Gastrointestinal Stromal Tumor Causes, Risk Factors, and Prevention

Risk Factors

A risk factor is anything that affects your chance of getting a disease such as cancer. Learn more about the risk factors for gastrointestinal stromal tumors.

- Gastrointestinal Stromal Tumor Risk Factors
- What Causes Gastrointestinal Stromal Tumors?

Prevention

The only known risk factors for gastrointestinal stromal tumors (GISTs) age and certain rare, genetic syndromes – cannot be changed. At this time we do not know of any way to protect against these cancers.

Gastrointestinal Stromal Tumor Risk Factors

A risk factor is anything that affects a person's chance of getting a disease like cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

But having a risk factor, or even several, does not mean that a person will get the

disease. And many people who get the disease may have few or no known risk factors.

Currently, there are very few known risk factors for gastrointestinal stromal tumors (GISTs).

Being older

These tumors can occur in people of any age, but they are rare in people younger than 40 and are most common in people aged 50 to 80.

Genetic syndromes

Most GISTs are sporadic (not inherited) and have no clear cause. In rare cases, though, GISTs have been found in several members of the same family. These family members have inherited a gene mutation (change) that can lead to GISTs.

Primary familial GIST syndrome: This is a rare, inherited condition that leads to an increased risk of developing GISTs. People with this condition tend to develop GISTs at a younger age than when they usually occur. They are also more likely to have more than one GIST.

Most often, this syndrome is caused by an abnormal *KIT* gene passed from parent to child. This is the same gene that is mutated (changed) in most sporadic GISTs. (See What Causes Gastrointestinal Stromal Tumors?) People who inherited this abnormal gene from a parent have it in all their cells, while people with sporadic GISTs only have it in the cancer cells.

Less often, a change in the *PDGFRA* gene causes this genetic syndrome. Defects in the *PDGFRA* gene are found in about 5% to 10% of sporadic GISTs.

Sometimes people with familial GIST syndrome also have skin spots like those seen in patients with neurofibromatosis (discussed below). Before tests for the *KIT* and *PDGFRA* genes became available, some of these people were mistakenly thought to have neurofibromatosis.

Neurofibromatosis type 1 (von Recklinghausen disease): This disease is caused by a defect in the *NF1* gene. This gene change may be inherited from a parent, but in some cases it occurs before birth, without being inherited.

People affected by this syndrome often have many benign (non-cancerous) tumors that form in nerves, called *neurofibromas*, starting at an early age. These tumors form under

the skin and in other parts of the body. These people also typically have tan or brown spots on the skin (called *café au lait spots*).

People with this condition have a higher risk of GISTs, as well as some other types of cancer.

Carney-Stratakis syndrome: People with this rare inherited condition have an increased risk of GISTs (most often in the stomach), as well as nerve tumors called *paragangliomas*. GISTs often develop when these people are in their teens or 20s. They are also more likely to have more than one GIST.

This syndrome is caused by a change in one of the succinate dehydrogenase (*SDH*) genes, which is passed from parent to child.

References

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What Causes Gastrointestinal Stromal Tumors?

We do not know exactly what causes most gastrointestinal stromal tumors (GISTs). But in recent years, scientists have made great progress in learning how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical in each of our cells that makes up our *genes*, which control how our cells function. We usually look like

our parents because they are the source of our DNA. But DNA affects more than just how we look.

Some genes control when cells grow and divide into new cells:

- Certain genes that help cells grow and divide are called *oncogenes*.
- Genes that help slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*.

Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Gene changes that can lead to GISTs

The gene changes that lead to most GISTs are now understood, but it's still not clear why these changes occur. There are no known lifestyle-related or environmental causes of GIST. Some might have causes that haven't been found yet, but many of these changes may just be random events that sometimes happen inside cells that unfortunately lead to cancer.

A few families have gastrointestinal stromal tumors (GISTs) caused by a gene mutation passed down from parent to child. (See Gastrointestinal Stromal Tumor Risk Factors.) But most gene mutations related to GISTs are not inherited. These changes occur for no apparent reason, and are called *acquired* or *sporadic*.

Changes in KIT or PDGFRA genes

The cancer cells of most patients with GISTs have a change in an oncogene called *KIT*. This gene directs cells to make a protein called KIT, which causes the cells to grow and divide. Usually the *KIT* gene is inactive in interstitial cells of Cajal (ICCs), which are the cells from which GISTs develop. The *KIT* gene is only active if there is a need for more ICCs. But in most GISTs the *KIT* gene is mutated and is always active, so the cells are always growing and dividing.

In about 5% to 10% of GISTs, the cancer cells have mutation in a different gene called *PDGFRA*, which causes the cells to make too much of a different protein (also called PDGFRA). This has the same effect on the cells as does KIT.

Most GISTs have changes in either the *KIT* or the *PDGFRA* gene, but not both.

Other gene changes

A small number of GISTs, especially those in children, do not have changes in either of these genes. Many of these tumors have changes in one of the *SDH* genes. Researchers are still trying to determine what other gene changes can lead to these cancers.

As doctors have learned more about the gene and protein changes in GIST cells, they have been able to use this information to help diagnose and treat these cancers. (See Targeted Therapy for Gastrointestinal Stromal Tumors[1].)

Hyperlinks

1. www.cancer.org/cancer/gastrointestinal-stromal-tumor/treating/targeted-therapy.html

References

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Can Gastrointestinal Stromal Tumors Be Prevented?

The risk of many types of cancer can be reduced with certain lifestyle changes (such as maintaining a healthy weight or quitting smoking), but the only known risk factors for

gastrointestinal stromal tumors (GISTs) age and certain rare, genetic syndromes – cannot be changed. At this time we do not know of any way to protect against these cancers.

References

Casali PG, Dei Tos AP, Gronchi A. Chapter 55: Gastrointestinal Stromal Tumor. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

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