

# PMM2-Congenital Disorder of Glycosylation

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*PMM2*-congenital disorder of glycosylation (*PMM2*-CDG, also known as congenital disorder of glycosylation type Ia) is an inherited condition that affects many parts of the body. The type and severity of problems associated with *PMM2*-CDG vary widely among affected individuals, sometimes even among members of the same family.

Keywords: genetic conditions

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## 1. Introduction

Individuals with *PMM2*-CDG typically develop signs and symptoms of the condition during infancy. Affected infants may have weak muscle tone (hypotonia), retracted (inverted) nipples, an abnormal distribution of fat, eyes that do not look in the same direction (strabismus), developmental delay, and a failure to gain weight and grow at the expected rate (failure to thrive). Infants with *PMM2*-CDG also frequently have an underdeveloped cerebellum, which is the part of the brain that coordinates movement. Distinctive facial features are sometimes present in affected individuals, including a high forehead, a triangular face, large ears, and a thin upper lip. Children with *PMM2*-CDG may also have elevated liver function test results, seizures, fluid around the heart (pericardial effusion), and blood clotting disorders. About 20 percent of affected infants do not survive the first year of life due to multiple organ failure.

The most severe cases of *PMM2*-CDG are characterized by hydrops fetalis, a condition in which excess fluid builds up in the body before birth. Most babies with hydrops fetalis are stillborn or die soon after birth.

People with *PMM2*-CDG who survive infancy may have moderate intellectual disability, and some are unable to walk independently. Affected individuals may also experience stroke-like episodes that involve an extreme lack of energy (lethargy) and temporary paralysis. Recovery from these episodes usually occurs over a period of a few weeks to several months.

During adolescence or adulthood, individuals with *PMM2*-CDG have reduced sensation and weakness in their arms and legs (peripheral neuropathy), an abnormal curvature of the spine (kyphoscoliosis), impaired muscle coordination (ataxia), and joint deformities (contractures). Some affected individuals have an eye disorder called retinitis pigmentosa that causes vision loss. Females with *PMM2*-CDG have hypergonadotropic hypogonadism, which affects the production of hormones that direct sexual development. As a result, females with *PMM2*-CDG do not go through puberty. Affected males experience normal puberty but often have small testes.

## 2. Frequency

More than 800 individuals with *PMM2*-CDG have been identified worldwide.

## 3. Causes

*PMM2*-CDG is caused by mutations in the *PMM2* gene. This gene provides instructions for making an enzyme called phosphomannomutase 2 (*PMM2*). The *PMM2* enzyme is involved in a process called glycosylation, which attaches groups of sugar molecules (oligosaccharides) to proteins. Glycosylation modifies proteins so they can perform a wider variety of functions. Mutations in the *PMM2* gene lead to the production of an abnormal *PMM2* enzyme with reduced activity. Without a properly functioning *PMM2* enzyme, glycosylation cannot proceed normally. As a result, incorrect oligosaccharides are produced and attached to proteins. The wide variety of signs and symptoms in *PMM2*-CDG are likely due to the production of abnormally glycosylated proteins in many organs and tissues.

### The Gene Associated with *PMM2*-Congenital Disorder of Glycosylation

- *PMM2*

## 4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## 5. Other Names for This Condition

- carbohydrate-deficient glycoprotein syndrome type Ia
- CDG Ia
- CDG1a
- CDGS1a
- congenital disorder of glycosylation type Ia
- Jaeken syndrome
- phosphomannomutase 2 deficiency
- PMM deficiency
- PMM2-CDG

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## References

1. de Lonlay P, Seta N, Barrot S, Chabrol B, Drouin V, Gabriel BM, Journal H, Kretz M, Laurent J, Le Merrer M, Leroy A, Pedespan D, Sarda P, Villeneuve N, Schmitz J, van Schaftingen E, Matthijs G, Jaeken J, Korner C, Munnich A, Saudubray JM, Cormier-Daire V. A broad spectrum of clinical presentations in congenital disorders of glycosylation I: a series of 26 cases. *J Med Genet.* 2001 Jan;38(1):14-9.
2. Grünewald S. The clinical spectrum of phosphomannomutase 2 deficiency (CDG-Ia). *Biochim Biophys Acta.* 2009 Sep;1792(9):827-34. doi:10.1016/j.bbadis.2009.01.003.
3. Haeuptle MA, Hennot T. Congenital disorders of glycosylation: an update on defects affecting the biosynthesis of dolichol-linked oligosaccharides. *Hum Mutat.* 2009 Dec;30(12):1628-41. doi: 10.1002/humu.21126. Review.
4. Jaeken J, Hennot T, Matthijs G, Freeze HH. CDG nomenclature: time for a change! *Biochim Biophys Acta.* 2009 Sep;1792(9):825-6. doi:10.1016/j.bbadis.2009.08.005.
5. Krasnewich D, O'Brien K, Sparks S. Clinical features in adults with congenital disorders of glycosylation type Ia (CDG-Ia). *Am J Med Genet C Semin Med Genet.* 2007 Aug 15;145C(3):302-6. Review.
6. Monin ML, Mignot C, De Lonlay P, Héron B, Masurel A, Mathieu-Dramard M, Lenaerts C, Thauvin C, Gérard M, Roze E, Jacqueline A, Charles P, de Baracé C, Drouin-Garraud V, Khau Van Kien P, Cormier-Daire V, Mayer M, Ogier H, Brice A, Seta N, Héron D. 29 French adult patients with PMM2-congenital disorder of glycosylation: outcome of the classical pediatric phenotype and depiction of an late-onset phenotype. *Orphanet J Rare Dis.* 2014 Dec 11;9:207. doi:10.1186/s13023-014-0207-4.
7. Sparks SE, Krasnewich DM. PMM2-CDG (CDG-Ia). 2005 Aug 15 [updated 2015 Oct 29]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1110/>

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