WHY I CARRY A MUTATION.
NOW WHAT?

If you carry a genetic mutation regardless of whether you have tumors or symptoms, it is important to be seen by a doctor(s) who has pheo para experience.

Regular screening using the urine or blood tests together with whole body imaging can catch tumors before they have symptoms. The frequency of screening depends upon your genetic mutation and medical history.

So for those with a known genetic mutation, regular screening using blood or urine tests together with whole body imaging can catch tumors early. Knowing your genetic mutation will also help to determine the frequency and a course of screening needed.

Recent research suggests that people who know they have a genetic mutation have less metastatic disease and a lower overall likelihood of complications and better overall health outcomes because of better follow-up and screening.

Approximately 30-40% of pheos and paragangliomas are hereditary.

PHEOCHROMOCYTOMA & PARAGANGLIOMA GENETICS

PheoPara Alliance

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More genes

MEN1 affects approximately 1/3,000 Americans. People with MEN1 have multiple cancers in the body like lung, breast, colon and pancreatic cancer. It is estimated that about 1/6,000 people inherit MEN1. It is inherited as an autosomal dominant trait that involves higher risk for medullary thyroid cancer and an increased risk for phaeo. MEN2 is caused by mutations in the RET proto-oncogene. It is estimated that about 1/10,000 have MEN2A and MEN2B. Both involve higher risk for medullary thyroid cancer and an increased risk for phaeo. MEN2B is more common than MEN2A.

All patients diagnosed with a pheo or para should talk to their doctor about genetic testing. If you have a genetic testing, your child have a 50/50 chance of inheriting it. Even if your children do not inherit the gene, they may not develop a tumor.
It is important to have genetic testing to identify current pheo para mutations and to advance research to discover new mutations.

**WHICH MUTATIONS ARE IMPORTANT?**

Patients with the following mutations are at a higher risk for developing pheo para. The information presented here is based on the most current research available, but new findings are constantly emerging. You can stay up to date on the latest research through reputable sources like the Pheo Para Alliance website.

**SDHx**

Hereditary Pheo Para Syndrome is the result of mutations in the Succinate Dehydrogenase Subunit Genes (SDHx). Patients with a SDHx mutation are at increased risk for pheo para and related conditions, such as GIST, renal cell carcinoma and kidney cancer. See the chart below for further information. The SDH genes include SDHB, SDHD, SDHA & SDHC.

**DIFFERENCES BETWEEN**

**SDHx MUTATIONS**

<table>
<thead>
<tr>
<th>Common Tumor Location</th>
<th>SDHB</th>
<th>SDHD*</th>
<th>SDHC</th>
<th>SDHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single/Multiple Tumors</td>
<td>para &gt; pheo</td>
<td>para H/N &gt; pheo</td>
<td>para H/N/cheest</td>
<td>para</td>
</tr>
<tr>
<td>Family History of Pheo/Para</td>
<td>multiple</td>
<td>multiple</td>
<td>single</td>
<td>single</td>
</tr>
<tr>
<td>Risk of Malignancy</td>
<td>medium</td>
<td>high</td>
<td>low</td>
<td>low/med</td>
</tr>
<tr>
<td>*When inherited from the father. H/N = head and neck</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SDHB**

Mutations in SDHB are one of the most common causes of familial pheo para, and are more likely to be metastatic. There is also an increased risk of cancerous tumors in the kidney and GI tract. SDH carriers who do not currently have a tumor have ~20-40% chance of developing one by the age of 60. (2)

@pheopara connecting with others who have the same genetic mutation can be comforting.

**SDHD**

This mutation is passed down through families by paternal inheritance. If you have SDHD, your child will have a 50% chance of inheriting the mutation, but the risk for developing pheo para is increased only if it is inherited from the father. If the mutation is inherited from the mother those children are not at higher risk of developing pheo para, but they can still pass on the mutation to their children. Someone who carries a mutation in the SDHD gene inherited by their father, but does not currently have a tumor has ~40% chance of developing one by the age of 60.

**SDHA**

SDHA mutations are common in the general population, but the development of tumors is rare. There is only a small chance that someone who carries this mutation will have a tumor. Because of this, tumors and SDHA mutations are often found incidentally. In the unlikely event that a tumor occurs, current research suggests that these tumors may behave aggressively. (3)

**SDHC**

SDHC is extremely rare, and much research still needs to be done. Tumors associated with this mutation often present in the head, neck and chest. It is unlikely that someone who carries an SDHC mutation but does not currently have a tumor will develop one by the age of 60.

**VHL**

Von Hippel Lindau (VHL) affects 1/36,000 and is characterized by tumors in up to ten areas of the body. With careful monitoring, early detection, and appropriate treatment, the most harmful consequences can be greatly reduced or completely prevented. Approximately 20% of patients will develop pheochromocytoma. (4)