Birt-Hogg-Dubé syndrome (BHD)

Birt-Hogg-Dubé syndrome (BHD) is a hereditary condition with symptoms that generally don't appear until adulthood.

What are the effects of Birt-Hogg-Dubé (BHD) syndrome?

People with BHD can have:

- **Benign (non-cancerous) skin tumors**, usually on the face, head, neck, or upper chest. These typically do not develop into cancerous tumors.
- **Lung cysts** (air or fluid-filled space surrounded by a thin wall) usually in both lungs. These cysts may rupture and cause a spontaneous pneumothorax (collapsed lung) due to air leaking out of the lungs and into the chest space.
- **An increased risk for kidney tumors**, often on both kidneys (bilateral) and in different places within the kidney (multifocal). The kidney tumors most often seen in people with BHD include **oncocytomas**, which are benign but can grow quite large, as well as **oncocytic hybrid tumors** and **chromophobe renal cell carcinomas (RCCs)**, which tend to be fairly slow-growing types of kidney cancer[1]. Other types of kidney cancer, such as clear cell RCC and papillary renal carcinoma, have also been linked with BHD, but these are rare.

What causes Birt-Hogg-Dubé (BHD) syndrome?

BHD is caused by a mutation (change) in the *FLCN* gene. *FLCN* is thought to be a tumor suppressor gene[2]. It normally makes a protein called **folliculin**, which helps keep tumors from forming by keeping cell growth under control. In people with BHD, the mutated *FLCN* gene is unable to make a functional folliculin protein. As a result, people with BHD are more likely to develop non-cancerous and cancerous tumors.

People can have BHD by inheriting a mutated *FLCN* gene from either parent. If a person has BHD, they have a 50/50 chance of passing the *FLCN* gene mutation on to each of their children.

Options exist for people who carry an *FLCN* gene mutation and might want to have children. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is Birt-Hogg-Dubé (BHD) syndrome?

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Minor criteria

- Having many lung cysts, in both lungs, not caused by another known medical condition
- Being diagnosed with kidney cancer, either before age 50, having tumors in both kidneys (or having more than one tumor in the same kidney), or having an oncocytic hybrid tumor
- Having a first-degree family member (parent, sibling, or child) who has been diagnosed with BHD

How often should people with Birt-Hogg-Dubé (BHD) be screened for cancer?

People with BHD have an increased risk of developing kidney cancer, so doctors often recommend that these people get regular imaging tests to look for kidney tumors.

If kidney cancer is not found when a person is first diagnosed with BHD, doctors typically recommend that they be screened with either a CT scan or MRI of the abdomen at least every 3 years. Ultrasound of the abdomen is generally not used alone for this purpose, as it may not detect small kidney tumors.

Screening guidelines may change over time as new technologies are developed and more is learned about BHD. It is important to talk with your health care team about appropriate screening tests for you.

How is Birt-Hogg-Dubé (BHD) managed?

People with BHD can have tumors or other growths in different organs (including the skin, lungs, and kidneys), so they typically have a team of doctors to address each of these. For example:

If **skin tumors** are present, a dermatologist (skin doctor) will discuss options for treatment with you. These may include laser therapy, cryotherapy, or even surgery. However, the skin tumors may return. Thus, life-long skin and psychological care is needed.

If **lung cysts** are present, a pulmonologist (lung doctor) may advise you not to take part

in pressure-sensitive activities such as scuba diving or air travel. These activities may increase your risk for developing a spontaneous pneumothorax (gas in the space between the lungs and the chest wall). If you do develop a pneumothorax, your pulmonologist will discuss your options, which might include observation (watching it closely to make sure it goes away) or medical management, such as putting in a chest tube or surgery.

If **kidney cancer** is present, a doctor who treats kidney cancer (urologist) will discuss with you options of either monitoring the tumors closely or considering treatment such as surgery. This is usually based on size and location of the tumors, your health, and how well your kidneys are working. If you need surgery , the goal is usually to avoid removing the entire kidney if possible (with a partial nephrectomy), so that you can keep long-term kidney function.

Each person's case is managed differently, based on their individual situation. Decisions should be made by you and your team of medical specialists, depending on your symptoms and needs.

Questions to ask the health care team

If you are concerned about your kidney cancer risk, talk with your health care team. It might be helpful to bring someone along to your appointments to take notes.

Consider asking your health care team the following questions:

- What is my risk of developing kidney cancer?
- Am I at higher risk for developing any other types of cancer?
- What can I do to reduce my risk of developing cancer?
- What cancer screening tests should I get?

If you are concerned about your family history and think your family may have BHD, consider asking the following questions:

- If I have had a collapsed lung/pneumothorax, could it be linked with a genetic condition such as BHD?
- Does my family history increase my risk of developing kidney cancer?
- Are the skin tumors I or my family members have consistent with a diagnosis of BHD?
- Should I speak with a genetic counselor or other genetics specialist? If so, will you refer me?

- Should I consider genetic testing[3]?

Hyperlinks

1. www.cancer.org/cancer/types/kidney-cancer.html
2. www.cancer.org/cancer/understanding-cancer/genes-and-cancer/oncogenes-tumor-suppressor-genes.html
3. www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-risk.html

References

Benusiglio PR, Giraud S, Deveaux S, et al. Renal cell tumour characteristics in patients with the Birt-Hogg-Dubé cancer susceptibility syndrome: A retrospective, multicentre study. *Orphanet J Rare Dis*. 2014;9(163).

Cowen EW. Birt-Hogg-Dubé syndrome. UpToDate. 2023. Accessed at https://www.uptodate.com/contents/birt-hogg-dube-syndrome on January 24, 2024.

Menko FH, van Steensel MA, Giraud S, et al. Birt-Hogg-Dubé syndrome: Diagnosis and management. *Lancet Oncol*. 2009;10(12):1199-1206.

Muller ME, Daccord C, Taffé P, et al. Prevalence of Birt-Hogg-Dubé syndrome determined through epidemiological data on spontaneous pneumothorax and Bayes theorem. *Front Med (Lausanne)*. 2021;8: 631168.

Pavlovich CP, Grubb RL, Hurley K, et al. Evaluation and management of renal tumors in the Birt-Hogg-Dubé syndrome. *J Urol*. 2005;173(5):1482-1486.

Pavlovich CP, Walther MM, Eyler RA, et al. Renal tumors in the Birt-Hogg-Dubé syndrome. *Am J Surg Pathol*. 2002;26(12):1542-1552.

Savatt JM, Shimelis H, Moreno-De-Luca A, et al. Frequency of truncating FLCN variants and Birt-Hogg-Dubé-associated phenotypes in a health care system population. *Genet Med*. 2022;24(9):1857-1866.

Shuch B, Vourganti S, Ricketts CJ, et al. Defining early-onset kidney cancer: Implications for germline and somatic mutation testing and clinical management. *J Clin*

Oncol. 2014;32(5):431-437.

Stamatakis L, Metwalli AR, Middelton LA, et al. Diagnosis and management of BHD-associated kidney cancer. *Fam Cancer*. 2013;12(3): 397-402.

Toro JR, Pautler SE, Stewart L, et al. Lung cysts, spontaneous pneumothorax, and genetic associations in 89 families with Birt-Hogg-Dubé syndrome. *Am J Respir Crit Care Med.* 2007;175(10):1044-1053.

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