

POST-POLIO HEALTH

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Stem Cell Therapy for Post-Polio Syndrome

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The media is abuzz with talk of stem cells, and there is hope of curing diseases, such as Parkinson's and muscular dystrophy, and spinal cord injury, using stem cell technology. What about polio? It was delightful to see a press release from the Salk Institute this spring, which added post-polio syndrome to the list of targets for stem cell therapy.¹

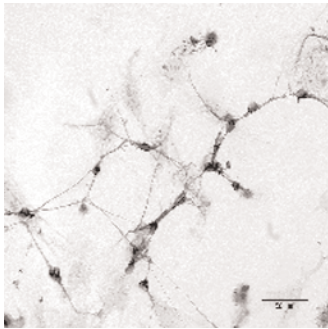


FIGURE 1. Motor neurons produced in the lab from embryonic stem cells. Note the stringy axons and small bushy end fibers.

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A refresher on stem cells

There are two broad types of stem cells with several subtypes:

EMBRYONIC STEM CELLS are derived from the human blastocyst — the result of five days of cell division after sperm and egg fuse into a fertilized egg (zygote). The human blastocyst is a sphere with about 30 stem cells inside, and these cells have many useful properties for therapy. Prodded with chemical messengers, they can develop into most of the cells of the adult body; i.e., they are pluripotent. In a lab dish, they can be maintained, dividing into new stem cells, for more than a year. They could easily be used for production of nerve cells or muscle fibers for post-polio therapy.

However, since the stem cells are not from the patient who will use them, they are easily rejected. This problem can be solved if the stem cells are cloned first by the patient donating a nucleus to a human egg cell and then allowing five days for development until stem cells are evident in the blastocyst. This is called *therapeutic cloning* or nuclear exchange. Therapeutic cloning requires new legislation and is currently not supported in the United States. Further, embryonic stem cells can transform into cancerous cells easier than the second type of stem cell, or adult stem cells.

ADULT STEM CELLS exist in many parts of the body, such as in the bone marrow, brain, blood, muscle, and internal organs. They are difficult to isolate because, in comparison to the tissue they are within, they represent a very small fraction of cells. However, many adult stem cells are pluripotent and can be prodded to develop into muscle, nerve, skin, and a variety of cell types. Because the patients can provide the stem cells for their own therapy, the stem cells are not rejected. Adult stem cells are not as prodigious as embryonic cells and cannot be maintained in the lab as long. Theoretically, as the technology progresses, adult stem cells should be able to serve as cellular material for new nerve cells and skeletal muscle fiber. (See Figure 1.)

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The Research Fund of Post-Polio Health International (PHI)

What? Call for Proposals. **How much?** \$25,000 for 2005.

Deadline? March 1, 2004 for Phase 1. **Decision:** October 15, 2004.

Where? Details at www.post-polio.org or call 314-534-0475.

Some procedures may require embryonic stem cells and others may do better with adult stem cells.² In the United States, there are currently very few samples of embryonic stem cells available, which government grants can fund. The American Medical Association (AMA) recently lobbied to have this reconsidered. No news yet.

Many polio survivors have weak paraspinal and deep muscles that support the spine, which can be very disabling. The spine is destabilized, resulting in impingement on adjacent nerves, which causes pain and new weakness. Because of their close proximity to the spinal cord, these muscles may be enervated by newly grafted motor neurons. These new ideas in remediation of post-polio syndrome should be considered in the context of stem cell therapy.

Challenge for use in old polio

Old polio presents several challenges that are different from the disorders usually discussed as targets for stem cell therapy. For example, in a spinal cord injury there is a loss of cells at the break in the spinal cord — where the body of nerve cells resides. Outside the cord, each cell projects into a long tube, sometimes three feet or more, which ends at a muscle fiber within a muscle. Theoretically, these long tubes, or axons, end with a few branches that connect to the muscle cells. In a spinal cord injury, these fibers and axons within the peripheral muscles usually remain intact. What needs to be done is to connect a new nerve body with the axon already there.


In post-polio syndrome, it is the end branches of the axons that are dying off while the nerve cell itself may continue living or eventually die. If scientists successfully implant new nerve cells in the anterior horn of the spinal cord, can the cells extend axons and connective end branches out through the tissues to a target muscle fiber? In polio, once muscle fibers have lost their nerve connections, they struggle to survive. Muscle fibers typically will atrophy and become non-functional after losing nerve stimulation. Therefore, muscle fibers may also need to be replaced. This is much more difficult than implanting new nerve cells in one place such as in Parkinson's disease or spinal cord injury.

Yet, there are things that can be done. For example, new nerve cells or support cells can be implanted to either fuse into existing weak motor nerve cells or provide protective chemicals for support.³ This would allow existing motor nerves to function longer and possibly even sprout more.

Another approach may be to try to strengthen muscles closer to the spinal cord. Muscles such as the paraspinal or hip muscles, if damaged, can result in more disability than more distant muscles, like the calf. So it may be possible to have a positive impact on muscles at or above the hip, where they cause the most disability if weakened. Regardless, there are several promising approaches, including the use of scaffolding biological materials, such as chondroitin, to guide new nerves to their targets.⁴

Several signaling factors act between stem cells, allowing them to differentiate and grow in the lab or in the body. As stem cell research progresses, more of these growth and differentiation factors for cell specialization, adaptation, and connection should be uncovered.

Recently, a few new cases of polio were reported in African countries free of polio for two years. As health officials prepare to contain the stocks of poliovirus in anticipation of the eradication of acute poliomyelitis, they face several obstacles.

Read more. 

Looking ahead

Imagine a combination of mechanisms (some of which are already known) that can signal motor neurons (nerve cells) to form connections with new muscle fibers. Muscle signaling cell adhesion molecules (CAM) can attract the placement of nerve synapses (connections) to muscle. Without even using stem cells, new derivative cellular chemicals can guide cells to the proper muscle fibers in a trouble area. There are many other possibilities. The only question is how long will it be until effective therapies emerge from stem cell research.

Much of the advancement in stem cell therapies and much of the realization of future promise will come as a result of lab work using model organisms like mice. A model of spinal cord damage, resulting in complete paralysis, has been mitigated in a rat with neurons derived from mouse embryonic stem cells. After treatment, the rat was able to use its hind legs in walking motions where-as prior to treatment it could not.⁵

Rodents can be easily engineered genetically and cloned, without implanted cell rejection. Using a mouse as a polio model (*Polio Network News*, Vol. 18, No. 4), there is a new opportunity to study post-polio rehabilitation with stem cells. The possibility of using this polio mouse model for stem cell studies involving polio is clear, due to the success in using rodents to further the understanding of cell differentiation and the possibilities of stem cell therapy.⁶

The most vexing problem for polio survivors may be the speed at which stem cell therapy advancement occurs. The clock is ticking. If rapid advancement in the use of this technology occurs in the next ten years or so, those who had polio in the '40s and '50s may benefit. If not, these polio survivors may just miss the next milestone in medicine — the ability to regenerate muscle and nerve tissue.

So close to the remedy, and yet so far. ●

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Edward P. Bollenbach (edward.bollenbach@snet.net) received a BA in Biology and an MA in Biology from the State University of New York at New Paltz, New York. In his professional work, he focused on bacteria and fungi, and, as he began to experience polio's late effects, he decided to use his scientific knowledge to clarify information about post-polio syndrome.

He co-authored an article in 2002 with Marcia Falconer, PhD, Ottawa, Ontario, Canada, "Late functional loss in nonparalytic polio," *Am J Phys Med Rehabil*, Jan-Feb, 79(1), 19-23.

