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Background Information on spinal cord injury

The spinal cord is the delicate tissue encased in the spinal column. It runs from the base of the brain to the middle of the back. The spinal cord conveys information between the brain, the limbs, the trunk and organs of the body.

Any injury to the spinal cord damages this information highway and therefore leads to paralysis, loss of sensation and loss of function of several internal organs (see Box 1).

The spinal cord is made up of millions of nerve cells that send projections up and down the cord, and out into other parts of the body. The information that allows us to sit, run, go to the toilet and breathe travels along these projections, called nerves.

Although the hard vertebrae of the spinal column protect the spinal cord, they can still be broken or dislocated, causing damage to the nerves and/or loss of cells.

Cells that are lost in the spinal cord cannot be replaced by the body. Consequently, the function of the spinal cord becomes impaired.

Road traffic accidents, falls, sporting accidents (like being thrown from a horse, or a diving accident), gunshot or knife wounds are all possible causes of spinal cord injury.

Few injuries sever the spinal cord completely; most injuries cause vertebrae to compress or fracture, crushing the nerves in the process.

Infections, cysts and tumours, if they develop in the spinal cord, can also lead to injury, without actually damaging the vertebrae.

Some congenital diseases (those that are present at birth) affect the structure of the spinal column and may also cause damage to the spinal cord.

Damage to the blood vessels that flow into the spinal cord can also injure the spinal cord if the nerve cells are starved of oxygen and food/nutrients carried to them by the blood vessels.

01. What is a spinal cord injury?
The severity of the injury, and the segment of the spinal cord which it affects, determines the degree of impairment.

Injuries to the vertebrae of the neck can lead to paralysis of most of the body from the neck down, including arms and legs. This is called tetraplegia.

Damage to the vertebrae of the middle back leads to paralysis of the lower body and legs. This is called paraplegia.

Until 50 years ago spinal cord injury meant certain death for most victims. Those who survived the initial injury faced a lifetime confined to a wheelchair or a bed, fighting off infections and complications (such as blood clots).

Today, thanks to research, improved emergency care, medical treatments and rehabilitation are part of current practice. However, these methods cannot so far repair most spinal injuries. Scientists, doctors and therapists are optimistic that spinal cord injury may eventually be reparable using new therapies.

**Causes and numbers of spinal cord injuries**

There are estimated to be 40,000 people with spinal cord injury in the UK. Every year, a further 1200 injuries occur – that’s around 3 injuries a day. The average age at injury is 31, with the greatest frequency between 15 and 25 years.

In the UK, the majority of spinal cord injuries are caused by falls (downstairs, from heights, etc), followed closely by road traffic accidents.
02. How does the spinal cord work?

The spinal cord is often described as a cable made up of millions of wires, running between the brain and the rest of the body. The cells that carry the information are called neurones; the “wires” of the spinal cord are the projections of the neurones, called axons.

Axons carry signals either downward from the brain, or upward towards the brain.

Some of these axons can be very long, so that they run the length of the spinal cord, which can be up to 45cm in an adult man.

Axons that carry similar signals, or extend to similar areas, bundle together in tracts, or nerves.

Each axon can make connections with many other neurones simultaneously, thus setting up a network of messages and information.

The nerves that carry messages down the spinal cord (from the brain) cause some sort of action at the final destination; they are called motor nerves. They control the muscles of internal organs (heart, stomach, intestines, etc) and those of the legs and arms. They also help regulate blood pressure, body temperature, and the response to stress.

The nerves that travel up the cord (to the brain) carry sensory information from the skin, joints and muscles (touch, pain, temperature) and from internal organs (heart, lungs, etc). These are the sensory nerves.

The spinal cord also contains circuits of neurones that control reflex movements, such as the knee jerk reflex that causes the lower part of your leg to automatically shoot up when your knee is tapped. These circuits are self-contained in the spinal cord, therefore they function without any input from the brain (see Box 2).
More on the structure of the spinal cord

The nerves leave or enter the spinal cord at the segment that is appropriate for their final destination, through small openings between the vertebrae. For example, the motor axons that connect to arm muscles will exit the spinal cord through openings between the vertebrae of the neck. Those that connect to trunk muscles exit from vertebrae along the back.

The axon tracts run on the outside of the spinal cord. The bodies of the neurones, their support cells (called glia) and blood vessels all gather at the inner portion of the spinal cord.
03. What happens when the spinal cord is injured?

The initial damage to the spinal cord triggers a cascade of events that spread around the injury site and last for days.

Any effort to develop strategies that will halt this cascade of events or repair the inflicted damage requires a thorough understanding of the processes involved, how they succeed each other, and how they interact.

The injury itself directly pulls nerve cells apart; the cells burst open, releasing toxic substances that kill neighbouring cells. The axons lose their insulation (called myelin) and eventually disintegrate. Cells that die or are lost in the spinal cord cannot be replaced, and so the information pathway is blocked.

Blood vessels may be crushed, become leaky or even burst, causing heavy bleeding at the site of injury which may spread to other areas of the spinal cord.

Within minutes, the spinal cord swells to fill the entire space within the spinal canal. As a result, blood flow is cut off. The swelling and the excessive bleeding interrupt delivery of oxygen and nutrients to cells, causing many of them to die.

Cells of the immune system gather at the injury site, causing uncontrolled inflammation. The immune system’s role is to protect the body from infection; the white blood cells circulate in the blood vessels and do not usually come into contact with cells of the nervous system.

However, after injury to the spinal cord, because vessels burst, the white blood cells accumulate near the nerve cells. The white blood cells see the nerves as ‘foreign’ and attack them, triggering inflammatory responses, including more cell death.

Days or weeks after the injury, cells of the spinal cord from within the injury area begin to commit suicide, by a process called apoptosis.

The nerve cells that are most prone to suicide are those that make up the insulating myelin sheath around axons, called oligodendrocytes. Without this insulation, axons are unable to carry signals, and eventually disintegrate.
The cumulative toll of all these events is that, a few weeks after the injury, a scar tissue is formed across the injury site. This scar acts as a physical barrier which any regrowing axons cannot cross to connect to cells on the other side.
The most important considerations when dealing with spinal cord injuries are to minimise the amount of damage to the spinal cord, on the one hand, and prevent additional damage, on the other. These concerns apply both when moving a patient and during the first weeks after the injury, during the so-called acute phase.

There are, as yet, no treatments that completely revert the damage caused to the spinal cord. However, doctors are agreed that high-quality medical care immediately after the injury and aggressive rehabilitation strategies can go a long way in helping patients regain both physical and emotional independence.

The steroid drug methylprednisolone is often given to patients within the first eight hours after their injury. This drug seems to significantly limit the extent of damage and improve patients’ recovery. It appears to work by reducing cell death near the injury site by decreasing inflammation at the site.

During the acute phase of the injury, which covers the first few weeks after the initial damage, braces, rods or ties are applied to the patient. The aim is to apply traction to the spinal column to stabilize it and prevent further damage.

Rehabilitation programmes are a central part of treating spinal cord injuries. They combine physiotherapy with skill-building activities and counselling. Their aim is to provide physical, social and emotional support to the patients.

A rehabilitation team will typically include a physiatrist (a doctor specialising in rehabilitation), physical and occupational therapists, recreational therapists, rehabilitation nurses and psychologists, vocational counsellors, nutritionists and other specialists.

For the patient to get the most out of a rehabilitation programme, it is crucial that he/she is actively supported by family and friends.
Many research teams, all over the world, are working to understand what actually happens when the spinal cord is injured. Their hope is that, in dissecting out the different phases of spinal cord injury, it will be possible to identify targets for therapeutic interventions that will halt or even reverse the devastation triggered by the initial damage.

A spinal cord injury is complex: it involves different kinds of damage (cell death, inflammation); different types of cells are damaged (neurones and their supporting cells, glia); the environment of the spinal cord changes drastically during the first few weeks after injury (immune cells flow in, toxic substances are released, a scar is formed).

It is therefore likely that a combination of therapies will need to be developed, each acting at the appropriate time-point, and on the correct targets.

Any attempt to develop a treatment entails thoroughly understanding the physical environment of the injury.

Researchers are trying to find answers to one or several of the following questions:

**01.** How can surviving cells be protected from further damage?

**02.** How can nerve cells that have died or are non-functional be replaced?

**03.** How can we stimulate re-growth of axons and make them establish the correct connections?

**04.** How can we retrain the circuits of neurones so that body functions are restored?
How may stem cell research contribute to spinal cord repair?

A stem cell has the capacity to give rise to many different types of cells. Because of this amazing capability, there is great potential for the use of stem cells to treat the damage inflicted on the cells of the spinal cord, after injury.

There are three ways in which stem cells may potentially contribute to repair the spinal cord.

01. They may be used to replace the neurones that have died as a result of the injury.

02. They may be used to generate new supporting cells that will re-form the insulating myelin sheath and, consequently, stimulate re-growth of damaged axons.

03. When introduced into the spinal cord shortly after injury, these cells may protect the cells at the injury site from further damage, by releasing protective factors. Stem cells may also stimulate self-repair by producing growth factors.

All research into the use of stem cells in spinal cord injuries has been undertaken using animal models (mainly mice and rats).

Several questions remain to be answered, but each new study brings scientists a step closer to applying stem cells, and the specialised cells grown from them, to the treatment of human spinal cord injuries.
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