Von Hippel-Lindau syndrome

Alternate names: von Hippel-Lindau disease, VHL syndrome

What is von Hippel-Lindau syndrome?

Von Hippel-Lindau syndrome is a rare condition that makes a person more likely to develop certain types of tumors. These tumors can be either benign (non-cancerous) or malignant (cancerous).

People with von Hippel-Lindau syndrome may develop the following:

- Central nervous system and retina tumors called hemangioblastomas. These blood vessel tumors are usually benign, but they may cause health problems depending on their location.
- Benign tumors of the inner ear called endolymphatic sac tumors, which can cause hearing loss
- Kidney cysts or cancer
- Pancreatic cysts or cancer
- Adrenal gland tumors known as pheochromocytomas. The adrenal glands are located on top of each kidney, and they produce important hormones.
- Genital tract tumors called papillary cystadenomas

Von Hippel-Lindau syndrome is hereditary, which means it can be passed from parents to their children. The severity of the condition and which body areas are affected can vary from person to person, even within the same family.

What causes von Hippel-Lindau syndrome?

Von Hippel-Lindau syndrome is caused by changes in a gene known as *VHL*. Genes carry information telling cells within the body how to function. The *VHL* gene helps to control how cells grow, divide and die. It also plays an important role in regulating how blood vessels develop.

Most people without von Hippel-Lindau syndrome carry two working copies of the *VHL* gene in their cells. One copy is inherited from the mother and one from the father. Cells from people with von Hippel-Lindau syndrome carry one working copy of *VHL* and one copy that is changed. This change causes the gene to not work properly. It is called a *VHL* mutation.

Most children with von Hippel-Lindau syndrome inherit the *VHL* gene mutation from a parent who also has the syndrome. About 1 in 5 or 20% of people with von Hippel-Lindau syndrome have a new *VHL* mutation that did not come from a parent. These children have no history of the syndrome in their family. In these cases, the change either happened in an egg or sperm cell when the child was formed or in one of the child's cells during pregnancy. These children are the first in their families to have von Hippel-Lindau syndrome. No matter how they acquired the *VHL* mutation, people with von Hippel-Lindau syndrome have a 50% or 1 in 2 chance of passing it on to their children.

As people with von Hippel-Lindau syndrome get older, the remaining working copy of *VHL* often becomes changed within some of their cells. When both copies of the gene are changed, benign tumors or cancers can develop.

What is the tumor risk for children with von Hippel-Lindau syndrome?

People with von Hippel-Lindau syndrome are at a higher risk of developing tumors in areas that contain blood vessels. These include hemangioblastomas in the central nervous system (brain, spinal cord) and retina (the back of the eye) as well as endolymphatic sac tumors in the inner ear. The age of diagnosis varies widely, but patients are most commonly diagnosed between ages 12–35 years. Often, these tumors must be removed to prevent medical problems like vision or hearing loss.

People with von Hippel-Lindau syndrome are also at higher risk of developing other tumor types. These tumor types include clear cell renal carcinoma (kidney cancer), pheochromocytomas, pancreatic cancer, and papillary cystadenomas. The most commonly diagnosed cancer is clear cell renal carcinoma, which occurs in about 40% of people with von Hippel-Lindau syndrome. Patients may also develop cysts in the pancreas and kidney. The age of diagnosis among these tumor types varies. The most common ages for diagnosis are between 12–50 years.

How are people with von Hippel-Lindau syndrome screened for tumors?

A health care provider who knows this condition well should manage people with von Hippel-Lindau syndrome. Screening is recommended for all people with von Hippel-Lindau syndrome. The goal of screening is finding and treating tumors early to allow the best outcome for patients. While many of the tumors associated with von Hippel-Lindau syndrome are benign (non-cancerous), they may cause serious complications, such as hearing loss (endolymphatic sac tumors) or high blood pressure (pheochromocytomas).

Test	**Age at first test**	**Frequency**	**Reason for screening**
Complete physical exam	Infancy	Yearly	Looking for signs and symptoms related to von Hippel-Lindau syndrome
Indirect Ophthalmoscopy (a test to see inside the eye)	Infancy	Yearly	Looking for retinal hemangioblastomas. If present, increase screenings to every 6 months or as recommended by ophthalmologist
Blood pressure monitoring	Infancy	Yearly	Looking for pheochromocytomas
Plasma free metanephrines (blood test)	5 years	Yearly	Looking for pheochromocytomas
Abdominal ultrasound	8 years	Yearly until age 11 years, then every other year	Looking for pheochromocytomas and other abdominal tumors

Abdominal MRI (with contrast)	11 years	Every other year	Looking for pheochromocytoma and other abdominal tumors
Brain and spine MRI (with contrast)	Puberty or 11 years, whichever is earlier	Every 2 years	Looking for hemangioblastomas and papillary cystadenomas
Hearing tests	5 years	Every 2-3 years	Looking for endolymphatic sac tumor. If abnormal, radiologic testing should also be performed

How is genetic testing for von Hippel-Lindau syndrome done?

The health care provider may suspect von Hippel-Lindau syndrome after looking at a person's medical or family history. In most cases, a health care provider or genetic counselor will ask questions about a person's health and the health of other family members.

The genetic counselor or health care provider will record which family members have developed tumors, and if so, the types of tumors and ages at which these tumors occurred. From this information, they will create a family tree. Health care providers and genetic counselors will examine the family tree to find out:

- If there are more tumors than normal,
- Whether tumors occurred at younger than expected ages, or
- If the types of tumors match up with what might be observed in those with von Hippel-Lindau syndrome.

If von Hippel-Lindau syndrome is suspected in a child or other family members, the health care provider or genetic counselor will likely recommend genetic testing of the *VHL* gene.

Diagnostic genetic testing

If health care providers or genetic counselors suspect a person has von Hippel-Lindau syndrome, diagnostic testing may take place as follows:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. A person's genes are made of DNA.
- Both copies of the *VHL* gene are checked for possible changes. A genetic specialist compares the two copies of the patient's *VHL* gene to a normal *VHL* gene. If there are differences, the specialist decides if they might be a cause of von Hippel-Lindau syndrome.
- If a *VHL* mutation is found, the genetic counselor will work with the family in the following ways:
    - To help the family understand the tumor risks related to von Hippel-Lindau syndrome
    - To find out if other family members should consider testing
    - To help with decisions about prenatal genetic testing

Prenatal genetic testing

Parents may undergo prenatal testing to find out if the pregnancy is affected with a known *VHL* mutation in the family. Testing may take place either before pregnancy occurs or during pregnancy.

People considering prenatal testing should work with a genetic counselor to review the pros and cons of the testing. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

Testing that occurs before pregnancy — Testing that happens before pregnancy is called preimplantation genetic testing (PGT). This special type of genetic testing is done along with in vitro fertilization (IVF). PGT offers a way to test embryos for a known *VHL* mutation before placing them into the uterus.

Testing that occurs during pregnancy —Testing can be used to see if a pregnancy is affected with a known *VHL* mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)—**during the first trimester (first three months)
- **Amniocentesis—**during the second trimester or later (last six months)

Collected tissue can be checked for the presence of the *VHL* mutation identified in the family.

Both of these tests carry minor risks and should be discussed with an experienced doctor or genetic counselor.

Special concerns

Genetic testing for von Hippel-Lindau syndrome is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with the health care provider or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with von Hippel-Lindau syndrome can feel sad, anxious or angry. Parents who pass on a *VHL* mutation to one or more of their children can feel guilty. Some people with a *VHL* mutation could have trouble getting disability coverage, life insurance, or long-term care insurance in some states. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with Von Hippel-Lindau syndrome?

Children with von Hippel-Lindau syndrome are at risk of developing multiple types of tumors during their lifetimes. They should monitor their health and adopt healthy habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any tumor can be found early at the most treatable stage.

People with this syndrome should watch closely for general signs or symptoms that could signal tumors:

- Aches, pains, lumps or swelling that cannot be explained
- Headaches, vomiting, changes in vision or nerve function that do not go away
- Hearing loss, ringing in the ears, or dizziness
- Increases in blood pressure
- Pain in the abdomen

Other ideas to reduce the risk of tumors include the following:

- Eat a healthy diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke
- Avoid excess sun exposure and always wear sunscreen, hat and protective clothing when out in the sun

What other information and resources are there for children with von-Hippel Lindau syndrome and their families?

Other resources about von Hippel-Lindau syndrome include the following:

- Von Hippel-Lindau (VHL) Alliance (*www.vhl.org*)
- Genetics Home Reference: (*ghr.nlm.nih.gov/condition/von-hippel-lindau-syndrome*)

Other resources:

- Making Sense of Your Genes: A Guide to Genetic Counseling (*www.ncbi.nlm.nih.gov/books/NBK115508/*)
- Young People with Cancer: A Parent's Guide (*www.cancer.gov/publications/patient-education/young-people*)

Sources:

1. GeneReviews: Von Hippel-Lindau Disease (*www.ncbi.nlm.nih.gov/books/NBK1463/*)
2. Von Hippel-Lindau (VHL) Alliance (*www.vhl.org*)

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