Hereditary Diffuse Gastric Cancer

This section has been reviewed and approved by the Cancer.Net Editorial Board [1], August / 2012

Overview

What is hereditary diffuse gastric cancer?

Hereditary diffuse gastric cancer (HDGC) is an inherited condition associated with an increased risk of gastric (stomach) cancer [2]. The stomach is located in the upper abdomen and plays a central role in digesting food. When food is swallowed, it is pushed down the esophagus (the muscular tube that connects the throat with the stomach) and enters the stomach. The muscles in the stomach mix the food and release gastric juices that help break down and digest the food. The food then moves into the small intestine for further digestion. Some people commonly refer to the stomach as the entire abdomen. However, doctors make a distinction between the stomach, which is an organ, and the abdomen, which is the area of the body between the chest and pelvic bones that holds many organs.

Diffuse gastric cancer is a specific type of stomach cancer [2] that tends to affect much of the stomach rather than staying in one area of the stomach. The average age for someone with HDGC to be diagnosed with stomach cancer is 38; gastric cancers not associated with this syndrome tend to occur in individuals older than 60. Women with HDGC also have an increased risk of lobular breast cancer [3]. People with HDGC may also have some increased risk of colorectal cancer [4].

What causes HDGC?

HDGC is a genetic condition. This means that the cancer risk and other features of HDGC can be passed from generation to generation in a family. The gene associated with HDGC is called *CHD1*. A mutation (alteration) in the *CHD1* gene gives a person an increased risk of developing gastric cancer and other cancers associated with HDGC. Researchers believe that other genes may be associated with HDGC, and studies are ongoing to learn more about this condition.

How is HDGC inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. HDGC follows an autosomal dominant inheritance pattern, in which a mutation happens in only one copy of the gene. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

How common is HDGC?

The specific number of families with HDGC is unknown. The overall incidence of gastric cancer [2] varies in different parts of the world. In the United States, it is estimated that less than 1% of the population will develop stomach cancer. The highest rate of gastric cancer is found in China, Japan, and other countries in Southeast Asia, as well as in Central and South America.

How is HDGC diagnosed?

Guidelines for the diagnosis of HDGC syndrome have been proposed, but may change over time as more is learned about this condition. Currently, the diagnosis of HDGC is suspected if a person or family meets any of the criteria listed below:

- At least two cases of stomach cancer [2] in a family, with at least one being diffuse gastric cancer and diagnosed before age 50
- At least three cases of stomach cancer at any age in a family, with at least one being diffuse gastric cancer
- A person diagnosed with diffuse gastric cancer before age 45
- A person diagnosed with both diffuse gastric cancer and lobular breast cancer [3]
- A person diagnosed with diffuse gastric cancer and another family member diagnosed with lobular breast cancer
- A person diagnosed with diffuse gastric cancer and another family member diagnosed with signet cell adenocarcinoma of the colon [4]

Genetic testing for mutations in the *CDH1* gene is available. However, only about 30% of families that appear to have HDGC will have a mutation found in the *CDH1* gene. Therefore, both clinical and genetic aspects must be considered in counseling individuals about the potential for their family to have HDGC, and talking with a genetic counselor or geneticist (a doctor with training in genetic diseases and conditions) that is familiar with the syndrome is recommended.

What are the estimated cancer risks associated with HDGC?

Not everyone who inherits a gene mutation for HDGC will develop cancer. In people who have this gene mutation, the risk for diffuse gastric cancer is estimated to be about 65% for men and 80% for women. Women with HDGC also have about a 40% risk of lobular breast cancer [3]. The risk of colorectal cancer [4] in people with HDGC has not been estimated.

What are the screening options for HDGC?

Screening for stomach cancer [2] is suggested for people known to be at risk for HDGC. However, the effectiveness of current screening techniques for the early diagnosis of stomach cancer is not proven. Screening recommendations may also change over time as new technologies are developed and more is learned about HDGC. It is important to talk with your doctor about appropriate screening tests.

Current Options for Screening

- Endoscopy [5] (also known as an upper gastrointestinal [GI] study; this procedure uses a thin, flexible tube with a light inserted into the body to examine a specific region)
- Chromoendoscopy (endoscopy using dye to help detect cancer)
- Endoscopic ultrasound [6] (which uses sound waves to find a tumor in the body)

Additional Screening for Women

Women at risk for HDGC should be considered at high risk for breast cancer [3] and should talk with their doctor about breast cancer screening options at the age of 35, or ten years before the age of the youngest affected relative. Screening options include:

- Monthly breast self-examinations
- Clinical breast examinations (examination by a doctor or nurse) every six months
- Regular breast imaging with mammograms [7], ultrasound [6], and/or magnetic resonance imaging [8] (MRI).

Other Screening

Colonoscopy [9], every one to two years, should be considered in families where both gastric cancer and colorectal cancer [4] have been diagnosed. Colorectal cancer screening should begin five to 10 years earlier than the earliest diagnosis of colorectal cancer in the family or by age 50, whichever is sooner.

Learn more about what to expect when having common tests, procedures, and scans [10].

Questions to ask the doctor

If you are concerned about your risk of cancer, talk with your doctor. Consider asking the following questions of your doctor:

- What is my risk of developing stomach cancer [2]?
- What is my risk of developing other types of cancer?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think you or other family members may have HDGC, consider asking the following questions:

- Does my family history increase my risk of stomach cancer [2]?
- Should I meet with a genetic counselor?
- Should I consider genetic testing [11]?

Additional resources

Guide to Stomach Cancer [2]

Guide to Breast Cancer [3]

Guide to Colorectal Cancer [4]

What to Expect When You Meet With a Genetic Counselor [12]

No Stomach for Cancer, Inc.

http://www.nostomachforcancer.org [13]

National Cancer Institute

www.cancer.gov [14]

American Cancer Society

www.cancer.org [15]

Cancer*Care*

www.cancercare.org [16]

To find a genetic counselor in your area, ask your doctor or visit these websites:

National Society of Genetic Counselors

www.nsgc.org [17]

National Cancer Institute:

www.cancer.gov/cancertopics/genetics/directory [18]

Links:
[1] http://www.cancer.net/about-us
[2] http://www.cancer.net/node/19645
[3] http://www.cancer.net/node/18618
[4] http://www.cancer.net/node/18701
[5] http://www.cancer.net/node/24731
[6] http://www.cancer.net/node/24714
[7] http://www.cancer.net/node/24584
[8] http://www.cancer.net/node/24578
[9] http://www.cancer.net/node/24481
[10] http://www.cancer.net/node/24959
[11] http://www.cancer.net/node/24895
[12] http://www.cancer.net/node/24907
[13] http://www.nostomachforcancer.org/
[14] http://www.cancer.gov/
[15] http://www.cancer.org/
[16] http://www.cancercare.org/
[17] http://www.nsgc.org/
[18] http://www.cancer.gov/cancertopics/genetics/directory