von Hippel Lindau Syndrome

von Hippel-Lindau (VHL) is an autosomal dominant hereditary cancer predisposition syndrome caused by mutations in the VHL gene and has a 21% new (de novo) mutation rate.

The tumours most commonly observed in families with VHL include renal cell carcinoma, pheochromocytoma, multisystem angiomas and hemangiomas. VHL tumours tend to occur at younger ages than their sporadic counterparts with mean ages of diagnosis from 22-50.

VHL testing for an eligible affected index case can be ordered by an endocrinologist or oncologist using the appropriate Cancer Genetics Lab requisition.

Referral Criteria

Note: close relatives include children, brothers, sisters, parents, aunts, uncles, grandchildren & grandparents on the same side of the family. History of cancer in cousins and more distant relatives from the same side of the family may also be relevant.

- family member with a confirmed VHL gene mutation – refer for carrier testing
- person with any pheochromocytoma
- person with clear cell renal cell carcinoma and a close relative with clear cell renal cell carcinoma
- person with 2 or more of the following lesions:
  - retinal angioma
  - spinal or cerebellar hemangioblastoma
  - adrenal or extra-adrenal pheochromocytoma
  - renal cell carcinoma
  - multiple renal and pancreatic cysts
  - less common: endolymphatic sac tumors, papillary cystadenomas of the epididymis or broad ligament, or neuroendocrine tumors of the pancreas
- person with family history of VHL and 1 or more of the above lesions
- person with 1 or more close relatives with any of the above

Referral of children is appropriate for this syndrome because it may inform their medical management.

Lifetime Cancer Risks for VHL mutation carriers

Providing cancer risks for an individual with VHL is challenging because of the ranges of risk reported in the literature and widely variable expressivity between and within families. The table below provides estimated lifetime risks.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>retinal angiomas</td>
<td>up to 92%</td>
</tr>
<tr>
<td>renal cell carcinoma</td>
<td>up to 80%</td>
</tr>
<tr>
<td>cerebellar hemangioblastoma</td>
<td>up to 85%</td>
</tr>
<tr>
<td>epididymal cystadenoma (males)</td>
<td>up to 60%</td>
</tr>
<tr>
<td>spinal hemangioblastoma</td>
<td>up to 50%</td>
</tr>
<tr>
<td>pheochromocytoma</td>
<td>up to 30%</td>
</tr>
<tr>
<td>endolymphatic sac tumour</td>
<td>up to 11%</td>
</tr>
</tbody>
</table>

This document is provided as a general resource and is not meant to replace hereditary cancer risk assessment. www.bccancer.bc.ca/health-professionals/clinical-resources/hereditary-cancer for Referral Form or call 604-877-6000, local 672198 with questions.
Cancer Risk Management Recommendations for VHL mutation carriers

Clinical management of individuals with VHL is challenging because of the wide spectrum of associated tumours and the lack of evidence to support screening for these tumours. Guidelines remain primarily based on expert opinion.

1. MRI of the brain stem, spine, and abdomen at ages 12, 15, and 18, with abdominal ultrasound in intervening years, followed by MRI every 2 years from age 20.
2. Annual physical examination from 2 years of age
3. Consider annual catecholamine assessment – plasma free metanephrines have the highest sensitivity
4. Annual ophthalmologic review from 2 years of age
5. Audiometry if symptomatic and consider baseline audiometry at age of school entry

Additional information

The following websites offer support and information which may be helpful to people living with VHL:

- Canadian VHL Alliance: www.cvhla.ca
- VHL Alliance: www.vhl.org

References available on request.
Reviewed October 2017