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Genetics of Hereditary Breast and Ovarian Cancer

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The majority of cancer cases are not attributable to hereditary causes. However, cancer can be hereditary in some families. Many factors can increase the probability that the cancers in a family may be hereditary. Some of these factors are: early onset of cancer (e.g. premenopausal breast cancer), more than one primary (new) cancer in an individual, the same cancer in two or more close relatives on the same side of the family, unusual presentation of cancer (e.g. breast cancer in a male), and related cancers (such as breast/ovarian/pancreatic cancer) found in the same family. Individuals of Ashkenazi Jewish ancestry are also at greater risk for hereditary breast and ovarian cancer. In addition, emerging data suggest that certain features are overrepresented in hereditary breast and ovarian cancer syndrome, including medullary and 'triple negative' tumors (estrogen receptor (ER) negative, progesterone receptor (PR) negative and HER2 negative or 'ER-/PR-/HER2-').

Several gene changes (mutations) have been discovered which predispose individuals to breast and ovarian cancer. Two genes account for a majority of hereditary breast and ovarian cancer cases. These are *BRCA1* (breast cancer-1) and *BRCA2* (breast cancer-2).

Both of these genes are passed down in families in a pattern called autosomal dominant. This means that a parent who carries a mutation in the gene has a 50% chance of passing on that mutation to each of their children. It also means that if a person carries such a mutation, their siblings have a 50% chance to carry the mutation.

Genetic testing for mutations in *BRCA1* and *BRCA2* has become clinically available within the past twenty years. The available data suggests that women who carry mutations in the *BRCA1/2* genes have between a 50-75% risk to develop breast cancer and a 15-60% risk to develop ovarian cancer (this includes cancer of the fallopian tubes and the peritoneum, or the membrane covering the organs in the abdomen) by the time they are 70 years of age. These figures are significantly higher than the 12-13% lifetime risk for breast cancer and the 1-2% lifetime risk for ovarian cancer in the general population. Individuals with *BRCA1/2* mutations also have a greater chance of developing additional primary breast cancers in remaining breast tissue (as high as ~20-60% lifetime risk). The risk for male breast cancer, pancreatic cancer, and melanoma is highest in individuals with *BRCA2* mutations but may also be elevated in individuals with *BRCA1* mutations.

Individuals who learn they have a *BRCA1* or *BRCA2* mutation are offered special surveillance and risk reduction options. Genetic testing for *BRCA1* and *BRAC2* is available at age 18, as there are no known childhood cancers for individuals with mutations. High-risk screening typically begins at age 25 for women and age ~35 for men.