Duchenne Muscular Dystrophy

What is Duchenne muscular dystrophy (DMD)?

Duchenne muscular dystrophy, also known as DMD, is the most common childhood onset hereditary neuromuscular disorder affecting 1 in 3,500 to 1 in 5,000 male births. It is a severe and progressive muscle wasting disease that leads to loss of mobility and deterioration in health over time.

The earliest presenting symptoms are difficulties in walking upstairs, easy falling, or waddling gait. These symptoms are usually recognised between 3 to 6 years of age. Most patients become wheelchair dependent around 8-10 years of age. They also need assisted ventilation support and cardiac medicine at adolescence. As weakness worsens, scoliosis and joint contractures develop.

Following the recommended Standard of Care (SOC) and regular steroid treatment, most patients with DMD can prolong their independent ambulation till the age of 12. One-third of the patients also have learning, neurobehavioural or cognitive problems. Most of the patients die early between 20 to 40 years of age from either cardiac failure or respiratory failure.

What causes Duchenne muscular dystrophy?

DMD is caused by mutations in DMD gene on the X-chromosome. The mutations in the DMD gene prevent the production of functional dystrophin protein. The dystrophin protein is found in the inner membrane of the skeletal and cardiac muscle cells maintaining the stability of the muscle cell membrane from easy damage. The lack of dystrophin protein in the skeletal muscles results in progressive muscle damage from repeated muscle contraction leading to muscle atrophy and weakness. The lack of dystrophin protein in the heart muscles causes dilated cardiomyopathy and arrhythmia. The inadequate dystrophin protein in the brain also causes learning difficulty, cognitive impairment and / or neurobehavioural disorders.

What are the presenting symptoms and signs of DMD?

Symptoms

- Motor difficulties (e.g. easy falling, tip toe walking)
- Delayed motor development (e.g. delay in walking)
- Proximal weakness reported (e.g.difficulty in getting up from sitting to standing)

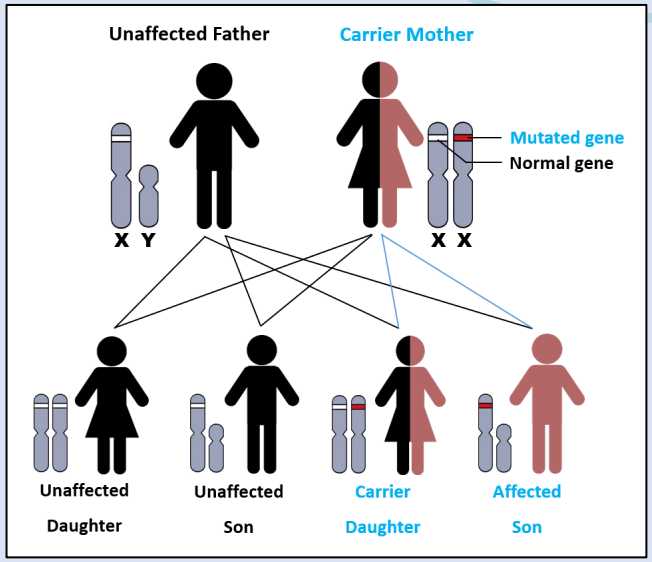
Signs

- Calves pseudohypertrophy
- Gower sign: Child relies on his hands to crawl up his legs to stand from sitting position due to weakness of his proximal muscles
- Hyporeflexia or areflexia
- Without muscle pain, child has markedly elevated creatine kinase level

How is Duchenne muscular dystrophy inherited?

DMD is an X-linked recessive disorder with the condition caused by DMD gene mutation located on the short arm (p) of the X-chromosome (Xp21.2) and manifest mainly in males. For a male with only 1 copy of X-chromosome, he will develop DMD if he has the mutation of the DMD gene. Although most boys with DMD inherit the abnormal gene from their mothers as the carriers, some may develop the disease as a result of a spontaneous mutation of the DMD gene (de novo or sporadic cases).

A mother who is a DMD carrier has a 50 % chance to pass on the genetic mutation to her children. Her son who receives the defective DMD gene will have the disease. Her daughter who receives the defective gene will become a carrier.



How is Duchenne muscular dystrophy diagnosed?

A diagnosis of DMD is made based on detailed clinical history, a thorough clinical evaluation, and several specialized tests including creatine kinases and genetic study.

Type of DMD gene mutations	How often does the mutation cause DMD?	Genetic Test
Exon deletions	60 - 70%	MLPA
Exon duplications	10%	MLPA
Point mutations and other small intragenic changes (including 'nonsense' mutations)	15 - 30%	DMD gene sequencing or whole exome sequencing

If the above genetic findings are negative, muscle biopsy should be arranged to evaluate the expression of dystrophin protein and other associated muscle membrane proteins in the skeletal muscle biopsy. If the dystrophin expression is absent in the muscle biopsy but the above genetic studies show negative finding, patients might be recruited to further research study based on their clinical condition. Whole genome sequencing and muscle biopsy transcriptome study will be proceeded under research arrangement.

Are there treatments for Duchenne muscular dystrophy?

No curative treatment is available for DMD at this stage. Standard of care management for DMD includes multi-speciality care.

Physiotherapy, occupational therapy, and rehabilitation can help to maintain muscle strength, prevent joint contractures, and improve range of motion. Regular use of oral steroid – prednisolone or deflazacort – can delay motor deterioration and prolong the time of independent ambulation. At the later stage of the disease, rehab equipment such as brace, orthosis, walking aids and wheelchair help to improve functional independence. When there is breathing difficulty, non-invasive ventilation use can improve breathing. Cardiac treatment is helpful if dilated cardiomyopathy is evidenced. Those with spinal curve progression require spinal brace support and may need scoliosis surgery. Endocrine care and adequate vitamin D and calcium level promotes bone health.

For further enquiries on the treatment options, please consult your attending doctor.

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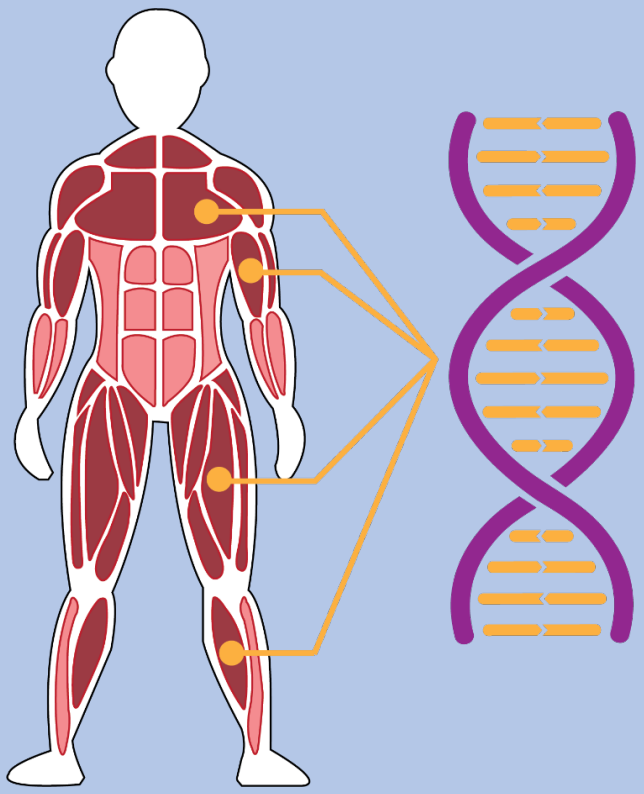
DUCHENNE MUSCULAR DYSTROPHY INFORMATION



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