

Russell-Silver syndrome

Description

Russell-Silver syndrome is a growth disorder characterized by slow growth before and after birth. Babies with this condition have a low birth weight and often fail to grow and gain weight at the expected rate (failure to thrive). Head growth is normal, however, so the head may appear unusually large compared to the rest of the body. Affected children are thin and have poor appetites, and some develop recurrent episodes of low blood glucose (hypoglycemia) as a result of feeding difficulties. Adults with Russell-Silver syndrome are short; the average height for affected men is about 151 centimeters (4 feet, 11 inches) and the average height for affected women is about 140 centimeters (4 feet, 7 inches).

Many children with Russell-Silver syndrome have a small, triangular face with distinctive facial features including a prominent forehead, a narrow chin, a small jaw, and downturned corners of the mouth. Other features of this disorder can include an unusual curving of the fifth finger (clinodactyly), asymmetric or uneven growth of some parts of the body, and digestive system abnormalities. Russell-Silver syndrome is also associated with an increased risk of delayed development, speech and language problems, and learning disabilities.

Frequency

The exact incidence of Russell-Silver syndrome is unknown. Worldwide estimates range from 1 in 30,000 to 1 in 100,000 people.

Causes

The genetic causes of Russell-Silver syndrome are complex. The disorder often results from the abnormal regulation of certain genes that control growth. Research has focused on genes located in particular regions of chromosome 7 and chromosome 11.

People normally inherit one copy of each chromosome from their mother and one copy from their father. For most genes, both copies are expressed, or "turned on," in cells. For some genes, however, only the copy inherited from a person's father (the paternal copy) is expressed. For other genes, only the copy inherited from a person's mother (the maternal copy) is expressed. These parent-specific differences in gene expression are caused by a phenomenon called genomic imprinting. Both chromosome 7 and

chromosome 11 contain groups of genes that normally undergo genomic imprinting; some of these genes are active only on the maternal copy of the chromosome, while others are active only on the paternal copy. Abnormalities involving these genes appear to be responsible for many cases of Russell-Silver syndrome.

Researchers suspect that 30 to 50 percent of all cases of Russell-Silver syndrome result from changes in a process called methylation on the short (p) arm of chromosome 11 at position 15 (11p15). Methylation is a chemical reaction that attaches small molecules called methyl groups to certain segments of DNA. In genes that undergo genomic imprinting, methylation is one way that a gene's parent of origin is marked during the formation of egg and sperm cells. Russell-Silver syndrome has been associated with changes in methylation involving the *H19* and *IGF2* genes, which are located near one another at 11p15. These genes are thought to be involved in directing normal growth. A loss of methylation disrupts the regulation of these genes, which leads to slow growth and the other characteristic features of this disorder.

Abnormalities involving genes on chromosome 7 can also cause Russell-Silver syndrome. In 7 percent to 10 percent of cases, people inherit both copies of chromosome 7 from their mother instead of one copy from each parent. This phenomenon is called maternal uniparental disomy (UPD). Maternal UPD causes people to have two active copies of some imprinted genes and no active copies of others. An imbalance in certain active paternal and maternal genes on chromosome 7 underlies the signs and symptoms of the disorder.

In about 40 percent of people with Russell-Silver syndrome, the cause of the condition is unknown. It is likely that changes involving imprinted genes on chromosomes other than 7 and 11 play a role. Researchers are working to identify additional genetic changes that underlie this disorder.

[Learn more about the genes and chromosomes associated with Russell-Silver syndrome](#)

- *H19*
- *IGF2*
- chromosome 11
- chromosome 7

Inheritance

Most cases of Russell-Silver syndrome are sporadic, which means they occur in people with no history of the disorder in their family.

Rarely, Russell-Silver syndrome can run in families. In some affected families, the condition appears to have an autosomal dominant pattern of inheritance. Autosomal dominant inheritance means one copy of a genetic change in each cell is sufficient to cause the disorder. In other families, the condition appears to have an autosomal recessive pattern of inheritance. Autosomal recessive inheritance means both copies of

a gene are altered in each cell. 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.

Other Names for This Condition

- RSS
- Silver-Russell dwarfism
- Silver-Russell syndrome
- SRS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Russell-Silver syndrome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0175693/>)

Genetic and Rare Diseases Information Center

- Silver-Russell syndrome (<https://rarediseases.info.nih.gov/diseases/4870/index>)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Russell-Silver syndrome%22](https://clinicaltrials.gov/search?cond=%22Russell-Silver%20syndrome%22))

Catalog of Genes and Diseases from OMIM

- SILVER-RUSSELL SYNDROME 1; SRS1 (<https://omim.org/entry/180860>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28russell-silver+syndrome%5BTIAB%5D%29+OR+%28silver-russell+syndrome%5BTIAB%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D%29%22>)

References

- Abu-Amro S, Monk D, Frost J, Preece M, Stanier P, Moore GE. The genetic aetiology of Silver-Russell syndrome. *J Med Genet*. 2008 Apr;45(4):193-9. doi:10.1136/jmg.2007.053017. Epub 2007 Dec 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18156438>)
- Eggermann T, Spengler S, Gogiel M, Begemann M, Elbracht M. Epigenetic and genetic diagnosis of Silver-Russell syndrome. *Expert Rev Mol Diagn*. 2012 Jun;12(5):459-71. doi: 10.1586/erm.12.43. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22702363>)
- Eggermann T. Russell-Silver syndrome. *Am J Med Genet C Semin Med Genet*. 2010 Aug 15;154C(3):355-64. doi: 10.1002/ajmg.c.30274. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20803658>)
- Gicquel C, Rossignol S, Cabrol S, Houang M, Steunou V, Barbu V, Danton F, Thibaud N, Le Merrer M, Burglen L, Bertrand AM, Netchine I, Le Bouc Y. Epimutation of the telomeric imprinting center region on chromosome 11p15 in Silver-Russell syndrome. *Nat Genet*. 2005 Sep;37(9):1003-7. doi: 10.1038/ng1629. Epub 2005 Aug 7. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16086014>)
- Saal HM, Harbison MD, Netchine I. Silver-Russell Syndrome. 2002 Nov 2 [updated 2019 Oct 21]. 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/NBK1324/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301499>)
- Wakeling EL, Brioude F, Lokulo-Sodipe O, O'Connell SM, Salem J, Bliet J, Canton AP, Chrzanowska KH, Davies JH, Dias RP, Dubern B, Elbracht M, Giabicani E, Grimberg A, Gronskov K, Hokken-Koelega AC, Jorge AA, Kagami M, Linglart A, Maghnie M, Mohnike K, Monk D, Moore GE, Murray PG, Ogata T, Petit IO, Russo S, Said E, Toumba M, Turner Z, Binder G, Eggermann T, Harbison MD, Temple IK, Mackay DJ, Netchine I. Diagnosis and management of Silver-Russell syndrome: first international consensus statement. *Nat Rev Endocrinol*. 2017 Feb;13(2):105-124. doi: 10.1038/nrendo.2016.138. Epub 2016 Sep 2. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27585961>)
- Wakeling EL. Silver-Russell syndrome. *Arch Dis Child*. 2011 Dec;96(12):1156-61. doi: 10.1136/adc.2010.190165. Epub 2011 Feb 24. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/21349887>)

Last updated September 1, 2016