

Bell's palsy Cure using Mesenchymal Stem Cells: A Case Report

Patrick E Sewell Jr * 

President, Regenerative Methods Corporation, North and Central America

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ABSTRACT

Bell's palsy is the most common cause of facial paralysis. The majority of affected patients have complete resolution of symptoms, but a disturbing percentage retain some or all of their neurological deficits. Existing therapies are frustratingly ineffective and decades old. I've had success using Mesenchymal Stem Cells to treat traumatic motor and sensory nerve damage, so I decided to apply that technique to a case of chronic Bell's palsy. The results are very exciting with this patient recovering approximately 95% of his chronic neurological deficits.



Keywords: Mesenchymal Stem Cells • Bell's Palsy • Peripheral Nerve Damage • Nerve Regeneration • Schwaan Cells

*Correspondence:

Patrick E Sewell Jr

drsewell@regenerative-
biologyandmedicine.com

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INTRODUCTION

Bell's palsy is a common cranial neuropathy of unknown etiology accounting for 80% of cases of acute unilateral lower motor neuron facial paralysis. The annual incidence is 1 in every 3000 persons with a lifetime risk of 1 in 60. Bell's palsy can occur at any age, the incidence rises with age, and the median age at onset is 40 years. It has no race or sex predilection. Approximately 71% of persons fully recover within 6 months, while the remaining 29% have partial or complete persistent neurological deficits. Recurrence rates vary between 6% and 15% in published studies [1-3].

The clinical presentation of Bell's palsy is a rapid onset of symptoms progressing over 48 hours. Difficulty moving facial muscles on physical exam is the primary diagnostic test. The electrical conductivity of the facial nerve can be measured by electromyography confirming the diagnosis and quantitating the degree of nerve damage [4]. Partial or complete facial muscle weakness is accompanied by symptoms of dysgeusia, hyperacusis, postauricular pain, facial numbness, and facial pain. With complete paralysis, one sees incomplete eyelid closure and impaired forehead wrinkling. The facial nerve is composed of motor, sensory, and parasympathetic fibers which explains the clinical presentation of muscle weakness or paralysis. The symptoms of altered facial sensations as well as vestibular and pharyngeal dysfunction are a result of connections between the facial nerve and adjacent nerves including cranial nerves 5, 8, 9, and 10. The involvement of the parasympathetic fibers explains the reduction in salivation and lacrimation [2]. Because of facial disfigurement, there are significant psychological complications for patients and their families [2,4]. Patients with chronic facial palsy are at risk of anxiety and social isolation, thus they often benefit from counseling.



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Although the etiology is unknown, there is an association with cold exposure as well as certain viral infections including Lyme disease, herpes simplex virus, varicella-zoster virus, and HSV-1 [5,6]. Other infections are associated with Bell's palsy such as acute otitis media and parotitis [5]. The herpes simplex viral genome is detected in the facial nerve endoneurial fluid in 79% of cases [3]. Immune, infectious, ischemic, and mechanisms resulting in focal edema, demyelination, and cell death are implicated in the pathology [2,4]. Vaccinations are also implicated in Bell's palsy including the various COVID-19 vaccines and the Influenza vaccine [7-9].

Conventional treatment consists of steroids and antiviral medication. Nonpharmacologic therapies include facial exercises, acupuncture, physiotherapy, and neuromuscular retraining. Other measures such as eye protection (sunglasses, eye patches, lubricating tears, or ointments) are routinely used to prevent corneal abrasions, ulceration, and keratitis. Other options for persistent symptoms include facial physiotherapy for weakness, botulinum toxin injections for facial asymmetry, and surgery to facilitate eyelid closure. Recently recurrent Transcranial Magnet Therapy (TCM) has been used to accelerate nerve recovery in Bell's palsy [10].

CASE PRESENTATION

This patient's symptoms started in October of 2011 when the patient had a sudden onset of left facial paralysis and numbness. He sought immediate medical attention and

began oral prednisone within 90 minutes of the appearance of his symptoms. The following day he saw a neurologist who assessed his Bell's palsy as the worst case in his experience. He continued the prednisone and instituted an eye patch for 2 months, and the use of a straw for drinking for 1 year. He began a 20-week course of bland and electrical acupuncture. He had some mild improvement from the acupuncture but exposure to cold and wind resulted in a relapse of symptoms. His clinical course was marked by unpleasant events such as cheek trauma from his teeth. Cold weather, wind, and stress seemed to exacerbate his symptoms. His facial paralysis remained significant for the next 11 years until September 24th, 2022. On that date, I treated the patient with subcutaneous and deep injections of Mesenchymal Stem Cells.

Injection of Mesenchymal Stem Cells was performed using stem cells provided by the REGENELBS Company located in the country of Mexico. The MSCs were injected under ultrasound guidance and injection was performed around the facial nerve just proximal to where it enters the parotid gland as well as the facial nerve branches near the 1st, 2nd, and 3rd divisions of the 5th cranial nerve. A total of 4 treatments were administered over 9 months. The injections were performed using a sterile technique. At each of the 4 injection sites, 10 million Mesenchymal Stem Cells were injected using ultrasound guidance. There were no adverse effects or complications from the injections.

Figure 1 demonstrates an absence of left forehead muscle contraction consistent with near-complete paralysis. Figure

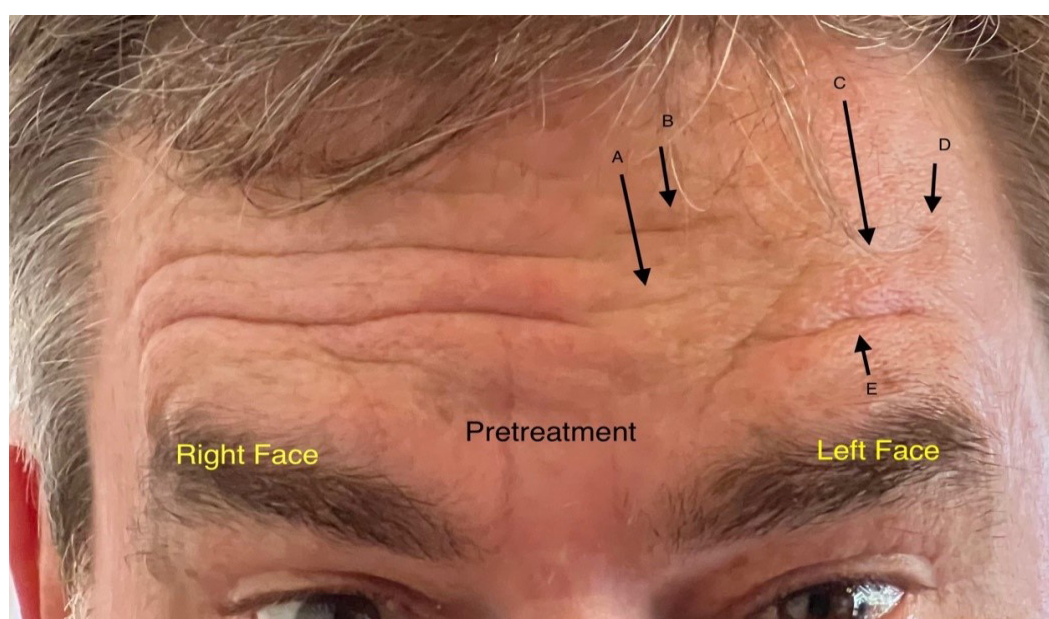


Figure 1: Pre-treatment traditional type photograph (the right side of the photograph is the subject's left side of the face) of the left forehead demonstrates markedly decreased left forehead muscle contraction manifesting as a paucity of forehead creases. The area of decreased muscle contraction is identified by the 5 black arrows labeled A, B, C, D, & E, and should be compared to the normal muscle contraction of the right forehead in this photo.

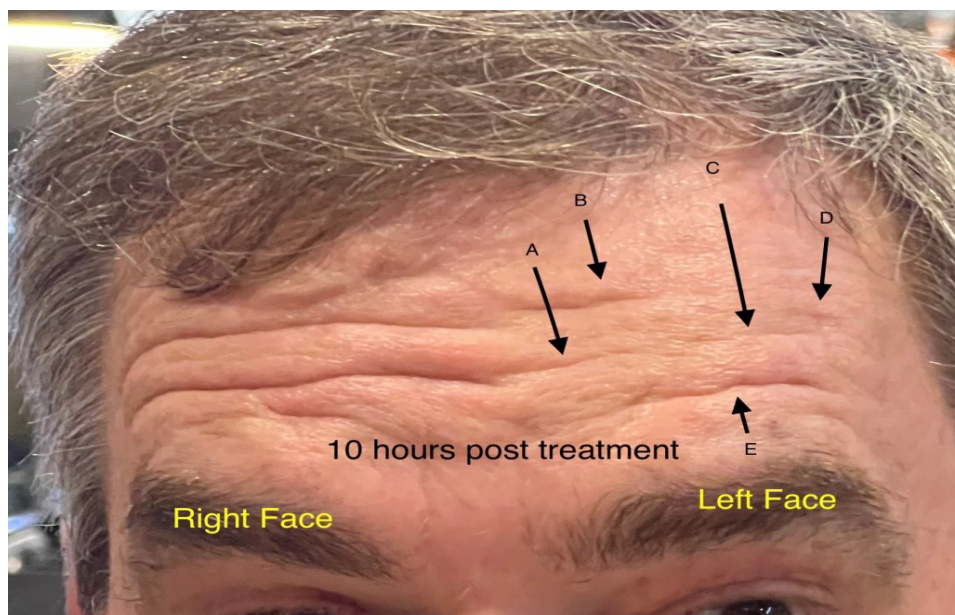


Figure 2: Ten hours after the first injection of stem cells consists of a traditional type photograph (the right side of the photograph is the subject's left side of the face) and demonstrates a visible increase in the left forehead muscle contraction compared to the pre-treatment photograph labeled Figure 1. As in figure 1, the area of decreased muscle contraction is identified by the 5 black arrows labeled A, B, C, D, and E.



Figure 3: Traditional type photograph (the right side of the photograph is the subject's left side of the face) obtained Pre-treatment demonstrates severe left facial muscle paralysis with an asymmetric smile and left eyelid approximation.

2 demonstrates improved contraction of the left forehead muscles 10 hours after the initial injection. Also of note was the reported return of sensation to his face at the 10-hour post-injection mark. His forehead muscle function was visibly improved as demonstrated in Figure 2 when compared to Figure 1.

Figure 3 demonstrates the left deficit in the left facial muscles around the left eye and left mouth facial muscle before injection. Comparison of Figure 3 with Figure 4 of the same area that was obtained at 8 days post-injection and

Figure 5 of the same area that was obtained 287 days post-injection demonstrates progressive improvement of the left facial muscle function used in forming a smile as well as the muscles around the eye.

At the 10-hour post-injection photo, both I and the patient felt he had recovered approximately 75% of his motor and sensory deficit. Three additional injections administered over the next 9 months yielded further improvement in his motor and sensory function. Ultimately, he regained approximately 95% of his motor and sensory function.

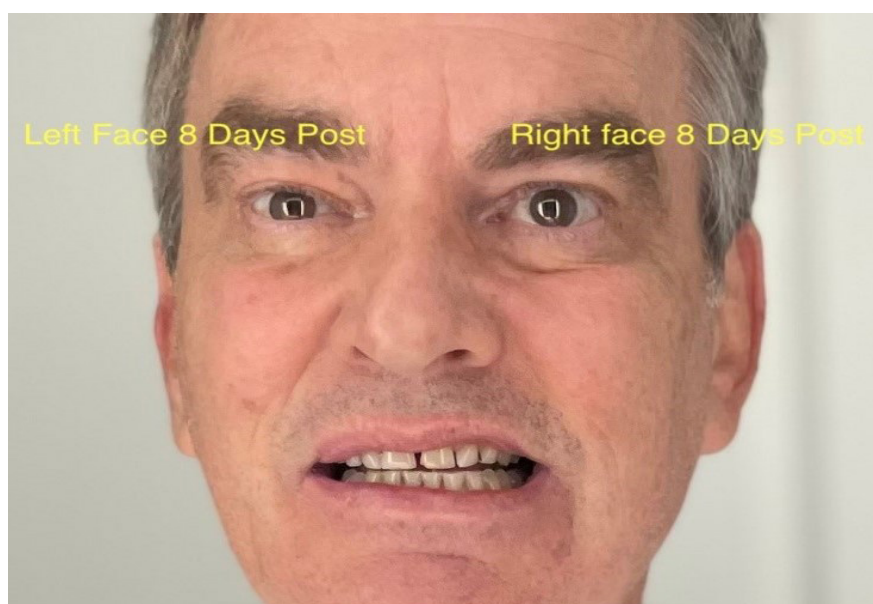


Figure 4: Self-portrait type photograph (the right side of the photograph is the subject's right side of the face) obtained Eight days post-treatment demonstrates a noticeable improvement in left facial muscle function compared to the pre-treatment.



Figure 5: Self-portrait type photograph (the right side of the photograph is the subject's right side of the face) obtained 287 days post-treatment demonstrates significant left facial muscle function with near left and right symmetry.

DISCUSSION

Stem cells are undifferentiated cells of an organism capable of indefinitely generating more cells of the same type as well as differentiating into other types of cells. Stem cells arise from two main sources: Embryos and adult tissues.

Stem cells are classified by their capability to differentiate into other cell types.

- Unipotent stem cells give rise to cells of their type.
- Oligopotent stem cells differentiate into a few cell types.
- Multipotent stem cells differentiate into hematopoietic stem cells.
- Pluripotent stem cells differentiate into almost all cell types.
- Totipotent stem cells give rise to all possible cell types [11].

Stem cells can differentiate into special cells that produce regenerative factors including bioactive molecules, cytokines, special extracellular matrix molecules, special growth factors, trophic molecules, and regulating molecules. These regenerative factors increase cellular plasticity, are neuroprotective, and allow for the differentiation of the stem cells into cells promoting re-myelination [12].

Peripheral nerve injury is characterized by sensory, motor, and autonomic dysfunction. After nerve injury, the Schwann cells proliferate. Macrophage recruitment clears the axonal and myelin debris. Schwann cells produce growth-promoting factors such as glial-derived neurotrophic factor, ciliary neurotrophic factor, neuroregulin 1, and insulin-like growth factor-1 [13]. The injury destroys the integrity of axons and Schwann cells and disrupts the myelin sheath. The myelin sheath is a significant factor in nerve function. A myelin sheath-encased axon has significantly greater conduction velocities compared to a damaged or absent myelin sheath. In the peripheral nerve system, Schwann cells play a pivotal role in the cellular regenerative process regulating the functions of axons as well as the regenerative processes. Schwann cells can dedifferentiate into additional regenerative support cells [13-15].

Regenerative preclinical work with Schwann cells yielded promising results however clinical studies discovered significant difficulties in harvesting and culture of Schwann cells. It was also discovered that prolonged denervated Schwann cells lose their ability to produce growth-promoting factors and stimulate regeneration [11]. A significant drawback of using Schwann cells is the need

to collect cells surgically. Culture and laboratory expansion of Schwann cells is also problematic [15].

Stem cells have been used in place of Schwann cells for central and peripheral nerve regeneration. Unlike Schwann cells, undifferentiated stem cells have a strong expansion capacity. Stem cells are known to differentiate into Schwann-like cells which secrete proteins that promote myelin formation and accelerate axonal growth [14]. Stem cells have significant characteristics that make them well-suited for use in tissue regeneration. Their differentiation potential is multidirectional. They are universally accepted due to their low immunogenicity. Mesenchymal stem cells, which can be derived from adipose tissue, bone marrow, and the umbilical cord, have been shown to address the issues that develop with nerve damage including axonal repair [12,13].

The future direction in peripheral nerve regeneration is the addition of neurotrophic factors which will significantly enhance the neural regenerative properties of stem cells. Some of the most important neurotrophic factors include:

Brain-derived Neurotrophic Factor (BDNF) plays a key role after neural injuries and is shown to have advantageous effects on outgrowing axons.

Nerve Growth Factor (NGF) has also a beneficial effect on the elongation of outgrowing sensory axons in addition to enhancing SCs motility.

- Glial Cell Line-Derived Neurotrophic Factor (GDNF) acts like a chemoattractant for Schwann cells.
- Sox11 is a very important transcription factor upregulating in response to peripheral nerve injury. Its expression can affect myelination, axonal elongation, and levels of BDNF. It also can help with the survival of neurons through the expression of TNF receptor-associated factor-associated NF- κ B activator (TANK).
- Vascular Endothelial Growth Factor (VEGF) can improve outcomes of nerve regeneration through improving microcirculation.
- Insulin-like Growth Factor (IGF) was found to have stimulant effects on mitosis of SCs and axonal elongation [11].

Sir Charles Bell lived in London England from 1774 to 1842 and he was the first to identify the anatomical basis of Bell's palsy. He was the first scientist to study animal facial nerve function. His most famous publication of Bell's palsy was posted in 1828 and involved a man with unilateral facial paralysis secondary to blunt force trauma from a bull resulting in permanent facial paralysis [4]. The treatment

of Bell's palsy was ineffectual at that time. Advances in the study of anatomy and physiology along with the advent of modern pharmaceuticals resulted in the application of steroids for the treatment of Bell's palsy. Despite 200 or so years of treating Bell's palsy, there have been no significant advances in the treatment regimen after the application of steroids. As mentioned previously, the recent use of recurrent transcranial magnetic therapy in a small study suggested this technology yields a more rapid recovery of neurological deficits however there is no evidence at this time that transcranial magnetic therapy can change the incidence of chronic Bell's palsy. More research is needed.

With the recent expansion in the field of regenerative medicine along with the more widely available supply of stem cells comes the opportunity to apply such science and technology to a disease such as Bell's palsy. Given the evidence of neural axon regeneration and remyelination

of nerves from the application of stem cells, I feel neurological disorders such as Bell's palsy will experience a breakthrough in treatment success. This single case is a great starting point. A large number of patients worldwide suffer from chronic Bell's palsy. The wide availability of stem cell technology lends itself to a large patient clinical trial. The results should be evident in a short timeframe and such a trial could revolutionize the treatment of Bell's palsy, as well as other similar diseases.

CONCLUSION

The application of Mesenchymal Stem Cells to the superficial and deep tissues in the distribution of the facial nerve and its branches resulted in the restoration of facial nerve function. Mesenchymal Stem Cells will likely prove to be a significant therapeutic agent in the treatment of chronic Bell's palsy as well as other peripheral nerve injury.

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