

Advances in Spinal Cord Injury Management Frequently Asked Questions



This handout is intended for people with spinal cord injury (SCI), their partners and relatives. It aims to provide information about current spinal cord injury research, most of which to date has been focused on SCI resulting from traumatic causes, such as motor vehicle accidents, sporting injuries, assault and falls. SCI resulting from non-traumatic causes, such as spinal infections, vascular accidents, multiple sclerosis, motor neuron disease, or tumours are beyond the scope of this handout.

What happens after a spinal cord injury? How is the spinal cord damaged?

To understand the basis of some of current SCI-related research, it is helpful to understand what happens when a person has an accident and sustains a SCI.

The spinal cord is protected by the surrounding spinal column, which is made up of 33 bones (vertebral bodies) stacked on top of each other (Figure 1). The vertebral bodies are separated by discs which act as “shock absorbers”. The bones and discs are held together by strong ligaments which are also supported by muscles.

A large external force to the spinal column can cause the vertebral bodies, discs and ligaments to break, and their fragments can be forced into the spinal cord (Figure 2). This can damage or bruise delicate spinal cord tissue, the coverings of the spinal cord and the blood vessels which supply the spinal cord.

Injury to our body tissues results in ***inflammation***, a process marked by changes in blood flow and leaking of fluid and cells from blood vessels into the damaged area of the spinal cord. Within a few minutes, the spinal cord starts to swell with the fluid and new cells coming to “fight” the injury. However, swelling of the spinal cord can cut off the blood vessels supplying oxygen and essential nutrients to the cord, causing more nerve cells (neurons) to die.

In addition, inflammation sets off a cascade of events that may worsen damage. For example, too much release of chemicals can damage supporting and protective cells (oligodendrocytes).

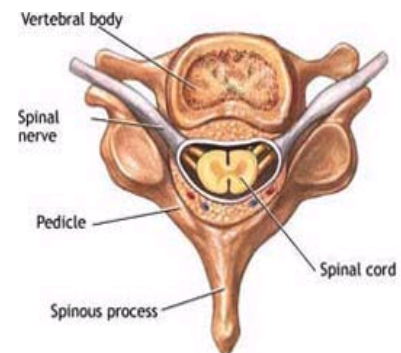


Figure 1 Cross-section of spinal cord and nerve roots protected by surrounding vertebra

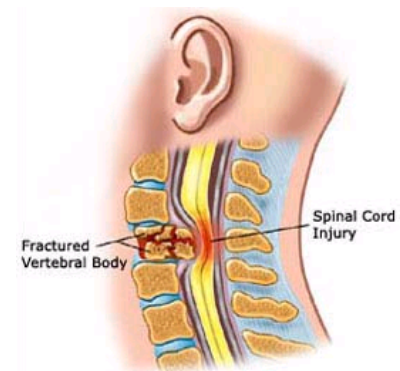


Figure 2 Fractured vertebral body with bony fragments impinging on the spinal cord

www.aqavic.org.au/sci_facts/whats_sci.html

These chemicals can also prevent surviving nerve cells from working properly or damage parts of the nerve cells, such as the insulation (called myelin – Figure 3) around the nerve cells (this damage is referred to as **demyelination**). A process called **apoptosis** also occurs after SCI, where cells “suicide” days or weeks after injury.

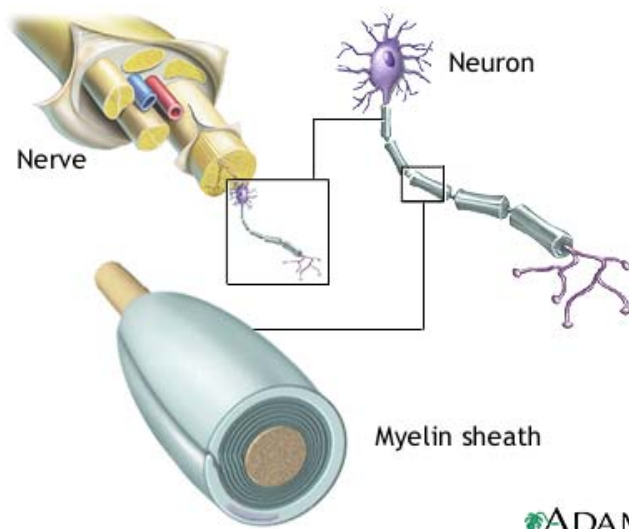


Figure 3 Diagram showing nerve bundle with individual nerve cell (neuron) and myelin sheath

ADAM.

These mechanisms of secondary damage expand the area of initial damage (Figure 4), causing more nerve cells from the brain to be disconnected from the nerve cells that perform body functions. Similar to other parts of the body, a scar could form which could act as a physical barrier to nerve cells that are trying to regenerate and reconnect.

Tissue Loss after Spinal Cord Injury

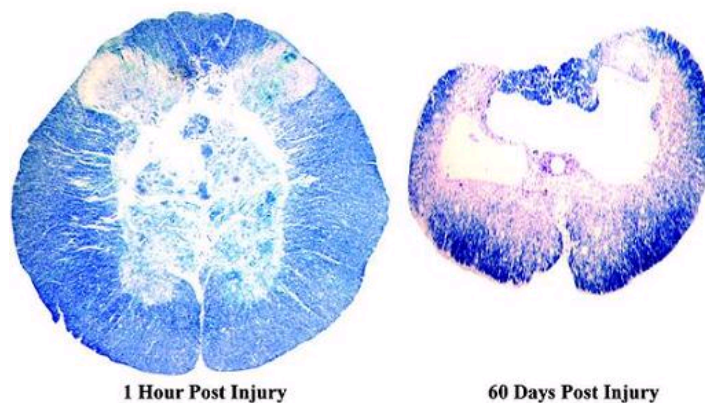


Figure 4: Spinal cord damage expands over time. The left image shows a rat spinal cord 1 hour after injury. By 60 days post SCI, there is only a thin rim of tissue.

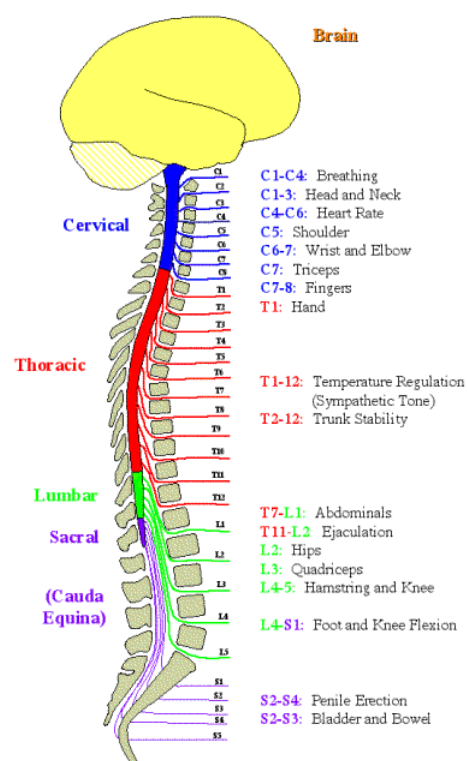
Researchers are working to better understand the reasons why there is more tissue loss after the initial damage. It is hoped that this will ultimately lead to being able to apply this knowledge to prevent and limit damage from spinal cord trauma, which in turn would lead to improved recovery.

How does spinal cord injury impact on our body functions?

The spinal cord functions as a bridge between the brain, which receives and interprets information before issuing commands, and the peripheral nervous system. The peripheral nervous system controls our breathing, heart rate, blood pressure, skin sweating, temperature control, bladder, bowel, sexual and other vital organ functions. It has a central role in coordinating movements, interpreting different types of sensations and regulating reflex activity.

The disability resulting from a SCI depends on the level where the spinal cord was damaged (Figure 5) as well as the extent of damage. This may involve:

- Loss of voluntary movement
- Loss of sensation
- Bladder, bowel and sexual dysfunction
- Variable heart rate (slow, fast or irregular)
- Unstable blood pressure, which can be too low (called orthostatic hypotension) or too high (autonomic dysreflexia)
- Blood clots forming in the leg (deep venous thrombosis), which can break off and lodge in lungs (pulmonary emboli)
- Breathing problems (shallow breathing and trouble coughing which may need ventilation support or can make one more susceptible to lung infections)
- Skin breakdown (from decreased sensation and movement)
- Pain (from damage to nerves in spinal cord or to musculoskeletal structures)
- Spasms and spasticity (from excessive unregulated reflex activity)
- Impact on psychological health and social interactions
- Impact on function and community participation – ability to self care, work, participate in recreation activities



http://www.reeve.uci.edu/anatomy/images/scns_1b.gif

Figure 5 Diagram showing key functions at different spinal cord levels

Injury to the spinal cord above T1 level results in tetraplegia (where the arms are affected), whereas injury below T1 results in paraplegia. With rehabilitation, the person is helped to maximize their medical and functional outcomes.

Functional outcomes may vary by individual, as there are many factors involved. For a description of what function can be expected for a certain level of injury, please refer to the Paralyzed Veterans America Website where you can access consumer guide entitled Expected Outcomes: What You Should Know. (www.pva.org/)

What should I be aware of if I'm considering participating in a research study or a new treatment?

There has been considerable media coverage on new treatments for SCI in the last few years, some of which involves transplantation of 'stem cells'. Although they are advertised as having beneficial effects with glowing testimonials, there is often little scientific evidence (such as properly conducted clinical trials) for these claims. These treatments are often offered in countries where there may be less rigorous government regulation for consumer protection.

As a consumer, it is important to be convinced that a treatment that is offered will be effective, as there may be significant health risks and financial costs involved. The treatment should have been tested by a well designed research study and replicated by other institutions. Well designed research is objective and free from any preconceived notions, expectations or prejudices (“biases”) in order to determine if a treatment is effective or not.

If you are thinking of participating in a research study, look for the following characteristics which should:

- Clearly state the intended effect of the treatment being studied.
- Include an experimental group (that receives the treatment) and a control group (which receives an inactive treatment or “placebo”).
- Be “randomised” so that you have an equal chance of being assigned to a treatment or a placebo group.
- Make clear what you could stand to gain or lose from the trial. Side effects and complications that can result from this treatment should be described in detail. For example, is it possible that you could lose any muscle and sensory function, develop a spinal infection, have worsening of spasms or pain or affect your energy or mood?
- Has the proposed treatment undergone extensive testing in animals to ensure it is safe and shown to have a beneficial effect on function that has been repeated by several independent groups of scientists.
- Include extensive testing of your baseline function before treatment to compare with function after the trial.
- Have an adequate number of people recruited to detect a meaningful difference from the treatment.
- Be at no cost to yourself.
- Have obtained approval from the local ethics committee to be carried out and should have a stamp on the consent form. Check that this is on every page. Make sure that you understand all the conditions and have your questions answered before you consent. You have the right to withdraw at any time if so desired.

YOU SHOULD BEWARE OF:

- Organisations that promise outcomes that seem too good to be true or a “cure”. Be wary that some are unscrupulous and these treatments come at high cost.
- Complications from the proposed treatment. If you develop any, your insurance agency or funding body may refuse to cover the health care costs sustained from treating any complication arising.
- Furthermore, participation in unproven treatments may also preclude you from participating in future legitimate trials.

If you are considering participating in a trial that involves an intervention (treatment), you should check that the trial has been registered on the World Health Organisation International Clinical Trials Registry Platform (ICTRP) (<http://www.who.int/ictcp/en/>) or the Australian New Zealand Clinical Trials Registry (<http://www.anzctr.org.au/>). These websites improve research transparency and gives an overview of what is being done internationally.

There is also an excellent resource entitled “Experimental treatments for spinal cord injury: what you should know if you are considering participation in a clinical trial.” This is a guide produced by the International Campaign for Cures of spinal cord injury Paralysis.

<http://icord.org/documents/iccp-clinical-trials-information/>

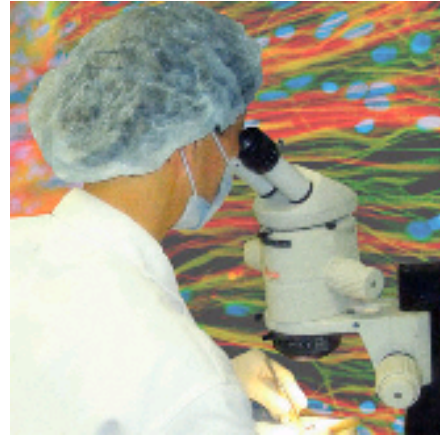


Figure 6 Front page illustration of ICCP guide

What can be done to maximise recovery from spinal cord injury?

There have been many advances in treatment of spinal cord injury and numerous areas of research are ongoing to help maximise the potential for recovery after spinal cord injury. A simple way to understand some of these advances is to classify them based on our understanding of what happens after a spinal cord injury:

a) Prevention

As there are no fully restorative therapies as yet, preventing the spinal cord injury from occurring in the first place is the best medicine. Examples of prevention initiatives are engineering safer cars and roads, compulsory use of seat belts, weapon restrictions and referees enforcing rules in sports.

b) Neuroprotection

The interventions discussed in this section are concerned with limiting secondary damage and protecting surviving nerve cells once the initial insult has occurred. Most interventions of this type are thought most useful when applied early after SCI (within 1-2 weeks).

An important consideration immediately after trauma is to prevent further injury to the spine and spinal cord. Ambulance officers and emergency staff have protocols to follow to minimise movement of the spine by applying a hard collar and transporting the patient on a rigid board, assist breathing (which may involve inserting a tube into the person's airway) and monitor vital signs, such as blood pressure, heart rate and oxygen levels.



lifemedicalsupplier.com

Figure 7 Child on rigid board with hard collar on.

Methylprednisolone is a steroid drug which has been administered to patients with SCI if they present within 8 hours of injury, in an attempt to decrease inflammation. There have been questions raised about its effectiveness and safety and some doctors will not routinely administer this medication in Australia. Researchers are working on other compounds that have an anti-inflammatory effect, as well as ways to block the release of harmful chemicals after SCI. Some of these have been trialed in people with stroke and similar agents could be tested in patients with SCI.

There is emerging evidence that early surgery (within 7 days) to relieve pressure on the cord may improve outcomes and reduce complication rates in patients with SCI. However, this may not apply to all types of traumatic spinal cord injury as the mechanisms of injury can differ. Work is also being done in the field of cooling the body for several hours following injury to see if this limits spinal cord damage.

c) Promoting regrowth, remyelination and regeneration

The work done in this field focuses on trying to get nerve cells to grow, repair and regenerate.

In adults, the spinal cord contains chemicals that stop growth. For regeneration to occur, these chemicals need to be switched off.

In addition, chemicals that tell nerve cells to grow, where to grow towards, how much to grow and which nerve cells to connect to, need to be switched on. For

example, various growth factors have been discovered that can promote nerve survival and outgrowth. Debris such as dead cells and scar material also need to be cleared away. Another challenge is to help surviving nerve cells that have lost their protective covering (myelin), which helps nerve cells transmit signals more effectively.

Delivery of the correct combination and timing of release of growth factors, cells and other chemicals is needed to engineer this complex process and scientists all over the world are working on different aspects of this. We do not know at this stage which chemicals to use, how much to use, where within the spinal cord to deliver these molecules and when after injury to put them in the spinal cord.

d) Cellular replacement

The general idea in this field is to replace the loss of nerves (neurons) and their supporting cells by transplanting reliable cells that can “bridge the gap” and help to reconnect axons (fix “broken circuits”). Some of these cells are:

Schwann cells that make myelin (outer insulation covering around nerve). It is thought that it might help to repair the myelin sheaths that are lost after a spinal cord injury. Studies are ongoing into animal models of spinal cord injury to see if there is a definite benefit.

Olfactory ensheathing glia, which are cells that support the nerve which conveys smell sensation to the brain from the nose. These can be taken from the person with SCI (called autologous transplantation – shown below in Figure 6) or from other donors or embryos (allogeneic transplantation). Some countries, including Australia, are conducting early trials in this area to see if this is safe in the long term in a small number of people. However, trials that have been conducted thus far are not able to tell us if implanting these cells has led to definite functional improvements.

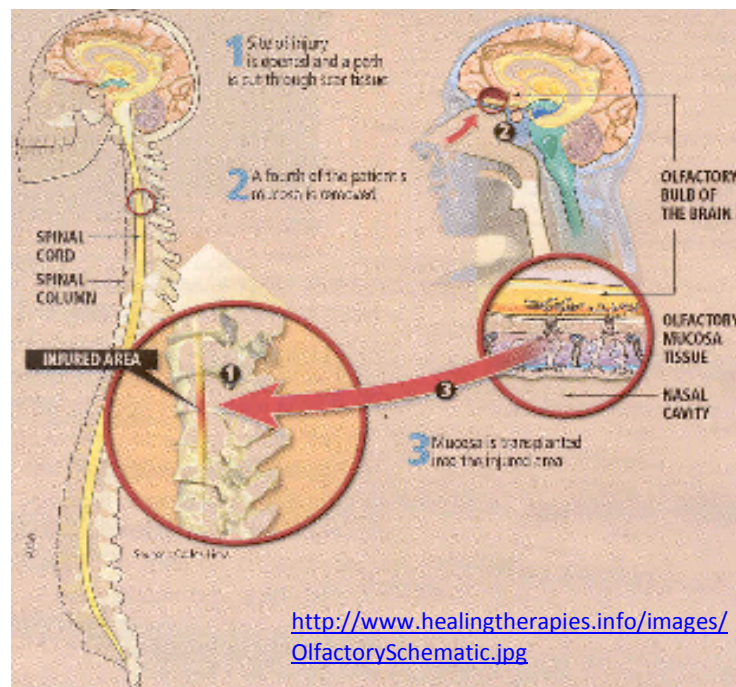


Figure 8: Diagram showing how nasal olfactory cells being harvested, grown and then replaced into the same person

Fetal spinal cord cells are derived from discarded embryos. Some success in animal models has been reported where some movement has been restored in limbs. However, results in humans are less conclusive. There are also ethical concerns raised by people opposed to the use of stem cells obtained from aborted fetuses.

Stem cells have the capacity to divide and become different cell types. They can be derived from embryos or various organs in children or adults. Stem cells are being extensively studied in many areas of medicine in hopes that it will treat diseases such as diabetes, heart disease, Parkinson's disease and spinal cord injury. However, the road to a cure is still long and uncertain, as there are still many things we do not understand about how stem cells behave. For example, we know that stem cells can sometimes turn into cancerous cells and form tumours.

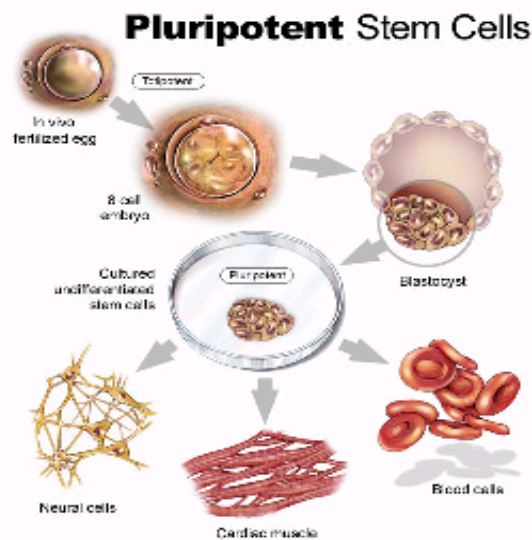


Figure 9 Diagram illustrating how stem cells may differentiate into various cell types

<http://www.csa.com/discoveryguides/stemcell/images/pluri.jpg>

Further research is required to tell us what signals are needed to tell stem cells to grow and repair damage, if we need to implant support cells as well, and if these will eventually replace nerve function as desired. We also need to know when is the best time to do this after SCI and if there are any bad effects in the long term.

Apart from animal experiments, many human studies (clinical trials) need to be conducted before we can finally determine if stem cell transplants are safe and effective or not. A Position Paper on Stem Cell Research has recently been prepared by the Australia New Zealand Spinal Cord Injury Network (ANZSCIN) in conjunction with the Australian New Zealand Spinal Cord Society (ANZSCoS) and is available at <http://www.anzscin.org>.

This is similar to the Position statement on the sale of unproven cellular therapies for spinal cord injury The International Campaign for Cures of Spinal Cord Injury Paralysis (see references).

e) Enhancing/replacing surviving functions

There are many exciting discoveries in the field of rehabilitation, aiming to maximise and enhance surviving functions. We know that there are networks of nerve cells in animals' spinal cords called central pattern generators (CPGs) that produce rhythmic walking patterns. These networks may be able to be retrained after a spinal cord injury by repetition of movements that activate muscles needed for walking and standing.

There are programs around the world that are investigating this by supporting the patient's body weight with a harness while therapists or machines move the patient's legs on a treadmill (Figure 10). Other studies are also using electrical stimulation and assisted exercises to see if this will improve walking and balance.

It will be critically important to better understand the mechanisms by which activity-based (also known as task-specific) exercise therapy and other rehabilitation techniques enhance functional recovery after injury to determine the most effective rehabilitation programs to compliment any new drug or cellular treatments.



Figure 10 Body weight supported treadmill training

Functional Electrical Stimulation (FES) and Neural Prosthesis Systems

FES can provide the user with control of muscles to assist function via an electrical stimulator delivering programmed patterns of small electrical impulses to nerves that activate movement. Electrodes can be taped to skin overlying target muscles or surgically implanted. The user can control the electrical stimulation by using a computer interface device. There are a variety of ways of controlling movement. For example, electrodes placed in the arm to provide hand function can be controlled by a device which detects movements of the opposite shoulder.

FES systems have been shown to have benefits for improving bladder, bowel and sometimes sexual function (Figure 11), exercising paralysed muscles and maintaining muscle bulk, improving cardiovascular health, maintaining bone mass, and helping to improve function such as upper

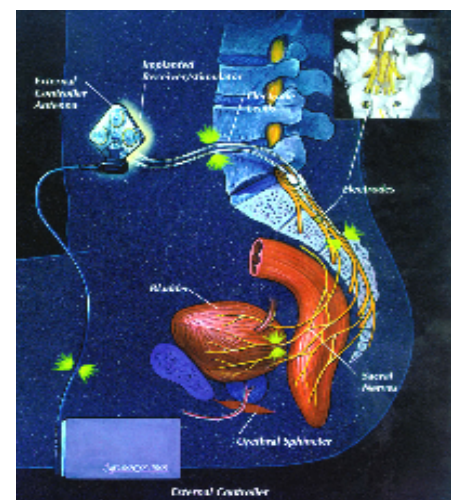


Figure 11 Brindley Sacral Anterior Root Stimulator (Finetech, UK) with electrodes placed within spinal canal over sacral nerves supplying bladder and bowel function

and lower limb movement. However, there are many limitations to their use including the high cost and specialised technical knowledge required to implant, implement and maintain these systems. Furthermore, the movements produced are slow and robotic, making it somewhat impractical to utilise. There are also risks of hardware failure and surgical complications from some of the procedures, which requires consideration before embarking on this intervention. There are a few research projects into FES walking/cycling in Australia. Please see resources section at end of document for a list of these.

Early work is being done into neural prostheses (replacement body parts) to replace the role of the spinal cord in relaying messages. In animal experiments, microwires have been implanted into the area of the brain which controls movement to record activity. This brainwave activity is relayed to a computer that processes the data and then sends commands to a robotic arm. It is hoped that this device can be used to control prosthetic limbs, assistive devices such as a wheelchair or even the person's own arms and legs. Although exciting, this work is very experimental and early and it will take some decades before this work is validated for effectiveness, tested for safety and be available for patients.



virtualworldlets.net

Figure 12 Illustration of brain controlled wheelchair

Exercise Programs

The specialised Spinal Cord Injury Rehabilitation Units in Australia provide comprehensive multidisciplinary rehabilitation services which are individualised and aim to help people with SCI reach their maximum functional potential. Doctors, physiotherapists, occupational therapists, orthotists, social workers, psychologists, dieticians and nurses work together to prescribe what is appropriate for each individual. In addition, there are local gym-based exercise programs such as “Burn Rubber Burn” in the community for a nominal cost.

There are emerging programs in the USA and Australia (such as the “Walk On” program) offering intensive exercise after discharge from SCI Units. They are not a replacement for an inpatient rehabilitation program. These programs require commitment and have a high financial cost and are not affiliated with the spinal units, and therefore medical officers in the spinal units may not be able to provide medical clearance for participation in these programs. These programs are not suitable for everyone with a SCI and it is important that the individual make an informed decision. References at the end may help assist with this.

All the interventions discussed in this section need to be subjected to well designed randomised clinical trials to see if they are effective or not, regardless if they are stem cell therapies or physical therapies/programs.

f) Managing complications arising from spinal cord injury

As you are aware, spinal cord injury affects many organ systems and body functions. Over recent years, research has improved our understanding of how and why these complications develop and can be treated, or even better prevented in first place. Some of the significant advances in medical treatments and technology include new pharmacological (drug based) interventions and different routes of medication delivery than oral, such as intravesical injections (into the bladder wall) and intrathecal delivery of medication (directly into spinal fluid space around cord). There are also a range of non-pharmacological (non drug based) interventions, such as physical therapy (exercise, stretching, cold, heat, TENS, etc), equipment and devices, neural prostheses etc, psychological approaches (eg. cognitive behavioural therapy), educational interventions and complimentary (alternative) therapies, for which the evidence of effectiveness is currently not as strong.

To illustrate some of the advances, let us look what is going on in the fields of pain and spasticity.

Pain is common after spinal cord injury and can impact significantly on a person's function and quality of life. Much of the research into pain is focusing on understanding why and how pain occurs after spinal cord injury, as well as the different types of pain. We now know that the earlier we treat pain, the greater the chances of reducing the development of chronic pain later on. Physical therapies such as massage, heat, shoulder exercise and acupuncture are being investigated to see if they reduce pain. New medications have become available in the last few years which are proving more effective in treating nerve pain. There is also further research investigating medications which might interfere with nerve chemicals implicated in the development of pain syndromes. Apart from oral medications, studies have been conducted to investigate if some medications delivered to the spinal cord space or into the veins help with pain.

No discussion on pain can be complete without considering the social, emotional and mental factors that impact on pain. More and more, people are realising that medications alone are not effective in managing pain. Interventions such as cognitive behavioural therapy (for example challenging catastrophic ways of thinking, distraction techniques and relaxation therapies) are being trialed and most units will have a clinical psychologist available to help people with SCI develop better strategies for managing their pain.

There are many medications available for treating spasms currently, but their efficacy is often limited by side effects. Botulinum toxin acts to relax stiff muscles, but it is temporary (lasting only 3-6 months) and expensive. Botulinum toxin is also now being used to control bladder spasms in some people where oral medications are ineffective or have serious side effects.

More invasive methods, such as implanting pump systems to deliver anti-spasmodic medications directly into the fluid space around the spinal cord and surgery are more invasive options that can be considered, but carry with them the risks and complications of surgery, hardware failure and dependence on institutions. The management of spasticity continues to be a challenge to most doctors and people with SCI .

g) Health promotion

There is growing interest in how to maintain and promote physical and mental health for the long term in people with spinal cord injury, for example by keeping active, having a good diet, avoiding smoking and having regular health checks. We are starting to understand how spinal cord injury impacts on aging, for example the muscles and joints of the upper limbs can age faster due to greater use and impact of everyday life in a wheelchair. On the other hand, aging can also impact on spinal cord injury, by affecting a person's functional reserve. Research is being done into how we can pick up problems earlier and when best to screen people for these problems.

If you would like further information on how to keep healthy for as long as possible and pick up problems earlier, please contact us on (02) 9808 9666 for a fact sheet on Aging and Health Maintenance after Spinal Cord Injury. We also have other useful information, for e.g. on "What to do when you are hospitalised". There is also a list of useful resources and list of programs available at the end of this document.

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Resources:

For further information on participation in research studies and more details about the advances in spinal cord injury, please refer to the following.

“Experimental treatments for spinal cord injury: what you should know if you are considering participation in a clinical trial.” This is a guide produced by the International Campaign for Cures of spinal cord injury Paralysis.

http://www.icord.org/ICCP/Experimental_treatment_for_SCI-summary.pdf

Australia New Zealand Spinal Cord Injury Network (ANZSCIN)

<http://www.anzscin.org> provides ANZSCIN/ANZSCoS Position Statement on Stem Cell Research, as well as information about clinical trials being conducted in Australia and New Zealand.

Position statement on the sale of unproven cellular therapies for spinal cord injury The International Campaign for Cures of Spinal Cord Injury Paralysis

<http://www.nature.com/sc/journal/v47/n9/full/sc2008179a.html>

The NSW State Spinal Cord Injury Service website provides information on services, resources, publications, education programs, data and research, and links to relevant websites for clinicians managing people with a spinal cord injury. It also has a Directory of Information and Support, which provides guidance about sources of support and information on the psychological and social consequences of spinal cord injury.

<http://www.health.nsw.gov.au/gmct/spinal/>

Spinal Cord Injuries Australia. This site has a link to many helpful resources, including a publication entitled “Community Survival Kit”.

<http://www.scia.org.au/>

ParaQuad NSW website contains information, news, events about living in the community with a spinal cord injury in addition to health information targeting people with spinal cord injuries and their carers.

<http://www.paraquad.org.au/>

The D-Ability site focuses on maximising abilities through recreation, travel, leisure, sport and the arts for people with spinal cord injuries.

<http://d-ability.org/>

Burn Rubber Burn is an exercise program developed for individuals with a spinal cord injury. It is a circuit based exercise program incorporating resistance and cardiovascular training, focusing on health and wellbeing. This site includes details about program locations, cost and contact details.

http://www.pycnsw.org/prime_sparts_burnrubber

A site for physiotherapists containing 600 exercises appropriate for people with spinal cord injuries and other neurological disabilities.

<http://www.physiotherapyexercises.com/>

Websites outside of Australia:

Christopher and Dana Reeve Foundation (USA)

<http://www.christopherreeve.org>

National Institute of Neurological Disorders and Stroke (USA)

http://www.ninds.nih.gov/disorders/sci/detail_sci.htm

Miami Project to Cure Paralysis/ Buoniconti Fund (USA)

<http://www.themiamiproject.org>

Paralyzed Veterans of America (USA)

<http://www.pva.org>

World Health Organisation International Clinical Trials Registry Platform (ICTRP)

<http://www.who.int/ictcp/en/>