PHARMACY DEPARTMENT HOSPITAL SEGAMAT

BULLETIN PHARMACY (4/2014)

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AMYOTROPHIC LATERAL SCLEROSIS (ALS)

Have you ever heard of the ALS Ice Bucket Challenge? It went viral over the internet and across the world recently. It is a campaign to raise public awareness to ALS, it also raised substantial amount of donation with over 3 million donations worldwide for ALS research. When you search for ALS in Malaysia on the internet, there is close to none of information about it.

What is ALS?

Amyotrophic lateral sclerosis (ALS), sometimes called *Lou Gehrig's disease*, is a rapidly progressive, invariably fatal neurological disease that attacks the nerve cells *(neurons)* responsible for controlling voluntary muscles (muscle action we are able to control, such as those in the arms, legs, and face). The disease belongs to a group of disorders known as *motor neuron diseases,* which are characterized by the gradual degeneration and death of motor neurons.[1]

HISTORY OF ALS

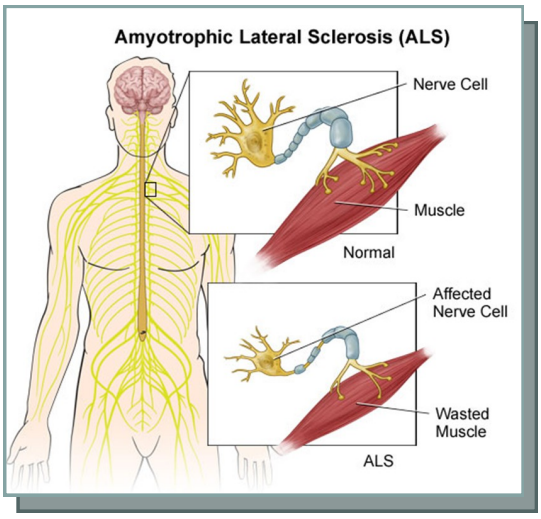
Jean- Marie Charcot (1825-1893) noted the first reports of the characteristics of ALS in 1874, and named the fatal syndrome based on what he found. He was a noted French neurologist who has been called "the Father of Neurology", and explained how the central nervous system works [6]

PATHOPHYSIOLOGY

Motor neurons are nerve cells located in the brain, brain stem, and spinal cord that serve as controlling units and vital communication links between the nervous system and the voluntary muscles of the body. Messages from motor neurons in the brain (called *upper motor neurons)* are transmitted to motor neurons in the spinal cord (called *lower motor neurons)* and from them to particular muscles. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, and stop sending messages to muscles. Unable to function, the muscles gradually weaken, waste away *(atrophy)*, and have very fine twitches *(*called *fasciculations)*. Eventually, the ability of the brain to start and control voluntary movement is lost.[2]

ALS causes weakness with a wide range of disabilities. Eventually, all muscles under voluntary control are affected, and individuals lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, people lose the ability to breathe without ventilatory support. Most people with ALS die from respiratory failure, usually within 3 to 5 years from the onset of symptoms. However, about 10 percent of those with ALS survive for 10 or more years. Although the disease usually does not impair a person's mind or intelligence, several recent studies suggest that some persons with ALS may have depression or alterations in cognitive functions involving decision-making and memory.[2]

ALS does not affect a person's ability to see, smell, taste, hear, or recognize touch. Patients usually maintain control of eye muscles and bladder and bowel functions, although in the late stages of the disease most individuals will need help getting to and from the bathroom.[2]



RISK FACTORS[3]

- **Heredity:** 5-10% of the people with ALS inherited it.
- **Age:** commonly occurs in people aged 40-60 years old.
- **Sex:** Before the age of 65, slightly more men than women develop ALS. This sex difference disappears after age 70.
- **Smoking:** Smoking cigarettes appears to increase a person's risk of ALS to almost twice that of a nonsmoker. The more years spent smoking, the greater the risk
- **Lead exposure.** Some evidence suggests that exposure to lead in the workplace may be associated with the development of ALS.

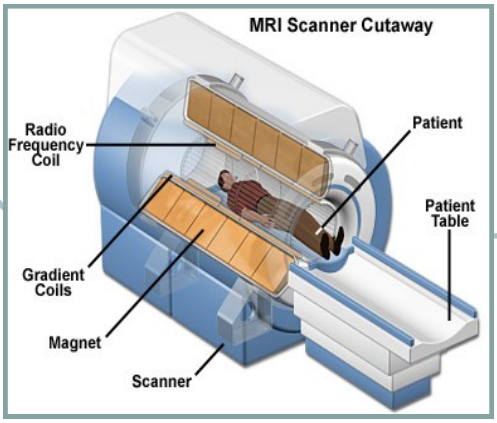
SIGNS & SYMPTOMS [1,2]

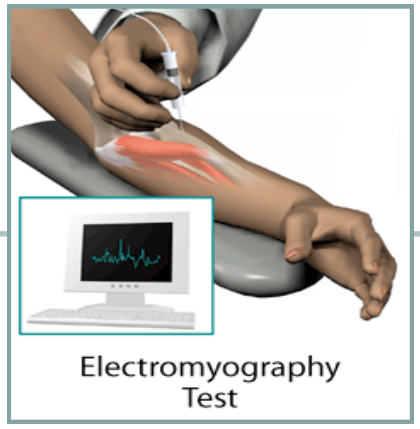
- Twitching and cramping of muscles, especially those in the hands and feet
- Loss of motor control in the hands and arms
- Impairment in the use of the arms and legs
- Tripping and falling
- Dropping things
- Persistent fatigue
- Uncontrollable periods of laughing or crying
- Slurred or thick speech and difficulty in projecting the voice
- Difficulty breathing
- Difficulty swallowing
- Paralysis

"Most people with ALS die from respiratory failure, usually within 3 to 5 years from the onset of symptoms. However, about 10 percent of those with ALS survive for 10 or more years" [4]

TEST & DIAGNOSIS[3]

- **Laboratory tests** (including blood and urine studies and thyroid functioning tests)
- **Muscle and/or nerve biopsy.** A procedure performed to remove tissue or cells from the body for examination under a microscope.
- **Spinal tap (also called a lumbar puncture).** A special needle is placed into the lower back, into the spinal canal; This is the area around the spinal cord; The pressure in the spinal canal and brain can then be measured. A small amount of cerebral spinal fluid (CSF) can be removed and sent for testing to determine if there is an infection or other problems. CSF is the fluid that bathes the brain and spinal cord.
- **X-ray.** A diagnostic test which uses invisible electromagnetic energy beams to produce images of internal tissues, bones, and organs onto film
- **Magnetic resonance imaging (MRI).** A diagnostic procedure that uses a combination of large magnets, radiofrequencies, and a computer to produce detailed images of organs and structures within the body
- **Electrodiagnostic tests, such as electromyography (EMG) and nerve conduction study (NCS).** Studies that evaluate and diagnose disorders of the muscles and motor neurons. Electrodes are inserted into the muscle, or placed on the skin overlying a muscle or muscle group, and electrical activity and muscle response are recorded.





MANAGEMENT [5]

BREATHING

The physician may recommend *noninvasive ventilation* to compensate for weakened muscles by assisting the movement of air in and out of the lungs. Noninvasive ventilation usually consists of two basic elements: an "interface," such as a mask or nose inserts, and air delivered under pressure by a small, portable machine such as *BiPAP* for *bilevel positive airway pressure*. A different type of breathing assistance device called a *diaphragm pacing system* was approved in ALS by the U.S. Food and Drug Administration (FDA). The NeuRx Diaphragm Pacing System (DPS) rhythmically stimulates breathing through an external pacer unit attached to electrodes that are surgically implanted in the diaphragm. Another aspect of respiratory care that's important in ALS is *assisted coughing*. An assisted coughing device, which pushes air into the airways through a mask and then quickly reverses air flow, can help clear the airways and prevent infection.

MANAGEMENT (CONT...)

COGNITIVE & BEHAVIOUR CHANGES

Although ALS is considered a disease of the motor (movement) system, cognitive (thinking) and behavioral changes also may occur in this disease. Memory is generally well-preserved in ALS. Instead, the person with ALS may become unduly angry or irritable. Another phenomenon that sometimes occurs in ALS is known as *pseudobulbar affect (PBA),* in which the person experiences uncontrollable bouts of laughing or crying out of proportion to the situation. In 2010, the drug *Nuedexta* was approved to treat this symptom.

COMMUNICATION

Speaking ability is lost when ALS affects the muscles of the mouth and throat that control speech and the muscles that help move air over the vocal cords. A speech therapist can teach the person with ALS special techniques for conserving energy and making speech more understandable. Speech therapists may suggest voice banking, which involves recording a number of common phrases that later can be programmed into a computer or communication device, enabling individuals with ALS to continue speaking in their own voice when they communicate via assistive technology. In some cases, a dentist can make a device called a *palatal lift* that can help compensate for certain types of weakness in the roof of the mouth.

DEPRESSION

According to the 2009 ALS Care Guidelines, there have been no controlled trials of treatment for depression in ALS. Many clinicians have found that antidepressants or anti-anxiety medication can have a positive effect.

DROLLING

Drooling, is common in ALS, because of weakness of the muscles of the mouth and throat. Oral medication *amitriptyline* may be helpful in drying up saliva thereby reducing drooling, as may injections of *botulinum toxin type A* into the salivary glands. There is good evidence that drooling can be controlled using the drug botulinum toxin type B, injected into the glands near the jaw that make saliva. Radiation of the salivary glands to reduce saliva production also has been used for treatment of this condition when other measures fail.

EATING, DRINKING AND NUTRITION

Recent evidence shows that maintaining one's weight may increase survival with ALS. Severe weight loss means muscle loss. Adequate fluid intake also is essential, for hydration and avoiding constipation. Other challenges include arm/hand weakness that limits self-feeding, decreased appetite and constipation. Early solutions involve changing the consistency of food and liquids — usually thickening the liquids and avoiding large pieces of food — as well as changing swallowing techniques. If swallowing becomes difficult or unsafe and/or if eating takes a great deal of time and energy, a feeding tube may be recommended.

HAND FUNCTION

Occupational therapists specialize in helping people find and use tools to cope with progressive weakness in hand muscles. Special grips for writing and eating utensils, devices that fit over keys to make them easier to turn, zipper pulls and button hooks can help make weakening hands more functional, and help preserve independence in activities of daily living

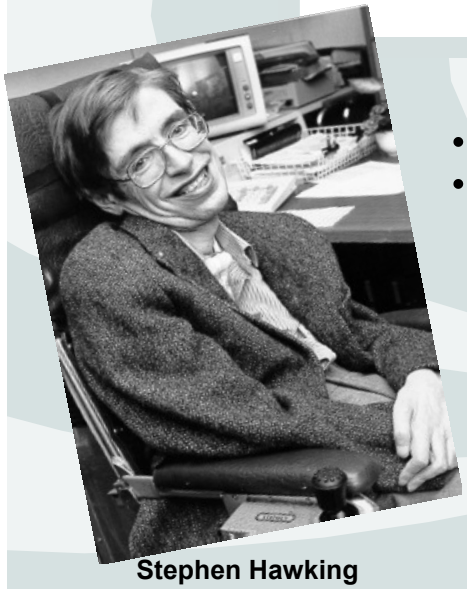
MEDICATIONS

The drug *riluzole (Rilutek)* has a modest effect on slowing disease progression and prolonging survival. Vitamin supplements may be recommended if swallowing difficulties result in reduced intake of nutrients including vitamins C and E, are thought to have beneficial effects on the nervous system and overall health. In 2010, a medication called Nuedexta was approved specifically for an aspect of ALS called *pseudobulbar affect*.

MOBILITY

Fatigue, falling and increased difficulty walking often are experienced as ALS progresses. Avoiding falls is of paramount importance and can prevent trauma that could accelerate ALS disease progression. In addition to using mobility equipment to avoid falls, be sure to move area rugs, install grab bars and eliminate clutter wherever possible. In the early stages of ALS, mobility equipment such as a cane, walker or a supportive brace (*orthosis*) provide help in getting around. A lightweight ankle-foot orthosis, or *AFO*, keeps the foot from dropping and adds steadiness when walking. When walking becomes difficult, riding in a manual wheelchair for long distances can conserve energy for short-distance walking, and also help prevent injury. In later stages of the disease, a power wheelchair is usually the preferred means of mobility. Other valuable power chair options include elevating seats, chairs that turn into standers, motorized leg rests and custom seating.

FAMOUS PEOPLE WITH ALS

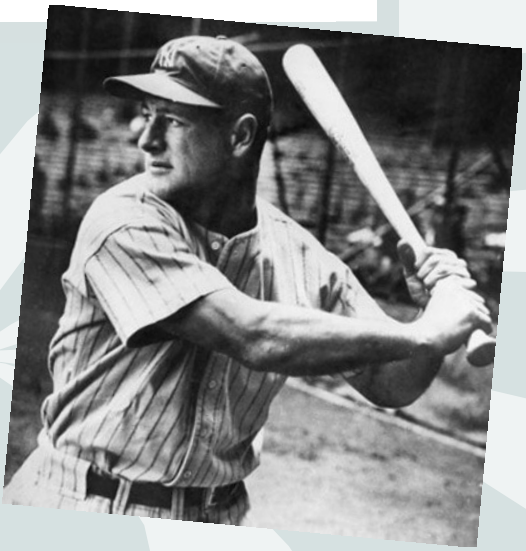


Stephen Hawking

- Professor (Theoretical Physics & Cosmology)
- 8 Jan 1942 - Present

Mokhtar Dahari

- Malaysian football player
- 13 Nov 1953 - 11 July 1991



Lou Gehrig

- American baseball player
- 19 June 1903 – 2 June 1941

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1. http://www.alsa.org/about-als/what-is-als.html
2. http://www.medicinenet.com/amyotrophic_lateral_sclerosis/article.htm
3. http://www.mayoclinic.org/diseases-conditions/amyotrophic-lateral-sclerosis/basics/risk-factors/con-20024397
4. http://www.ninds.nih.gov/disorders/amyotrophiclateralsclerosis/detail_als.htm#267704842
5. http://mda.org/disease/amyotrophic-lateral-sclerosis/medical-management
6. http://dev.nsta.org/evwebs/2150/history.htm

ADVERSE DRUG REACTION REPORT

Hospital Segamat

Date	Medication	ADR	Treatment	Reporter
18/8/2014	IV Streptokinase 1.5MU STAT	Urticaria	IV Hydrocortisone, IV Piriton	Ms. Jessica Chin

MADRAC UPDATE

HUMAN PAPILLOMAVIRUS (HPV) VACCINE: COMPLEX REGIONAL PAIN SYNDROME (CRPS)

About HPV Vaccination

The World Health Organisation (WHO) recommends the introduction of human papillomavirus (HPV) vaccination into national immunisation programmes where cervical cancer prevention is a public health priority and it is programmatically feasible. The Malaysian HPV Immunisation Programme was launched in September 2010, targeting teenage girls aged 13 years. A catch-up programme for women aged 18 years was launched in July 2012 under the National Population and Family Development Board (LPPKN). There are currently two (2) HPV vaccines registered in Malaysia: Cervarix® (containing HPV types 16 & 18) and Gardasil® (containing HPV types 6, 11, 16 & 18).

Background of safety issue

In June 2013, the Japanese Ministry of Health, Labor and Welfare (MHLW) suspended active recommendation of HPV vaccination after almost 2,000 adverse reactions to the HPV vaccines were reported within three years, including long-term pain and numbness1. Several cases of complex regional pain syndrome (CRPS) have been highlighted in Japan, where more than 8 million doses of HPV vaccine have been distributed. Although no regulatory action was taken against the HPV vaccine license holders, the MHLW instructed local governments not to promote the use of the vaccines while further studies were being conducted on the adverse events, particularly CRPS

In January 2014, the MHLW Vaccines Safety Committee announced that the chronic pain appeared to be psychosomatic in nature (i.e. anxiety due to vaccination). An expert advisory committee continues to review the situation and has yet to conclude whether to return to proactive recommendation of HPV vaccination.

Complex Regional Pain Syndrome (CRPS)

CRPS is a chronic pain most often affecting one of the limbs, usually after an injury or trauma to that limb. It can affect both men and women. Children do not get it before age five and only very rarely before age ten, but it is not uncommon in teenagers2. The WHO ADR database contains 52 cases of CRPS related to HPV vaccination reported between 2009 and 2014*. Thirteen (13) of these reports were submitted from Japan.

The key symptom of CRPS is prolonged pain. The pain may feel like a burning or "pins and needles" sensation. It may spread to the entire limb or travel to the opposite extremity. People with CRPS also experience constant or intermittent changes in temperature, skin color, and swelling of the affected limb due to abnormal microcirculation. This is caused by damage to the nerves controlling blood flow and temperature. The exact pathogenesis of CRPS is still unclear. In more than 90% of cases, the condition is triggered by a clear history of trauma or injury. Limited data suggest that CRPS also may be influenced by genetics. The outcome of CRPS varies from person to person. Almost all children and teenagers have good recovery.

ADR REPORTS

Since the launch of the National HPV Immunisation Programme in 2010 until the end of 2013, a total of 6,867 adverse events following immunisation (AEFI) reports have been received by the Drug Safety Monitoring Centre through the active surveillance program. The majorities of these reactions were of mild to moderate severity, not long-lasting, and were documented in the package inserts. Frequently reported reactions include injection site pain, swelling, erythema, and generalised weakness. None of the reports related to prolonged injection site pain or body ache post-HPV vaccination.

CRPS is classified by the WHO as an autonomic nervous system disorder. To date, no CRPS or other adverse event related to autonomic nervous system disorders have been reported in Malaysia post-HPV vaccination. CRPS-associated symptoms such as muscle ache (87 reports), body aching (588) and limb weakness (480) have been reported but were mostly mild in nature and the patients subsequently recovered.

Conclusion

It is plausible that CRPS could develop following the injection of any vaccine. However, to date, the WHO Global Advisory Committee on Vaccine Safety (GACVS) has not found any safety issue that would alter the current recommendations for the use of HPV vaccines5,6**. The NPCB will continue to monitor this issue closely.**

Healthcare professionals are advised to report any suspected adverse events related to HPV vaccination to NPCB. Besides that, patients and their parents should be educated on the benefits of HPV vaccination in cervical cancer prevention as well as possible rare adverse events such as anaphylaxis. Healthcare providers in the private sector are advised to distribute the simplified AEFI reporting form to patients or their parents after HPV vaccination, as is done in the government setting. Please remind patients to seek medical attention and submit the form if any adverse reactions occur.

References

1. The Asahi Shimbun: *Health Ministry Withdraws Recommendation for Cervical Cancer Vaccine*. [June 2013]
2. National Institute of Neurological Disorders and Strokes: *Complex Regional Pain Syndrome Fact Sheet.* [Accessed: March 2014]
3. Cervarix® Package Insert. Malaysia. [Version: September 2012]
4. Gardasil® Package Insert. Malaysia. [Version: February 2011]
5. WHO Global Advisory Committee on Vaccine Safety (March 2014). *Statement on the continued safety of HPV vaccination.*
6. WHO Global Advisory Committee on Vaccine Safety (June 2013). *Weekly epidemiological record: Update on Human Papillomavirus*
Vaccines. 29:309-312.

Pharmacy Activities

Majlis perpisahan Cik Kee Geok Cheng

Dinner Jabatan farmasi di Port Dickson

Jamuan hariraya peringkat Hospital Segamat