Hereditary Breast Cancer

Our knowledge and options for genetic testing for hereditary breast cancer has increased in recent years. While most cases of breast cancers are not hereditary, an estimated 5-10% of breast cancer is due to a hereditary cause. In some families with multiple women with breast cancer, the underlying genetic cause for the breast cancer in these families remains unclear.

Finding a hereditary explanation for why some people develop breast cancer can help to:
- Guide the course of cancer treatment or decision about surgery
- Provide a reason for why they or their relatives were diagnosed with cancer
- Clarify the risk for other cancers to guide screening or surveillance

Inherited mutations in two genes, called BRCA1 and BRCA2, account for the majority of hereditary breast cancer cases. Women who have mutations in the BRCA1/2 genes have a greater than 60% risk to develop breast cancer and as much as a 13 to 58% risk to develop ovarian cancer, including cancer of the fallopian tubes and peritoneum, by age 70. These figures are significantly higher than the 12-13% lifetime risk for breast cancer and 1-2% lifetime risk for ovarian cancer in the general population. Men with mutations in the BRCA1/2 genes have up to a 9% risk to develop breast cancer and up to a 20% risk to develop prostate cancer. These figures are significantly higher than the 0.1% lifetime risk for male breast cancer and 12% lifetime risk for prostate cancer in the general population. Men and women also have a 4-8% risk to develop pancreatic cancer and an increased risk for melanoma, particularly those with a BRCA2 mutation.

Genetic testing is one way to understand if a person has a hereditary risk for breast cancer. If a person has genetic testing and finds that he or she has a mutation associated with hereditary breast cancer, then it means he or she was born with an increased risk to develop certain types of cancers. The risk for breast and other cancers associated with mutations in these genes can vary (see next page). Genetic testing can look for several hereditary cancer syndromes by testing a panel of genes, including the BRCA1 and BRCA2 genes, as well as additional genes related to hereditary breast cancer. Some of the genes have not been studied as long as other genes and some genes only have a possible association with breast cancer risk. For these less studied genes, information about the associated cancer risks and screening recommendations may change over time.

In addition, results of genetic testing are important information to share with relatives because they may have also inherited the same increased risk to develop cancer. A parent who has a mutation in one of these breast cancer genes has a 50% chance of passing the mutation on to each of his or her children. It also means his or her siblings have a 50% chance to have the mutation. When a hereditary explanation is found in a family, relatives can have genetic testing to better understand their risk to develop cancer, which can help guide their decisions about cancer screening, prevention, and management.
### High Risk Breast Cancer Genes

<table>
<thead>
<tr>
<th>Genes</th>
<th>Lifetime Risk of Breast Cancer</th>
<th>Increased Risk for Other Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRCA1</strong>&lt;br&gt;<strong>BRCA2</strong></td>
<td>Female risk: 50-75%&lt;br&gt;Male risk: up to 9%</td>
<td>- Ovarian cancer&lt;br&gt;- Pancreatic cancer&lt;br&gt;- Prostate cancer&lt;br&gt;- Melanoma</td>
</tr>
<tr>
<td><strong>CDH1</strong></td>
<td>41-60%</td>
<td>- Diffuse stomach cancer&lt;br&gt;- Possible increased risk for colorectal cancer</td>
</tr>
<tr>
<td><strong>PALB2</strong></td>
<td>41-60%</td>
<td>- Pancreatic cancer&lt;br&gt;- Ovarian cancer&lt;br&gt;- Possible increased risk for male breast, and prostate cancer</td>
</tr>
<tr>
<td><strong>PTEN</strong></td>
<td>40-60% but may be higher in some families</td>
<td>- Thyroid, uterine, colorectal, kidney cancer, and melanoma</td>
</tr>
<tr>
<td><strong>STK11</strong></td>
<td>40-60%</td>
<td>- Colorectal, stomach, pancreatic, small intestine, lung, ovarian, endometrial, and cervical cancer&lt;br&gt;- Increased risk for multiple polyps in small intestine</td>
</tr>
<tr>
<td><strong>TP53</strong></td>
<td>60% or higher</td>
<td>- Lifetime risk for developing cancer is approximately 90% in women and 73% in men&lt;br&gt;- Risk to develop multiple different types of cancer</td>
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### Low to Moderate Risk Breast Cancer Genes

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<tbody>
<tr>
<td><strong>ATM</strong></td>
<td>15-40%</td>
<td>- Pancreatic cancer&lt;br&gt; - Ovarian cancer (slightly increased)&lt;br&gt; - Possible increased risk for prostate cancer</td>
</tr>
<tr>
<td><strong>CHEK2</strong></td>
<td>15-40%</td>
<td>- Colorectal cancer&lt;br&gt; - Possible increased risk for prostate cancer and melanoma</td>
</tr>
<tr>
<td><strong>NF1</strong></td>
<td>15-40%</td>
<td>- Causes Neurofibromatosis Type 1&lt;br&gt; - Nervous system tumors including benign and cancerous brain, spine, and eye tumors&lt;br&gt; - Gastrointestinal Stromal Tumors (GIST)</td>
</tr>
<tr>
<td><strong>BARD1</strong></td>
<td>15-40%</td>
<td>- Unknown or limited evidence for other cancers at this time</td>
</tr>
<tr>
<td><strong>RAD51C, RAD51D</strong></td>
<td>15-40%</td>
<td>- Ovarian cancer&lt;br&gt; - Possible risk for other cancers</td>
</tr>
</tbody>
</table>

### Genes with Possible Breast Cancer Association

<table>
<thead>
<tr>
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<th>Lifetime Risk of Breast Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRIP1</strong></td>
<td>Not well understood or defined at this time</td>
</tr>
<tr>
<td><strong>Lynch syndrome</strong></td>
<td>Slightly elevated above the 12% risk in the general population, for some but not all genes</td>
</tr>
</tbody>
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### Genes with No Established Breast Cancer Risk Association

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</tr>
</thead>
<tbody>
<tr>
<td><strong>CDKN2A, NBN</strong></td>
<td>No established association</td>
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