What Is Carcinoid Syndrome?

Carcinoid syndrome is caused by carcinoid tumors—small, malignant or benign tumors that most commonly arise in the mucosa of the gastrointestinal tract. Carcinoid syndrome is the set of symptoms that may occur in patients who have carcinoid tumors. Not all people with carcinoid tumors have carcinoid syndrome. The syndrome occurs when carcinoid tumors overproduce substances such as serotonin that normally circulate throughout your body. This overproduction of serotonin and other hormones is what causes the symptoms of carcinoid syndrome.

Other (non-carcinoid) tumors can also cause symptoms similar to those of carcinoid syndrome. These can include tumors in the duodenum and the lung. Another such tumor is called a VIPoma. "VIP" stands for Vasoactive Intestinal Peptide. VIPomas are extremely rare and can cause severe, watery diarrhea that requires immediate care.

If you have carcinoid syndrome, or diarrhea caused by a VIPoma, it is important to visit your healthcare provider regularly. Your healthcare provider will also explain your treatment options.
What Causes Carcinoid Syndrome?

Carcinoid syndrome occurs when carcinoid tumors overproduce hormones and other substances that normally circulate throughout your body. One of the most important substances that is overproduced is serotonin—one of the body's natural chemical messengers. When excess serotonin reaches tissues in the gastrointestinal tract, the lungs, or the skin, it causes the symptoms of carcinoid syndrome.

Carcinoid tumors often do not produce noticeable symptoms until they spread to the liver. That's because most of the blood circulation from the gastrointestinal tract must pass through the liver before it reaches the rest of the body. The liver has strong enzymes that break down and neutralize most of the excess serotonin and other substances produced by the carcinoid tumors, preventing them from reaching tissues where they can cause symptoms. When carcinoid tumors metastasize to the liver, the substances they overproduce can more easily reach your bloodstream, and reach tissues where they can cause symptoms.

Serotonin breaks down into smaller parts, called metabolites. The most important serotonin metabolite is 5-HIAA (5-hydroxyindoleacetic acid). The 5-HIAA test measures the amount of this metabolite in your blood, and can therefore be used to estimate the extent of your disease. Chromogranin-A (CgA) is a protein found in carcinoid cells that may be secreted into the blood. CgA can also be measured to check the extent of carcinoid syndrome.

Diagnosing and Monitoring Carcinoid Syndrome

Doctors often have difficulty diagnosing carcinoid syndrome in its early stages. There are several reasons for this. Most of the symptoms are fairly common, and they are "nonspecific," meaning similar to symptoms that can be caused by many things. Flushing, for example, can also be a menopausal symptom, a reaction to alcohol, or a side effect of a drug.
However, two symptoms that might suggest carcinoid syndrome rather than another condition include:

- "Dry" flushing (flushing with no sweating), as opposed to "wet" flushing (flushing with sweating), which occurs as a symptom of menopause, for example
- Nighttime diarrhea (or nocturnal diarrhea), as opposed to diarrhea during the day, which might be more likely to be caused by irritable bowel syndrome, for example

Adding to the challenge is the fact that carcinoid syndrome is a fairly rare condition. Your doctor might not have been looking for carcinoid syndrome when your symptoms first started. That's why, if you've gotten to the point of getting your carcinoid syndrome diagnosed, you are more fortunate than many patients. You're well on your way toward helping to manage carcinoid syndrome.

There are several tests that your doctor can use to diagnose carcinoid syndrome and to monitor it once it has been diagnosed. It's important to be monitored regularly for changes in your symptoms or test results. Regular doctor visits will also help you get the best possible outcome.

On this page, you'll learn about:

- Chromogranin A (CgA) Testing
- 5-Hydroxyindoleacetic Acid (5-HIAA) Testing
- Somatostatin Receptor Scintigraphy (SRS) [OctreoScan®] Testing
- Why Early Diagnosis of Carcinoid Syndrome Is Important

*OctreoScan® is a registered trademark of Mallinckrodt, Inc.

Chromogranin A (CgA) Testing

The Chromogranin A (CgA) blood test is a good marker to help detect and monitor the activity of
carcinoid tumors in general. This includes carcinoid tumors that secrete certain hormones that are associated with carcinoid syndrome as well as carcinoid tumors that do not cause carcinoid syndrome. Elevated levels of CgA are found in 80-100% of patients with carcinoid tumors.

A CgA test is fast, easy to perform, and accurate. However, increased levels of this marker may also be caused by other factors such as renal failure, chronic atrophic gastritis or the use of proton-pump inhibitors.

**How the Test Is Done**

A blood sample is taken and then tested with a CgA-specific enzyme-conjugated antibody. The antibody and enzyme bind the CgA protein as a "sandwich"—the purpose of the antibodies is to bind with the CgA protein, while the enzymes produce color. The intensity of the color is proportional to the specimen's CgA concentration. The CgA test uses CgA-specific antibodies to measure the level of CgA in the body.

Measurements may vary with meal consumption so patients are required to fast before a CgA test. CgA tests are performed every 3 to 6 months.

**5-Hydroxyindoleacetic Acid (5-HIAA) Testing**

5-HIAA testing is a 24-hour urine test that is specific to carcinoid tumors—levels of 5-HIAA are not elevated with other types of tumors. This test is the most common biochemical test for carcinoid tumors associated with carcinoid syndrome.

Elevated levels of 5-HIAA, a by-product produced when serotonin breaks down in the body, can be detected from a urine sample. Serotonin is one of the key body chemicals released by carcinoid tumors that are associated with carcinoid syndrome. The test can positively detect carcinoid tumors 73% of the time, and is generally regarded as an accurate test. However, the level of 5-HIAA only becomes elevated when carcinoid tumors have metastasized to the liver, making the potential for a cure less likely. 5-HIAA testing is useful to estimate the extent of
disease and survival.

Sometimes you can have what is called a false-positive test result. This happens when you eat foods rich in serotonin and your urine 5-HIAA levels go up. That is why your healthcare provider will probably advise you not to eat the following foods for 24 hours before you take the test:

- Bananas
- Walnuts
- Plantains
- Hickory nuts
- Pineapple
- Pecans
- Kiwi fruit
- Avocados
- Plums
- Tomatoes
- Eggplant

There are several drugs—for example, many that are contained in cough and cold medicines—that also affect the urine level of 5-HIAA. Your healthcare provider may tell you to avoid taking these drugs for 24 hours before you take the test.

*Consult with your physician about which medications are appropriate to take before this test.*

**How the 5-HIAA Test Works**

When serotonin breaks down in the body, it is converted first to 5-HT and then to 5-HIAA, which is excreted into the urine. A urine sample is collected, and the level of 5-HIAA in the urine is measured. By measuring the level of 5-HIAA in the urine, doctors are able to calculate the amount of serotonin in the body.

**Somatostatin Receptor Scintigraphy (SRS) [OctreoScan®] Testing**
SRS testing is a commonly used imaging test used for detecting carcinoid tumors. The SRS test images all of the body's systems, and detects both tumors and metastases when somatostatin receptors are present (about 90% of carcinoid tumors). The SRS test cannot detect tumors and metastases that do not express somatostatin receptors. The advantage of SRS testing over conventional imaging such as a CT scan or MRI is the ability to image all body regions with high sensitivity and selectivity, allowing evaluation of tumors for therapy. Another advantage is that SRS testing can help show the density of somatostatin receptors.

**How SRS Testing Works**

The somatostatin analogue radiolabeled octreotide is administered intravenously, 4 hours before the imaging. The radiolabeled octreotide binds with somatostatin receptors and produces an image during the SRS test, which lasts 15-20 minutes. Twenty-four hours after the injection, the results of the scan are obtained.

**Imaging Tests**

When positive readings are obtained on biochemical testing, imaging tests are recommended to confirm the diagnosis. Imaging methods your doctor may select depend on the suspected site of the tumor and may include any of the following:

- Computed tomography (CT) scan
- Magnetic resonance imaging (MRI)
- Endoscopic ultrasonography

Why Early Diagnosis of Carcinoid Syndrome Is Important

Carcinoid tumors are often difficult to diagnose because there are few if any symptoms. In fact, many carcinoid tumors are found through unrelated surgery or at autopsy. But, if metastasis occurs, patients may experience the uncomfortable and sometimes debilitating symptoms of carcinoid syndrome.

Unfortunately, the symptoms of carcinoid syndrome are often too vague for doctors to rule out other possible conditions, and they may misdiagnose the disease as something else, such as irritable bowel syndrome. Misdiagnosis then puts patients at a higher risk for carcinoid crisis, a dangerous condition that can occur at the time of surgery, which can be a life threatening complication of carcinoid syndrome.

Because of the difficulty involved, there may be a delay of approximately 5-7 years in correctly diagnosing carcinoid syndrome. This emphasizes the need for early recognition of the symptoms of carcinoid syndrome, and continued testing for the disease.
The Goals of Treatment

When treating carcinoid tumors and carcinoid syndrome, your doctor is most concerned with preserving your overall health and lifestyle. The goals of treatment are to remove the carcinoid tumor or reduce its size, and to help manage its impact on you.

Removing or Reducing the Size of the Tumor

The first choice in treating carcinoid tumors is often removing the tumor or reducing its size using surgery. However, if patients have severe carcinoid syndrome, it may mean that carcinoid tumors have metastasized to (spread into) the liver. In this case, some doctors may suggest a procedure called hepatic artery embolization—either with or without chemotherapy. Hepatic artery embolization decreases blood supply to the liver in an attempt to kill the tumor cells, which may lead to less discomfort from symptoms for 6 months to one year.

Your treatment may depend on the size of the tumor, whether or not it has spread, and where the tumor is located. Your healthcare professional will want to discuss all of these points with you.

Biochemical Monitoring
To track your disease, your healthcare provider will use biochemical monitoring. Biochemical monitoring involves measuring the amount of certain body substances that are released by carcinoid tumors. The substances that are monitored on an ongoing basis are the same ones that are measured to diagnose carcinoid syndrome. On this page, you can learn more about the monitoring of these substances, which include:

- Chromogranin A (CgA)
- 5-Hydroxyindoleacetic Acid (5-HIAA)

It is very important that levels of these substances be checked regularly by your healthcare provider.

**Chromogranin A (CgA) Testing**

CgA is a protein found in carcinoid tumor cells. The protein may be released into the bloodstream. Therefore, CgA levels are measured by a blood test. The CgA test is considered an accurate test available both for detecting carcinoid tumors and for monitoring their activity. This includes carcinoid tumors that secrete certain hormones that are associated with carcinoid syndrome as well as carcinoid tumors that do not cause carcinoid syndrome. High levels of CgA are found in 80% to 100% of people with carcinoid syndrome.

**Preparing for the CgA test**
Your CgA level can be measured using a simple blood test. Your level will vary depending upon what you have eaten, so your healthcare provider will tell you to fast—that is, not to eat or drink anything for a certain number of hours—before you take the test.

**How often to take the CgA test**

Your healthcare provider will tell you how often to get a CgA test. Most people who are being treated for carcinoid syndrome need to have the test every 3 to 6 months.

**What the results mean**

The target number for your CgA test varies with the laboratory running the test. In general, though, if your numbers go down, it means your disease is under control. CgA levels that are very high (up to 1000 times normal levels) may indicate that carcinoid tumors have spread.

**5-Hydroxyindoleacetic Acid (5-HIAA) Testing**

5-HIAA—more specific to carcinoid syndrome than CgA—is a by-product that is produced when the body breaks down serotonin. Serotonin is one of the key body chemicals released by carcinoid tumors that are associated with carcinoid syndrome and plays a role in many of the signs and symptoms of carcinoid syndrome. The body gets rid of 5-HIAA in the urine. Therefore, 5-HIAA levels are measured in the urine. By measuring the level of 5-HIAA in the urine, healthcare providers can calculate the amount of serotonin in the body. The 5-HIAA test is the most common biochemical test for carcinoid syndrome.
Preparing for the 5-HIAA test

Certain foods have a high serotonin content, and eating them before a 5-HIAA test can increase your levels. Therefore, your healthcare provider will probably tell you not to eat the following foods for 24 hours before you take the test:

- Bananas
- Walnuts
- Plantains
- Hickory nuts
- Pineapple
- Pecans
- Kiwi fruit
- Avocados
- Plums
- Tomatoes
- Eggplant

Several drugs can also affect the level of 5-HIAA in your urine, so your healthcare provider will probably tell you to avoid taking any of these drugs for 24 hours before you begin collecting urine for a 5-HIAA test.

Consult with your physician about which medications are appropriate to take before this test.

How often to take the 5-HIAA test
Your healthcare provider will tell you how often to get a 5-HIAA test. Most people who are being treated for carcinoid syndrome need to have the test every 3 to 6 months. The test is performed using urine samples collected during a 24-hour period.

**What the results mean**

In general, if your numbers go down, it means your disease is under control. Elevated 5-HIAA levels may indicate carcinoid heart disease.

**Keeping Track of Your Levels**

Keeping records of your CgA or 5-HIAA level (or both) over time can help you keep track of how well your treatment is working.