Birt-Hogg-Dubé syndrome

Birt-Hogg-Dubé syndrome is a rare disorder that affects the skin and lungs and increases the risk of certain types of tumors. Its signs and symptoms vary among affected individuals.

Birt-Hogg-Dubé syndrome is characterized by multiple noncancerous (benign) skin tumors, particularly on the face, neck, and upper chest. These growths typically first appear in a person's twenties or thirties and become larger and more numerous over time. Affected individuals also have an increased chance of developing cysts in the lungs and an abnormal accumulation of air in the chest cavity (pneumothorax) that may result in the collapse of a lung. Additionally, Birt-Hogg-Dubé syndrome is associated with an elevated risk of developing cancerous or noncancerous kidney tumors. Other types of cancer have also been reported in affected individuals, but it is unclear whether these tumors are actually a feature of Birt-Hogg-Dubé syndrome.

Frequency

Birt-Hogg-Dubé syndrome is rare; its exact incidence is unknown. This condition has been reported in more than 400 families.

Causes

Mutations in the \( FLCN \) gene cause Birt-Hogg-Dubé syndrome. This gene provides instructions for making a protein called folliculin. The normal function of this protein is unknown, but researchers believe that it may act as a tumor suppressor. Tumor suppressors prevent cells from growing and dividing too rapidly or in an uncontrolled way. Mutations in the \( FLCN \) gene may interfere with the ability of folliculin to restrain cell growth and division, leading to uncontrolled cell growth and the formation of noncancerous and cancerous tumors. Researchers have not determined how \( FLCN \) mutations increase the risk of lung problems, such as pneumothorax.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered \( FLCN \) gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the mutation from one affected parent. Less commonly, the condition results from a new mutation in the gene and occurs in people with no history of the disorder in their family.

Having a single mutated copy of the \( FLCN \) gene in each cell is enough to cause the skin tumors and lung problems associated with Birt-Hogg-Dubé syndrome. However, both copies of the \( FLCN \) gene are often mutated in the kidney tumors that occur with this condition. One of the mutations is inherited from a parent, while the other occurs by
chance in a kidney cell during a person's lifetime. These genetic changes disable both copies of the *FLCN* gene, which allows kidney cells to divide uncontrollably and form tumors.

**Other Names for This Condition**

- BHD
- fibrofolliculomas with trichodiscomas and acrochordons
- Hornstein-Birt-Hogg-Dubé syndrome
- Hornstein-Knickenberg syndrome

**Diagnosis & Management**

**Genetic Testing Information**

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Multiple fibrofolliculomas
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0346010/

**Research Studies from ClinicalTrials.gov**

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Birt-Hogg-Dube+syndrome%22

**Other Diagnosis and Management Resources**

- BHD Foundation: Practical Considerations
  https://www.bhdsyndrome.org/for-families/practical-considerations/
- GeneReview: Birt-Hogg-Dube Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1522
- MedlinePlus Encyclopedia: Collapsed Lung
  https://medlineplus.gov/ency/article/000087.htm

**Additional Information & Resources**

**Health Information from MedlinePlus**

- Encyclopedia: Collapsed Lung
  https://medlineplus.gov/ency/article/000087.htm
- Health Topic: Kidney Cancer
  https://medlineplus.gov/kidneycancer.html
• Health Topic: Lung Diseases
  https://medlineplus.gov/lungdiseases.html

• Health Topic: Skin Conditions
  https://medlineplus.gov/skinconditions.html

Genetic and Rare Diseases Information Center
• Birt-Hogg-Dube syndrome
  https://rarediseases.info.nih.gov/diseases/2322/birt-hogg-dube-syndrome

Additional NIH Resources
• National Cancer Institute: Kidney Cancer Home Page
  https://www.cancer.gov/types/kidney

Educational Resources
• BHD Foundation: Information Pamphlets
  https://www.bhdsyndrome.org/for-families/information-pamphlets/

• MalaCards: birt-hogg-dube syndrome
  https://www.malacards.org/card/birt_hogg_dube_syndrome

• Orphanet: Birt-Hogg-Dube syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=122

Patient Support and Advocacy Resources
• American Cancer Society: Kidney Cancer
  https://www.cancer.org/cancer/kidney-cancer.html

• BHD Foundation
  https://www.bhdsyndrome.org/

• Kidney Cancer Association
  https://www.kidneycancer.org/

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/birt-hogg-dube-syndrome/

Clinical Information from GeneReviews
• Birt-Hogg-Dube Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1522

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28birt-hogg-dubé+syndr ome%5BTIA%5D%29%29+OR+%28birt-hogg-dube+syndrome%5BTIAB%5D %29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last +1440+days%22%5Bdp%5D
**BIRT-HOGG-DUBE SYNDROME**  
http://omim.org/entry/135150

**Sources for This Summary**

- Happle R. Hornstein-Birt-Hogg-Dubé syndrome: a renaming and reconsideration. Am J Med Genet A. 2012 Jun;158A(6):1247-51. doi: 10.1002/ajmg.a.35330. Epub 2012 May 11.  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22581760

- Khoo SK, Giraud S, Kahnoski K, Chen J, Motorna O, Nickolov R, Binet O, Lambert D, Friedel J, Lévy R, Ferlicot S, Wolkenstein P, Hammel P, Bergerheim U, Hedblad MA, Bradley M, Teh BT, Nordenskjöld M, Richard S. Clinical and genetic studies of Birt-Hogg-Dubé syndrome. J Med Genet. 2002 Dec;39(12):906-12. Erratum in: J Med Genet. 2003 Feb;40(2):150..  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12471204  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1757219/

- Nickerson ML, Warren MB, Toro JR, Matrosova V, Glenn G, Turner ML, Duray P, Merino M, Choyke P, Pavlovich CP, Sharma N, Walther M, Munroe D, Hill R, Maher E, Greenberg C, Lerman MI, Linehan WM, Zbar B, Schmidt LS. Mutations in a novel gene lead to kidney tumors, lung wall defects, and benign tumors of the hair follicle in patients with the Birt-Hogg-Dubé syndrome. Cancer Cell. 2002 Aug;2(2):157-64.  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12204536

- Pavlovich CP, Walther MM, Eyler RA, Hewitt SM, Zbar B, Linehan WM, Merino MJ. Renal tumors in the Birt-Hogg-Dubé syndrome. Am J Surg Pathol. 2002 Dec;26(12):1542-52.  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12459621

- Schmidt LS, Nickerson ML, Warren MB, Glenn GM, Toro JR, Merino MJ, Turner ML, Choyke PL, Sharma N, Peterson J, Morrison P, Maher ER, Walther MM, Zbar B, Linehan WM. Germline BHD-mutation spectrum and phenotype analysis of a large cohort of families with Birt-Hogg-Dubé syndrome. Am J Hum Genet. 2005 Jun;76(6):1023-33. Epub 2005 Apr 25.  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15852235  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1196440/

- Schmidt LS, Warren MB, Nickerson ML, Weirich G, Matrosova V, Toro JR, Turner ML, Duray P, Merino M, Hewitt S, Pavlovich CP, Glenn G, Greenberg CR, Linehan WM, Zbar B. Birt-Hogg-Dubé syndrome, a genodermatosis associated with spontaneous pneumothorax and kidney neoplasia, maps to chromosome 17p11.2. Am J Hum Genet. 2001 Oct;69(4):876-82. Epub 2001 Aug 30.  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11533913  
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1226073/

- Toro JR. Birt-Hogg-Dubé Syndrome. 2006 Feb 27 [updated 2014 Aug 7]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Merfodd HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1522/  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301695

- Warren MB, Torres-Cabala CA, Turner ML, Merino MJ, Matrosova VY, Nickerson ML, Ma W, Linehan WM, Zbar B, Schmidt LS. Expression of Birt-Hogg-Dubé gene mRNA in normal and neoplastic human tissues. Mod Pathol. 2004 Aug;17(8):998-1011.  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15143337

Reprinted from Genetics Home Reference:  
https://ghr.nlm.nih.gov/condition/birt-hogg-dube-syndrome
