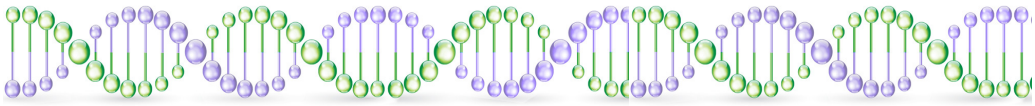
# Information Sheet



# Von Hippel Lindau syndrome and the VHL gene

Von Hippel Lindau syndrome affects around 1 in 36,000 people. It is caused by a mutation in the VHL gene.

The VHL gene is involved in cell growth. Inherited mutations in the VHL gene result in cysts and tumours made up of blood vessels, called haemangioblastoma. It is also associated with a rare tumour involving the adrenal gland, called a pheochromocytoma. Pheochromocytoma can secrete adrenalin and other hormones. Knowing that you have VHL is important as it allows screening to prevent the growths and cysts from causing damage or becoming cancerous. Screening needs to start at a young age.

**What are the clinical signs of Von Hippel Lindau syndrome?**
The common features of Von Hippel Lindau syndrome include:

- Haemangioblastoma
- Endolymphatic Sac Tumours
- Multiple cysts in the pancreas and kidneys
- Pheochromocytoma
- Epididymal cystadenomas

**What are Haemangioblastoma?**
Haemangioblastoma are abnormal growth of blood vessels. They tend to occur in the cerebellum (lower part of the brain) and spinal cord. When they occur in the eye, they are called retinal angioma. They rarely become cancer but can damage surrounding tissues if they grow large and, in the case of the eye, cause blindness if not detected early. Haemangioblastoma affect 50% to 90% of people with Von Hippel Lindau syndrome at some time in their lives.

If a retinal angioma develops before age 40, there is a 20 to 30% chance that person carries a VHL mutation and genetic testing would be Medicare funded.

**What are Endolymphatic Sac Tumours of the inner ear?**
Endolymphatic sac tumours are cysts affect the inner and can cause hearing loss, tinnitus, vertigo and problems with the facial nerve. They are not cancer. . Surgery is curative.

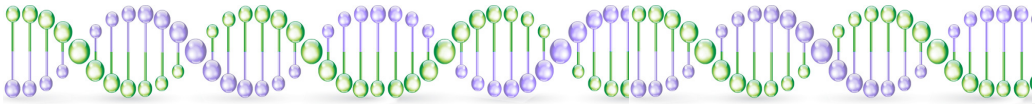
Only 5% or so of individuals with Von Hippel Lindau syndrome develop endolymphatic sac tumours. However, if an individual has an endolymphatic sac tumour, there is a 50% chance that they carry a VHL mutation and genetic testing would be Medicare funded.

**Cysts involving the kidney and pancreas**
Kidney cysts are quite common. In VHL however, there may be lots of cysts and they can occur at a young age. A kidney cancer, called a clear cell renal cell carcinoma (RCC), develops if the cysts are not removed when they get to a certain size. Without screening, 80% of people with VHL would get a RCC at an average age of 40.

The cysts in the pancreas can develop into tumours called neuroendocrine tumours. Most tumours don't secrete hormones and rarely they can be become cancers.

..../2

# Von Hippel Lindau syndrome and the VHL gene



**What are Pheochromocytoma?**
Pheochromocytoma are rare. They are diagnosed in 1 to 10 people per million people each year. They are usually small growths in the adrenal glands, which sits above the kidneys. They cause problems by secreting the "fight or flight" hormone adrenalin. Rarely, they can develop into cancer.

In addition to the VHL gene, hereditary causes include:

- SDH genes including SDHB, SDHC and SDHD and Hereditary Paraganglioma and Pheochromocytoma syndrome
- RET gene and Multiple Neuroendocrine syndrome Type 2 (MEN2)
- NF1 gene and Neurofibromatosis type 1
- the TMEM127 and MAX genes

**What are Epididymal Cystadenomas?**
Epididymal cystadenomas are a rare growth in men affecting the epididymis (the tube that connects the testis to the vas deferens and carries sperm). They are not cancer and do not affect fertility. Epididymal cystadenoma are often felt as a small (grain-of-rice sized) painless lump. More than half of the men with Von Hippel Lindau syndrome will develop epididymal cystadenomas affecting one or both testicles. Genetic testing should be considered and may be Medicare funded.

**How is Von Hippel Lindau syndrome managed?**

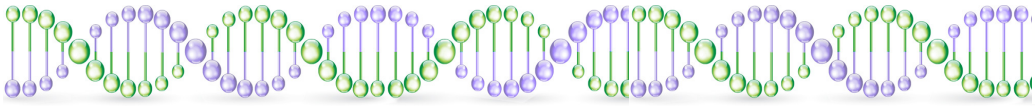
- Eye checks start at birth and are done every year by an ophthalmologist
- An MRI of the brain and spine is recommended every 2 years from age 10
- Hearing checks should start around age 4 and be repeated every few years during childhood
- Screening of the pancreas and kidneys with an MRI alternated with an ultrasound every year starting at age 10. This allows the growth to be removed before problems or cancers arise. It is not usually necessary to remove the whole kidney or pancreas, just the cyst or growth
- Screening for pheochromocytoma starts at age 2, measuring blood pressure and checking the blood for breakdown products of adrenalin

**Is Von Hippel Lindau syndrome inherited?**
Yes. Von Hippel Lindau syndrome is a hereditary cancer syndrome caused by a mutation in the VHL gene. There is a 50% chance of a person who carries a germline VHL mutation, whether male or female, passing the mutation to their son or daughter. If a mutation is identified, then predictive testing is available for blood relatives and is Medicare funded.

**What are De Novo VHL mutations?**
In individuals with Von Hippel Lindau syndrome, 20% of the time, they are the first person in their family to carry a VHL mutation. This is called a “de novo” mutation, meaning "from new". That is, the mutation occurred either in the making of that particular sperm or egg or the first few cell divisions after fertilisation. In this situation, the parents are not affected but the mutation can be passed on to the next generation.

…./3

# Von Hippel Lindau syndrome and the VHL gene



**Does this sound like you or your family?**
Have you had a haemangioblastoma or an endolymphatic sac tumour? Has a VHL mutation been detected in a blood relative? Genetic testing is available and may be Medicare funded.

Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

More information is available on our website, including links to the following:

- The VHL Alliance is based in the USA but has branches you can contact via email in Australia and has information on research studies.
- The Cancer Genetics section of the Cancer Institute's eviQ website provides up-to-date Australian-based management guidelines as well as the lifetime risk of tumours and cancers for individuals with VHL.
- The US National Library of Medicine website has more information about this syndrome.

Clinics in Sydney. Telehealth throughout Australia including to rural and regional areas
All Correspondence: PO Box 845, Broadway, NSW, 2007
All appointments: (+61 2) 9304 0438 Fax: (+61 2) 9304 0468 E:info@SydneyCancerGenetics.com.au