Down syndrome

Description

Down syndrome is a chromosomal condition that is associated with intellectual disability, a characteristic facial appearance, and weak muscle tone (hypotonia) in infancy. All affected individuals experience cognitive delays, but the intellectual disability is usually mild to moderate.

People with Down syndrome often have a characteristic facial appearance that includes a flattened appearance to the face, outside corners of the eyes that point upward (upslanting palpebral fissures), small ears, a short neck, and a tongue that tends to stick out of the mouth. Affected individuals may have a variety of birth defects. Many people with Down syndrome have small hands and feet and a single crease across the palms of the hands. About half of all affected children are born with a heart defect. Digestive abnormalities, such as a blockage of the intestine, are less common.

Individuals with Down syndrome have an increased risk of developing several medical conditions. These include gastroesophageal reflux, which is a backflow of acidic stomach contents into the esophagus, and celiac disease, which is an intolerance of a wheat protein called gluten. About 15 percent of people with Down syndrome have an underactive thyroid gland (hypothyroidism). The thyroid gland is a butterfly-shaped organ in the lower neck that produces hormones. Individuals with Down syndrome also have an increased risk of hearing and vision problems. Additionally, a small percentage of children with Down syndrome develop cancer of blood-forming cells (leukemia).

Delayed development and behavioral problems are often reported in children with Down syndrome. Affected individuals can have growth problems and their speech and language develop later and more slowly than in children without Down syndrome. Additionally, speech may be difficult to understand in individuals with Down syndrome. Behavioral issues can include attention problems, obsessive/compulsive behavior, and stubbornness or tantrums. A small percentage of people with Down syndrome are also diagnosed with developmental conditions called autism spectrum disorders, which affect communication and social interaction.

People with Down syndrome often experience a gradual decline in thinking ability (cognition) as they age, usually starting around age 50. Down syndrome is also associated with an increased risk of developing Alzheimer disease, a brain disorder that results in a gradual loss of memory, judgment, and ability to function. Approximately half of adults with Down syndrome develop Alzheimer disease. Although Alzheimer disease

is usually a disorder that occurs in older adults, people with Down syndrome commonly develop this condition earlier, in their fifties or sixties.

Frequency

Down syndrome occurs in about 1 in 700 newborns. About 5,300 babies with Down syndrome are born in the United States each year, and approximately 200,000 people in this country have the condition. Although women of any age can have a child with Down syndrome, the chance of having a child with this condition increases as a woman gets older.

Causes

Most cases of Down syndrome result from trisomy 21, which means each cell in the body has three copies of chromosome 21 instead of the usual two copies.

Less commonly, Down syndrome occurs when part of chromosome 21 becomes attached (translocated) to another chromosome during the formation of reproductive cells (eggs and sperm) in a parent or very early in fetal development. Affected people have two normal copies of chromosome 21 plus extra material from chromosome 21 attached to another chromosome, resulting in three copies of genetic material from chromosome 21. Affected individuals with this genetic change are said to have translocation Down syndrome.

A very small percentage of people with Down syndrome have an extra copy of chromosome 21 in only some of the body's cells. In these people, the condition is called mosaic Down syndrome.

Researchers believe that having extra copies of genes on chromosome 21 disrupts the course of normal development, causing the characteristic features of Down syndrome and the increased risk of health problems associated with this condition.

Learn more about the chromosome associated with Down syndrome

- chromosome 21

Inheritance

Most cases of Down syndrome are not inherited. When the condition is caused by trisomy 21, the chromosomal abnormality occurs as a random event during the formation of reproductive cells in a parent. The abnormality usually occurs in egg cells, but it occasionally occurs in sperm cells. An error in cell division called nondisjunction results in a reproductive cell with an abnormal number of chromosomes. For example, an egg or sperm cell may gain an extra copy of chromosome 21. If one of these atypical reproductive cells contributes to the genetic makeup of a child, the child will have an extra chromosome 21 in each of the body's cells.

People with translocation Down syndrome can inherit the condition from an unaffected parent. The parent carries a rearrangement of genetic material between chromosome 21 and another chromosome. This rearrangement is called a balanced translocation. No genetic material is gained or lost in a balanced translocation, so these chromosomal changes usually do not cause any health problems. However, as this translocation is passed to the next generation, it can become unbalanced. People who inherit an unbalanced translocation involving chromosome 21 may have extra genetic material from chromosome 21, which causes Down syndrome.

Like trisomy 21, mosaic Down syndrome is not inherited. It occurs as a random event during cell division early in fetal development. As a result, some of the body's cells have the usual two copies of chromosome 21, and other cells have three copies of this chromosome.

Other Names for This Condition

- 47,XX,+21
- 47,XY,+21
- Down's syndrome
- Trisomy 21
- Trisomy G

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Complete trisomy 21 syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0013080/)

Genetic and Rare Diseases Information Center

- Down syndrome (https://rarediseases.info.nih.gov/diseases/10247/down-syndrome)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (https://clinicaltrials.gov/ct2/results?cond=%22down+syndrome%22)

Catalog of Genes and Diseases from OMIM

- DOWN SYNDROME (https://omim.org/entry/190685)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Down+Syndrome%5BMAJR%5D%29+AND+%28Down+syndrome%5BTI%5D%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

References

- Antonarakis SE, Lyle R, Dermitzakis ET, Reymond A, Deutsch S. Chromosome 21and down syndrome: from genomics to pathophysiology. Nat Rev Genet. 2004Oct; 5(10):725-38. doi: 10.1038/nrg1448. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15510164)
- Capone G, Goyal P, Ares W, Lannigan E. Neurobehavioral disorders in children, adolescents, and young adults with Down syndrome. Am J Med Genet C Semin MedGenet. 2006 Aug 15;142C(3):158-72. doi: 10.1002/ajmg.c.30097. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16838318)
- Carter JC, Capone GT, Gray RM, Cox CS, Kaufmann WE. Autistic-spectrumdisorders in Down syndrome: further delineation and distinction from otherbehavioral abnormalities. Am J Med Genet B Neuropsychiatr Genet. 2007 Jan5; 144B(1):87-94. doi: 10.1002/ajmg.b.30407. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16958028)
- Chapman RS, Hesketh LJ. Behavioral phenotype of individuals with Downsyndrome. Ment Retard Dev Disabil Res Rev. 2000;6(2):84-95. doi:10.1002/1098-2779(2000)6:23.0.CO;2-P. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10899801)
- Cohen WI. Current dilemmas in Down syndrome clinical care: celiac disease,thyroid disorders, and atlanto-axial instability. Am J Med Genet C Semin MedGenet. 2006 Aug 15;142C(3):141-8. doi: 10.1002/ajmg.c.30102. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16838307)
- de Graaf G, Buckley F, Skotko BG. Estimates of the live births, naturallosses, and elective terminations with Down syndrome in the United States. Am JMed Genet A. 2015 Apr;167A(4):756-67. doi: 10.1002/ajmg.a.37001. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25822844)
- de Graaf G, Buckley F, Skotko BG. Estimation of the number of people with Downsyndrome in the United States. Genet Med. 2017 Apr;19(4):439-447. doi:10.1038/gim.2016.127. Epub 2016 Sep 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27608174)
- Kumin L. Speech intelligibility and childhood verbal apraxia in children withDown

syndrome. Downs Syndr Res Pract. 2006 Jul;10(1):10-22. doi:10.3104/reports.301. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16869369)

- Lott IT, Head E. Alzheimer disease and Down syndrome: factors in pathogenesis. Neurobiol Aging. 2005 Mar;26(3):383-9. doi: 10.1016/j.neurobiolaging.2004.08.005. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15639317)
- Lubec G, Engidawork E. The brain in Down syndrome (TRISOMY 21). J Neurol. 2002Oct;249(10):1347-56. doi: 10.1007/s00415-002-0799-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12382149)
- Roizen NJ, Patterson D. Down's syndrome. Lancet. 2003 Apr 12;361(9365):1281-9.doi: 10.1016/S0140-6736(03)12987-X. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12699967)
- Shapiro BL. Down syndrome and associated congenital malformations. J NeuralTransm Suppl. 2003;(67):207-14. doi: 10.1007/978-3-7091-6721-2_18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15068252)
- Sherman SL, Allen EG, Bean LH, Freeman SB. Epidemiology of Down syndrome. MentRetard Dev Disabil Res Rev. 2007;13(3):221-7. doi: 10.1002/mrdd.20157. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17910090)
- Steingass KJ, Chicoine B, McGuire D, Roizen NJ. Developmental disabilitiesgrown up: Down syndrome. J Dev Behav Pediatr. 2011 Sep;32(7):548-58. doi:10.1097/DBP.0b013e31822182e0. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21743353)
- Zigman WB, Lott IT. Alzheimer's disease in Down syndrome: neurobiology andrisk. Ment Retard Dev Disabil Res Rev. 2007;13(3):237-46. doi:10.1002/mrdd.20163. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17910085)

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