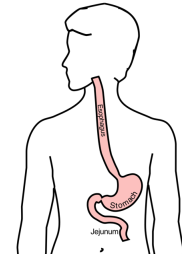


Stomach Cancer and CDH1 Gene

1

Anatomy

Food moves from the throat
 → esophagus
 → stomach
 → small bowel (jejunum)



2

Hereditary Diffuse Gastric Cancer

- Genetic condition in which family members have high rates of gastric cancer
- Most affected members develop gastric cancer by age 40
- Affected family members pass the susceptibility to half their children

3

Genetics of Hereditary Diffuse Gastric Cancer

- Altered copy of the CDH1 gene found to be responsible
- We each carry two copies of the CDH1 gene
 - Altered copy is passed on to half of children
- Family members with the altered CDH1 gene tend to develop cancer

4

Clinically Apparent Gastric Cancer

Among patients with HDGC who have visible stomach cancer, this is termed “clinically apparent”

5

Cancer Risk in HDGCd

Among family members in HDGC families with an altered CDH1 gene:

- Men have 70% risk of stomach cancer by age 80
- Women have 50-80% risk of stomach cancer by age 80
 - Increased risk of endometrial cancer

6

Genetic Testing

- Blood test can detect copies of the altered CDH1 gene
- Recommended in all patients under age 50 with stomach cancer
- Requires meeting with a genetic counselor

7

Prophylactic Gastrectomy in HDGC

- Preventive surgery to remove the stomach can be performed
- Surgery dramatically reduces risk of gastric cancer
- Surgery is usually done before age 40

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Prophylactic Gastrectomy in HDGC

Among family members with HDGC who carry the CDH1 gene

If preventive surgery is performed, 90-95% of cases have microscopic tumor in the removed stomach

9

Hereditary Diffuse Gastric Cancer

Inherited condition in which an altered copy of the CDH1 gene is passed from generation to generation

Presence of the gene can be detected by genetic testing

Affected person can pass the gene to (on average) half of their children

Affected persons carry the CDH1

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Hereditary Diffuse Gastric Cancer

Affected individuals have microscopic cancers beginning to form in the top layer of the stomach at an early age

Majority of affected individuals will develop visible cancer by age 40

By age 80, 70% of men and 56-83% of women are estimated to be at risk to develop visible cancer however some recent studies place this risk at 50%/33%

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CDH1

CDH1 carriers with visible cancer are termed "clinically apparent"

CDH1 carriers with clinically apparent cancers which are large enough to cause symptoms generally are likely to have spread to lymph nodes at the time of diagnosis

12

Prophylactic Gastrectomy

- Recommended for CDH1 carriers between ages 18-40
- Cancer rarely is found to have spread to lymph nodes
- Requires removing all of stomach tissue

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CH1 and Family History

Among patients with CDH1 mutation and a family history of gastric cancer who undergo preventive total gastrectomy, 90% have early stages of gastric cancer

Among patients with CDH1 mutation without a family history of gastric cancer, 2 out of 3 (67%) are estimated to have early stages of gastric cancer

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Treatment options for CDH1 Carriers

Total Gastrectomy

- Surgical removal of all of stomach
- Permanent alteration in eating
- Requires Small Frequent meals
- Feeding jejunostomy

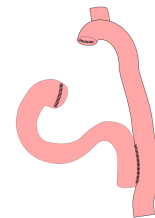
Surveillance

- Endoscopy every 6-12 months
- Unknown how long this is required.

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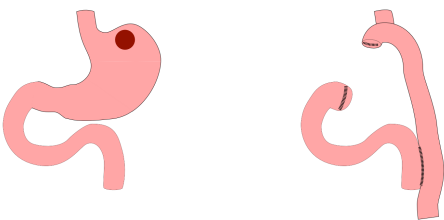
Total Gastrectomy

- Removes all of the stomach
- Reconstruction with small intestine
- Needed for those with CDH1 mutations



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Total Gastrectomy



17