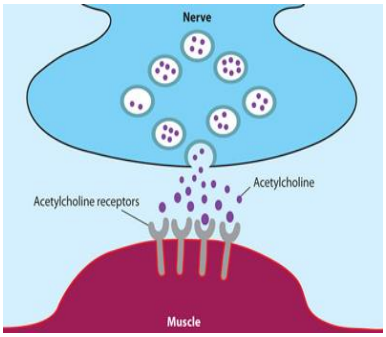
Updated October 2016

Muscular Dystrophy New Zealand

Congenital Myasthenic Syndrome- Information Fact Sheet

What is Congenital Myasthenic Syndrome?



Source: mda.org.au

Congenital Myasthenic Syndrome (CMS) is a family of inherited neuromuscular conditions characterised by skeletal muscle weakness that worsens with physical exertion. Cardiac and smooth muscle are usually not involved. Coordination, sensation, and tendon reflexes are normal; cognitive skills are usually normal as well. Muscular weakness is due to problems in the neuromuscular junction -which is the area between the ends of nerve cells and muscle cells where signals are relayed to trigger muscle movement. This causes communication in this area to be adversely affected. Symptoms of muscle weakness typically begin in early childhood, however they can also begin in adolescence and adulthood. The severity of the myasthenia varies greatly, with some people experiencing minor weakness and others having such severe weakness that they are unable to walk. Prevalence of CMS is unknown.

What are the different types of Congenital Myasthenic Syndrome?

The types of CMS are grouped into three main categories depending on the part of the neuromuscular junction affected. These include presynaptic (the nerve cell), postsynaptic (the muscle cell) or synaptic (the space in between the nerve and the muscle cell).

Presynaptic CMS is characterised by insufficient release of acetylcholine, a neurotransmitter that controls muscle contractions. This affects 7-8% of individuals with CMS.

Postsynaptic CMS have two forms, and affect a total of approximately 75-80% of individuals with the condition. One is characterised by missing acetylcholine receptors or receptors that don't stay open long enough called "fast-channel CMS" and the second is characterised by acetylcholine receptors that are open for too long, called "slow-channel CMS".

Synaptic CMS is characterised by a deficiency of acetylcholinesterase, an enzyme which breaks down acetylcholine. This affects 14-15% of individuals with the condition. Identification of the specific subtype is important in patient care for determining the most effective treatment.

419 Church Street East, Penrose, Auckland 1642 | P O Box 12063, Penrose, Auckland 1061
0800 800 337 | info@mda.org.nz | www.mda.org.nz

Charity Registration Number CC31123

Muscular Dystrophy New Zealand

What are the features of Congenital Myasthenic Syndrome?

The features of CMS are often present at birth; however, they sometimes are not noticeable until before adolescence. People will have visible facial weakness and it may be noted that infants are slow to meet their crawling or walking milestones. Infants with the condition can also have periods of shallow breathing often at times of infection, fever or excitement which can cause periods of no breathing and cyanosis (blue skin or lips). An abnormal, high-pitched, musical breathing sound caused by a blockage in the throat or voice box (larynx) can also be heard in CMS infants when taking in a breath. Symptoms of CMS consist of muscle weakness, particularly in the mouth and throat causing difficulty chewing, swallowing or feeding and causing choking spells. The eye muscles are also commonly affected causing droopy eyelids (ptosis). Curvature of the spine (scoliosis) and in some cases contractures can also be present.

What causes Congenital Myasthenic Syndrome?

CMS is an inherited neuromuscular condition; therefore, it is caused by defective genes necessary for making the acetylcholine receptor or other components or proteins of the neuromuscular junction. Mutations in the *CHRNE* gene are responsible for more than half of all cases. A large number of cases are also caused by mutations in the *RAPSN*, *CHAT*, *COLQ*, and *DOK7* genes. Except for slow-channel CMS, the inheritance pattern for the different types of CMS is autosomal recessive. This means that it takes two copies of the defective gene, one from each parent, for the disease to be present. Slow-channel CMS is autosomal dominant; therefore, it only takes one copy of the gene from one parent to cause the disease which means that there is a 50% chance of an affected parent to pass on the disease to their child.

Diagnosis of Congenital Myasthenic Syndrome

A full comprehensive family history and physical examination will occur as part of the diagnostic process. The physician will be looking specifically for weakness and fatigue, particularly where the weakness includes droopy eyelids. A physical assessment of the strength of eyelids and skeletal muscles may be assessed by asking the patient to look towards the ceiling without blinking for one-two minutes or holding their arms out for as long as possible.

If physical tests are consistent with myasthenia, blood tests will be ordered to detect antibodies to the acetylcholine receptor. A negative test will rule out myasthenia gravia (MG), an autoimmune disease and indicate possible CMS. However, it does not rule out seronegative types of MG. Electrodiagnostic tests could then be

performed where an electrode is placed on the surface of a major muscle and deliver a small shock to the nerve or records the responses in the muscle to contraction.
An intravenous injection of Tensilon, a fast-acting acetylcholinesterase inhibitor could be administered as part of the diagnostic process where a temporary increase in strength after the injection would indicate CMS.
Biopsy and absence of major pathological findings on a piece of muscle tissue as well as genetic testing can further conclude the type of CMS along with a family history of myasthenic syndrome will support this diagnosis.

Management of Congenital Myasthenic Syndrome

- Non-invasive ventilation at night time to help with breathing difficulties. Apnea monitors are recommended for young children.
- Pyridostigmine, a cholinesterase inhibitor, to encourage messages to travel from the nerve to the muscle. This is used for presynaptic CMS and postsynaptic fast-channel CMS.
- 3,4-diamino-pyridine' DAP, increases acetylcholine release which causes electrical messages to last longer. To be used for postsynaptic fast-channel CMS.
- Ephedrine and albuterol to improve muscle strength.
- Quinidine or fluoxetine to help faulty acetylcholine receptors to close for post synaptic slow-channel CMS.

There are no current medications available to treat synaptic CMs.

Certain drugs should be avoided as they are known to affect neuromuscular transmission and exacerbate symptoms of the condition (e.g., ciprofloxacin, chloroquine, procaine, lithium, phenytoin, beta-blockers, procainamide, quinidine).

Research into Congenital Myasthenic Syndrome

Current research studies are focusing on the development of a new mouse model of a congenital myasthenic syndrome; genetic analysis of a worm with a slow-channel myasthenic syndrome; studies of how the nerve-muscle function forms and also methods to improve diagnosis, treatment and prevention of congenital myasthenic syndrome.

Muscular Dystrophy New Zealand

Support for people with Congenital Myasthenic Syndrome

The MDA Fieldworkers are available for support. They have in-depth knowledge of a range of neuromuscular conditions, and will have a better 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 real practical suggestions that have worked for others to offer as well. This service is offered free of charge to MDA members and is funded through donations and grants.
Contact your local MDA Branch to be put in contact with your fieldworker.

The MDA Support Network allows people with similar circumstances or challenges to come together to share their experiences and provide each other with emotional and moral support in addition to practical advice and information. By bringing together people with common experiences, support networks can provide an invaluable addition to medical care. The MDA of New Zealand Support Network currently has over 700 members throughout New Zealand who want to be in touch with others living with neuromuscular conditions. Please see the MDA website www.mda.org.nz for contact details and more information that you might find relevant for you and your whanau.

Information in this fact sheet was primarily sourced from:

- https://www.mda.org/disease/congenital-myasthenic-syndromes/medical-management
- http://www.congenitalmyasthenicsyndrome.info/
- https://www.myaware.org/congenital-myasthenia
- https://ghr.nlm.nih.gov/condition/congenital-myasthenic-syndrome#statistics
- http://www.ncbi.nlm.nih.gov/books/NBK1168/
- GARD: Genetic and rare diseases information centre: https://rarediseases.info.nih.gov/diseases/11902/congenital-myasthenic-syndrome

419 Church Street East, Penrose, Auckland 1642 | P O Box 12063, Penrose, Auckland 1061
0800 800 337 | info@mda.org.nz | www.mda.org.nz

Charity Registration Number CC31123