thanatophoric dysplasia

Thanatophoric dysplasia is a severe skeletal disorder characterized by extremely short limbs and folds of extra (redundant) skin on the arms and legs. Other features of this condition include a narrow chest, short ribs, underdeveloped lungs, and an enlarged head with a large forehead and prominent, wide-spaced eyes.

Researchers have described two major forms of thanatophoric dysplasia, type I and type II. Type I thanatophoric dysplasia is distinguished by the presence of curved thigh bones and flattened bones of the spine (platyspondyly). Type II thanatophoric dysplasia is characterized by straight thigh bones and a moderate to severe skull abnormality called a cloverleaf skull.

The term thanatophoric is Greek for "death bearing." Infants with thanatophoric dysplasia are usually stillborn or die shortly after birth from respiratory failure; however, a few affected individuals have survived into childhood with extensive medical help.

Frequency

This condition occurs in 1 in 20,000 to 50,000 newborns. Type I thanatophoric dysplasia is more common than type II.

Genetic Changes

Mutations in the *FGFR3* gene cause thanatophoric dysplasia. Both types of this condition result from mutations in the *FGFR3* gene. This gene provides instructions for making a protein that is involved in the development and maintenance of bone and brain tissue. Mutations in this gene cause the FGFR3 protein to be overly active, which leads to the severe disturbances in bone growth that are characteristic of thanatophoric dysplasia. It is not known how *FGFR3* mutations cause the brain and skin abnormalities associated with this disorder.

Inheritance Pattern

Thanatophoric dysplasia is considered an autosomal dominant disorder because one mutated copy of the *FGFR3* gene in each cell is sufficient to cause the condition. Virtually all cases of thanatophoric dysplasia are caused by new mutations in the *FGFR3* gene and occur in people with no history of the disorder in their family. No affected individuals are known to have had children; therefore, the disorder has not been passed to the next generation.

Other Names for This Condition

- Dwarf, thanatophoric
- thanatophoric dwarfism
- thanatophoric short stature

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Thanatophoric dysplasia type 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1868678/
- Genetic Testing Registry: Thanatophoric dysplasia, type 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1300257/

Other Diagnosis and Management Resources

- GeneReview: Thanatophoric Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1366

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

- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html
- Health Topic: Dwarfism
  https://medlineplus.gov/dwarfism.html
- Health Topic: Respiratory Failure
  https://medlineplus.gov/respiratoryfailure.html

Genetic and Rare Diseases Information Center

- Thanatophoric dysplasia
  https://rarediseases.info.nih.gov/diseases/85/thanatophoric-dysplasia

Educational Resources

- Disease InfoSearch: Thanatophoric dysplasia
  http://www.diseaseinfosearch.org/Thanatophoric+dysplasia/9674
- MalaCards: thanatophoric dysplasia type i
  http://www.malacards.org/card/thanatophoric_dysplasia_type_i
- MalaCards: thanatophoric dysplasia type ii
  http://www.malacards.org/card/thanatophoric_dysplasia_type_ii
- Orphanet: Thanatophoric dysplasia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2655

Patient Support and Advocacy Resources

- International Skeletal Dysplasia Registry, UCLA
  http://ortho.ucla.edu/isdr
- Little People of America, Inc.
  http://www.lpaonline.org
- Little People UK
  http://littlepeopleuk.org/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/skeldysp.html
- The MAGIC Foundation
  https://www.magicfoundation.org/

GeneReviews

- Thanatophoric Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1366

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22thanatophoric+dysplasia%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Thanatophoric+Dysplasia%5BMAJR%5D%29+AND+%28thanatophoric+dysplasia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- THANATOPHORIC DYSPLASIA, TYPE I
  http://omim.org/entry/187600
- THANATOPHORIC DYSPLASIA, TYPE II
  http://omim.org/entry/187601

Sources for This Summary

- Cohen MM Jr. Some chondrodysplasias with short limbs: molecular perspectives. Am J Med Genet. 2002 Oct 15;112(3):304-13. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12357475
- Foldynova-Trantirkova S, Wilcox WR, Krejci P. Sixteen years and counting: the current understanding of fibroblast growth factor receptor 3 (FGFR3) signaling in skeletal dysplasias. Hum Mutat. 2012 Jan;33(1):29-41. doi: 10.1002/humu.21636. Epub 2011 Nov 16. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22045636
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3240715/
- GeneReview: Thanatophoric Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1366
- Martínez-Frías ML, de Frutos CA, Bermejo E, Nieto MA; ECEMC Working Group. Review of the recently defined molecular mechanisms underlying thanatophoric dysplasia and their potential therapeutic implications for achondroplasia. Am J Med Genet A. 2010 Jan;152A(1):245-55. doi: 10.1002/ajmg.a.33188. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20034074
- Pannier S, Martinovic J, Heuertz S, Delezoide AL, Munnich A, Schibler L, Serre V, Legeai-Mallet L. Thanatophoric dysplasia caused by double missense FGFR3 mutations. Am J Med Genet A. 2009 Jun;149A(6):1296-301. doi: 10.1002/ajmg.a.32880.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19449430
- Vajo Z, Francomano CA, Wilkin DJ. The molecular and genetic basis of fibroblast growth factor receptor 3 disorders: the achondroplasia family of skeletal dysplasias, Muenke craniosynostosis, and Crouzon syndrome with acanthosis nigricans. Endocr Rev. 2000 Feb;21(1):23-39. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10696568
- Waller DK, Correa A, Vo TM, Wang Y, Hobbs C, Langlois PH, Pearson K, Romitti PA, Shaw GM, Hecht JT. The population-based prevalence of achondroplasia and thanatophoric dysplasia in selected regions of the US. Am J Med Genet A. 2008 Sep 15;146A(18):2385-9. doi: 10.1002/ajmg.a.32485.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18698630

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