



Isolated Pierre Robin sequence

Pierre Robin sequence is a set of abnormalities affecting the head and face, consisting of a small lower jaw (micrognathia), a tongue that is placed further back than normal (glossoptosis), and blockage (obstruction) of the airways. Most people with Pierre Robin sequence are also born with an opening in the roof of the mouth (a cleft palate). This feature is not generally considered necessary for diagnosis of the condition, although there is some disagreement among doctors.

Some people have the features of Pierre Robin sequence as part of a syndrome that affects other organs and tissues in the body, such as Stickler syndrome or campomelic dysplasia. These instances are described as syndromic. When Pierre Robin sequence occurs by itself, it is described as nonsyndromic or isolated. Approximately 20 to 40 percent of cases of Pierre Robin sequence are isolated.

This condition is described as a "sequence" because one of its features, underdevelopment of the lower jaw (mandible), sets off a sequence of events before birth that cause the other signs and symptoms. Specifically, having an abnormally small jaw affects placement of the tongue, and the abnormally positioned tongue can block the airways. In addition, micrognathia and glossoptosis affect formation of the palate during development before birth, which often leads to cleft palate.

The combination of features characteristic of Pierre Robin sequence can lead to difficulty breathing and problems eating early in life. As a result, some affected babies have an inability to grow and gain weight at the expected rate (failure to thrive). In some children with Pierre Robin sequence, growth of the mandible catches up, and as adults these individuals have normal-sized chins.

Frequency

Isolated Pierre Robin sequence affects an estimated 1 in 8,500 to 14,000 people.

Genetic Changes

Changes in the DNA near the *SOX9* gene are the most common genetic cause of isolated Pierre Robin sequence. It is likely that changes in other genes, some of which have not been identified, are also involved in the condition. Doctors speculate that nongenetic factors, for example conditions during pregnancy that restrict growth of the jaw, may cause some cases of isolated Pierre Robin sequence.

The *SOX9* gene provides instructions for making a protein that plays a critical role in the formation of many different tissues and organs during embryonic development. The *SOX9* protein regulates the activity of other genes, especially those that are important for development of the skeleton, including the mandible.

The genetic changes near the *SOX9* gene that are associated with isolated Pierre Robin sequence are thought to disrupt regions of DNA called enhancers, which normally regulate the activity of the *SOX9* gene. These changes reduce *SOX9* gene activity. As a result, the *SOX9* protein cannot properly control the genes essential for normal development of the lower jaw, causing micrognathia, and consequently, glossoptosis, airway obstruction, and, often, cleft palate.

Inheritance Pattern

Isolated Pierre Robin sequence is usually not inherited. It typically results from new (de novo) genetic changes and occurs in people with no history of the disorder in their family. When the condition is inherited, it follows an autosomal dominant pattern, which means one copy of the DNA alteration in each cell is sufficient to cause the disorder.

Syndromic Pierre Robin sequence is inherited in the same pattern as the condition it is associated with.

Other Names for This Condition

- glossoptosis, micrognathia, and cleft palate
- Pierre Robin syndrome
- Pierre-Robin syndrome
- Robin sequence
- Robin syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Robin sequence
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0031900/>

Other Diagnosis and Management Resources

- Boston Children's Hospital: Cleft Lip and Cleft Palate Treatment and Care
<http://www.childrenshospital.org/conditions-and-treatments/conditions/c/cleft-lip-and-cleft-palate>
- Seattle Children's Hospital: Robin Sequence Treatments
<http://www.seattlechildrens.org/medical-conditions/chromosomal-genetic-conditions/robin/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>

- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Micrognathia
<https://medlineplus.gov/ency/article/003306.htm>
- Encyclopedia: Pierre Robin Syndrome
<https://medlineplus.gov/ency/article/001607.htm>
- Health Topic: Craniofacial Abnormalities
<https://medlineplus.gov/craniofacialabnormalities.html>

Genetic and Rare Diseases Information Center

- Pierre Robin sequence
<https://rarediseases.info.nih.gov/diseases/4347/pierre-robin-sequence>

Educational Resources

- Centers for Disease Control: Facts About Cleft Lip and Cleft Palate
<https://www.cdc.gov/ncbddd/birthdefects/cleftlip.html>
- Children's Craniofacial Association: A Guide to Understanding Pierre Robin Sequence
https://ccakids.org//assets/syndromebk_pierrerobin.pdf
- Disease InfoSearch: Pierre Robin Sequence
<http://www.diseaseinfosearch.org/Pierre+Robin+Sequence/5751>
- MalaCards: isolated pierre robin sequence
http://www.malacards.org/card/isolated_pierre_robin_sequence
- Orphanet: Isolated Pierre Robin syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=718
- University of California Davis Children's Hospital
https://www.ucdmc.ucdavis.edu/children/clinical_services/cleft_craniofacial/anomalies/pierre.html

Patient Support and Advocacy Resources

- Children's Craniofacial Association
<https://ccakids.org/>
- Cleft Palate Foundation
<http://www.cleftline.org/>
- Foundation for Faces of Children
<https://facesofchildren.org/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/pierre-robin-sequence/>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Pierre-Robin+sequence%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Pierre+Robin+Syndrome%5BM+AJR%5D%29+AND+%28Pierre-Robin+sequence%5BTIAB%5D%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

OMIM

- PIERRE ROBIN SYNDROME
<http://omim.org/entry/261800>

Sources for This Summary

- Amarillo IE, Dipple KM, Quintero-Rivera F. Familial microdeletion of 17q24.3 upstream of SOX9 is associated with isolated Pierre Robin sequence due to position effect. *Am J Med Genet A*. 2013 May;161A(5):1167-72. doi: 10.1002/ajmg.a.35847. Epub 2013 Mar 26.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23532965>
- Benko S, Fantes JA, Amiel J, Kleinjan DJ, Thomas S, Ramsay J, Jamshidi N, Essafi A, Heaney S, Gordon CT, McBride D, Golzio C, Fisher M, Perry P, Abadie V, Ayuso C, Holder-Espinasse M, Kilpatrick N, Lees MM, Picard A, Temple IK, Thomas P, Vazquez MP, Vekemans M, Roest Crolius H, Hastie ND, Munnich A, Etchevers HC, Pelet A, Farlie PG, Fitzpatrick DR, Lyonnet S. Highly conserved non-coding elements on either side of SOX9 associated with Pierre Robin sequence. *Nat Genet*. 2009 Mar;41(3):359-64. doi: 10.1038/ng.329. Epub 2009 Feb 22.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19234473>
- Côté A, Fanous A, Almajed A, Lacroix Y. Pierre Robin sequence: review of diagnostic and treatment challenges. *Int J Pediatr Otorhinolaryngol*. 2015 Apr;79(4):451-64. doi: 10.1016/j.ijporl.2015.01.035. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/25704848>

- Gordon CT, Attanasio C, Bhatia S, Benko S, Ansari M, Tan TY, Munnich A, Pennacchio LA, Abadie V, Temple IK, Goldenberg A, van Heyningen V, Amiel J, FitzPatrick D, Kleinjan DA, Visel A, Lyonnet S. Identification of novel craniofacial regulatory domains located far upstream of SOX9 and disrupted in Pierre Robin sequence. *Hum Mutat.* 2014 Aug;35(8):1011-20. doi: 10.1002/humu.22606.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24934569>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4389788/>
- Jakobsen LP, Ullmann R, Christensen SB, Jensen KE, Mølsted K, Henriksen KF, Hansen C, Knudsen MA, Larsen LA, Tommerup N, Tümer Z. Pierre Robin sequence may be caused by dysregulation of SOX9 and KCNJ2. *J Med Genet.* 2007 Jun;44(6):381-6.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17551083>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2740883/>
- Mackay DR. Controversies in the diagnosis and management of the Robin sequence. *J Craniofac Surg.* 2011 Mar;22(2):415-20. doi: 10.1097/SCS.0b013e3182074799. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21403570>
- Tan TY, Farlie PG. Rare syndromes of the head and face-Pierre Robin sequence. *Wiley Interdiscip Rev Dev Biol.* 2013 May-Jun;2(3):369-77. doi: 10.1002/wdev.69. Epub 2012 May 14.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23799581>
- Thouvenin B, Djadi-Prat J, Chalouhi C, Pierrot S, Lyonnet S, Couly G, Abadie V. Developmental outcome in Pierre Robin sequence: a longitudinal and prospective study of a consecutive series of severe phenotypes. *Am J Med Genet A.* 2013 Feb;161A(2):312-9. doi: 10.1002/ajmg.a.35773. Epub 2013 Jan 9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23303695>

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/isolated-pierre-robin-sequence>

Reviewed: December 2016

Published: April 17, 2018

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