Diamond-Blackfan anemia

Description

Diamond-Blackfan anemia is a disorder that primarily affects the bone marrow. People with this condition often also have physical abnormalities affecting various parts of the body.

The major function of bone marrow is to produce new blood cells. In Diamond-Blackfan anemia, the bone marrow malfunctions and fails to make enough red blood cells, which carry oxygen to the body's tissues. The resulting shortage of red blood cells (anemia) usually becomes apparent during the first year of life. Symptoms of anemia include fatigue, weakness, and an abnormally pale appearance (pallor).

People with Diamond-Blackfan anemia have an increased risk of several serious complications related to their malfunctioning bone marrow. Specifically, they have a higher-than-average chance of developing myelodysplastic syndrome (MDS), which is a disorder in which immature blood cells fail to develop normally. Individuals with Diamond-Blackfan anemia also have an increased risk of developing a bone marrow cancer known as acute myeloid leukemia (AML), a type of bone cancer called osteosarcoma, and other cancers.

Approximately half of individuals with Diamond-Blackfan anemia have physical abnormalities. They may have an unusually small head size (microcephaly) and a low frontal hairline, along with distinctive facial features such as wide-set eyes (hypertelorism); droopy eyelids (ptosis); a broad, flat bridge of the nose; small, low-set ears; and a small lower jaw (micrognathia). Affected individuals may also have an opening in the roof of the mouth (cleft palate) with or without a split in the upper lip (cleft lip). They may have a short, webbed neck; shoulder blades that are smaller and higher than usual; and abnormalities of their hands, most commonly malformed or absent thumbs. About one-third of affected individuals have slow growth leading to short stature.

Other features of Diamond-Blackfan anemia may include eye problems such as clouding of the lens of the eyes (cataracts), increased pressure in the eyes (glaucoma), or eyes that do not look in the same direction (strabismus). Affected individuals may also have kidney abnormalities; structural defects of the heart; and, in males, the opening of the urethra on the underside of the penis (hypospadias).

The severity of Diamond-Blackfan anemia may vary, even within the same family.

Increasingly, individuals with "non-classical" Diamond-Blackfan anemia have been identified. This form of the disorder typically has less severe symptoms. For example, some affected individuals have mild anemia beginning later in childhood or in adulthood, while others have some of the physical features but no bone marrow problems.

Frequency

Diamond-Blackfan anemia affects approximately 5 to 7 per million newborn babies worldwide.

Causes

Diamond-Blackfan anemia can be caused by mutations in one of many genes, including the *RPL5*, *RPL11*, *RPL35A*, *RPS10*, *RPS17*, *RPS19*, *RPS24*, and *RPS26* genes. These and other genes associated with Diamond-Blackfan anemia provide instructions for making ribosomal proteins, which are components of cellular structures called ribosomes. Ribosomes process the cell's genetic instructions to create proteins.

Each ribosome is made up of two parts (subunits) called the large and small subunits. The ribosomal proteins produced from the *RPL5*, *RPL11*, and *RPL35A* genes are among those found in the large subunit. The proteins produced from the *RPS10*, *RPS17*, *RPS19*, *RPS24*, and *RPS26* genes are among those found in the small subunit.

Some ribosomal proteins are involved in the assembly or stability of ribosomes. Others help carry out the ribosome's main function of building new proteins. Studies suggest that some ribosomal proteins may have other functions, such as participating in chemical signaling pathways within the cell, regulating cell division, and controlling the self-destruction of cells (apoptosis).

Approximately 25 percent of individuals with Diamond-Blackfan anemia have mutations in the *RPS19* gene. About another 25 to 35 percent of individuals with this disorder have mutations in the *RPL5*, *RPL11*, *RPL35A*, *RPS10*, *RPS17*, *RPS24*, or *RPS26* gene. Mutations in any of these genes are believed to cause problems with ribosome function. Studies indicate that a shortage of functioning ribosomes may increase the self-destruction of blood-forming cells in the bone marrow, resulting in anemia. Abnormal regulation of cell division or inappropriate triggering of apoptosis may contribute to the other health problems that affect some people with Diamond-Blackfan anemia. Scientists are working to determine why the blood abnormalities and physical problems can vary so much between individuals.

Mutations in many other genes, some of which have not been identified, account for the remaining Diamond-Blackfan anemia cases. While mutations in genes that provide instructions for ribosomal proteins cause most cases of Diamond-Blackfan anemia, gene changes affecting proteins that interact with ribosomal proteins or that play other roles in blood-forming processes have been identified in a few individuals with this disorder.

Learn more about the genes associated with Diamond-Blackfan anemia

- GATA1
- RPL11
- RPL35A
- RPL5
- RPS10
- RPS17
- RPS19
- RPS24
- RPS26

Additional Information from NCBI Gene:

- RPL15
- RPL26
- RPL27
- RPL31
- RPL36
- RPS15
- RPS27
- RPS27A
- RPS28
- RPS29
- RPS7
- TSR2

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In approximately 45 percent of cases, an affected person inherits the mutation from one affected parent. The remaining cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- Aase syndrome
- Aase-Smith syndrome II
- BDA

- BDS
- Blackfan Diamond anemia
- Blackfan-Diamond disease
- Blackfan-Diamond syndrome
- Chronic congenital agenerative anemia
- Congenital erythroid hypoplastic anemia
- Congenital hypoplastic anemia of Blackfan and Diamond
- Congenital pure red cell anemia
- Congenital pure red cell aplasia
- DBA
- Erythrogenesis imperfecta
- Hypoplastic congenital anemia
- Inherited erythroblastopenia
- Pure hereditary red cell aplasia

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Diamond-Blackfan anemia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1260899/)

Genetic and Rare Diseases Information Center

- Blackfan-Diamond anemia (https://rarediseases.info.nih.gov/diseases/6274/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Diamond-Blackfan anemia%22)

Catalog of Genes and Diseases from OMIM

- DIAMOND-BLACKFAN ANEMIA 10; DBA10 (https://omim.org/entry/613309)
- DIAMOND-BLACKFAN ANEMIA 11; DBA11 (https://omim.org/entry/614900)

- DIAMOND-BLACKFAN ANEMIA 12; DBA12 (https://omim.org/entry/615550)
- DIAMOND-BLACKFAN ANEMIA 13; DBA13 (https://omim.org/entry/615909)
- DIAMOND-BLACKFAN ANEMIA 14 WITH MANDIBULOFACIAL DYSOSTOSIS; DBA14 (https://omim.org/entry/300946)
- DIAMOND-BLACKFAN ANEMIA 15 WITH MANDIBULOFACIAL DYSOSTOSIS; DBA15 (https://omim.org/entry/606164)
- DIAMOND-BLACKFAN ANEMIA 16; DBA16 (https://omim.org/entry/617408)
- DIAMOND-BLACKFAN ANEMIA 17; DBA17 (https://omim.org/entry/617409)
- DIAMOND-BLACKFAN ANEMIA 1; DBA1 (https://omim.org/entry/105650)
- DIAMOND-BLACKFAN ANEMIA 2; DBA2 (https://omim.org/entry/606129)
- DIAMOND-BLACKFAN ANEMIA 3; DBA3 (https://omim.org/entry/610629)
- DIAMOND-BLACKFAN ANEMIA 4; DBA4 (https://omim.org/entry/612527)
- DIAMOND-BLACKFAN ANEMIA 5; DBA5 (https://omim.org/entry/612528)
- DIAMOND-BLACKFAN ANEMIA 6; DBA6 (https://omim.org/entry/612561)
- DIAMOND-BLACKFAN ANEMIA 7; DBA7 (https://omim.org/entry/612562)
- DIAMOND-BLACKFAN ANEMIA 8; DBA8 (https://omim.org/entry/612563)
- DIAMOND-BLACKFAN ANEMIA 9; DBA9 (https://omim.org/entry/613308)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Anemia,+Diamond-Blackfan%5BMAJR%5D%29+AND+%28Diamond-Blackfan+anemia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

References

- Ball S. Diamond Blackfan anemia. Hematology Am Soc Hematol Educ Program. 2011;2011:487-91. doi: 10.1182/asheducation-2011.1.487. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22160079)
- Boria I, Garelli E, Gazda HT, Aspesi A, Quarello P, Pavesi E, Ferrante D,Meerpohl JJ, Kartal M, Da Costa L, Proust A, Leblanc T, Simansour M, Dahl N,Frojmark AS, Pospisilova D, Cmejla R, Beggs AH, Sheen MR, Landowski M, Buros CM,Clinton CM, Dobson LJ, Vlachos A, Atsidaftos E, Lipton JM, Ellis SR, Ramenghi U,Dianzani I. The ribosomal basis of Diamond-Blackfan Anemia: mutation and databaseupdate. Hum Mutat. 2010 Dec;31(12):1269-79. doi: 10.1002/humu.21383. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20960466) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4485435/)
- Boultwood J, Pellagatti A, Wainscoat JS. Haploinsufficiency of ribosomalproteins and p53 activation in anemia: Diamond-Blackfan anemia and the 5q-syndrome. Adv Biol Regul. 2012 Jan;52(1):196-203. doi:10.1016/j.advenzreg.2011.09.008. No

abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21930148)

- Danilova N, Gazda HT. Ribosomopathies: how a common root can cause a tree ofpathologies. Dis Model Mech. 2015 Sep;8(9):1013-26. doi: 10.1242/dmm.020529. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26398160) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4582105/)
- Ellis SR, Gleizes PE. Diamond Blackfan anemia: ribosomal proteins going rogue. Semin Hematol. 2011 Apr;48(2):89-96. doi: 10.1053/j.seminhematol.2011.02.005. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21435505)
- Ellis SR. Nucleolar stress in Diamond Blackfan anemia pathophysiology. BiochimBiophys Acta. 2014 Jun;1842(6):765-8. doi: 10.1016/j.bbadis.2013.12.013. Epub2014 Jan 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24412987)
- Farrar JE, Dahl N. Untangling the phenotypic heterogeneity of Diamond Blackfananemia. Semin Hematol. 2011 Apr;48(2):124-35. doi:10.1053/j.seminhematol.2011.02.003. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21435509) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3078697/)
- Ito E, Konno Y, Toki T, Terui K. Molecular pathogenesis in Diamond-Blackfananemia. Int J Hematol. 2010 Oct;92(3):413-8. doi: 10.1007/s12185-010-0693-7. Epub2010 Sep 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20882441)
- Mills EW, Green R. Ribosomopathies: There's strength in numbers. Science. 2017Nov 3;358(6363):eaan2755. doi: 10.1126/science.aan2755. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29097519)
- Narla A, Hurst SN, Ebert BL. Ribosome defects in disorders of erythropoiesis.Int J Hematol. 2011 Feb;93(2):144-149. doi: 10.1007/s12185-011-0776-0. Epub 2011Feb 1. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21279816) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3689295/)
- Sieff C. DBA Syndrome. 2009 Jun 25 [updated 2025 Jul 31]. In: Adam MP, Bick S, Mirzaa GM, Wallace SE, Amemiya A, editors. GeneReviews(R) [Internet].Seattle (WA): University of Washington, Seattle; 1993-2026. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK7047/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301769)
- Vlachos A, Blanc L, Lipton JM. Diamond Blackfan anemia: a model for thetranslational approach to understanding human disease. Expert Rev Hematol. 2014Jun;7(3):359-72. doi: 10.1586/17474086.2014.897923. Epub 2014 Mar 26. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24665981)

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