Critical congenital heart disease

Critical congenital heart disease (CCHD) is a term that refers to a group of serious heart defects that are present from birth. These abnormalities result from problems with the formation of one or more parts of the heart during the early stages of embryonic development. CCHD prevents the heart from pumping blood effectively or reduces the amount of oxygen in the blood. As a result, organs and tissues throughout the body do not receive enough oxygen, which can lead to organ damage and life-threatening complications. Individuals with CCHD usually require surgery soon after birth.

Although babies with CCHD may appear healthy for the first few hours or days of life, signs and symptoms soon become apparent. These can include an abnormal heart sound during a heartbeat (heart murmur), rapid breathing (tachypnea), low blood pressure (hypotension), low levels of oxygen in the blood (hypoxemia), and a blue or purple tint to the skin caused by a shortage of oxygen (cyanosis). If untreated, CCHD can lead to shock, coma, and death. However, most people with CCHD now survive past infancy due to improvements in early detection, diagnosis, and treatment.

Some people with treated CCHD have few related health problems later in life. However, long-term effects of CCHD can include delayed development and reduced stamina during exercise. Adults with these heart defects have an increased risk of abnormal heart rhythms, heart failure, sudden cardiac arrest, stroke, and premature death.

Each of the heart defects associated with CCHD affects the flow of blood into, out of, or through the heart. Some of the heart defects involve structures within the heart itself, such as the two lower chambers of the heart (the ventricles) or the valves that control blood flow through the heart. Others affect the structure of the large blood vessels leading into and out of the heart (including the aorta and pulmonary artery). Still others involve a combination of these structural abnormalities.

People with CCHD have one or more specific heart defects. The heart defects classified as CCHD include coarctation of the aorta, double-outlet right ventricle, D-transposition of the great arteries, Ebstein anomaly, hypoplastic left heart syndrome, interrupted aortic arch, pulmonary atresia with intact septum, single ventricle, total anomalous pulmonary venous connection, tetralogy of Fallot, tricuspid atresia, and truncus arteriosus.

Frequency

Heart defects are the most common type of birth defect, accounting for more than 30 percent of all infant deaths due to birth defects. CCHD represents some of the most serious types of heart defects. About 7,200 newborns, or 18 per 10,000, in the United States are diagnosed with CCHD each year.

Causes

In most cases, the cause of CCHD is unknown. A variety of genetic and environmental factors likely contribute to this complex condition.

Changes in single genes have been associated with CCHD. Studies suggest that these genes are involved in normal heart development before birth. Most of the identified mutations reduce the amount or function of the protein that is produced from a specific gene, which likely impairs the normal formation of structures in the heart. Studies have also suggested that having more or fewer copies of particular genes compared with other people, a phenomenon known as copy number variation, may play a role in CCHD. However, it is unclear whether genes affected by copy number variation are involved in heart development and how having missing or extra copies of those genes could lead to heart defects. Researchers believe that single-gene mutations and copy number variation account for a relatively small percentage of all CCHD.

CCHD is usually isolated, which means it occurs alone (without signs and symptoms affecting other parts of the body). However, the heart defects associated with CCHD can also occur as part of genetic syndromes that have additional features. Some of these genetic conditions, such as Down syndrome, Turner syndrome, and 22q11.2 deletion syndrome, result from changes in the number or structure of particular chromosomes. Other conditions, including Noonan syndrome and Alagille syndrome, result from mutations in single genes.

Environmental factors may also contribute to the development of CCHD. Potential risk factors that have been studied include exposure to certain chemicals or drugs before birth, viral infections (such as rubella and influenza) that occur during pregnancy, and other maternal illnesses including diabetes and phenylketonuria. Although researchers are examining risk factors that may be associated with this complex condition, many of these factors remain unknown.

Inheritance Pattern

Most cases of CCHD are sporadic, which means they occur in people with no history of the disorder in their family. However, close relatives (such as siblings) of people with CCHD may have an increased risk of being born with a heart defect compared with people in the general population.

Other Names for This Condition

- CCHD
- critical congenital heart defects

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Congenital heart disease
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0152021/
- Genetic Testing Registry: Ebstein anomaly of the tricuspid valve
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0013481/
- Genetic Testing Registry: Heterotaxy, visceral, 2, autosomal
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1415817/
- Genetic Testing Registry: Hypoplastic left heart syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0152101/
- Genetic Testing Registry: Hypoplastic left heart syndrome 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3280795/
- Genetic Testing Registry: Persistent truncus arteriosus
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0041207/
- Genetic Testing Registry: Pulmonary atresia with intact ventricular septum
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0344975/
- Genetic Testing Registry: Pulmonary atresia with ventricular septal defect
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0344976/
- Genetic Testing Registry: Tetralogy of Fallot
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0039685/
- Genetic Testing Registry: Transposition of the great arteries
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0040761/
- Genetic Testing Registry: Transposition of the great arteries, dextro-looped 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151221/
- Genetic Testing Registry: Tricuspid atresia (disease)
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0243002/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22critical+congenital+heart+disease%22+OR+%22critical+congenital+heart+defects%22

Other Diagnosis and Management Resources

- Baby's First Test: Critical Congenital Heart Disease
  https://www.babysfirsttest.org/newborn-screening/conditions/critical-congenital-heart-disease-cchd
- Boston Children's Hospital
  http://www.childrenshospital.org/conditions-and-treatments/conditions/c/congenital-heart-defects
- Centers for Disease Control and Prevention: Screening for Critical Congenital Heart Defects
  https://www.cdc.gov/ncbddd/heartdefects/cchd-facts.html
- Children's Hospital of Philadelphia
  https://www.chop.edu/conditions-diseases/congenital-heart-disease
- Cincinnati Children's Hospital Medical Center
  https://www.cincinnatichildrens.org/patients/child/encyclopedia/defects
- Screening, Technology, and Research in Genetics (STAR-G)
  http://www.newbornscreening.info/Parents/otherdisorders/CCHD.html
- University of California, San Francisco Fetal Treatment Center: Congenital Heart Disease
  https://fetus.ucsf.edu/congenital-heart-disease

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Coarctation of the Aorta
  https://medlineplus.gov/ency/article/000191.htm
- Encyclopedia: Double Outlet Right Ventricle
  https://medlineplus.gov/ency/article/007328.htm
- Encyclopedia: Ebstein's Anomaly
  https://medlineplus.gov/ency/article/007321.htm
- Encyclopedia: Hypoplastic Left Heart Syndrome
  https://medlineplus.gov/ency/article/001106.htm
- Encyclopedia: Pulmonary Atresia
  https://medlineplus.gov/ency/article/001091.htm
- Encyclopedia: Tetralogy of Fallot
  https://medlineplus.gov/ency/article/001567.htm
- Encyclopedia: Total Anomalous Pulmonary Venous Return
  https://medlineplus.gov/ency/article/001115.htm
- Encyclopedia: Transposition of the Great Vessels
  https://medlineplus.gov/ency/article/001568.htm

- Encyclopedia: Tricuspid Atresia
  https://medlineplus.gov/ency/article/001110.htm
- Encyclopedia: Truncus Arteriosus
  https://medlineplus.gov/ency/article/001111.htm
- Health Topic: Congenital Heart Defects
  https://medlineplus.gov/congenitalheartdefects.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Hypoplastic left heart syndrome
  https://rarediseases.info.nih.gov/diseases/6739/hypoplastic-left-heart-syndrome
- Transposition of the great arteries
  https://rarediseases.info.nih.gov/diseases/7795/transposition-of-the-great-arteries

Additional NIH Resources

- National Heart Lung and Blood Institute: What Is Tetralogy of Fallot?
  https://www.nhlbi.nih.gov/health-topics/congenital-heart-defects

Educational Resources

- Centers for Disease Control and Prevention: Congenital Heart Defects
  https://www.cdc.gov/ncbddd/heartdefects/
- KidsHealth from Nemours
  https://kidshealth.org/en/parents/if-heart-defect.html
- Lucile Packard Children's Hospital at Stanford
  https://www.stanfordchildrens.org/en/topic/default?id=factors-contributing-to-congenital-heart-disease-90-P01788
- MalaCards: critical congenital heart disease
  https://www.malacards.org/card/critical_congenital_heart_disease
- March of Dimes
  https://www.marchofdimes.org/complications/congenital-heart-defects.aspx
- Merck Manual Consumer Version
  https://www.merckmanuals.com/home/children-s-health-issues/birth-defects-of-the-heart/overview-of-heart-defects
- Orphanet: Hypoplastic left heart syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2248
- Orphanet: Pulmonary atresia - intact ventricular septum
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1208

- Orphanet: Pulmonary atresia with ventricular septal defect
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1207
- Orphanet: Tetralogy of Fallot
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3303
- Orphanet: Tricuspid atresia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1209
- Orphanet: Truncus arteriosus
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3384

Patient Support and Advocacy Resources

- Adult Congenital Heart Association
  https://www.achaheart.org/
- American Heart Association
  https://www.heart.org/en/health-topics/congenital-heart-defects
- Contact a Family (UK)
  https://contact.org.uk/advice-and-support/health-medical-information/conditions/h/heart-defects/
- Kids With Heart National Association for Children's Heart Disorders
  https://kidswithheart.org/
- Resource List from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/conghart.html

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Heart+Defects,+Congenital%5BMAJR%5D%29+AND+%28%28critical+congenital+heart+disease%5BTIAB%5D%29+OR+%28critical+congenital+heart+defect*%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- COARCTATION OF AORTA
  http://omim.org/entry/120000
- CONGENITAL HEART DEFECTS, MULTIPLE TYPES, 6
  http://omim.org/entry/613854
- CONOTRUNCAL HEART MALFORMATIONS
  http://omim.org/entry/217095
- EBSTEIN ANOMALY
  http://omim.org/entry/224700

- HETEROTAXY, VISCERAL, 2, AUTOSOMAL
  http://omim.org/entry/605376
- HYPOPLASTIC LEFT HEART SYNDROME 1
  http://omim.org/entry/241550
- HYPOPLASTIC LEFT HEART SYNDROME 2
  http://omim.org/entry/614435
- PULMONARY ATRESIA WITH INTACT VENTRICULAR SEPTUM
  http://omim.org/entry/265150
- PULMONARY ATRESIA WITH VENTRICULAR SEPTAL DEFECT
  http://omim.org/entry/178370
- TETRALOGY OF FALLOT
  http://omim.org/entry/187500
- TOTAL ANOMALOUS PULMONARY VENOUS RETURN 1
  http://omim.org/entry/106700
- TRANSPOSITION OF THE GREAT ARTERIES, DEXTRO-LOOPED 1
  http://omim.org/entry/608808
- TRICUSPID ATRESIA
  http://omim.org/entry/605067

Sources for This Summary

- Centers for Disease Control and Prevention: Screening for Critical Congenital Heart Defects
  https://www.cdc.gov/ncbddd/heartdefects/cchd-facts.html
- Fahed AC, Gelb BD, Seidman JG, Seidman CE. Genetics of congenital heart disease: the glass half empty. Circ Res. 2013 Feb 15;112(4):707-20. doi: 10.1161/CIRCRESAHA.112.300853. Review. Erratum in: Circ Res. 2013 Jun 7;112(12):e182.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23410880
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3827691/
- Grochowski CM, Loomes KM, Spinner NB. Jagged1 (JAG1): Structure, expression, and disease associations. Gene. 2016 Jan 15;576(1 Pt 3):381-4. doi: 10.1016/j.gene.2015.10.065. Epub 2015 Nov 6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26548814
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4673022/
- Jenkins KJ, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, Elixson M, Warnes CA, Webb CL; American Heart Association Council on Cardiovascular Disease in the Young. Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation. 2007 Jun 12;115(23):2995-3014. Epub 2007 May 22. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17519397

- Mahle WT, Newburger JW, Matherne GP, Smith FC, Hoke TR, Koppel R, Gidding SS, Beekman RH 3rd, Grosse SD; American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research; American Academy of Pediatrics Section on Cardiology And Cardiac Surgery; Committee On Fetus And Newborn. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the AHA and AAP. Pediatrics. 2009 Aug;124(2):823-36. doi: 10.1542/peds.2009-1397. Epub 2009 Jul 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19581259
- Richards AA, Garg V. Genetics of congenital heart disease. Curr Cardiol Rev. 2010 May;6(2):91-7. doi: 10.2174/157340310791162703.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21532774
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2892081/
- Wessels MW, Willems PJ. Genetic factors in non-syndromic congenital heart malformations. Clin Genet. 2010 Aug;78(2):103-23. doi: 10.1111/j.1399-0004.2010.01435.x. Epub 2010 May 17. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20497191
- Zaidi S, Choi M, Wakimoto H, Ma L, Jiang J, Overton JD, Romano-Adesman A, Bjornson RD, Breitbart RE, Brown KK, Carriero NJ, Cheung YH, Deanfield J, DePalma S, Fakhro KA, Glessner J, Hakonarson H, Italia MJ, Kaltman JR, Kaski J, Kim R, Kline JK, Lee T, Leipzig J, Lopez A, Mane SM, Mitchell LE, Newburger JW, Parfenov M, Pe'er I, Porter G, Roberts AE, Sachidanandam R, Sanders SJ, Seiden HS, State MW, Subramanian S, Tikhonova IR, Wang W, Warburton D, White PS, Williams IA, Zhao H, Seidman JG, Brueckner M, Chung WK, Gelb BD, Goldmuntz E, Seidman CE, Lifton RP. De novo mutations in histone-modifying genes in congenital heart disease. Nature. 2013 Jun 13;498(7453):220-3. doi: 10.1038/nature12141. Epub 2013 May 12.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23665959
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3706629/
- van der Bom T, Zomer AC, Zwinderman AH, Meijboom FJ, Bouma BJ, Mulder BJ. The changing epidemiology of congenital heart disease. Nat Rev Cardiol. 2011 Jan;8(1):50-60. doi: 10.1038/nrcardio.2010.166. Epub 2010 Nov 2. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21045784

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/critical-congenital-heart-disease

Reviewed: August 2020
Published: August 17, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services