

What is gastrointestinal stromal tumour (GIST)?

GIST is a rare form of cancer that occurs in the GI (or digestive) tract. It is called a stromal tumour because the cancer starts in the stroma, or the connective tissues controlling the movements of the gut.¹ GIST begins in the interstitial cells of Cajal (ICC), special cells found in the walls of the digestive tract that control its regular movements.² Although GISTs can occur in almost any part of the digestive system, they most commonly grow in the stomach (50–70%) or small intestine (20–30%), and less commonly in the large intestine and rectum (5–15%) and esophagus (<5%).³ (See Figure 1: The gastrointestinal tract and surrounding organs)

Not all GISTs are cancerous – some are benign, meaning they don't grow into other areas or spread to other parts of the body.² If the GIST is malignant (cancerous), also it may spread (metastasize) to other parts of the body, most often within the abdomen, and to the liver in particular.² Cancers are named after the part of the body where they start. So, even if GIST spreads to your liver, it is still called GIST (metastatic GIST), not liver cancer.²

How does GIST develop?²

We don't know exactly what causes GIST. But our understanding of cancer tells us that certain changes in DNA, the chemical that carries the instructions for almost everything our cells do, can cause normal cells to become cancerous. In particular, when our cells grow and divide, and a copy of the original cell's DNA is made, an error can occur, which can result in a defect, or mutation, in a gene.

Some of our genes, called *oncogenes*, promote cell growth and division. Other genes that slow down cell division or cause cells to die at the right time are called *tumour suppressor* genes. We know that a cancer can be caused by mutations in DNA that turn on *oncogenes* or turn off *tumour suppressor* genes. Sometimes mutations that increase the risk of cancer are passed from parent to child, but this does not happen often with GIST. These mutations mostly occur for no real reason, and are called sporadic.

In most people with GIST, the cancer cells have a mutation in an oncogene called *c-kit*, a gene found in all cells of the body. The protein this gene creates, called KIT, is only turned on when the body needs more interstitial cells of Cajal (ICCs), the starting place for GIST. In most GISTs, the *c-kit* gene is mutated and never turns off, which may explain why the cancer forms, since the cells are always growing and dividing.

In some GISTs, a mutation causes the cell to make too much of a protein called PDGFRA, which has the same effect as KIT. Both KIT and PDGFRA act as enzymes called tyrosine kinases, which are important in the diagnosis and treatment of GIST.

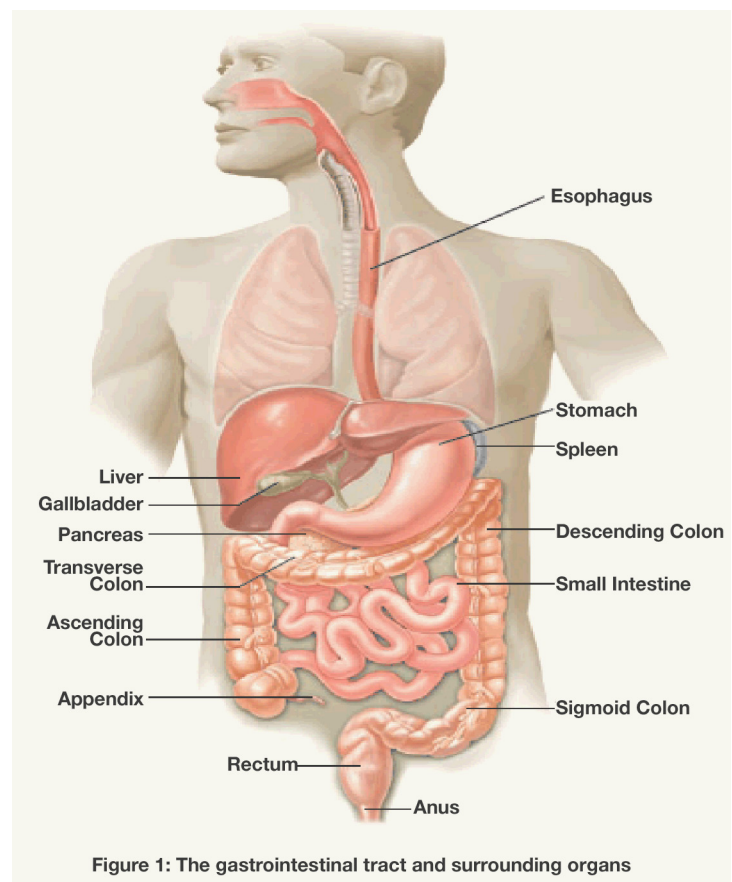


Figure 1: The gastrointestinal tract and surrounding organs

How common is GIST?¹

- In Canada, up to nearly 700 people may develop GIST this year (10 – 20 people per million)
- GIST occurs equally among men and women, and is not more common in any one race
- GIST can affect any age group, although it occurs most often in people over the age of 50

What are the risk factors and how can I help prevent GIST?²

Presently, aside from the small number of GIST cases that involve an inherited gene, the risk factors for developing GIST are not known. Effective ways to prevent GIST are also not known at this time.

What are the symptoms of GIST?²

Although many GISTs do not produce symptoms initially, they may cause signs and symptoms such as:

- Abdominal pain
- Blood in stool or vomit
- A lump that you can feel

In some cases, the GIST may grow in the throat and cause problems with swallowing. Or, the GIST may grow into the intestine and block it, causing severe gut pain and vomiting. This is called intestinal obstruction, and usually requires emergency surgery to remove the blockage.

How is GIST diagnosed and staged?²

GIST cancer can be difficult to diagnose. It may be hidden in the stomach area and may not cause any physical symptoms in its early stages. And, with no current effective screening tests or recommendations for routine testing, GIST can often grow quite large or spread to another organ before being discovered. Occasionally, a GIST may be found early during routine tests such as a colonoscopy screen testing (for colon cancer), an x-ray, a CT scan, or even abdominal surgery for another problem.²

The following tests are used to diagnose and stage GIST:²

- Physical exam
- Imaging tests such as endoscopy, barium x-ray, endoscopic ultrasound, CT scan [computerized tomography], MRI [magnetic resonance imaging], or PET [positron emission tomography]
- Biopsy
- Immunohistochemistry for KIT protein (CD117)
- Blood tests
- Histologic grading (microscopic analysis)

The staging of a tumour describes the size of the tumour, its location and if it has spread or not. The higher the stage, the more dangerous the tumour has become. Doctors use several diagnostic tests to determine the stage of a tumour. Once all the tests have been completed, a stage can be assigned. Stage descriptions vary for different types of cancers.²

Currently, there is no standard staging system for GIST.² Two factors are commonly used to determine the risk of a GIST being malignant (cancerous) or not: the size of the tumour and the mitotic count (the actual number of dividing cells). The larger the size and the higher the mitotic count, the higher the risk. Smaller tumours (less than 5 cm across) tend to be less likely to spread, which can lead to better outcomes. The best outlook is for tumours less than 2.5 cm across.²

Defining Risk of Aggressive Behaviour in GISTs		
	Size (largest diameter)	Mitotic Count
Very low risk	<2 cm	<5 / 50 HPF
Low risk	2–5 cm	<5 / 50 HPF
Intermediate risk	<5 cm	6–10 / 50 HPF
	5–10 cm	<5 / 50 HPF
High risk	>5 cm	>5 / 50 HPF
	>10 cm	Any mitotic rate

Fletcher et al., 2002

How is GIST treated?

Surgery is the main treatment used, with the goal being to remove all of the cancer. For smaller tumours, surgery can often remove all the cancerous tissue. For larger tumours or those growing into other organs, complete removal may still be the goal, though this may involve removing portions of the other organs.²

Unlike many other cancers, GIST does not respond very often to chemotherapy, so it is rarely used.² Radiation also does little to shrink GISTs, so it is seldom used, and only then to help relieve symptoms such as pain.² If the tumour cannot be completely removed, a doctor may try treating the patient with a targeted therapy called a tyrosinekinase (TK) inhibitor to help shrink the tumour to make it easier to remove.² By turning off the KIT and PDGF proteins, therapies or TK inhibitors help block the signals that tell cancerous cells to grow and divide.² Speak to your healthcare provider to find out more about which treatments are available in Canada and how they may help you.²

Your doctor may ask you if you would like to participate in a clinical trial. Therapy for cancer is constantly evolving as the medical profession continues to look for better treatments. Clinical trials are studies that are done to determine whether a new therapy is safe and effective. The new therapy is then compared to the standard treatment to determine which one is better.²

It is entirely your choice whether or not you wish to participate in a clinical trial. By participating, you may receive a new drug that is not yet available in Canada; you will also be contributing to the development of better cancer treatments for many patients. If you decide not to participate in a clinical trial, you will continue to receive the best treatment your doctor decides is appropriate for you.²

For information about ongoing clinical trials speak to your doctor and/or refer to the following resources:

Canadian Cancer Society Research Institute

www.cancer.ca/research/

The Canadian Cancer Society also provides information about specific clinical trials. **Call the national, bilingual toll-free Cancer Information Service at 1-888-939-3333.**

United States National Cancer Institute

www.cancer.gov/clinicaltrials

(Provides helpful information about international clinical trials, including some being conducted in Canada)

Living with GIST

Having a GIST affects many aspects of a person's life. Although every person is different, people often experience shock, denial, distress and similar feelings when they are told that they have cancer. This can be especially true when the diagnosis is GIST, a rare form of cancer.

Talking about your feelings is difficult, but it can help you get the support you may need and help nurture a close and loving bond among friends and family members.

Telling people⁶

Telling others about your situation can be one of the most difficult parts of a cancer diagnosis. Do your best to have a private, quiet conversation free from distractions. Try to ease into the conversation slowly, and give the information in small chunks. And remember to be honest about your own feelings. You will get different reactions from different people, with some people even withdrawing from you over time because of their discomfort in dealing with your situation. Don't take it personally, and surround yourself with people who listen well, make you feel comfortable and respond supportively.

If you need to tell a child about someone having cancer, take care to make the information understandable to the child and be prepared to have to repeat things more than once. It's important to make sure that the child doesn't assume blame for what has happened. If you are worried about talking to a child about these issues, consider asking a healthcare professional to be present.

Sexual relationships⁷

Almost all cancer patients experience some sexual problems at some time during the course of their illness, due to stress, physical problems or interpersonal problems. However, sexual activity is an important part of normal life, and people with GIST can remain sexually active.

It often helps if you and your partner discuss the issue of sexuality and any fears around it that either person might have. Take it slowly and make plans based on what you can do and what feels comfortable. If discussion is difficult, a sexual counsellor can be helpful.

Returning to work and activities^{2, 8}

Cancer and its treatment can make you feel very tired. If you do feel tired, returning to work may be difficult. Take one step at a time and start with just an hour or two of work per day.

People affected by cancer may become depressed. You may find that you are unable to take pleasure in the things that normally make you happy. Fortunately, this condition is treatable. If you are unable to get back into your normal activities, even though you are physically capable of doing so, consider the possibility that you may be experiencing depression and inform your healthcare team.

Patient Resources

The following groups can offer you support and information about cancer. Learning more about your disease and treatment, or talking with other people affected by cancer, may help you to cope with your illness.

The Canadian Cancer Society (CCS)

www.cancer.ca

CCS Cancer Information Service: Call toll-free 1-888-939-3333. TTY 1-866-786-3934

The CCS is a resource for patients and healthcare professionals alike. The CCS website has news, facts and useful tips for you and your family, including:

- current news stories about cancer studies
- information on many types of cancer
- new clinical trials in Canada
- stories about cancer survivors
- tips for coping with cancer
- links to support groups

GIST Support International (GSI)

www.gistsupport.org

GSI supports GIST patients and their families and friends, and has information on current GIST research. The GSI website can offer you:

- contact with people from around the world who are dealing with GIST
- tips for coping with GIST
- an e-mail chat group for sharing support and news
- news about research and clinical trials that may affect you

The National Cancer Institute (NCI) [U.S.]

www.cancer.gov

The NCI website (U.S.) is a large source of facts about cancer, treatments and clinical trials, including trials taking place in Canada.

Life Raft Group Canada

www.liferaftgroup.ca

References

1. **Cancer Research UK.** What is the treatment for GIST – Gastrointestinal Stromal Tumour?
Available at: www.cancerhelp.org.uk/about-cancer/cancer-questions/what-is-the-treatment-for-gist-gastrointestinal-stromal-tumour
Accessed December 22, 2009.
2. **American Cancer Society.** Gastrointestinal Stromal Tumor (GIST) Detailed Guide.
Available at: www.cancer.org/docroot/CRI/content/CRI_2_4_7x_Gastrointestinal_Stromal_Tumors_Detailed_Guide.asp
Accessed December 22, 2009.
3. **Medscape.** Gastrointestinal Stromal Tumors: eMedicine Gastroenterology.
Available at: emedicine.medscape.com/article/179669-overview
Accessed December 22, 2009.
4. **Crohn's and Colitis Foundation of Canada.** Anatomy and Function of the GI Tract.
Available at: www.ccfcc.ca/English/info/ibd.html
Accessed December 22, 2009.
5. **GIST Support International.** Prognosis for GIST.
Available at: www.gistsupport.org/about-gist/prognosis.php
Accessed December 22, 2009.
6. **Canadian Cancer Society.** Telling people about a cancer diagnosis.
Available at: www.cancer.ca/Canada-wide/About%20cancer/Coping%20with%20cancer/Telling%20people%20about%20a%20cancer%20diagnosis.aspx?sc_lang=en
Accessed December 23, 2009.
7. **Canadian Cancer Society.** Sexuality.
Available at: www.cancer.ca/Canada-wide/Support%20Services/CW-Coping%20with%20cancer/CW-Sexuality.aspx?sc_lang=en
Accessed December 23, 2009.
8. **Canadian Cancer Society.** Sadness and depression.
Available at: www.cancer.ca/Canada-wide/About%20cancer/Coping%20with%20cancer/Living%20with%20cancer/Sadness%20and%20depression.aspx?sc_lang=en
Accessed December 23, 2009.