Hyperparathyroidism/Endocrine Tumor Panel

Features of Hereditary Hyperparathyroidism/Endocrine Tumors

Genetic testing with the Hyperparathyroidism/Endocrine Tumor Panel may be appropriate if your personal and/or family history is suggestive of a hereditary predisposition to cancer and/or tumors. This includes:

- A personal history of two or more endocrine tumors or disorders including hyperparathyroidism, pituitary adenoma, thyroid cancer, benign thyroid disease, carcinoid tumors, or neuroendocrine tumors of the pancreas or gastrointestinal tract.
- A personal history of parathyroid carcinoma.
- A personal history of multi-glandular hyperparathyroidism.
- Multiple relatives on the same side of the family diagnosed with endocrine tumors and/or hyperparathyroidism.

Genes Included on the Hyperparathyroidism/Endocrine Tumor Panel are Listed in the Table Below

**High-Risk Genes**
- Well-studied • Greater than 4-fold risk of developing one or more cancers • Can cause a moderate risk for other cancers • National or expert opinion guidelines for screening and prevention are established

**Moderate-Risk Genes**
- Well-studied • Approximately 2- to 4-fold risk of developing one or more cancers • May increase risk for other cancers • Limited guidelines for screening and prevention

**Newer-Risk Genes**
- Not as well-studied • Precise lifetime risks and tumor spectrum not yet determined • Guidelines for screening and prevention are limited or not available

**Lifetime Cancer and/or Tumor Risks**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Lifetime Cancer and/or Tumor Risks*</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>Colorectal (up to 93%), Small bowel (4-12%), Gastric, Thyroid (up to 3%), Pancreatic, Brain, Liver, Desmoid tumors, Gastrointestinal polyps</td>
</tr>
<tr>
<td>CDC73</td>
<td>Hyperparathyroidism, Parathyroid cancer and tumors, Jaw tumors, Renal tumors, Uterine tumors</td>
</tr>
<tr>
<td>MEN1</td>
<td>Hyperparathyroidism, Parathyroid tumors (95%), Pancreatic neuroendocrine tumors, Pituitary tumors, Central nervous system tumors, Pheochromocytomas and other neuroendocrine tumors</td>
</tr>
<tr>
<td>PRKAR1A</td>
<td>Myxomas-cardiac (20-40%) and cutaneous, Testicular tumors (40%), Pituitary tumors (10-20%), Thyroid (10%), Schwannomas (up to 10%), among others</td>
</tr>
<tr>
<td>PTEN</td>
<td>Female breast (25-85%), Thyroid (3-38%), Endometrial (5-28%), Colorectal, Renal, Melanoma, Gastrointestinal polyps, Lhermitte-Duclos disease</td>
</tr>
<tr>
<td>RET</td>
<td>Thyroid-medullary (greater than 90%), Pheochromocytoma (up to 50%), Hyperparathyroidism (up to 30%)</td>
</tr>
<tr>
<td>CHEK2</td>
<td>Female breast, Male breast, Colorectal, Gastric, Prostate, Thyroid</td>
</tr>
<tr>
<td>AIP</td>
<td>Pituitary Tumors</td>
</tr>
<tr>
<td>CASR</td>
<td>Hyperparathyroidism, Parathyroid tumors</td>
</tr>
<tr>
<td>CDKN1B</td>
<td>Hyperparathyroidism, Pituitary tumors, Gastro-entero-pancreatic neuroendocrine tumors, Parathyroid tumors</td>
</tr>
<tr>
<td>DICER1</td>
<td>Lung tumors, Thyroid tumors, Renal tumors, Ovarian tumors, Embryonal rhabdomyosarcoma-cervix, Pituitary blastoma, Pineoblastoma, among others</td>
</tr>
</tbody>
</table>

* Most commonly associated cancer/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant.
Possible Outcomes of Genetic Testing:

There are four possible outcomes of genetic testing: positive (pathogenic variant), likely pathogenic variant, variant of uncertain significance (VUS), and negative. Genetic counseling is recommended prior to genetic testing to understand the benefits and limitations of testing.

A positive result indicates a genetic variant (change) was identified in a specific gene and that variant is pathogenic (harmful). With a positive test result, the risk to develop a particular disease (in this case, cancer and/or tumors) is increased.

A likely pathogenic variant result indicates that there is a variant in a specific gene for which there is significant, but not conclusive, evidence of an increased risk to develop a particular disease (in this case, cancer and/or tumors).

A variant of uncertain significance (VUS) result means that a change in a specific gene was identified, however the effect of the variant cannot be clearly established. There may be conflicting or incomplete information in the medical literature about this variant and its association with an increased risk of cancers and/or tumors is unknown. In other words, it cannot be determined yet whether this variant is associated with an increased risk of cancer and/or tumors or it is a harmless (normal) variant.

A negative result means that no reportable variants were identified.

Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a positive (pathogenic variant) test result indicating an increased risk for cancer and/or tumors. Guidelines and recommendations for early detection and/or risk reduction are specific to the gene in which the pathogenic variant was found.

Recommendations may include:

- Blood or urine analysis
- Imaging exams, such as a MRI, CT and/or ultrasound
- Clinical exams, such as dental, skin, hearing or eye exams
- Risk-reducing surgery

If you have a positive or a likely pathogenic variant result, your test report will include additional information regarding available medical management options.

If you have a negative or a variant of uncertain significance (VUS) test result, medical management should be based upon your personal and/or family history of cancer and/or tumors.

Once your test results are available, a discussion with your healthcare provider is recommended to determine the most appropriate medical management options for you and your family.

Regardless of the test results, consider sharing them with your family members so that they may discuss the results with their healthcare providers. If you have a positive or a likely pathogenic variant result, family members are at risk to have the same variant and should consider genetic testing to best understand their chance of developing cancer and/or tumors.

Resources

General
American Cancer Society
www.cancer.org
GeneDx
www.genedx.com/oncology
National Cancer Institute
www.cancer.gov

Hyperparathyroidism/Endocrine Resources
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)-Primary Hyperparathyroidism
www.niddk.nih.gov/health-information/endocrine-diseases/primary-hyperparathyroidism
The American Association of Endocrine Surgeons (AAES)
endocrinodiseases.org

Find a Genetic Counselor
Canadian Association of Genetic Counsellors
www.cagc-accg.ca
National Society of Genetic Counselors
www.nsgc.org