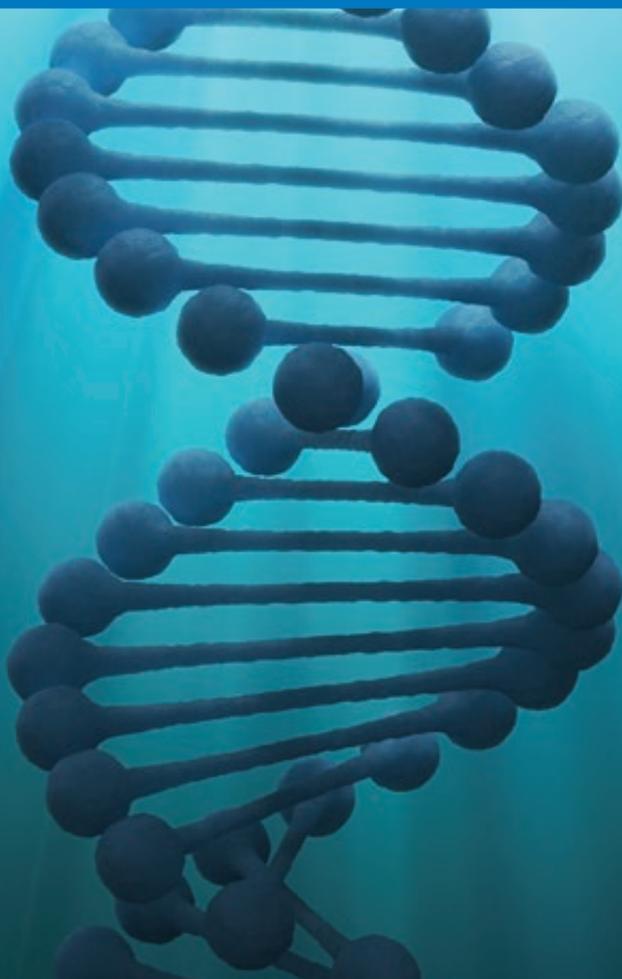


# Von Hippel-Lindau disease (VHL)

Information for patients



This booklet has been written to answer some of the questions people may have about von Hippel-Lindau (VHL) disease.

VHL is a rare disorder caused by a faulty gene. It is named after the two doctors who first described the disease, and affects about one in 35,000 people. Tumours develop in one or more parts of the body. Many of these tumours involve the abnormal growth of blood vessels in parts of the body which are particularly rich in blood vessels.

Areas most frequently affected are the eyes, the back of the brain (cerebellum), the spinal cord, the kidneys, the adrenal glands and the pancreas. People are affected differently, even within the same family. The only VHL tumour which tends to run in families affects the adrenal glands (phaeochromocytoma).

Different VHL features tend to develop at different ages. The eye angiomas often develop in childhood. Others, including tumours found in the cerebellum, spinal cord or adrenal glands (haemangioblastomas and phaeochromocytomas) can develop from late childhood onwards. The kidney tumours are usually the last things that develop, from the mid-twenties onwards.

The features of VHL can be divided into two groups. The first are those that if left untreated would go on to cause some kind of problem. The second group of features hardly ever cause symptoms and can just be regarded as helpful in diagnosing VHL.

Most often the tumours seen in VHL are classified as benign because they are not cancerous and do not have the potential to spread to other parts of the body. However, these tumours can have serious effects on the areas where they are found, which may need to be acted upon.

## Eyes

Patients with VHL may develop one or more (benign) eye tumours. The medical names for these are retinal haemangioblastomas. However, many doctors refer to them as retinal angiomas or haemangiomas. The retina is the internal lining at the back of the eyeball. How the angiomas affect vision depends on where they are in the eye.

The angiomas in VHL can usually be treated successfully with laser treatment. However, there are some angiomas, (particularly if they occur in the centre of the eye), that are difficult to treat because laser treatment may cause harm to the vision itself.

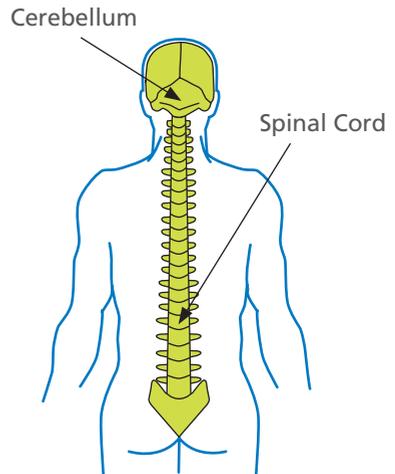
Early treatment of the angiomas prevents their enlargement and the risk of bleeding. It is recommended that people with VHL have regular eye checks (usually once a year) to monitor the development of angiomas.

## Brain and spinal cord

Haemangioblastomas, like the ones that occur in the eye, can occur in the brain and spinal cord in people with VHL. The symptoms they cause depend on where they are. The most common site is in the cerebellum. This is at the back of the brain and is involved in balance. Symptoms can include headaches, feeling unsteady, episodes of dizziness and sickness.

If haemangioblastomas occur near the spinal cord, different symptoms develop depending on where in the spine the tumour is. Symptoms can include pain in the back, altered sensation in one or more parts of the body, or difficulty in using a hand, arm or leg.

The nervous system tumours in VHL are usually treated surgically. As the tumours are benign, their complete removal is usually possible and the outcome of surgery successful.



## Kidneys

The kidney is affected in two ways. The commonest scan finding in somebody with VHL is multiple cysts in both kidneys. These usually do not affect how the kidney works or cause any symptoms. Occasionally there might be bleeding from the wall of one of the cysts and this can cause kidney pain, but this often settles without any specific treatment.

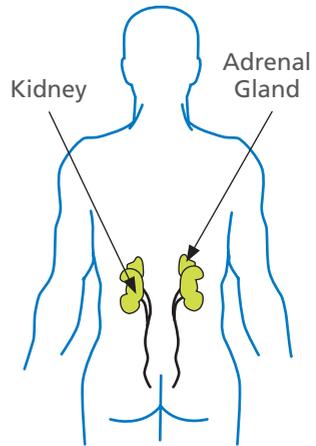
Kidney cancer is more common in people with VHL than in the general population. Sometimes the kidney cancer starts in the wall of one of the cysts and sometimes it starts as a solid tumour. Kidney cancer often only causes symptoms very late in its course, when it may already have spread to different parts of the body.

However, we know that if kidney cancers are detected early and removed before they grow to a size of approximately 3cm, in nearly every case the tumour will not come back or spread anywhere else in the body. Therefore we recommend a scan every year to look at the kidneys and check for any tumours. If any are found they are monitored carefully so people may have treatment at an appropriate time.

The treatment is usually either surgery to remove the tumour or newer techniques called radio-frequency ablation or cryotherapy. These are carried out by a radiology doctor and are less invasive than surgery.

## Adrenal gland

The adrenal gland lies just above the kidney. It is only affected in a small proportion of VHL families. The tumour that develops is called a phaeochromocytoma. It is the only disease feature where if one person in the family has been affected by phaeochromocytoma other relatives are also likely to be affected.

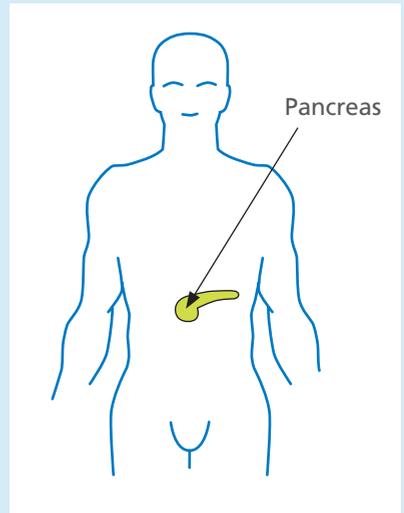


Tumours can produce chemicals that cause high blood pressure. If this goes untreated, the effects of continued high blood pressure can be severe. If a phaeochromocytoma is detected, surgery is recommended and is very successful. We specifically check for phaeochromocytoma by asking you to do a 24 hour urine collection every year.

## Pancreas

The pancreas, like the kidney, is a common site for cysts to develop in VHL. Just as in the kidney, these are usually only found on scanning and seldom cause symptoms.

Much more rarely patients with VHL have solid tumours in the pancreas and very occasionally these are cancerous. If a tumour is found in the pancreas of somebody with VHL, then treatment depends upon its size. Small tumours are often monitored by regular scans. Larger tumours can usually be removed successfully by surgery.



## Rarer features of VHL

Some features of VHL are very rare and are not routinely screened for. These include a rare kind of tumour related to the ear, called an endolymphatic sac tumour which can affect hearing.

Men with VHL can develop cysts or small tumours called cystadenomas in the epididymis, which is attached to the testicle. These tumours hardly ever cause symptoms.

Women with VHL can develop cystadenomas in their broad ligament (this runs from the womb to the pelvic floor). Again, these hardly ever cause symptoms.

## Diagnosis

All the tumours and cysts that occur in VHL can also happen as isolated events in the general population. A clue to somebody having VHL is that they have more than one of the tumours or cysts and that the tumours developed at a younger age than in the general population. For example, somebody with VHL would tend to have multiple angiomas in both eyes, whereas a single angioma after the age of 60 is unlikely to be due to VHL.

In people with no family history, the diagnosis is made if there is more than one haemangioblastoma in the eye or nervous system, or one haemangioblastoma and a VHL related tumour or cyst in the pancreas, kidney or adrenal gland.

In people with a family history of VHL, only one VHL related feature needs to be present for a diagnosis to be made.

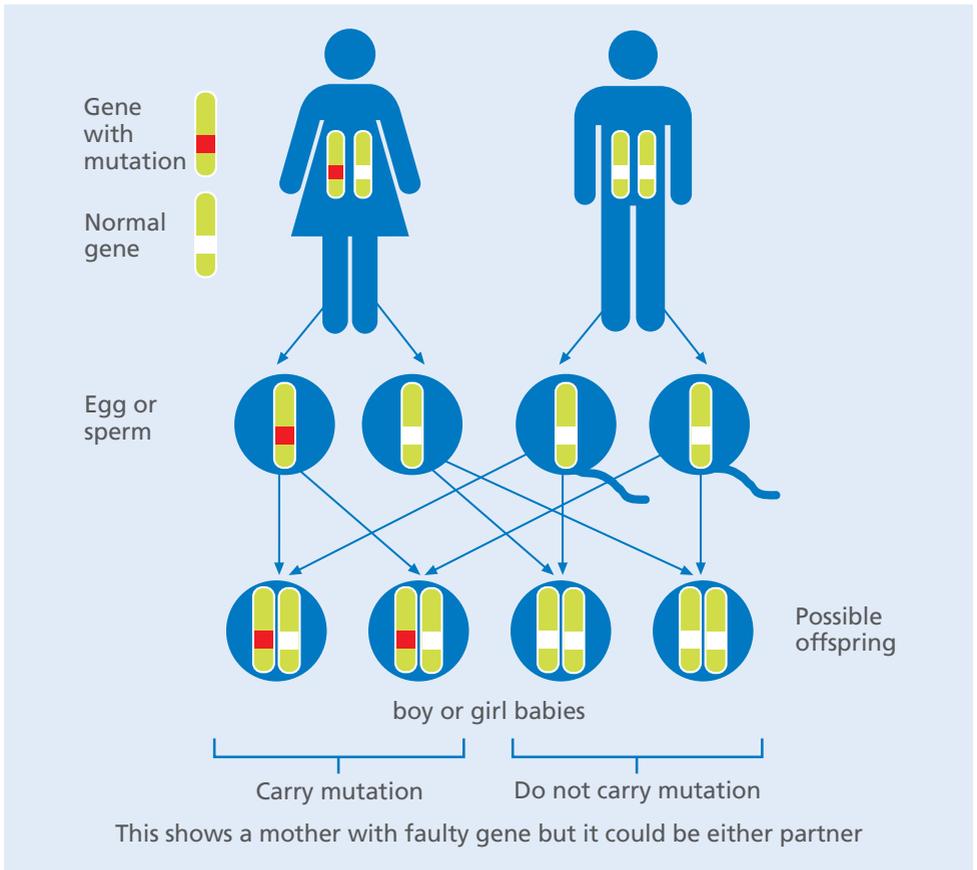
One of the difficulties about diagnosing VHL is that within families some people may only ever have one disease feature. Therefore to be cautious, young people with no family history and one disease manifestation (for example, a nervous system haemangioblastoma at a young age) are offered VHL screening just to make sure they do not have the disease.

The diagnosis of VHL has been made much easier recently by being able to look at the genetic code for VHL.

## Causes

VHL is often inherited from a parent. About a quarter of all people diagnosed with VHL have no family history of the disease, but can pass VHL on to their children.

Our bodies contain thousands of coded messages called genes that send instructions to our body on how to function; for example, what colour to make our eyes or how tall we will grow. The VHL gene makes a protein that is important for the normal function of cells. A mutation (fault) in this gene alters the message the gene sends to the body and causes an increased chance of one of the VHL tumours developing.



You may hear many different words used to describe a gene that is not working properly. The gene may be said to be faulty, altered or changed. The technical term is a mutation which means that the instruction that the gene sends to the body may be different, just as a spelling mistake may alter the meaning of a word.

We all have two copies of each of our genes; we get one copy from our mother, the other copy from our father. People with VHL have one faulty copy and one normal copy. When we have children we pass just one of each copy on; the other comes from the other parent.

Therefore, each of the children of someone with VHL has a one in two (50%) chance that they will inherit the altered gene. If a person has not inherited a mutation, then they cannot pass it on to their children.

## Gene testing

It is possible to look for a specific fault in the gene in an affected person. This can be done from a blood sample, since blood cells contain copies of all of our genes. This result will take a couple of months. It is known that current techniques are not yet good enough to find all gene changes, even when the diagnosis of VHL is certain.

If the fault in the gene is found then this information can be used to test other members of the family to see whether or not they also have the faulty gene. This test is much quicker taking two to four weeks for a result.

If the faulty gene has not been identified, then it may be possible to follow the gene through the family using DNA markers. This will give us a very good indication as to who is likely to carry the faulty gene within a family. Taking this information, alongside screening results, it may be possible to stop the screening programme on those people who are unlikely to have inherited the faulty gene.

## Screening

Complications of VHL disease are much easier to treat if they are detected early. For this reason, once the diagnosis is made it is recommended that patients enter an annual screening programme where different parts of the body involved in VHL can be checked out.

In this region, patients are offered an annual appointment at a joint neurological/genetics clinic. During the visit they have a consultation and general check up with a clinical geneticist, neurologist and genetic counsellor. They may have their blood pressure checked and a neurological examination performed. The patient also has a detailed eye examination with a consultant ophthalmologist at least once a year.

Depending on the age of the patient, MRI scans of the abdomen, brain or spinal cord are arranged. Finally, patients are asked to make a 24-hour urine collection after clinic to check for phaeochromocytomas.

The frequency of the different tests and screening programme reflects the natural history of the different features of VHL. For example, eyes and kidneys are checked on an annual basis. On the other hand, brain and spinal cord tumours grow slowly, and we know they can be present on scans for many years without causing symptoms. Therefore, some patients choose to have brain or spine scans only if they have symptoms. Other people prefer to have a brain or spine scan every few years.

If tumours are detected which need treatment the patient is referred to the specialist for that part of the body. They will discuss in detail how the particular problem should be treated. The majority of VHL tumours can be treated successfully, particularly when detected early.

## Tests

Your family history may suggest there is a possibility that you have inherited VHL disease, for example children of a parent with VHL disease each have a one in two (50%) risk of developing the disease regardless of whether they are boys or girls.

In the past all children at risk were offered screening very like that offered to people with definite VHL. The screening began with regular eye checks at five years and other checks were added in as the children grew into adulthood.

The development of a gene test for VHL has meant that children can be tested, (usually around the age of four or five) to see whether or not they need screening. Those who test negative are not at risk of passing VHL on to their own children in the future. Those with the faulty gene will be screened appropriately.

Some parents decide that they would rather the child made his or her own decision about gene testing when they are older. Therefore the child would be screened with eye checks and testing is then offered to them as they grow older and understand more about VHL and their risk. This test for children is only possible if we have been able to identify the specific VHL mutation in the family.

## Appointments

Because a person with VHL has a number of scans and appointments throughout the year it can be difficult to keep track of them all. We have developed a personal health record which you will be given at clinic which is a way of keeping all your information relating to VHL together.

## Pregnancy

In families where the faulty gene has been identified, it is possible to offer testing in pregnancy. This would usually be done at around 11 weeks by a test called chorionic villus sampling (CVS). In this technique, a sample is taken from the placenta. This tissue contains the foetus' genetic material and so we can see whether the pregnancy has inherited the faulty gene or not. Some people do not feel VHL is something they would want to test for in pregnancy. They go ahead and have their family and bring their children to clinic at the appropriate age. Others do not want to put children at risk of VHL but equally they would not want to terminate a pregnancy if the CVS test was positive.

There is also the possibility of a technique called pre-implantation genetic diagnosis (PGD). This is where the baby is conceived by an in-vitro fertilisation (IVF) procedure and the embryos tested for VHL before they are implanted. Those embryos that test negative for VHL would be implanted into the woman's uterus (womb). Such tests need a lot of consideration and are not widely available.

## Considerations

Some people experience a range of emotions when they are told they have VHL. Anger, shock, anxiety, worry about your health, guilt about possibly passing the gene on to children are all normal reactions.

Uncertainty is another problem. Because VHL is variable, even within families, we can't say how any one person will be affected in the future. As several family members can be affected this can also be difficult. Screening results and possible treatment interventions may be different for family members at different times. People in the family that do not inherit the gene can feel guilty when other close relatives have.

## Research

VHL is one of the diseases that has benefited from the developments in genetic research. Genetic testing has been possible for over 15 years. Now scientists are working to understand how the protein that the VHL gene codes for works. Various treatment trials in VHL are ongoing throughout the world.

One benefit of research would be if it led to a drug treatment that could be taken when the VHL tumours first appear, causing them to stop growing or even shrink. This is not yet possible but hopefully in the next ten or 20 years such treatments may become available.

## The team involved in your care are:

Consultant: .....

Tel no: .....

Genetic counsellor: .....

Tel no: .....

## Further information

If you need more advice or information about any aspect of VHL, please contact us at:

- **Wessex Clinical Genetics Service**

Princess Anne Hospital  
Coxford Road  
Southampton  
SO16 5YA

Telephone: **023 8120 6170**

Website: **[www.uhs.nhs.uk/genetics](http://www.uhs.nhs.uk/genetics)**

## Useful contacts

- **VHL Family Alliance**

Email: **[info@vhl.org](mailto:info@vhl.org)**

Website: **[www.vhl.org](http://www.vhl.org)**

This booklet was written by:

**Wessex Clinical Genetics Service**  
Princess Anne Hospital  
Coxford Road  
Southampton  
SO16 5YA

**If you need a translation of this document,  
an interpreter or a version in large print,  
Braille or on audiotape, please telephone  
023 8120 4688 for help.**

**[www.uhs.nhs.uk/genetics](http://www.uhs.nhs.uk/genetics)**

© 2016 University Hospital Southampton NHS Foundation Trust. All rights reserved.  
Not to be reproduced in whole or in part without the permission of the copyright holder.

Version 4. Published May 2016. Due for review May 2019. GEN018.01