UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

Von-Hippel Lindau (*VHL* mutations)

What You Should Know About Von-Hippel Lindau (VHL) Syndrome

Von-Hippel Lindau (VHL) syndrome is a rare condition that is caused by mutations in the *VHL* gene. Individuals with VHL are at increased risk to develop multiple tumors all over the body. Most of the tumors in individuals with VHL are not cancerous, but they can cause health problems.

Cancer/ Tumor Risks Associated with a *VHL* mutation

VHL is associated with the following risks:

- 25-70% risk for kidney cancer.
- 7-79% risk for benign tumors of the brain and spine (hemangioblastomas), which can lead to headaches, vomiting, dizziness, and sometimes difficulty walking.
- 25-60% risk for retinal hemangioblastomas, which are non-cancerous tumors in the eye. These tumors often do not have symptoms, but can occasionally cause vision loss.
- 15% risk for endolymphatic sac tumors (ELSTs), which are non-cancerous tumors in the ear that can be associated with hearing loss.
- Increased risk for benign tumors in the adrenal gland (called pheochromocytomas), which can cause high blood pressure.
- Increased risk for pancreatic tumors, which are usually non-cancerous.
- Increased risk for benign cystadenomas of the epididymis in males or the broad ligament near the fallopian tube in women. There can be a risk for sterility/ infertility associated with the removal of cystadenomas, or depending on the location of the cystadenomas.

The Risks to Family Members

VHL is inherited in an autosomal dominant fashion. This means that the children, brothers, sisters, and parents of an individual with VHL have a 50% (1 in 2) chance of having the mutation. Individuals with a *VHL* mutation may develop one tumor, more than one tumor, or none at all. Both males and females can inherit a familial *VHL* mutation and can pass that it on to their children.

Approximately 20% (1 in 5) of individuals with VHL do not have a family history of VHL, and thus have a new (de novo) mutation.

Managing Cancer Risks

Several organizations have proposed surveillance guidelines for individuals with VHL including the VHL Alliance and the American Association for Cancer Research (AACR). The VHL Alliance Active Surveillance guidelines are summarized below.

Ages 1-4

- Annual eye/retinal examination with indirect ophthalmoscope by an ophthalmologist. Pediatrician should look for signs of neurological disturbance, nystagmus, strabismus, white pupil, and abnormalities in blood pressure, vision, or hearing.

Ages 5-15

- Annual physical examination and neurological assessment by pediatrician informed about VHL, with particular attention to blood pressure (taken while lying down and standing), hearing impairment, neurological disturbance, nystagmus, strabismus, white pupil, and other signs indicating retinal problems.
- Annual dilated eye/retinal examination with indirect ophthalmoscope by ophthalmologist informed about VHL.
- Annual test for fractionated metanephrines, especially normetanephrine in a "plasma free metanephrine" blood test or in a 24-hour urine test. Abdominal MRI or MIBG scan only if biochemical abnormalities found.
- Annual abdominal ultrasonography starting at 8 years (or earlier) if indicated.
- Audiology assessment by an audiologist every 2-3 years. Annually if any hearing loss, tinnitus, or vertigo is found. In the case of repeated ear infections, MRI with contrast of the internal auditory canal using thin slices, to check for a possible ELST

Age 16+

- Annual physical examination by physician informed about VHL.
- Annual dilated eye/retinal examination with indirect ophthalmoscope by ophthalmologist informed about VHL.
- Annaul quality ultrasound and at least every other year when not pregnant, an MRI scan of abdomen with and without contrast to assess kidneys, pancreas, and adrenals.
- Annual test for fractionated metanephrines, especially normetanephrine in "plasma free metanephrines" blood test or 24-hour urine test. Abdominal MRI or MIBG scan if biochemical abnormalities found.
- Every 2-3 years, MRI scans should be ordered as no less than a 1.5T MRI with and without contrast of brain, cervical, thoracic, and lumbar spine, with thin cuts through the posterior fossa, and attention to inner ear/petrous temporal bone to rule out both ELST and hemangioblastomas of the neuraxis.
- Audiology assessment by an audiologist.

During Pregnancy (for women with VHL)

- Regular retinal checkup to anticipate potentially more rapid progression of lesions.
- Test for pheochromocytoma early, mid, and again late pregnancy to ensure no active pheochromocytoma during pregnancy or especially labor and delivery.
- During the 4th month of pregnancy, MRI—without contrast—to check on any known lesions of the brain and spine.
- If known retinal, brain, or spinal lesions, consider C-section.

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