of MS and may perform a **lumbar puncture** ("spinal tap")—sampling of the **cerebrospinal fluid** (the fluid that surrounds the brain and spinal cord)—to analyze for proteins associated with the disease.

Forms of MS

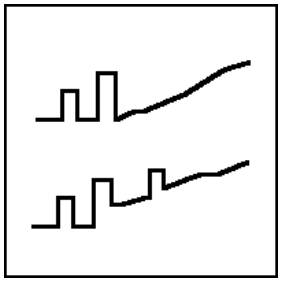
There are four main varieties as defined in an international survey of neurologists *[Lubin and Reingold, 1996]*. (All the graphs show level of disability over time - where two lines appear in the graph it denotes two possible courses of that form of MS.)

1. Relapsing/Remitting (RRMS):



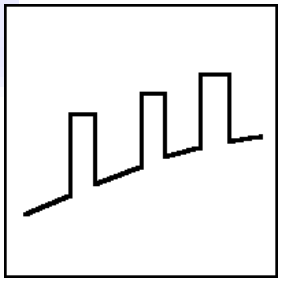
This is characterised by relapses (also known as exacerbations) during which time new symptoms can appear and old ones resurface or worsen. The relapses are followed by periods of remission, during which time the person fully or partially recovers from the deficits acquired during the relapse. Relapses can last for days, weeks or months and recovery can be slow and gradual or almost instantaneous. The vast majority of people presenting with Multiple Sclerosis are first diagnosed with relapsing/remitting. This is typically when they are in their twenties or thirties, though diagnoses much earlier or later are known. Around twice as many women as men present with this variety.

2. Secondary Progressive (SPMS):



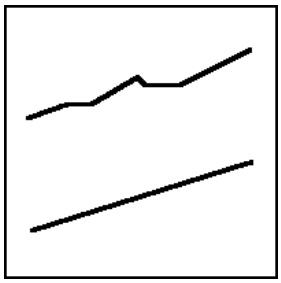
After a number of years many people who have had relapsing/remitting MS will pass into a secondary progressive phase of the disease. This is characterised by a gradual worsening of the disease between relapses. In the early phases of Secondary Progressive, the person may still experience a few relapses but after a while these merge into a general progression. People with secondary progressive may experience good and bad days or weeks, but, apart from some remission following relapsing episodes, no real recovery. After 10 years, 50% of people with relapsing/remitting MS will have developed secondary progressive *[Weinshenker et al, 1989, Runmarker and Andersen, 1993, Minderhoud et al, 1988]*. By 25 to 30 years, that figure will have risen to 90% *[Ref]*.

3. Progressive Relapsing Multiple Sclerosis (PRMS):



This form of MS follows a progressive course from onset, punctuated by relapses. There is significant recovery immediately following a relapse but between relapses there is a gradual worsening of symptoms.

4. Primary Progressive (PPMS):



This type of MS is characterised by a gradual progression of the disease from its onset with no remissions at all. There may be periods of a leveling off of disease activity and,

as with secondary progressive, there may be good and bad days or weeks. PPMS differs from Relapsing/Remitting and Secondary Progressive in that onset is typically in the late thirties or early forties, men are as likely women to develop it and initial disease activity is in the spinal cord and not in the brain. Primary Progressive MS often migrates into the brain, but is less likely to damage brain areas than relapsing/remitting or secondary progressive - for example, people with Primary Progressive are less likely to develop cognitive problems.

Treatment

Currently there is no cure for MS. However, there are treatments available that may slow its progression and alleviate associated symptoms.

- **Drug therapies.** Medications that target the body's immune system may decrease the frequency and duration of attacks. These medications can be used on a long-term basis and also to treat specific attacks. Additional medications may be prescribed for other symptoms such as pain or depression.

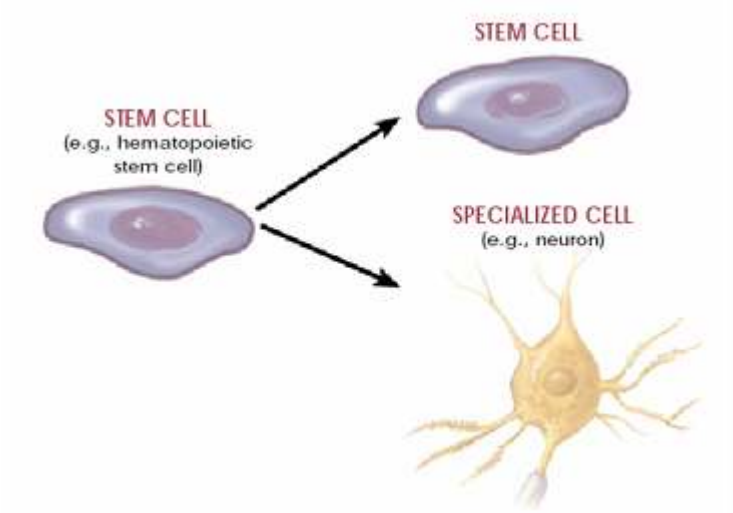
- **Additional therapies.** Because MS may affect the patient's ability to perform self-care and other activities of daily living, treatment may also include referral to specialists for physical and occupational therapy.

At the beginning of the disease there are many such drug treatment options.

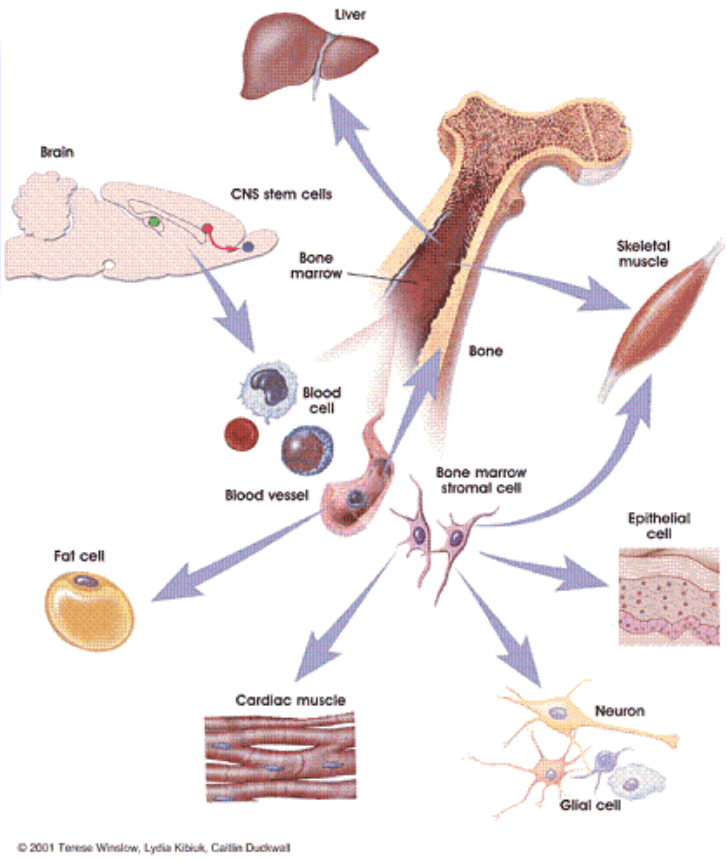
Your neurologist can assist you in finding the right drug therapy for you. Stem cells treatment is indicated where no other treatment options exists anymore. It is not known yet, if in an early phase stem cells can delay the progress of the disease.

About Stem Cells

The discovery of the stem cell had lead to a real revolution in modern medicine. Stem cells are in fact the "smart cells" of our body. The cells move themselves exactly to the place where they are needed and they form themselves exactly the type of tissue what is injured. In this way our body is repaired and continuously new cells and tissues are produced.



Stem cells have the capacity to multiply and to renew themselves almost indefinitely. This in contrast with nerve cells, muscle cells and blood cells. These cells cannot multiply themselves and have a limited life span. Stem cells however can also develop themselves into specialized cells.



In this picture more examples of the development of stem cells are given. Stem cells from the bone marrow can develop into liver, brain, cardiac muscle, nerve, fat and skin tissue.

Source: NIH

The Health-MS procedure: intrathecal administration of autologous stem cells

Introduction
In this document the treatment of MS patients by means of intrathecally administered stem cells is explained.

The procedure consists of the following phases: the qualification phase, the (bone marrow) collection phase, the sample processing phase, the transplantation phase and the follow-up phase.

Objectives

The objective of the treatment is to recover as much as possible the functions lost caused by Multiple Sclerosis (MS).

Type of the treatment: it concerns an autologous stem cells treatment, this means applying the patient's own stem cells, with the purpose to repair damaged cells or to reactivate existing cells.

Method of treatment: the stem cells collected from the bone marrow sample are intrathecally (directly in the spinal canal fluid) administered. The stem cells are at least a few days before the treatment, isolated from the bone marrow sample. The bone marrow sample is collected from the patient's iliac crist (hip bone).

Conditions for eligibility to this treatment

The patient will qualify for this stem cells treatment in the following conditions:

1. The patient has been diagnosed to have MS (see chapter "Description Multiple Sclerosis".
2. The patient has lost functions due to MS.
3. The Cells4health medical team has qualified the patient for treatment based on all information provided.
4. In the bone marrow of the patient must have enough, qualitatively as well as and quantitatively, stem cells. See Qualification phase for more details.
5. There are no alternative treatment available.

Qualification phase

In the qualification phase the specific situation of the patient is investigated to determine if he/she qualifies for the stem cell treatment.

The patient has to provide the required information for the evaluation.

The qualification consists of studying of all available relevant information. Based on that, the medical team appointed to evaluate the situation, will judge if the indication medically seen can be treated with stem cells. During that evaluation also possible complicating factors and alternative treatment by others are considered.

The required information for the evaluation is obtained from:

- ❒ Patient anamnesis.
- ❒ A neurology report about disorder of the patient.
- ❒ All other available relevant information in connection with the illness and disorder.
- ❒ If required, additional inquiry by a member of the medical team.

Optional:

- ❒ A MRI / CT scan of the patient.
- ❒ A MRI / CT report (radiology report).
- ❒ Observation of the physical functions of the patient by our medical team.

Collection phase

Prior to the collection of the bone marrow sample the patient has to fill in the assessment form (see Appendix). In case the patient uses blood diluting medicines, after scheduling the collection and discussing this with his/her physician, the patient has to discontinue using that medicine.

In this stage the patient has to report him/her selves at one of our clinics. The clinic has at that point received the stem cells collection kid.

The physician will collect a sample of about 150-200 ml bone marrow after applying local anesthetics. The collection of the sample is conducted as follows:
After applying local anesthetics a needle is inserted in the ilea crist (hip bone). Several tubes are filled with bone marrow.

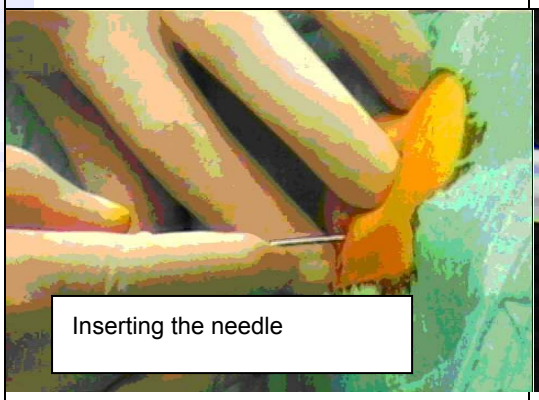
The following photo's show the course of the collection:

Arrival at the clinic

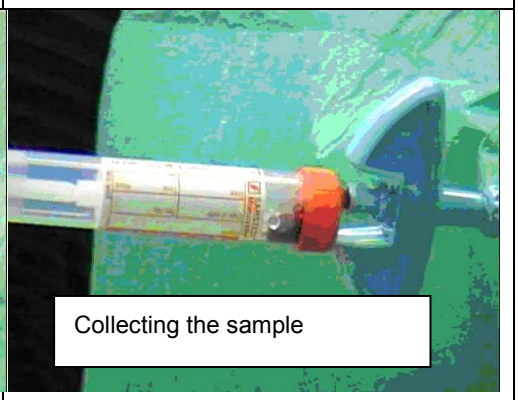
Preparation in the sterile environment

Disinfection of the collection site

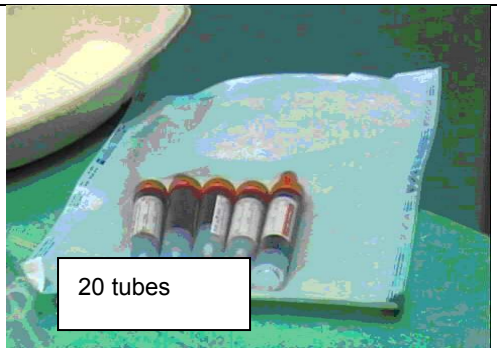
Injection of a local anesthetic



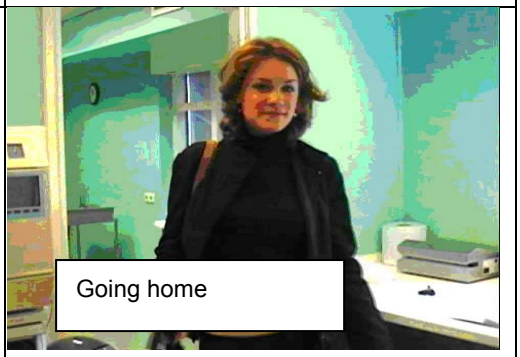
Inserting the needle



Collecting the sample



20 tubes



Going home

The insertion of the needle for the local anesthetic will be a bit painful (comparable with local anesthetic at the dentist). The insertion of the needle in the hip bone will almost not be felt. Up to 3 to 4 days after the collection the patient will feel the spot of the collection being a bit painful. Theoretically, it is possible to get an infection; the probability of getting that is minimized by working in a sterile environment. Normally, there are no side effects; except a "blue spot" for a few days.

The volume of the collected bone marrow is, in comparison to the volume which is used for transplantation for example treating leukemia, small (2 to 5 times less). The bone marrow sample, collected in sterile tubes, will then be transported urgently via courier to the laboratory. The sample must be at the laboratory within 48 hours after the collection.

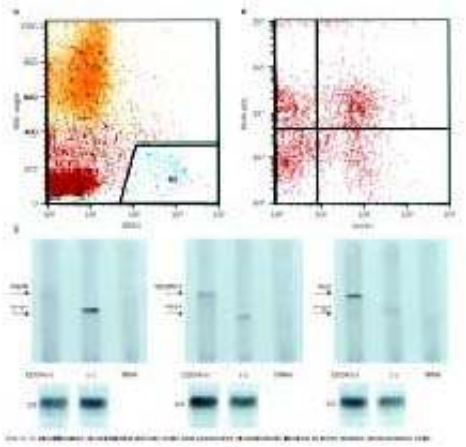
Processing phase

In the laboratory in Plymouth (UK) the samples are processed and tested on quality. The samples are transported to the clean room. The clean rooms are totally sterile and all technicians are wearing sterile cloths.

The processing consists of:

- Isolating the stem cells. In that process the red, the white blood cells and the plasma are separated. The sample is never in contact with the air and thus can not be contaminated.
- Counting the total number of stem cells.
- Measuring the vitality of the stem cells.

After the processing a report is prepared with the results.



The result is considered positive if:

1. There are more than two million (2.000.000) stem cells ($CD34^+$) present.
2. The stem cells present ($CD34^+$ cells) have a vitality higher than 80%.

In case the result is positive the isolated stem cells will be kept in several sterile tubes at minus 196°C in liquid nitrogen.

After the treatment has been planned, the stem cells will be transported in frozen condition to the medical centre via courier. The timing of the delivery of the stem cells is aligned with the treatment date and the treatment location..

Transplantation phase

Intrathecal injection

The patient can have his/her breakfast or lunch, as usual, prior to the transplantation.

The transplantation of the stem cells takes place intrathecally (4mL) as well as intravenously (2 to 4 mL). Via the intrathecal route means that the stem cells are administered by means of an injection directly into the spinal fluid. The physician will apply local anesthetic if needed. The treatment will have a duration of about half an hour. After the treatment the patient will stay in bed for three to four hours for observation. If there are no complications then he/she may return home.

As other minimally invasive medical interventions, also this stem cells therapy has a very small risk for infection. This risk is minimized by working in a sterile environment and having the patient taking an antibiotic prophylactically.

Follow-up phase

After the treatment there is a phone hotline 24 hours available per day for urgent consult and advise if needed.

Adverse events: After the administration of the stem cells the patient could experience nausea, headache, backache, and/or pain in the legs. These adverse events can be intensive but last usually not longer then two to three days.

A member of the medical team will contact the patient a number of times, by phone or email to inquire about the health conditions of the patient and about the result of the treatment. In this phase the patient will, on regular basis, fill in and submit a follow-up form.

The results that might be expected (see also testimonial and video link):

Although we have established that this therapy has been effective in the majority of patients (in more then 80% of the treated patients we see positive effects), Cells4health can neither guarantee the recovery of lost functions, nor the extent of the recovery. Also the duration of the possible recovery is unknown. In most cases the initial effect is observed around the seventh week after the treatment. That includes for example less spasm, less fatigue, increased energy, improvement of the mobility, more sensations, and/or improved bowel / bladder control, easier defecation and improvement in erectile dysfunction. Loss of functions never have been reported.

Costs

The total price for the treatment is € 5,500.-- . This amount covers the following items:

- The collection of the bone marrow sample and the transport of it to the laboratory
- The processing, temporary storage and the transport of the stem cells to the medical centre.
- The administration of the stem cells.
- The costs of the medical centre and administration costs.

The costs are excluding travel expenses and hotel accommodations.

There are no further costs; except for the treatment of complications and a stay at the medical centre would be required.

The total amount is payable after receiving the invoice; the invoice will be sent at least a week before treatment.

In case the bone marrow sample does not have enough stem cells, or the stem cells can not be administered due to medical reasons, then only the costs made up to then will be invoiced. In the situation of not enough stem cells the patient together with cells4health might decide to plan another collection of bone marrow.

Testimonial

The Courier 23 January 2006

Stem cell praise from MS sufferer

By Stefan Morkis

A DUNDEE man who has been living with multiple sclerosis for over 30 years has said his condition has improved significantly since undergoing stem cell treatment.

Sixty-year-old Ian Wood travelled to Brussels in Belgium earlier this month for the revolutionary treatment, provided by cells4health.com, a company that uses stem cell therapy to treat a host of different illnesses ranging from heart defects to spinal problems.

Ian was first diagnosed with MS in 1973 but began exhibiting symptoms four years earlier.

For the past 12 years he has been forced to use a wheelchair but says his balance has already improved since he finished the treatment less than two weeks ago.

"It has been really good and I don't want to pre-empt anything but there has certainly been an improvement and things are coming along," he said yesterday.

"I am able to go for a little walk in the mornings—my balance has improved and it takes much, much less effort than it did before.

"Little things like leaning forward are also much easier and other people have also noticed a difference."

Ian had cells removed from bone marrow in his hip and scientists then took regenerating cells from that and injected them into his spinal column to repair spinal damage.

Despite the fact that using stem cell treatment for MS is still a relatively new science, Ian said that all of the patients who were attending the clinic in Belgium had been optimistic about its potential benefits.

"There was a great atmosphere in the clinic. There were about nine or 10 people going through the treatment and there was a real team spirit," he said.

Although already delighted that some of his symptoms have been alleviated by the treatment, Ian said that he felt it would still be some time before the full benefits became apparent.

Mr Wood said, "I think there is more to come. There is a guy I am in contact with in Holland who also suffers from MS and he felt nothing for a month after the treatment and then he was suddenly able to walk with the help of a stick."

Mr Wood, who attends the Mackinnon Centre in Broughty Ferry, travelled to Belgium with his friend and fellow MS sufferer Moira Ogilvie, who also underwent the treatment.

Although she has not yet seen a significant improvement in her condition, Ian said that the possibilities opened up by stem cell therapy offered hope to MS sufferers.

"It certainly bodes well for the future," he said.

"As it stands there is no treatment for MS available on the health service but this i a ray of hope."

Link to a testimonial on video

http://www.cells4health.nl/video/C4h200511.wmv

Benno

Contact

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