Stem Cell Research: An Overview

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In the last few months, stem cell research has been brought into the spotlight by the presidential campaign as well as by the passing of Christopher Reeve, a leading advocate for increased funding of stem cell research. Stem cell research and therapy hold promise for treatment and/or cure of a wide range of diseases and conditions that affect millions of people.

What are stem cells?

Stem cells are known as the “building blocks” of life that give rise to different kinds of tissues or other cells in the body. They are of particular value because they are self renewing in the body, and large quantities of stem cells can be reproduced in the laboratory. Scientists can isolate, manipulate and regenerate these cells to be transplanted in the body’s organs to replace or repair damaged or dead cells.

Scientists primarily work with two kinds of stem cells: adult stem and embryonic stem cells. These cells come from both animals and humans.

Adult stem cells renew themselves continuously in some organs of the body. These cells have historically been used with success in the treatment of some diseases. For example, bone marrow stem cells are used to replace the blood cells of patients with leukemia and other cancers.

Although there has been some success with the use of adult stem cells to treat disease, there are some significant limitations. Adult stem cells are present in very small quantities, isolating them is difficult, multiplying them outside the body has not yet been possible in most cases, and they may only be able to develop into a limited number of cell types. The general consensus is that adult stem cells are less versatile and valuable than embryonic stem cells.

Embryonic stem cells are found in embryos 5 or 6 days after fertilization when the embryo becomes a hollow sphere called a “blastocyst.” Stem cells are removed from the blastocyst and placed into a culture dish to produce a stem cell “line.” Embryonic stem cells have the versatility and potential to become almost any type of cell or tissue and they are easy to isolate and grow in laboratories.

Stem Cell Research

Many scientists are conducting research to uncover the potential benefits of stem cells. Research conducted over the last 20 years on embryonic cells transplanted from animals has provided some important scientific breakthroughs. Research on human embryonic stem cells has only recently become available. Embryonic stem cells seem to provide the best promise for regenerating dead or damaged cells. Specifically, research on embryonic stem cells might lead to cures for cancer, Parkinson’s disease, and even spinal cord injury.

Another potential benefit of research involves the nuclear transplantation of...
stem cells. This technique involves the process of replacing the DNA of an unfertilized egg cell with the DNA from a person’s somatic cell, and then triggering the egg to divide to form a blastocyst. The stem cell that would be derived from such a blastocyst would thus contain the patient’s own DNA. This technique would genetically match stem cells to a person’s DNA, replace or repair damaged tissue, and avoid the often-common result of tissue incompatibility and the body’s rejection of transplanted tissues generated from stem cells.

Although there is much to learn from using existing stem cell lines, there are still many obstacles that need to be overcome. For example, there is concern about potential change in the genetic and biological properties of these stem cell lines, as over time, all cell lines in tissue culture change. And when the cells are implanted into an individual, the cells must be made to function with the body’s natural cells and avoid rejection. These are just a few of the challenges that lie ahead.

While there are numerous challenges, researchers in the scientific community believe that stem cell therapies will eventually revolutionize medicine. Initially, information from basic research may be used to further explore the causes of diseases which result from cell damage or degeneration and from cell death. Stem cell therapies may then attempt to replace cell loss and induce repair mechanisms by having the healthy cells become integrated into a patient’s body and begin to function like the patient’s own cells.

**The Controversy**

Human embryonic stem cell research has spurred a great deal of controversy. One debate is about the ethical and legal issues of when life begins and the rights of an embryo. Controversy is also specifically related to the source of embryonic cells. Some will only accept, or oppose, the use of stem cells derived from embryos created specifically for research from eggs and sperm donated by volunteers who have no reproductive intent. Others may only accept, or oppose, the use of cells derived from embryos produced in fertility clinics that are no longer needed for reproductive purposes.

**Funding**

In August 2001, President Bush announced that he would approve federal financial support for research that uses embryonic stem cells already being cultured in laboratories. However, no federal funding will be made available for the development of new lines that involve the creation or destruction of additional embryos.
Understanding Nutrition - Part I

Q What is important about cholesterol?

A Knowing your blood cholesterol level helps determine your risk for a heart attack and stroke. Your blood cholesterol level (also known as a lipid profile) is the total number of your Low-Density Lipoproteins (LDL) and High-Density Lipoproteins (HDL) cholesterol measurements and about 20% of your triglyceride level. LDL is "bad" cholesterol, and a high LDL level contributes to blockages in arteries. These blockages can lead to heart attacks and strokes. HDL is “good” cholesterol, and a high HDL level actually protects you against diseases. Your triglyceride level is a measure of fats that circulate in the blood. You blood cholesterol level should be checked at least every five years - or more often if you are a man over the age of 45 or a woman over 55.

Most doctors agree that people with spinal cord injuries (SCI) have to watch their cholesterol levels. They usually have lower levels of the good (HDL) cholesterol and higher levels of the bad (LDL) cholesterol. This fact may be partly due to how the impairment affects the body’s metabolism and partly due to lack of exercise. You can help improve cholesterol levels by:

♦ reducing cholesterol and total fats (especially saturated and trans fats) in your diet;
♦ losing weight;
♦ participating in regular physical activity;
♦ eating more fruits, vegetables, and foods high in complex carbohydrates, fiber and soy;
♦ eating foods with omega-3 polyunsaturated fatty acids and monounsaturated fatty acids such as fish, flaxseed, nuts, olive, canola and soybean oils;
♦ limiting sugars and alcohol in your diet;
♦ stopping smoking.

Q Are there "good" and "bad" fats?

A Your body needs fat, but all fats are high in calories and should be eaten sparingly. The American Heart Association recommends that no more than 30% of your total daily calories come from fat. However, fat calories are often hidden in foods, so you may need to read the Nutrition Facts label carefully.

Monounsaturated fat is probably the healthiest type of general fat. Monounsaturated fats are believed to lower your bad cholesterol level, provide essential fatty acids for healthy skin and the development of body cells, and may offer protection against breast and colon cancers.

Polyunsaturated fats are believed to lower both good and bad cholesterol levels. The healthiest polyunsaturated fat is Omega 3, which is found in fresh fish such as salmon, tuna, trout and mackerel, so eating fish often is recommended. Polyunsaturated fats are also found in vegetable oils made from soybean, corn, sunflower, safflower, and olive.

Saturated fats are unhealthy. They raise your bad cholesterol level, which increases your health risk. Foods that are highest in saturated fats include lard, meats, dairy products, palm and coconut oils.

Trans-fats are the unhealthiest of all fats. They actually raise your bad cholesterol level and lower your good cholesterol level. Most trans-fats are common in vegetable shortening, some margarines, crackers, candies, baked goods, cookies, snack foods, fried foods, salad dressings, and many processed foods. Some nutrition labels may not list trans-fats with other fats, but if you see the words “shortening” or “hydrogenated” on the food’s ingredient list, the food contains trans-fat.

<table>
<thead>
<tr>
<th>At Health</th>
<th>Total Cholesterol Level (mg/dL)</th>
<th>HDL Cholesterol Level (mg/dL)</th>
<th>LDL Cholesterol Level (mg/dL)</th>
<th>Triglyceride Level (mg/dL)</th>
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<tr>
<td>Low (desirable)</td>
<td>&lt; 200</td>
<td>≥ 60</td>
<td>&lt; 100</td>
<td>&lt; 150</td>
</tr>
<tr>
<td>High (undesirable)</td>
<td>&gt; 240</td>
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<td>≥ 200</td>
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< means less than  > means greater than  ≥ means greater than or equal to
Sleep apnea is a disorder characterized by pauses in breathing during sleep. People who are at higher risk for developing sleep apnea include persons who are obese and people with an absence or weakness of respiratory muscles. Sleep apnea occurs in about two percent of women and four percent of men.

There are three types of sleep apnea:

1. **Obstructive sleep apnea (OSA)** is caused by an obstruction in the airway.
2. **Central sleep apnea** is a delay in the signals from the brain instructing the body to breathe.
3. **Mixed sleep apnea** is a combination of OSA and central sleep apnea.

Obstructive sleep apnea is the most common of the three types of apnea. Generally, the obstruction of the airway occurs as a person falls asleep. The muscles of the soft palate and the uvula (see illustration) relax. There are no rigid structures such as cartilage or bone in this area to hold the airway open, so a person finds it increasingly hard to breathe. This usually results in loud snoring. The airway eventually collapses and becomes obstructed. Breathing becomes very shallow or stops. There is a drop in the blood oxygen level and a rise in the blood carbon dioxide level. When the brain senses these changes in blood levels, the brain reacts by sending a signal to wake the person so that breathing can be restored to normal. Once normal breathing resumes, the person usually falls asleep again and repeats the cycle throughout the night.

Common symptoms of OSA while sleeping are:

- Loud heavy snoring (often interrupted by silence and then gasps, chokes, or snorts).
- Restless sleep (repeated awakenings).

A person with OSA might wake up more than 100 times in one night. Each waking episode might last only a few seconds, but multiple interruptions in sleep can prevent in a person from reaching the deep stages of sleep that the body needs in order to rest and recover. This recovery is essential for people to be at their best in performing daily activities.

Common symptoms of OSA while awake are:

- Dry throat upon awakening.
- High blood pressure.
- Morning headaches.
- Sleepiness during the day.
- Lack of energy.
- Trouble concentrating.
- Memory lapses.
- Mood or behavior changes (irritability, anxiety depression and decreased interest in sex).

**Diagnosis and Treatment**

**Diagnosing** OSA begins with recognition that there is a problem. Some people may recognize common symptoms of OSA while awake. However, most people are not aware of their breathing patterns while sleeping. Sleep partners or close family members may be able to provide feedback on nightly symptoms of OSA.

The second step is to consult a doctor. Patients who are suspected to have OSA are usually referred to a sleep clinic for evaluation. A sleep test (polysomnography) can then be used to record body activities such as electrical activity of the brain, eye and muscle movements, heart rate, respiratory effort, air flow and blood oxygen levels during sleep. OSA is diagnosed if the person has more than five apneic episodes per hour.

Treatment is aimed at restoring regular nighttime breathing and relieving symptoms. Some mild cases of OSA might be treated with behavioral changes such as weight loss, changes in sleep positions, or reduced use of alcohol, smoking, and sleep medications. Treatment of moderate or severe OSA usually includes a Continuous Positive Airway Pressure (CPAP) mask that fits over a person’s mouth and nose during sleep. The air pressure forces air...
through the mask to keep the airway open during sleep. Surgery is another possible treatment option that might include removing tonsils, adenoids, and excess tissue at the back of the throat. Reconstruction surgery of the nose and jaw may also improve air flow.

**Sleep Apnea after Spinal Cord Injury**

Although research is limited, sleep apnea seems to be a significant respiratory complication for many individuals with spinal cord injury (SCI). Some estimates put the prevalence of sleep apnea in individuals with SCI at 10 times higher than in the general population. It seems that persons with SCI are also at greatest risk for OSA. A number of factors contribute to this belief. First, the majority of individuals with SCI are men, and many are obese with thick necks. These are known risk factors for OSA in the general population. Second, many individuals with SCI sleep primarily on their backs. This is another known risk factor for OSA in the general population. Third, it is common for individuals with SCI to take medications to manage secondary conditions. Some medications are used for calming muscle activity, which is also a known factor in slowing down respiratory function. Finally, most individuals with SCI now have a life expectancy near that of the general population, so they, too, will experience a natural decline in muscle strength and lung capacity as they age. This advancing weakness of respiratory muscles is yet another known risk factor for OSA.

Normal respiratory function is controlled by 4 muscle groups. The neck muscles normally work to expand your upper chest when inhaling. The intercostal muscles are located between the ribs and help to expand your ribs as you inhale. The abdominal muscles help people breathe deeply and cough. The diaphragm is normally the main muscle that people use when they inhale. This is a strong, dome-shaped muscle that separates the abdominal and chest cavities.

Respiratory problems occur when signals sent from the brain can no longer flow through the spinal cord to control the four respiratory muscle groups to breathe air into your body. Complete injuries in the thoracic or cervical regions usually result in the permanent loss of respiratory muscle function below the level of injury. The higher the level of injury, the greater the loss to the respiratory muscle control. Therefore, individuals with tetraplegia may be at a very high risk for OSA.

Although some individuals with tetraplegia rely on their neck muscles to help with breathing, they rely mostly on their diaphragm for breathing. However, the diaphragm is not at normal strength. This weakness is compounded by the fact that these muscles become inactive during deep sleep, which further hinders an individual’s ability to breathe.

**Diagnosis and Treatment after SCI**

Individuals with SCI who think they may have sleep apnea should ask their doctor for a referral to a sleep specialist. Breathing obstructions can result from other medical conditions or as a side-effect of medications, so a sleep test (polysomnography) is needed to diagnose sleep apnea. The main problem for individuals with SCI, especially those with tetraplegia, is that most sleep labs are not fully accessible. This fact is a major barrier to treatment because home-based diagnostic tests may not be covered by insurances. Individuals with SCI and their doctors need to work together to explore other options.

The goal of treatment for individuals with SCI is the same as with the general population, which is to restore regular nighttime breathing and relieve symptoms. OSA is often easily treated in the general population with a combination of methods, which might include weight loss, changes in sleeping positions, or the use of CPAP. However, treatment may not be as easy for individuals with SCI. Although weight loss is possible for most individuals with SCI (see page 7 for information on a new weight management program), changes in sleep positions may not be possible. Although CPAP may be an effective treatment for individuals with SCI, they may have limited mobility and not be able to adjust the mask during sleep. Finally, it takes time to recovery from surgery, and it may or may not be an effective treatment for restoring breathing and relieving symptoms. Again, individuals with SCI need to work with their doctors to find the best treatment option.

This drug is in the early stage of clinical development and has not been approved by the Food and Drug Administration for marketing. Spain Rehabilitation Center at the University of Alabama at Birmingham is being paid by a sponsor to conduct this study. Dr. Amie B. Jackson is Principal Investigator.

**Introduction**

There are currently no available therapies for restoring motor function in individuals with chronic spinal cord injury (SCI), a population estimated at 250,000 in the USA alone. Although many pharmaceutical (drug) products are used to treat individuals with SCI, these drugs are almost exclusively directed to the treatment of secondary medical conditions such as pain, spasticity, pressure sores and bladder infections. However, a treatment option with only minimal effectiveness in improving function might represent a major improvement in the quality of life of many individuals with SCI.

**Objective**

The primary objectives are to evaluate an experimental drug treatment for its effectiveness and safety on total motor score of American Spinal Injury Association (ASIA) manual motor test. The secondary objectives are to determine the drug's effect on voluntary movement in additional muscle groups, walking, strength and gait assessment, spasticity, sensory function, independence, and reported outcomes.

**Participants**

About 240 men and women with SCI will take part in this study at approximately 30 to 35 study centers throughout the United States and Europe. Each center will enroll patients until the total of 240 is reached. Spain Rehabilitation Center at the University of Alabama at Birmingham will enroll as many patients as possible until the total number of patients is completed at all centers.

Participants will be considered for enrollment into the study if they:

- are at least 18 months post injury;
- are between the ages of 18 and 65;
- have a neurological level of SCI between C4 and T10
- have a measurable range of motion at the hips, knees, and ankles and possess potential propulsive activity (no functional contractures);
- are women of childbearing age, they must be using two forms of birth control; and
- have an SCI categorized on the ASIA manual motor test as either
  1) ASIA C incomplete impairment with motor function preserved below the neurological level, and more than half of key muscles below the neurological level with a muscle grade less than 3 or
  2) ASIA D incomplete impairment with motor function preserved below the neurological level, and at least half of key muscles below the neurological level with a muscle grade of 3 or more.

**Methodology**

Participants will be randomized and assigned to one of four dosing groups with 60 patients in each group. Starting on Day 1, each group of 60 patients will receive oral drug doses of either a 100 mg, 200 mg, 400 mg, or a placebo (sugar pill) once a day for a period of 24 weeks. The four dosing groups will undergo the same evaluations and assessments in weeks 2, 4, 8, 12, 16, 20, and 24. One or two weekly follow-up visits will also be required. Participants will be compensated $50 per visit to cover costs such as transportation. Neither the participant nor the study personnel will know to which group individuals have been assigned.

**Potential Findings**

There may or may not be a direct medical benefit to study participants. However, findings learned from this study will likely benefit other individuals with SCI in the future.
Currently, there are about 60 stem cell lines resulting from excess human embryos identified by the National Institutes of Health (NIH) as produced before the August 2001 announcement.

Although the NIH is considered a vital funding source, there are few state laws and no federal law that prohibit funding from private sources. This means private funds can be used for the development and use of human embryonic stem cells derived from excess embryos created by in vitro fertilization for the purposes of research or by nuclear transplantation.

Supporters of human embryonic stem cell research believe federal funding would speed the progress of health benefits faster than private funding. Funding from the private sector is often tied to commercial applications, such as new drugs. Therefore, many companies in the private sector may not be inclined to fund basic stem cell research.

Sara Lerman, MPH is a Program Manager for the American Association of Spinal Cord Injury Nurses (www.aascin.org). This article was adapted with permission from an article appearing in the January 2005 issue of orbit (V2;N1), a monthly publication of United Spinal Association (www.unitedspinal.org/pages.php?catid=259).

INTRODUCING:

As a person with spinal cord injury (SCI), you can benefit from a healthy weight management program. However, most programs are not designed for persons with SCI. Your nutritional needs and physical abilities are probably different from people in the general population. For example, you are at higher risk for kidney problems if you follow diets low in carbohydrates and high in protein. Improper exercises can add stress and strain to your muscles and joints, which can cause chronic pain.

In 2003, the University of Alabama at Birmingham (UAB) finished a 4 year study of a modified version of the EatRight® Weight Management Program, which was originally developed in 1976 for the general population by a team of UAB physicians, dietitians and psychologists. The core of the original EatRight program remained intact, but modifications were made to meet the unique diet and physical demands of persons with SCI who were overweight or obese. Study participants attended weekly classes to learn the necessary skills for effective weight management. The modified program was shown to be safe and effective for weight loss, reducing medical risks and improving quality of life for persons with SCI.

UAB received a grant from the PVA Education Foundation to make this new program accessible to consumers. The EatRight® Home-Based Weight Management Program for Individuals with Spinal Cord Impairments was created to meet the unique nutritional and physical needs of persons with spinal cord injuries, dysfunctions and diseases. This comprehensive program utilizes video lessons and workbook assignments to guide you through the 12 proven elements of effective weight management:

1. Getting Started
2. Making Healthy Food Choices
3. Planning Meals
4. Shopping
5. Cooking
6. Setting Goals
7. Participating in Physical Activities
8. Dining Out
9. Understanding Nutrition
10. Improving Self-Talk
11. Reducing Stress
12. Maintaining Long-Term Success

For more information or to order this program, go to www.spinalcord.uab.edu/show.asp?durki=77527 or call 205-934-3283
Participants Needed for Studies on Chronic Pain and Spinal Cord Injury

1 - Participants with chronic pain are being asked to complete a 1-time telephone survey on the contribution of cognitive appraisal, coping, activity restriction, and social support in the relationship between pain and depression. Participants will get $25 for completing the survey. Contact Michael Wilson at 205-281-4273 or mwwilson@uab.edu to see if they qualify.

2 - People with chronic (for at least 6 months post-injury) neuropathic pain after SCI are being asked to test an experimental device that might reduce pain. Participants must be at least 18 years old and have moderate to severe pain below their level of injury. Participants will get up to $95 for completing the study. Interested participants can contact Sherry Sutfin at 205-934-3454 to see if they qualify.

Sleep Apnea

- [www.sleepapnea.org](http://www.sleepapnea.org)
- [www.sleepturbo.com/s_osa.html](http://www.sleepturbo.com/s_osa.html)
- [www.sleepdisorderchannel.net/osa/](http://www.sleepdisorderchannel.net/osa/)
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