



Hereditary Diffuse Gastric Cancer

Hereditary diffuse gastric cancer (HDGC) is an autosomal dominant cancer susceptibility syndrome characterized by multigenerational **diffuse** gastric cancer (DGC) and lobular breast cancer (LBC). Diffuse gastric cancer is a poorly differentiated adenocarcinoma that infiltrates into the stomach wall and causes thickening (linitis plastica) without forming a distinct mass. Diffuse gastric cancer is also referred to as signet ring carcinoma or isolated cell-type carcinoma.

Inherited *CDH1* mutations account for about 40% of HDGC families. Other genes associated with hereditary diffuse gastric cancer presentation include: *CTNNA1*, *BRCA2*, *PALB2* and *TP53*.

Referral Criteria

*Note: **close relatives** include: children, brothers, sisters, parents, aunts, uncles, grandchildren & grandparents **on the same side of the family**. History of cancer in cousins and more distant relatives from the same side of the family may also be relevant.*

- family member with a confirmed *CDH1* gene mutation – refer for carrier testing
- person with 1 or more of the following:
 - diffuse gastric cancer diagnosed at age 40 or younger
 - *in situ* signet ring cells and/or pagetoid spread of signet ring cells in the stomach confirmed by pathology
 - diffuse gastric cancer AND lobular breast cancer, 1 of which was diagnosed at age 50 or younger
 - bilateral lobular breast cancer at age 50 or younger
 - diffuse gastric cancer AND personal or family history of cleft lip/palate
 - a close relative with any of the above
- family with 1 or more of the following diagnosed in close relatives:
 - 1 case of diffuse gastric cancer and 1 case of signet ring colon cancer
 - 1 case of diffuse gastric cancer and 1 case of lobular breast cancer, with 1 diagnosis at age 50 or younger
 - 2 or more cases of gastric cancer, at least 1 of which is diffuse gastric cancer
 - 2 or more cases of lobular breast cancer at age 50 or younger

Lifetime Cancer Risks for *CDH1* Mutation Carriers

Diffuse gastric cancer: 70% for men, 56% for women

Lobular breast cancer: 42% for women

Other: possible increased risk for colorectal cancer, appendiceal signet ring cell carcinoma

Cancer Risk Management Recommendations for *CDH1* Mutation Carriers

Note: The recommendations provided below are general in nature. Individualized recommendations based on personal and/or family medical histories may be provided through Hereditary Cancer Program assessment and/or by other specialists involved in a person's current care.

1. **Prophylactic gastrectomy** (surgical removal of the stomach) should be considered. The timing of this operation may vary according to the preferences, age, physical and psychological fitness of the individual. It is complex decision that must include careful and thorough discussion with experts about the limitations of screening and the significant health effects of preventive surgery.
2. **Annual endoscopy** should be offered to mutation carriers (and at risk family members) who are not yet ready for gastrectomy. This should be done in a centre familiar with HDGC (preferably under a research protocol) and start in the late teens or early 20s, or 5-10 years younger than the youngest gastric cancer diagnosis in the family.
3. **Breast cancer screening** should include: annual mammograms and breast MRI beginning at age 30 or 10 years younger than the youngest breast cancer diagnosis in the family (but not before age 30), in conjunction with annual clinical examination of the breast and regional nodes.
4. **Risk-reducing mastectomy** or the use of medications known to reduce breast cancer risk (e.g. tamoxifen, raloxifene, anastrozole, exemestane) are considered by some women.
5. **Screening colonoscopy** every 3-5 years starting at age 40 (or 10 years younger than the youngest colon cancer diagnosis) if the family history includes close relatives with mucinous or signet ring cell colon cancer.

Additional Information

The following websites offer support and information which may be helpful to people living with HDGC:

- No Stomach For Cancer: www.nostomachforcancer.org

References available on request.

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