

Research for a Cure in Spinal Cord Injury

WHAT IS RESEARCH

Research is a thorough scholarly or scientific study to discover new knowledge in a subject or provide a new understanding about a known subject matter. Billions of dollars are spent each year in the form of "grants" to conduct research in untold areas of health and wellness. These grants are typically used by universities and organizations throughout the United States (US) to conduct research to gain or advance knowledge in a specific area.

RESEARCH PROCESS

The federal government is the biggest financial resource for research activities. Much of the funding is awarded by federal agencies such as the National Institutes of Health, the Center for Disease Control and Prevention and the National Institute on Disability and Rehabilitation Research, which also funds this information sheet. Typically, these and other agencies release announcements requesting that universities and organizations submit applications to conduct research.

Researchers submit applications for funding. The applications will normally contain a detailed description of the proposed study, a rationale for the need of the study, how the study will be conducted, a budget outline, key personnel, study participants, and anticipated results. Peer-reviewers score the applications, and the best scores are usually funded. The researchers then conduct the studies according to their proposed applications.

Research outcomes are typically published in Peer-Reviewed Journals as a means for researchers to report their findings to other researchers. There are hundreds of journals, and each journal features articles in specific areas of medicine. These articles explain individual study methods and results along with a discussion on the impact of the study. Future researchers read the articles to avoid repeating studies that fail and build upon studies that are successful.

You can search for journal articles at..

...www.ncbi.nlm.nih.gov

...www.medscape.com

...www.medlineplus.gov

In general, the main goal of this research is to contribute to the health and well-being of people. For example, medical professionals read medical journal articles to learn what treatments may or may not work in practice. Their patients, or consumers, benefit when doctors use their new knowledge based on research findings in their practice.

RESEARCH AND SCI

As an individual with spinal cord injury (SCI), you are likely to live a much longer, healthier life because of improvements in medical treatments gained through research. In fact, there have been approximately 20,000 SCI-related articles published in major medical journals over the past 40 years. Some articles report findings from animal research, but most articles report research results on groups of people with SCI or single case reports of individuals with SCI.

UNDERSTANDING RESEARCH RESULTS

It is important to remember that journal articles are intended for professionals. These articles are carefully written to avoid misleading the reader. For example, researchers often use words such as "may result in," "appears to be," and "has the potential to" instead of words like "does result in," "is the cause," and "is associated with." Researchers are careful not to imply direct cause and effect because it is near impossible to positively state that one single factor always result in a specific effect.

On the other hand, most consumers learn about research results through the media by reading articles in newspapers and magazines or watching television. The media will often summarize research results and offer misleading information. For example, a newspaper headline might read "New Drug Treatment

in Fight to Cure Paralysis." This title suggests that the drug is a "cure" for paralysis. However, the actual journal article might read "a new drug *appears to* improve motor movement of paralyzed mice." This statement acknowledges that the drug has a possibility of improving function in mice.

Instead of relying only on the media for information, it is important for consumers to do their own research before drawing a conclusion. Luckily, the Internet makes it much easier to get better informed on topics of interest. If you cannot access the Internet at work or home, you can at your local library. With Internet access you can find information on nearly every topic.

Craig Hospital (www.craighospital.org) offers 3 educational brochures as a guide to understanding research:

- I: Finding the Information You Need
- II: Medical & Research Articles
- III: Those Scary Statistics

ACUTE SCI _____

You might better understand strategies for a cure if you first learn about the spinal cord and what happens to it after injury. The spinal cord is a thick bundle of nerves that carries sensations and messages to and from the brain and the body. The nerves are enclosed

in the spinal canal, a bony passageway that is formed by the holes in the middle of every vertebra. An injury, or damage, to the nerves can affect sensation and movement of the whole body. The spinal cord may be injured if you have an injury to the neck or back that:

- ◆ breaks or dislocates the bones around the spinal cord;
- ◆ penetrates through or between the bones (such as a bullet); or
- ◆ crushes the disks between the bones and pushes them into the spinal canal.

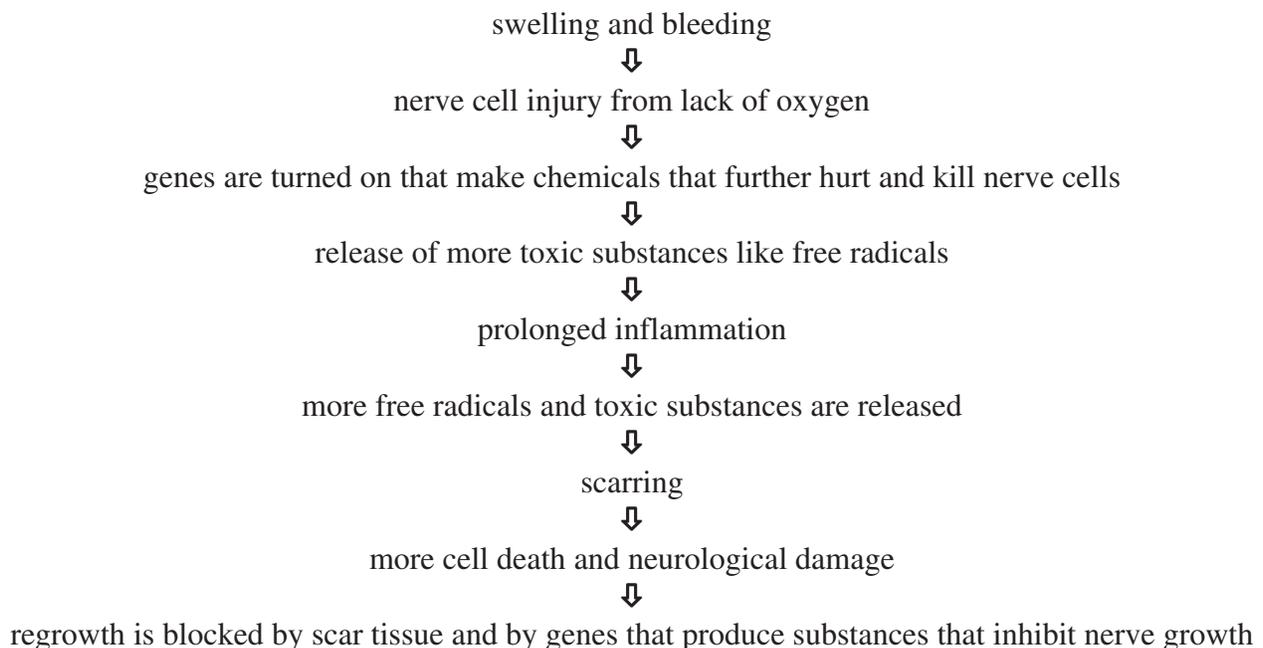
When the spinal cord is injured, a cascade of cellular and molecular events occur inside and around the damaged spinal nerves. This process starts immediately to destroy neurological function and can continue for weeks. This cascade of events (see the box below) essentially occurs in sequence. This damage to nerve cells and blood vessels occurs at first in the center of the spinal cord and spreads outward.

STRATEGIES FOR A CURE _____

The eventual cure for paralysis will likely involve a combination of 4 basic strategies for a cure. These strategies have not changed over the last few years, but notable advances have been made in each area.

1 - Neuro-Protective Agents are used to prevent or minimize the damage immediately after injury along

SEQUENCE OF CELLULAR AND MOLECULAR EVENTS INSIDE AND AROUND THE DAMAGED SPINAL NERVES



with long-term scar formation. The current effort is on developing precise surgical techniques at the injury site to stabilize and decompress the pressure around the spinal cord which allows for delivery of specific drug interventions. The second step is to develop more effective ways to deliver the drug directly to the nerve cells with the goal of improving neurologic outcomes.

To date, Methylprednisolone, GM-1 Ganglioside (Sygen), 4-Aminopyridine (4-AP), and Interleukin-10 have been studied. The use of Methylprednisolone after spinal cord injury is controversial. In general, studies suggest the drug is minimally significant at best. Yet, methylprednisolone continues to be widely used after injury. A multi-center study of Sygen has also shown mixed results. It showed no long-term improvement between non-treatment and treatment groups. However, treatment groups had earlier recovery than did the non-treatment group, but this benefit was only in the short-term. Also, some subgroups had improved recovery. Interleukin-10 and 4-AP offered no improvement in neurologic outcomes. Other drugs currently under investigation include Cyclohexamide, Glutamate (AMPA) Receptor Blockers, BAF, Hypothermia, and Opioid antagonists.

2 - Regeneration centers on manipulating the neural environment to facilitate nerve growth. Possible growth factors include Neurotrophin-3 (NT-3), Brain Derived Neurotrophic Factor (BDNF), acidic Fibroblast Growth Factor (aFGF), and Nerve Growth Factor (NGF). Electrical stimulation, transplant glial or schwann cell grafts may be considered. Regeneration also requires the ability to block the inhibitory processes that prevent spinal nerve growth, which might be accomplished by the Inhibitor-Neutralizing antibody (IN-1 Antibody). Finally, it is necessary to promote correct “connections” on both sides of the injury. This might be accomplished with Olfactory-Ensheathing Glial Cell implants, Growth Cones and Neural Glue, Netrins (substance produced by nerves which forms a structure on which new nerves will grow), and/or Schwann Cell Tubes (allows nerves to grow through the tube to the other side of the injury).

3 - Transplantation is a repair strategy. The four components of transplantation include multiple peripheral nerve bridges, grafted areas with fibrin-based tissue glue, the addition of growth factors (aFGF),

and stabilization of the spine to prevent re-injury. Transplantation types include peripheral nerves, fetal central nervous system tissue, stem cells, and genetic induction (genetic material in the form of viral or plasmid vectors delivers genes into surviving cells in the spinal cord which induce stem cell and neural tissue growth).

4 - Rehabilitation interventions are essential to help people regain and maintain strength, stamina, and balance once function is restored. Today, interventions include bioengineering, computerized, and advanced therapeutic techniques. Functional Electrical Stimulation (FES) is a likely treatment option to improve limb, bladder, bowel and respiratory functions. Other interventions might include surgical techniques to enhance regeneration and axonal sprouting (plasticity) to improve communication between the brain and body.

PARTICIPATING IN RESEARCH _____

Researchers from around the world are recruiting individuals with SCI to participate in clinical trial to determine the effectiveness of various treatments. Whenever you hear about “promising” research, it is very important to consider the source of information before participating. Most US researchers follow strict guidelines designed to protect participants from harm. US researchers also gain credibility for their results by publishing them in peer-reviewed journals. This process helps assure the public that results from research are based on credible evidence. On the other hand, researchers from other countries are not subject to these US standards.

SUMMARY _____

Medical advances made through research suggest that some type of cure is within reach. Right now, remyelination seems to be the simplest repair process to accomplish. It also seems easier to prevent or limit the early injury cascade rather than reverse the damage. In the end, however, a cure will not likely be one simple solution. A combination of treatments is more likely. Until the cure is known, you are encouraged to search the Internet to find answers to your questions and stay informed on ongoing research and outcomes.

SCI RESEARCH RESOURCES _____

ASSOCIATION OF ACADEMIC PHYSIATRIST

Phone: 410-637-8300

Email: aap@physiatry.org

www.physiatry.org

National organization of physiatrists affiliated with medical schools promoting the advancement of teaching and research in PM&R within an academic environment.

ASSOCIATION OF REHABILITATION NURSES

Phone: 800-229-7530

Email: info@rehabnurse.org

www.rehabnurse.org

Promotes professional rehabilitation nursing practice through education, advocacy, collaboration, and research to enhance the quality of life for persons with disability.

CENTER FOR DISEASE CONTROL AND PREVENTION

Phone: 800-CDC-INFO

Email: cdcinfo@cdc.gov

www.cdc.gov

CDC is globally recognized for conducting research and investigations and for its action oriented approach. CDC applies research and findings to improve people's daily lives and responds to health emergencies—something that distinguishes CDC from its peer agencies.

CENTER FOR INTERNATIONAL REHABILITATION RESEARCH INFORMATION AND EXCHANGE

Phone: 716-829-3141 ext.125

Email: ub-cirrie@buffalo.edu

http://cirrie.buffalo.edu/

Facilitate the sharing of information and expertise in rehabilitation research between the U.S. and other countries.

CENTER FOR PARALYSIS RESEARCH

Phone: 765-494-7600

Email: cpr@vet.purdue.edu

www.vet.purdue.edu/cpr

Develops and tests promising methods of treatment for SCI.

CENTER FOR RESEARCH ON WOMEN WITH DISABILITIES

Phone: 800-443-7693

Email: crowd@bcm.edu

www.bcm.tmc.edu/crowd

Promotes, develops, and disseminates information to expand life choices of women with disabilities.

CHRISTOPHER REEVE PARALYSIS FOUNDATION

Phone: 800-225-0292

Email: info@ChristopherReeve.org

www.christopherreeve.org

Funds research to develop effective treatments and a cure for paralysis, and funds quality of life grants for people with SCI.

MODEL SCI SYSTEM DISSEMINATION CENTER

Phone: 800-732-8124

Email: khart@bcm.tmc.edu

www.msdisdisseminationcenter.org

SCI related Abstracts, Books and Chapters, Consumer Journal Articles, E-Journal Articles, Educational Resources and Other Publications.

NATIONAL CENTER FOR THE DISSEMINATION OF DISABILITY RESEARCH

Phone: 800-266-1832

Email: NCDDR@sedl.org

www.ncddr.org

Conducts research activities that are designed to collect information that will assist in identifying the needs and most likely strategies that will assist in matching dissemination practices with intended user groups.

NATIONAL INSTITUTE ON DISABILITY AND REHABILITATION RESEARCH

Phone: 202-245-7640

www.ed.gov/about/offices/list/osers/nidrr/index.html

Conducts programs of research and related activities to maximize the full inclusion, social integration, employment, and independent living of individuals with disabilities.

NATIONAL INSTITUTES OF HEALTH

Phone: 301-496-4000

Email: NIHinfo@od.nih.gov

www.nih.gov

Grants news, applications, grants policy, NIH Guide, award data, eRA Commons, research training, research contracts, loan repayment programs, Small Business Research Programs.

NATIONAL REHABILITATION INFORMATION CENTER

Phone: 800-346-2742

Email: naricinfo@heitechservices.com

www.naric.com

Collects and disseminates the results of federally funded research projects via commercially published books, journal articles, and audiovisuals.

PARALYZED VETERANS OF AMERICA

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Email: info@pva.org

www.pva.org

The PVA is devoted to maximizing the quality of life for people with SCI/D through the PVA Research Foundation.

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