

The Genetic Testing Process

How can a simple blood test be so complicated?

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When genetic testing is offered, it can yield important information. But where should testing begin and what are the limitations? In addition to ensuring individuals have a full understanding of the benefits, risks and implications of test results; we must consider the best approach to provide the most useful information.

While genetic testing starts with a standard blood draw, genetic testing can be like looking for a needle in a haystack. This is especially true in the case of breast and ovarian cancer, where we are dealing with two large genes called *BRCA1* and *BRCA2* (*BRCA1/2*). Hundreds of different gene changes have been identified responsible for hereditary breast and ovarian cancer in different families. It is hard work to pinpoint the genetic culprit for a family's cancer and in some cases; the results are not always easy to interpret.

Testing in Alberta labs involves sequencing; a sensitive technique used to find gene changes. Unfortunately, this technique finds many types of gene changes, some of which may be simple variations that are likely harmless and not responsible for increasing an individual's risk for cancer. Additionally, this testing is not perfect; there remains a small chance that testing cannot detect a gene change. Lastly, we are still learning about genes that may be involved in hereditary breast or ovarian cancer. *BRCA1/2* are probably not the genetic culprit in all families. There are likely other genes responsible for hereditary breast or ovarian cancer in some families. Unfortunately, these genes have not yet been discovered.

For all of these reasons, when first determining whether a gene change in *BRCA1/2* is the cause for a family's inherited cancer, it is favorable to begin with a family member who is most likely to have a gene change. This generally means someone who has already been diagnosed with breast or ovarian cancer. However, even when we start by testing this person, three possible results need to be considered. Careful review of the family history can help in interpreting results.

1. **Positive result:** Testing finds a gene change known to affect gene function and increase the risk for breast and ovarian cancer. With this result, the genetic cause for a family's inherited cancer has been found.
2. **Indeterminate Result:** (Non-informative) Testing does not turn up any changes in the *BRCA1/2* gene. This could mean two things; current testing methods could not detect a gene change or another gene may be responsible for the cancer in a family.
3. **Inconclusive Result:** Testing detects a gene change of uncertain significance. This means that the gene change found may be responsible for a family's breast and/or ovarian cancers or simply a harmless variation. Inconclusive results can be frustrating for both the family and genetics team and are not unique to *BRCA1/2* testing. There are numerous research groups tackling this problem. With time, we are hopeful that many of these uncertain changes will be better understood.

When we find a gene change responsible for a family's cancer, genetic testing becomes straightforward. Now, testing of at risk family members would only require looking for that specific gene change. This takes less time and results are easier to interpret. A positive result means the person tested has inherited the family's predisposition to breast and ovarian cancer. A negative result means they did not inherit this predisposition. Their risks for cancer are now expected to be similar to the general population.

The decision to pursue genetic testing is personal and should always be left up to the individual after a thorough discussion of the benefits, risks and limitations of genetic testing. Genetic counselling is helpful in the process of deciding whether to be tested or not and understanding what genetic tests results mean.

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