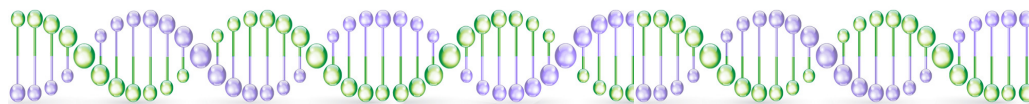


Information Sheet



Hereditary Diffuse Gastric Cancer syndrome and the CDH1 gene

Hereditary Diffuse Gastric Cancer syndrome is caused by inherited (germline) mutations in the CDH1 gene and rarely the CTNNA1 gene.

How common is Diffuse Gastric Cancer syndrome?

Hereditary Diffuse Gastric Cancer syndrome is very rare, affecting about 1 in 10,000 people. It was first described in 1998 in a New Zealand Maori family.

What does the CDH1 gene do?

The CDH1 gene encodes the protein E-cadherin. One of E-cadherin's roles is to help cells stick to one another (cell adhesion) to form tissues and another is control cell grow and division.

Do inherited CDH1 mutations cause cancer?

Hereditary diffuse cancer syndrome is caused by mutations affecting the CDH1 gene. It is associated with a very high risk of diffuse gastric cancer (up to 80% by age 80) and also lobular breast cancer in women (up to 60% by age 80), with most of the cancers occurring before age 40.

What is Diffuse Gastric Cancer?

Diffuse gastric cancer is a rare type of stomach cancer. It is also referred to as signet ring carcinoma because of how the cells look under the microscope. The cancers tend to grow just beneath the stomach lining, making them almost invisible when the stomach lining is viewed via a gastroscopy.

Also, because the E-cadherin protein isn't working, the cells grow in single rows rather than lumps and are more likely to break off and spread (metastasise).

How common is Diffuse Gastric Cancer?

Of the 2000 to 2500 new gastric cancers diagnosed each year in Australia, only a small amount are diffuse gastric cancers. However, more than 1 in 3 diffuse gastric cancers will be due to an inherited CDH1 gene mutation. Genetic testing is recommended for all people who are diagnosed with diffuse gastric cancer.

Four out of five people who carry a CDH1 mutation will develop diffuse gastric cancer, often at a young age.

Do CDH1 mutations cause breast cancer?

Yes. CDH1 mutations are associated with breast cancer of the lobular type.

Some lobular breast cancers are due to an inherited (germline) CDH1 mutation. Clues include:

- lobular breast cancer diagnosed before age 40.
- bilateral lobular breast cancer.
- 2 or more blood relatives with lobular breast cancer diagnosed before age 50.

A woman who has carries a CDH1 mutation (a germline mutation) is at high risk for lobular breast cancer. This risk starts to rise at age 30 and is 30% to 60% over her lifetime. The average woman has a 10 to 15% lifetime risk of any breast cancer.

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In all lobular breast cancers both copies of the E-cadherin gene are damaged. In fact, pathologists use the loss of the E-cadherin protein to help differentiate lobular breast cancers from the more common ductal kind. For most lobular breast cancers, the CDH1 genes were damaged as the cancer grew (somatic mutations - not inherited).

How is Hereditary Diffuse Gastric Cancer syndrome managed?

Because the gastric and breast cancers that occur do not form lumps, they can be very difficult to detected and may spread very early.

Gastrectomy (the removal of the stomach) is recommended at age 20 to prevent diffuse gastric cancer from occurring.

- Although you can live without a stomach, there is usually quite significant weight loss in the first 6 months following gastrectomy. That's why gastrectomy is not recommended in children: you need to balance the small risk against the need for growth and development.
- Gastrectomy is the only truly effective way to remove the risk.
- For individuals who don't want to have a gastrectomy unless a cancer is detected (prophylactic gastrectomy) but are fit enough and would consider surgery if a diffuse gastric cancer were detected, then endoscopic surveillance in expert centres could be considered. A specific protocol with screening every 6 months and involving multiple (30 to 60) random biopsies, is recommended.
- Prophylactic gastrectomy after age 70 is not recommended.

Breast screening or risk reducing surgery (mastectomy):

- Some women who carry a CDH1 mutation elect to pursue bilateral risk reducing mastectomies to reduce their lifetime risk of breast cancer to <2% (which is significantly lower than the population based risk of 10%).
- In the absence of surgery, annual breast MRI would be recommended. Breast MRIs are Medicare funded for women with germline CDH1 mutations from ages 30 to 50.

Is Diffuse Gastric Cancer syndrome inherited?

Yes. Diffuse Gastric Cancer syndrome is a hereditary cancer syndrome caused by a germline mutation in the CDH1 gene.

Does this sound like you or your family? Have you or a relative been diagnosed with diffuse gastric cancer or lobular breast cancer before age 40? Has a CDH1 mutation been detected in a blood relative? Genetic testing is available.

Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

More information is available on our website, including links to the following:

- No Stomach For Cancer is charity based in the USA that provides support for individuals and families affected by gastric cancer, including diffuse gastric cancer.
- The Cancer Genetics section of the Cancer Institute's eviQ website provides up-to-date Australian-based management guidelines
- The US National Library of Medicine website has more information about this syndrome.

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