Hereditary Spastic Paraplegia / Familial Spastic Paraparesis

Understanding this group of inherited disorders.

What is Hereditary Spastic Paraplegia?

Hereditary spastic paraplegia (HSP), also called familial spastic paraparesis (FSP), refers to a group of inherited disorders caused by various genetic alterations. Although there are various presentations of these conditions they all share common symptoms of weakness, spasticity (stiffness) and reduced ability to sense vibrations in the legs. Often the initial symptoms are mild difficulties in walking style (a spastic gait) due to leg stiffness. HSP tends to progress (get worse over time) quite slowly but, may eventually result in the person requiring the assistance of a cane, walker, or wheelchair. The number of people who have HSP varies from population to population ranging between 1.3 to 9.6 per 100,000 people. HSP affects both males and females similarly.

Types of HSP

HSP can present as "pure" with progressive lower limb spasticity and weakness or with other symptoms of a systemic or neurological nature (complicated HSP). These additional symptoms can include ataxia (lack of muscle coordination), epilepsy, impaired vision due to cataracts,

A walking stick is helpful for maintaining balance.

problems with the optic nerve and retina of the eye, cognitive impairment, peripheral neuropathy, and deafness.

Symptoms may begin in childhood or adulthood, depending on the particular HSP gene involved. When symptoms begin after childhood they usually progress slowly and steadily. If symptoms start in very early childhood they may not progress and therefore resemble spastic diplegic cerebal palsy. The severity of the condition varies widely with some people being severely disabled and others only mildly. Life expectancy for "pure" HSP is not affected.

Causes of HSP

Numerous genes are responsible for several forms of HSP, with more than 80 genetic causes of HSP identified to date, and many more will likely be identified in the future. HSP genes are designated "SPastic parapleGia, loci ("SPG") and numbered in order of their discovery (for example, SPG1 through SPG80). These genes generally encode proteins that normally help maintain the function of axons (which conduct nerve impulses) in the spinal cord. Loss of the conduction of information in these cells causes the symptoms experienced in HSP.

Inheritance

HSP has several forms of inheritance. Not all children in a family will necessarily develop symptoms, although they may be carriers of the abnormal gene

Depending on the specific gene defect that is causing the condition it is inherited in three ways which are described below:

X-linked recessive: The sex chromosomes X and Y determine if a baby will be a boy or a girl. X-Linked HSP is caused by defects in genes present on the X chromosome.

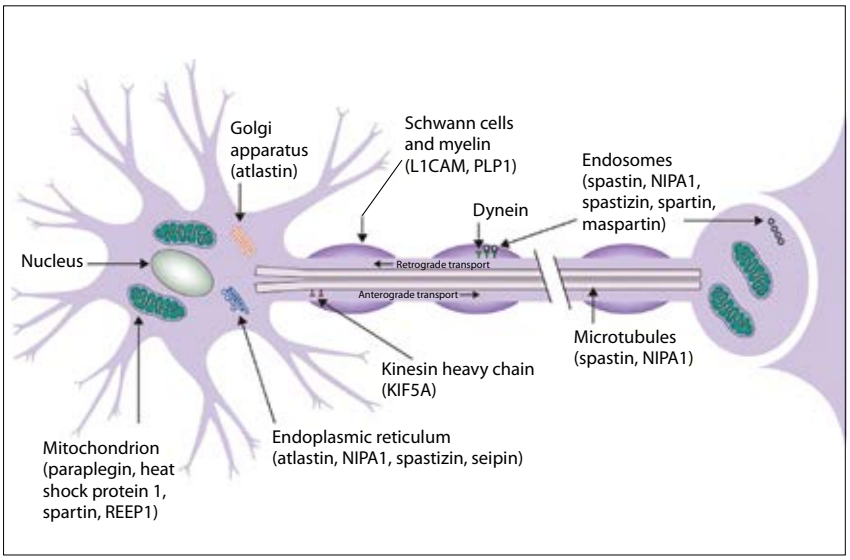

Diagram of nerves and transmission of signals. Photo credit: thelancet.com

One functioning copy is enough to prevent X-Linked HSP. Girls receive an X chromosome from mum and an X chromosome from dad and are described as XX. Boys receive an X from mum and a Y chromosome from dad and are described as XY. As boys have only one X chromosome if they inherit an X chromosome with a defective gene then they will have that condition. The mother is described as a 'carrier' and with one functioning gene is usually unaffected. A carrier mother has a 25% chance in each pregnancy of having an affected male child.

Autosomal dominant: This means that one defective copy is enough for the disease to present. The gene with the defect is found on one of the 22 pairs of chromosomes not involved in sex determination. Men and women are equally likely to be affected. A person with an autosomal dominant condition has a 50 percent chance in each pregnancy that their child will also be affected.

Autosomal recessive: This means that both copies of the abnormal gene must be defective for the disease to develop fully. In this situation each parent is a carrier of the same defective gene. Each child they have has a 25% chance of inheriting the disease.

If symptoms start in very early childhood they may not progress and therefore resemble spastic diplegic cerebal palsy.

Genetic counselling is available to families who have had a diagnosis of hereditary spastic paraplegia (as there are several different inheritance patterns it is important that the diagnosis is correct). This service provides information, helps families understand inheritance patterns and what this means for their family, as well as enabling people to make more informed family-planning decisions. You can access the free NZ genetic counsellor service via your GP, self-referral or talk to an MDANZ fieldworker who can assist you.

Diagnosis

The diagnosis of HSP is primarily by neurological examination and observation of a spastic gait as well as testing to rule out other disorders. Family history, genetic testing, laboratory tests, neurophysiologic testing, and neuroimaging can also help confirm a diagnosis.

MRI abnormalities, such as a thin corpus callosum (largest midline structure of the brain), may be seen in some of the complicated forms of HSP.

Management

There are no specific treatments to prevent, slow, or reverse HSP. There is a multidisciplinary team approach to management of the symptoms that present during the course of this condition and to improve balance, strength and agility. A neurologist, physiotherapist, occupational therapist, and a dietitian may all be needed at some point.

Current recommendations are:

- Daily physical therapy and exercise aiming towards improving cardiovascular fitness and maintaining and improving muscle strength and gait and reducing muscle tightness.
- Referral to an occupational therapist to make sure any assistive walking devices or ankle-foot orthotics are used if appropriate.

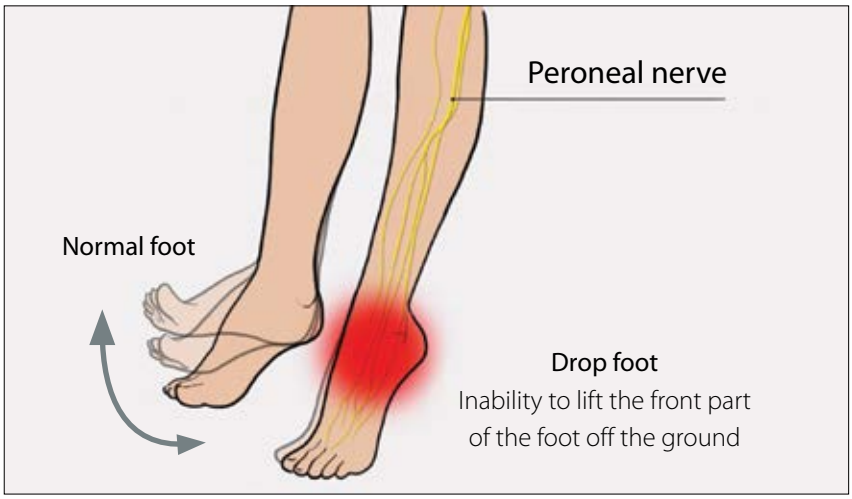

Diagram showing drop foot. Illustration: www.bodyorganics.com.au

They may have some practical suggestions that have worked for others to offer as well.

- Drugs to reduce muscle spasticity (including Botox injections) and reduce urinary urgency.
- Annual or as needed evaluations by a neurologist and physiotherapist to monitor any progression of the condition and to make sure treatment programmes are relevant.
- Avoid exposure to medications or chemicals that cause neuropathy if possible.

During Pregnancy

HSP symptoms generally do not change significantly during pregnancy, unless a medication treating symptoms is stopped during the course of the pregnancy. In general, uncomplicated HSP does not pose increased risk for pregnancy, labour, or delivery. In general, having uncomplicated HSP does not increase risk associated with obstetric anaesthesia.

Research

Current research is looking at the following methods of treating HSP:

- Gene therapy: a mechanism for supplementing defective genes with healthy genes in the tissues affected by neuromuscular disease;
- Gene silencing: turning off genetic instructions that cause the production of toxic proteins.

Support

Our fieldworkers are available for support. They have in-depth knowledge of a range of neuromuscular conditions, and will have an understanding of your needs and challenges. Have a chat over the phone or they can come to you for a kanohi ki te kanohi/face-to-face visit. They may have some practical suggestions that have worked for others to offer, as well as providing general support and a referral to health professionals. This service is offered free of charge to MDANZ members and is funded through donations and grants. See contact information at the back of *In Touch* to find a fieldworker.

Our Support Network facilitates people with similar circumstances or challenges to connect so they can share their experiences, and provide each other with emotional support, as well as practical advice and information. By bringing together people with common experiences, support networks can provide an invaluable addition to medical care. Our Support Network currently has over 600 members throughout New Zealand who want to be in touch with others livings with neuromuscular conditions. Please contact info@mda.org.nz more information.

Useful Websites

http://sp-foundation.org/

http://rarediseases.org/

References http://www.ninds.nih.gov/disorders/hereditary_spastic_paraplegia/hereditary_spastic_paraplegia.htm

https://umaine.edu/edhd/research/acc/what-is-agenesis-of-the-corpus-callosum-acc/

http://www.ncbi.nlm.nih.gov/books/NBK1509/ ®