

Congenital dyserythropoietic anemia

Description

Congenital dyserythropoietic anemia (CDA) is an inherited blood disorder that affects the development of red blood cells. This disorder is one of many types of anemia, which is a condition characterized by a shortage of red blood cells. This shortage prevents the blood from carrying an adequate supply of oxygen to the body's tissues. The resulting symptoms can include tiredness (fatigue), weakness, pale skin, and other complications.

Researchers have identified three major types of CDA: type I, type II, and type III. The types have different genetic causes and different but overlapping patterns of signs and symptoms.

CDA type I is characterized by moderate to severe anemia. It is usually diagnosed in childhood or adolescence, although in some cases, the condition can be detected before birth. Many affected individuals have yellowing of the skin and eyes (jaundice) and an enlarged liver and spleen (hepatosplenomegaly). This condition also causes the body to absorb too much iron, which builds up and can damage tissues and organs. In particular, iron overload can lead to an abnormal heart rhythm (arrhythmia), congestive heart failure, diabetes, and chronic liver disease (cirrhosis). Rarely, people with CDA type I are born with skeletal abnormalities, most often involving the fingers and/or toes.

The anemia associated with CDA type II can range from mild to severe, and most affected individuals have jaundice, hepatosplenomegaly, and the formation of hard deposits in the gallbladder called gallstones. This form of the disorder is usually diagnosed in adolescence or early adulthood. An abnormal buildup of iron typically occurs after age 20, leading to complications including heart disease, diabetes, and cirrhosis.

The signs and symptoms of CDA type III tend to be milder than those of the other types. Most affected individuals do not have hepatosplenomegaly, and iron does not build up in tissues and organs. In adulthood, abnormalities of a specialized tissue at the back of the eye (the retina) can cause vision impairment. Some people with CDA type III also have a blood disorder known as monoclonal gammopathy, which can lead to a cancer of white blood cells (multiple myeloma).

Several other variants of CDA have been described, although they appear to be rare and not much is known about them. Once researchers discover the genetic causes of

these variants, some of them may be grouped with the three major types of CDA.

Frequency

Several hundred cases of CDA have been reported worldwide. CDA type II is the most common form of the disorder, with more than 300 reported cases. CDA type III is the rarest form; it has been described in only a few families from Sweden, Argentina, and the United States. The incidence of CDA type I is unknown. Because CDA is so rare and its signs and symptoms overlap with those of other disorders, many cases likely remain undiagnosed or are incorrectly diagnosed as other disorders.

Causes

CDA type I usually results from mutations in the *CDAN1* gene. Little is known about the function of this gene, and it is unclear how mutations cause the characteristic features of CDA type I. Some people with this condition do not have identified mutations in the *CDAN1* gene, leading researchers to believe that mutations in at least one other gene can also cause this form of the disorder.

CDA type II is caused by mutations in the *SEC23B* gene. This gene provides instructions for making a protein that is involved in the transport of other proteins within cells. During the development of red blood cells, this protein may help ensure that proteins are transported to the areas where they are needed. Researchers are working to determine how mutations in the *SEC23B* gene lead to the signs and symptoms of CDA type II.

The genetic cause of CDA type III has not been identified. It likely results from mutations in a gene located on the long arm of chromosome 15 at a position designated 15q22. Researchers continue to search for the specific gene associated with this form of the condition.

The genetic changes responsible for CDA disrupt the normal development of red blood cells, a process called erythropoiesis. The term "dyserthropoietic" in the name of this condition means abnormal red blood cell formation. In people with CDA, immature red blood cells called erythroblasts are unusually shaped and have other abnormalities (such as extra nuclei). These abnormal erythroblasts cannot develop into functional mature red blood cells. The resulting shortage of healthy red blood cells leads to the characteristic signs and symptoms of anemia, as well as complications including hepatosplenomegaly and an abnormal buildup of iron.

[Learn more about the genes associated with Congenital dyserythropoietic anemia](#)

- *CDAN1*
- *SEC23B*

Inheritance

The inheritance pattern of CDA depends on the type of the disorder. CDA types I and II are inherited in an autosomal recessive pattern, which means both copies of the associated 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.

In several families, CDA type III appears to have an autosomal dominant pattern of inheritance. Autosomal dominant inheritance means that one copy of the altered gene in each cell is sufficient to cause the disorder. In these families, affected individuals often have a parent and other relatives with the condition.

Other Names for This Condition

- Anemia, dyserythropoietic, congenital
- CDA

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Congenital dyserythropoietic anemia (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0002876/>)

Genetic and Rare Diseases Information Center

- Congenital dyserythropoietic anemia (<https://rarediseases.info.nih.gov/diseases/1999/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Congenital dyserythropoietic anemia%22](https://clinicaltrials.gov/search?cond=%22Congenital+dyserythropoietic+anemia%22))

Catalog of Genes and Diseases from OMIM

- ANEMIA, CONGENITAL DYSERYTHROPOIETIC, TYPE IIIa; CDAN3A (<https://omim.org/entry/105600>)
- ANEMIA, CONGENITAL DYSERYTHROPOIETIC, TYPE II; CDAN2 (<https://omim.org/entry/105600>)

rg/entry/224100)

- ANEMIA, CONGENITAL DYSEERYTHROPOIETIC, TYPE Ia; CDAN1A (<https://omim.org/entry/224120>)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Anemia,+Dyserythropoietic,+Congenital%5BMAJR%5D%29+AND+%28%28congenital+dyserythropoietic+anemia*%5BTIAB%5D%29+OR+%28congenital+dyserythropoietic+anaemia*%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D)

References

- Denecke J, Marquardt T. Congenital dyserythropoietic anemia type II(CDAII/HEMPAS): where are we now? *Biochim Biophys Acta*. 2009 Sep;1792(9):915-20.doi: 10.1016/j.bbadis.2008.12.005. Epub 2008 Dec 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19150496>)
- Dgany O, Avidan N, Delaunay J, Krasnov T, Shalmon L, Shalev H, Eidelitz-Markus T, Kapelushnik J, Cattani D, Pariente A, Tulliez M, Cretien A, Schischmanoff PO, Iolascon A, Fibach E, Koren A, Rossler J, Le Merrer M, Yaniv I, Zaizov R, Ben-Asher E, Olender T, Lancet D, Beckmann JS, Tamary H. Congenital dyserythropoietic anemia type I is caused by mutations in codanin-1. *Am J Hum Genet*. 2002 Dec;71(6):1467-74. doi: 10.1086/344781. Epub 2002 Nov 14. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12434312>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC378595/>)
- Heimpel H, Anselstetter V, Chrobak L, Denecke J, Einsiedler B, Gallmeier K, Griesshammer A, Marquardt T, Janka-Schaub G, Kron M, Kohne E. Congenital dyserythropoietic anemia type II: epidemiology, clinical appearance, and prognosis based on long-term observation. *Blood*. 2003 Dec 15;102(13):4576-81. doi: 10.1182/blood-2003-02-0613. Epub 2003 Aug 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12933587>)
- Heimpel H, Schwarz K, Ebnother M, Goede JS, Heydrich D, Kamp T, Plaumann L, Rath B, Roessler J, Schildknecht O, Schmid M, Willemin W, Einsiedler B, Leichtle R, Tamary H, Kohne E. Congenital dyserythropoietic anemia type I (CDA I): molecular genetics, clinical appearance, and prognosis based on long-term observation. *Blood*. 2006 Jan 1;107(1):334-40. doi: 10.1182/blood-2005-01-0421. Epub 2005 Sep 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16141353>)
- Heimpel H. Congenital dyserythropoietic anemias: epidemiology, clinical significance, and progress in understanding their pathogenesis. *Ann Hematol*. 2004 Oct;83(10):613-21. doi: 10.1007/s00277-004-0892-5. Epub 2004 Jul 20. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15278299>)
- Renella R, Wood WG. The congenital dyserythropoietic anemias. *Hematol Oncol Clin North Am*. 2009 Apr;23(2):283-306. doi: 10.1016/j.hoc.2009.01.010.

Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19327584>)

- Sandstrom H, Wahlin A. Congenital dyserythropoietic anemia type III. *Haematologica*. 2000 Jul;85(7):753-7. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10897128>)
- Schwarz K, Iolascon A, Verissimo F, Trede NS, Horsley W, Chen W, Paw BH, Hopfner KP, Holzmann K, Russo R, Esposito MR, Spano D, De Falco L, Heinrich K, Joggerst B, Rojewski MT, Perrotta S, Denecke J, Pannicke U, Delaunay J, Pepperkok R, Heimpel H. Mutations affecting the secretory COPII coat component SEC23B cause congenital dyserythropoietic anemia type II. *Nat Genet*. 2009 Aug;41(8):936-40. doi: 10.1038/ng.405. Epub 2009 Jun 28. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19561605>)
- Tamy H, Dgany O, Proust A, Krasnov T, Avidan N, Eidelitz-Markus T, Tchernia G, Genevieve D, Cormier-Daire V, Bader-Meunier B, Ferrero-Vacher C, Munzer M, Gruppo R, Fibach E, Konen O, Yaniv I, Delaunay J. Clinical and molecular variability in congenital dyserythropoietic anaemia type I. *Br J Haematol*. 2005 Aug;130(4):628-34. doi: 10.1111/j.1365-2141.2005.05642.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16098079>)
- Tamy H, Dgany O. Congenital Dyserythropoietic Anemia Type I. 2009 Apr 21 [updated 2021 Jul 29]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. *GeneReviews*(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from <http://www.ncbi.nlm.nih.gov/books/NBK5313/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301759>)
- Wickramasinghe SN, Wood WG. Advances in the understanding of the congenital dyserythropoietic anaemias. *Br J Haematol*. 2005 Nov;131(4):431-46. doi: 10.1111/j.1365-2141.2005.05757.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16281933>)

Last updated July 1, 2009