

***FLCN* Mutations (Birt-Hogg-Dubé syndrome)**

What You Should Know About *FLCN* Mutations

Individuals with a mutation in the *FLCN* gene have a condition called Birt-Hogg-Dubé (BHD) syndrome. Individuals with BHD have an increased risk for kidney tumors, non-cancerous skin lesions, and spontaneous pneumothorax (collapsed lung).

Risks Associated with a *FLCN* Mutation

- **Skin Lesions:** Individuals with BHD typically have multiple benign (non-cancerous), small, skin-colored, domed papules over their face, neck, and upper-trunk. These are called fibrofolliculomas/trichodiscomas. About 90% of adults with BHD have one or more skin findings.
- **Lung Cysts and Pneumothorax:** Multiple lung cysts occur in 80-90% of individuals with BHD. Approximately 20-40% of individuals with BHD develop a spontaneous pneumothorax (collapsed lung).
- **Kidney tumors:** Individuals with BHD have an increased risk to develop kidney tumors. Kidney tumors associated with BHD tend to be bilateral (in both right and left kidneys), multifocal (multiple tumors in one kidney), and slow growing. Most of kidney tumors associated with BHD are classified as oncocytomas and chromophobe renal cell carcinoma.

Risks to Family Members

Mutations in the *FLCN* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *FLCN* mutation have a 1 in 2 (or 50%) chance of having the mutation. Individuals with a *FLCN* mutation may develop skin lesions, lung cysts, spontaneous pneumothorax, kidney tumors, or none of the above. Both males and females can inherit a familial *FLCN* mutation and both males and females can pass it on to their children.

Managing Cancer Risks

There are currently no consensus management guidelines for individuals with BHD syndrome. However, the following recommendations have been proposed based on expert opinion.

- **Skin Lesions:** No recommended surveillance. Laser ablation may improve the appearance of these lesions, but they can reappear over time.
- **Lung Cysts/Pneumothorax:** Baseline high-resolution computer tomography (HRCT) or CT to assess for the presence of lung cysts. Avoid high altitudes and high ambient pressures, which may increase their risk for spontaneous pneumothorax. This includes, but is not limited to, activities such as skydiving, or deep sea diving.
- **Kidney Tumors:** Baseline MRI of the kidneys, or abdominal/pelvic CT scan with contrast. If the baseline is normal, MRI or abdominal/pelvic CT scan with contrast every 2-3 years. Renal ultrasounds may be adequate in some patients.

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