Birt-Hogg-Dubé Syndrome [1]

What is Birt-Hogg-Dubé syndrome?

Birt-Hogg-Dubé syndrome (BHD) is a hereditary condition associated with multiple noncancerous (benign) skin tumors, lung cysts, and an increased risk of both benign kidney tumors and kidney cancer [2]. Symptoms of BHD generally do not appear until adulthood.

The most common skin tumors in BHD are called fibrofolliculomas. These are pale or flesh-colored tumors that occur in the hair follicles. Other skin tumors associated with BHD are called trichodiscomas and acrochordons. Acrochordons are also known as skin tags, and trichodiscomas are a growth of normal-appearing tissue that builds up into a noncancerous tumor. The lung cysts in BHD do not cause problems with breathing and do not increase the risk of lung cancer. There is an increased risk of spontaneous pneumothorax, which is air leaking out of the lungs and into the chest. Spontaneous pneumothorax may result in a collapsed lung. Many different types of kidney tumors have been seen in people with BHD. Multiple tumors may occur on both kidneys. Tumors tend to grow slowly, but they are likely to develop into kidney cancer [2].

What causes BHD?

BHD is a genetic condition. This means that the cancer risk and other features of BHD can be passed from generation to generation in a family. A mutation (change) in a specific gene called *FLCN,* which creates a protein called folliculin, is believed to cause most cases of BHD. *FLCN* is currently thought to be a tumor suppressor gene. A tumor suppressor gene?s natural role in the body is to make proteins that prevent tumor formation by limiting cell growth. Research is ongoing to learn more about BHD.

How is BHD inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. BHD follows an autosomal dominant inheritance pattern, in which a mutation happens in only one copy of the gene. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

Having the mutation in one copy of the gene is enough to cause BHD. However, current research shows that a person with BHD must have mutations in both copies of the *FLCN* gene in order for a tumor to appear. A person can be born with one mutated gene (the autosomal dominant inheritance pattern described above) and then acquire a mutation to the second copy of the *FLCN* gene at some point during his or her lifetime. Then, with both copies of the *FLCN* gene altered, the body loses its ability to suppress tumor growth.

Options exist for couples interested in having a child when they know that one of them carries a gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation Genetic Diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to have children who do not carry the mutation. A woman?s eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos which do not have the mutation. PGD has been in use for over a decade, and more recently has been used for several hereditary cancer predisposition syndromes. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is BHD?

BHD is considered to be rare. The exact number of people and families who have BHD is unknown. To date, about 60 families worldwide have been reported to have BHD.

How is BHD diagnosed?

BHD is suspected when a person has skin tumors associated with BHD, especially if that person or his or her family members have a history of lung cysts, spontaneous pneumothorax, or kidney cancer [2]. BHD is also suspected in families with multiple cases of kidney cancer, particularly if family members have had different types of kidney cancer. Genetic testing to look for mutations in the *FLCN* gene is available for people suspected of having BHD.

What are the estimated cancer risks associated with BHD?

BHD is associated with an increased risk for kidney cancer, particularly the chromophobe renal cell carcinoma (RCC) type of kidney cancer. The estimated risk for kidney cancer in people with BHD is around 15%. The risk of kidney cancer is significantly increased in people who smoke. Individuals with BHD or at risk for BHD should avoid smoking [3]. It is not known if people with BHD have an increased risk of other specific types of cancer.

What are the screening options for BHD?

There are no specific screening guidelines for BHD. Due to the risk of kidney cancer [2], some doctors suggest that individuals who have BHD or a family history of BHD have a yearly ultrasound [4] (which uses sound waves to create a picture of the internal organs) of their kidneys, beginning at age 25. Other doctors suggest an abdominal computed tomography [5] (CT or CAT; creates a three-dimensional picture of the inside of the body using x-rays) scan or magnetic resonance imaging [6] (MRI; uses magnetic fields, not x-rays, to produce detailed images of the body) every two years. Evaluation by a dermatologist (a doctor who specializes in diseases and conditions of the skin) and screening for lung cysts are also suggested.

Screening options may change over time as new technologies are developed and more is learned about BHD. It is important to talk with your doctor about appropriate screening tests.

Learn more about what to expect when having common tests, procedures, and scans [7].

Questions to ask the doctor

If you are concerned about your risk for kidney cancer [2], talk with your doctor. Consider asking the following questions:

- What is my risk of developing kidney cancer [2]?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

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

- Does my family history increase my risk of developing kidney cancer [2]?
- Are the skin tumors on me or on my family members consistent with a diagnosis of BHD?
- Should I meet with a genetic counselor?
- Should I consider genetic testing [8]?

Additional resources

Guide to Kidney Cancer [2]

What to Expect When You Meet With a Genetic Counselor [9]

Kidney Cancer Association
www.kidneycancer.org [10]

National Cancer Institute
www.cancer.gov [11]

American Cancer Society
www.cancer.org [12]

Cancer*Care*
www.cancercare.org [13]

To find a genetic counselor in your area, ask your doctor or visit the following websites:

National Society of Genetic Counselors
www.nsgc.org [14]

National Cancer Institute: Cancer Genetics Services Directory
www.cancer.gov/cancertopics/genetics/directory [15]

Links:
[1] http://www.cancer.net/cancer-types/birt-hogg-dub%C3%A9-syndrome
[2] http://www.cancer.net/node/31256
[3] http://www.cancer.net/node/28461
[4] http://www.cancer.net/node/24714
[5] http://www.cancer.net/node/24486
[6] http://www.cancer.net/node/24578
[7] http://www.cancer.net/node/24959
[8] http://www.cancer.net/node/24895
[9] http://www.cancer.net/node/24907
[10] http://www.kidneycancer.org/
[11] http://www.cancer.gov/
[12] http://www.cancer.org/
[13] http://www.cancercare.org/
[14] http://www.nsgc.org/
[15] http://www.cancer.gov/cancertopics/genetics/directory