Pelizaeus-Merzbacher disease (PMD)

What is Pelizaeus-Merzbacher disease?

Pelizaeus-Merzbacher disease (PMD) is a type of leukodystrophy, and affects the brain and spinal cord. There are two types of PMD, classic or connatal. The term "connatal" refers to the fact that this form is present from birth. Classic PMD is the most common type, however Connatal is the more severe of the two. PMD involves hypomyelination, which means that they nervous system has a reduced ability to form myelin (the substance covering nerve fibres). As a result the neurological function of those affected is reduced.

What is the PLP1 gene?

Changes or mutations in the PLP1 gene cause PMD. The PLP1 gene provides instructions for making 2 proteins, proteolipid protein 1, and a modified form of this protein called DM20.
Proteolipid protein 1 is primarily found in the nerves of the central nervous system, whereas DM20 is produced mainly in nerves connecting the brain and spinal cord to the muscles.

The majority of mutations that cause PMD duplicate the PLP1 gene, resulting in an increase in production of proteolipid protein 1 and DM20. Other mutations cause abnormal proteins to be produced. Excess or abnormal proteins cannot travel to the cell membrane, and therefore proteolipid protein 1 and DM20 are not available to form myelin.

What are the symptoms of PMD?

Classic PMD		Connatal PMD
Symptoms typically begin to appear in the first year of life. Symptoms of Classic PMD include weak muscle tone (hyptonia), involuntary eye movements, and delayed development of motor skills. Intellectual and motor skills develop throughout childhood, but development usually stops around adolescence, and these skills are slowly lost. As the condition worsens, nystagmus usually goes away but other movement disorders develop, including muscle stiffness, problems with movement and balance (ataxia), head and neck tremors, and involuntary tensing of the muscles (dystonia).		Symptoms are present at birth and are more severe than classic PMD. Symptoms include problems with feeding and consequent poor weight gain and growth, high-pitched breathing caused by an obstructed airway (stridor), nystagmus, progressive speech difficulties, severe ataxia, hypotonia, and seizures. Individuals with connatal PMD are never able to walk, and many are not able to purposefully use their arms. They also have problems producing speech (expressive language) but can generally understand speech (receptive language).

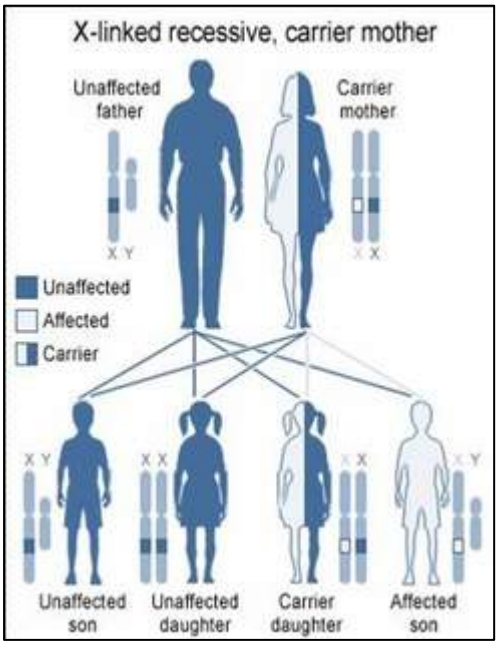
How is PMD diagnosed?

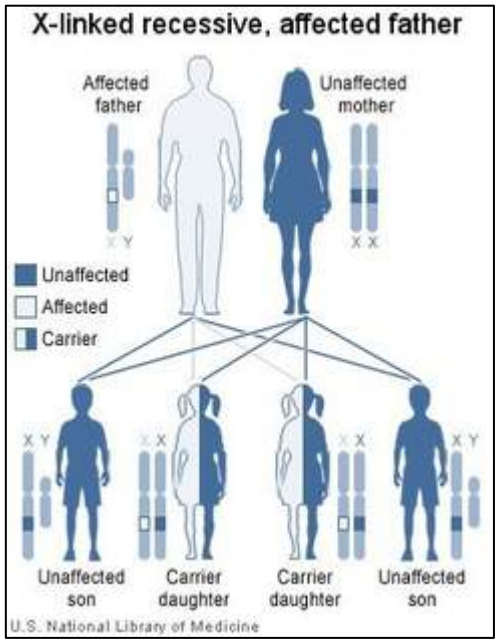
The presence of the symptoms will be suggestive of PMD. Genetic testing for PMD will look for changes (or mutations) in the PLP1 gene on the X chromosome.

Are family members at risk of PMD?
PMD is an X-linked condition, meaning the affected PLP1 gene is located on the X chromosome. As males have one X chromosome, and one Y chromosome, one copy of the affected PLP1 gene only their only X chromosome is sufficient to cause PMD. Having two copies of X chromosomes, women who have one affected PLP1 gene usually do not have any features of PMD, and are considered carriers. However, women with one copy of the affected PLP1 gene can show some signs of PMD, although less severe in nature.

Males affected with the PLP1 gene change will always pass on the affected X chromosome to his daughters, but never to his sons, as sons will always inherit their father's Y chromosome.

Females with an X chromosome affected by a change in the PLP1 gene have a 50/50 chance of passing the affected X chromosome to both their sons or daughters, each pregnancy.





Can PMD be treated?
There is no cure for PMD. Treatment is currently symptomatic and supportive, focussing on individual therapies for symptoms. This may include medication for seizures and the stiffness or abnormal muscle contractions that are a problem for many PMD patients.

Contact us
Ph: 1800 141 400 | M: 0418 755 994 | info@leuko.org.au | www.leuko.org.au |
PO Box 850 Mornington VIC 3931 | Facebook or Twitter @leukodystrophyaustralia

References
Genetics Home reference
United Leukodystrophy Foundation https://ulf.org/pelizaeus-merzbacher/