SHARSHERET®
The Jewish Breast & Ovarian Cancer Community

Contra Costa Community Sharsheret Panel
It's a Family Issue: Hereditary Cancer
March 10th, 2021

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The following information is provided by Josh Barnhart, BS, MS and Peggy Cottrell, MS, CGC as follow up to questions received during the panel.
Please note that they answered all questions to the best of their ability and if you have further questions, you can contact Sharsheret or consult your medical provider.

National Society of Genetic Counselors (NSGC) websites:

https://www.findageneticcounselor.com/ national directory of NSGC members
https://www.aboutgeneticcounselors.org/ consumer-facing NSGC website

Additional Questions

What are the differences between BRCA1 and BRCA2?

In terms of genetic risk, pathogenic variants in BRCA1 are associated with a greater risk for developing breast and ovarian cancer than that of BRCA2. However, pathogenic variants in BRCA2 are associated with a greater risk for developing male breast cancer, pancreatic cancer, prostate cancer, and melanoma that that of BRCA1. Additional differences include what chromosomes they are found on and their exact molecular role within our cells.

If the parent is negative, do the kids still need to be tested?

Yes, because the mutation can be inherited from either parent. If both parents have tested negative, it is less compelling for the child to be tested. However, there are rare new mutations that may occur, and also cases where someone's parents are not the genetic parents (sperm donor, adoption, non-paternity, etc).

Do you need a prescription or referral for genetic testing?

In general, a physician must order the test. Some genetic counselors work with providers who order the test, and others may ask you to get a prescription. A referral is needed with some insurance companies.

Is uterine cancer also hereditary?

Yes, uterine cancer can have hereditary components. In fact, 5-10% of uterine cancers have some genetic component that may explain the diagnosis. Therefore, individuals with multiple family members with uterine cancer or if family members had uterine cancer younger than 50 should consider a genetic counseling consult to discuss if there may be some underlying genetic component.

Is there any genetic testing for brain cancer?

Cancers of the central nervous system, which includes the brain and spinal cord, may be inherited. Genetic testing is available, and you should definitely work with a specialist.

Is thyroid cancer and being Ashkenazi related?

Thyroid cancer is a relatively common cancer, and it's not unusual for it to happen in people who are young. It is not seen more often in Ashkenazi individuals.

Is the BRCA gene mutation or other gene mutations associated with any childhood cancers? Our grandson was diagnosed with brain cancer at age 11 (egg yolk tumor).

BRCA1 and *BRCA2* are not associated with childhood cancers.

My first cousins have the genetic mutation. My dad died from pancreatic cancer and my mom was a stomach cancer survivor. I do not have the genetic mutation. Do we know how many generations can be affected? If I was negative, does it mean my kids are negative also?

Genetic mutations can be passed down throughout families for an endless number of generations. When every individual has children, they pass on 50% of their genetic material to each child. Therefore, it is possible that a mutation can continue to be passed on to every generation if the 50% of the genetic material that is passed on includes the genetic mutation that we're concerned about. However, if the 50% of genetic material passed on does not include the genetic mutation, then it is not passed on to future generations. If you tested negative, this means you do not have the genetic mutation that your first cousins have. Therefore, you do not have the possibility to pass on this genetic mutation to your children since you are negative. However, your children's father still makes up 50% of your children's genetic makeup, so we cannot rule out that something could be coming from his side of the family which could potentially affect your children.

What cancers are associated with the CHEK2 mutation? What options are available to those who test positive?

Pathogenic variants in CHEK2 are currently known to be associated with an elevated risk for developing breast, colon, thyroid and prostate cancer. Currently, some options that are available to patients who test positive are things like additional screening, such as annual Breast MRI screening starting at the age of 40 alongside annual mammograms. Also, colonoscopies starting at age 40 and having them every 5 years is also recommended. Some individuals may consider things like prostate and thyroid cancer screening starting from an earlier age but these are often discussed in the context of a family history. Whereas, the two screenings I mentioned previously are recommended for all patient who have test positive for a pathogenic variant in CHEK2.

What does a heterozygous mutation mean?

All of our genes come in pairs because we get one from our mother and one from our father. A heterozygous mutation refers to when you have one mutation in a gene that the other gene does not have. For example, let's say you have a heterozygous mutation in BRCA2, and it is coming from your father's side of the family. If your report showed a heterozygous mutation this would refer to the fact that one of your BRCA2 genes was found to have the same mutation as your father. However, this means that you have another copy of the BRCA2 gene that is functioning correctly. Therefore, since only one gene is mutated, and the other gene does not have that same genetic mutation you are said to have a heterozygous mutation. If you were to get the same genetic mutation from both your father and your mother it would be known as a homozygous mutation.

How old should a young woman be to start getting mammograms if she is BRCA2 positive?

According to national guidelines, women who are *BRCA1* or *BRCA2* positive are recommended to get an annual MRI starting at age 25, and add a mammogram at a 6 month interval to the MRI at age 30 (so imaging every 6 months starting at age 30).

When is whole genome testing recommended (non-Jewish parent) or just single nucleotide poly (SNP) recommended?

Whole genome testing would be testing all of the genes (~20,000 genes) on every chromosome, and that is almost never done for cancer. A panel test looks at anywhere from 8 - 100 genes associated with a variety of cancer types. I usually recommend a panel test that looks at the full sequence of the cancer genes even if a person has Ashkenazi ancestry, and would only recommend testing for founder mutations (the 3 "SNPs" in *BRCA1* and *BRCA2* that make up the majority of mutations identified in Ashkenazi individuals) as part of a study. It isn't less expensive anymore to just look at the founder mutations.

Do you suggest oophorectomy for patients with a BRCA mutation?

National guidelines recommend that women with a *BRCA1* mutation have their ovaries removed between 35 - 40, and women with a *BRCA2* mutation have their ovaries removed between 40 - 45.

My daughter tested positive for BRCA2, and was told that she had a 25-80% chance of developing breast cancer over her lifetime. Can you explain why the spread is so wide?

There are a lot of other factors that can increase or decrease the risk of breast cancer, even when there is a strong hereditary predisposition. These may include, but are not limited to, diet, alcohol consumption, exposures to carcinogens, and other hereditary factors that we don't know how to look for yet. Chance also plays a big role. Multiple studies have been done that come out with differing risk numbers.

Are there current recommendations for pancreatic cancer screening for people with BRCA?

It is best to have screening done as part of a pancreatic cancer screening study or at a specialized pancreatic cancer center. You can ask your physician to help you find such a location. Screening might include an endoscopic ultrasound or a specialized MRI of the pancreas (MRCP). There are not specific or standard screening recommendations, because pancreatic cancer is generally difficult to screen for.

If one sibling tests positive, will all the siblings? Can one be positive, and another be negative?

No, they won't all necessarily be positive. When a parent tests positive, there is a 50% chance that any of their children will test positive. So yes, one sibling can be positive and another can be negative.

Is there current research into other mutations that haven't been identified? I have strong family history but no mutations.

Yes, there is currently lots of research being done to identify new mutations. Some Sharsheret callers and their families are being followed by researchers who hope to discover new mutations as they have lots of family history, but everyone in the family has tested negative for all known gene mutations.

Email asax@sharsheret.org to ask questions,
get connected to Sharsheret support,
Sharsheret's genetic counselor,
or to bring Sharsheret to your school, doctor's office, or community.