LUNG CARCINOID TUMOR

What Is Cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells often travel to other parts of the body where they begin to grow and replace normal tissue. This process, called metastasis, occurs as the cancer cells get into the bloodstream or lymph vessels of our body. When cells from a cancer like breast cancer spread to another organ like the liver, the cancer is still called breast cancer, not liver cancer.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person's DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Remember that not all tumors are cancerous. Benign (noncancerous) tumors do not spread to other parts of the body (metastasize) and, with very rare exceptions, are not life threatening.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Cancer is the second leading cause of death in the United States. Half of all men and one-third of all women in the US will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

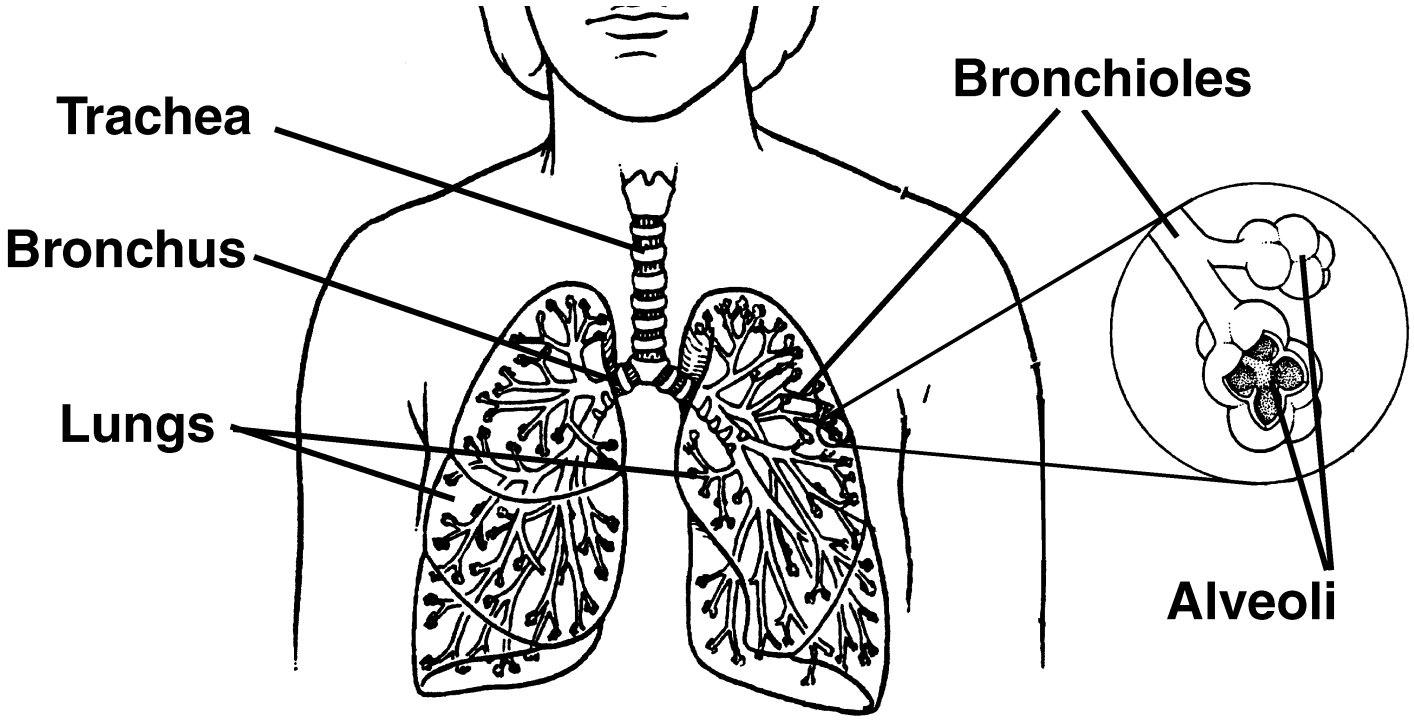
What Is a Lung Carcinoid Tumor?

The Lungs

The lungs are 2 sponge-like organs found in your chest cavity. Your right lung has 3 sections, called lobes. The left lung has 2 lobes.

It is smaller because the heart takes up more room on that side of the body. The lungs bring air in and out, taking in oxygen and getting rid of carbon dioxide gas, a waste product of the body.

The lining, which surrounds the lungs and helps to protect them and to facilitate the sliding motion during breathing, is called the *pleura*. The chest cavity is called the *pleural cavity*. The *trachea* (windpipe) brings air down into the lungs. It divides into tubes called the *bronchi*, which divide into smaller branches called the *bronchioles.* At the end of the bronchioles are tiny air sacs known as *alveoli.*



The Diffuse Neuroendocrine System

The *diffuse neuroendocrine system* is made up of cells that are in certain ways like nerve cells and in other ways like cells of *endocrine* (hormone-producing) glands. These cells do not form an actual organ like the pancreas, adrenal, or thyroid. Instead, they are scattered throughout other organs like the lungs, stomach, and intestines.

Neuroendocrine cells produce hormones like adrenalin and adrenalin-like substances. This may help control air flow and blood flow in the lungs and may help control growth of other types of lung cells. These neuroendocrine cells may detect decreased oxygen or increased carbon dioxide in the air we breathe and then release chemical messages to help the lungs adjust to changes in air composition. People who live at higher altitudes have more lung neuroendocrine cells, apparently because there is less oxygen in the air they breathe.

Neuroendocrine Cancers

Like most cells in your body, lung neuroendocrine cells sometimes undergo certain changes that cause them to grow too much and form tumors. The tumors that develop from neuroendocrine cells are known as *neuroendocrine tumors* or *neuroendocrine cancers.*

There are 4 types of neuroendocrine lung tumors. The most serious type, *small cell lung cancer* (SCLC), is one of the most rapidly growing and spreading of all cancers. It is discussed in a separate American Cancer Society lung cancer document. *Large cell neuroendocrine carcinoma* is a rare cancer that, with the exception of the size of the cells forming the cancer, is very similar to SCLC in its prognosis and in how patients are treated. *Carcinoid tumors,* also known as *carcinoids,* comprise the other 2 types of lung neuroendocrine cancer: *typical carcinoid* and *atypical carcinoid.* This document will only cover these 2 types of tumors.

Carcinoid Tumors

The 2 types of carcinoid tumors are distinguished from each other by their appearance under the microscope.
- *Typical carcinoids* grow slowly and only rarely spread beyond the lungs.
- *Atypical carcinoids* grow a little faster and are somewhat more likely to spread to other organs.
- Typical carcinoids are 9 times as common as atypical ones.
- Atypical carcinoids have more cells in the process of dividing and look more like a fast-growing tumor.

In addition to being classified as typical or atypical based on how they look under a microscope, carcinoids are sometimes also classified according to where they form within the lung.
- *Central carcinoids* form in the walls of large airways near the center of the lungs.
- *Peripheral carcinoids* develop in the narrower airways toward the edges of the lungs.

This distinction is important because the tumor's location affects which symptoms a patient will have. (See the section "How Are Lung Carcinoid Tumors Diagnosed?") Nearly all central carcinoid tumors are also typical carcinoids. Most peripheral carcinoids are also typical carcinoids.

What Are the Key Statistics About Lung Carcinoid Tumor?

Less than 1% of all lung tumors are lung carcinoid tumors. Most lung carcinoids are small. They vary from 0.5 cm (slightly smaller than ¼ inch) to 2 cm (a little over ¾ inch) at the time of diagnosis. Patients with carcinoids larger than 3 cm (almost 1 ¼ inch), atypical carcinoids, or carcinoids that have spread to lymph nodes have a worse outlook for chances of survival (prognosis).

The 5-year survival rates for patients with typical and atypical lung carcinoids are around 95% and 70%, respectively. The ranges reflect different survival rates quoted by several medical journal articles. For both types of carcinoids, the 10-year survival rates are about 10% lower than the 5-year rates. The 5-year survival rate for patients whose carcinoid tumors have not spread (metastasized) to their lymph nodes is 85%. For those patients with lymph node metastasis, the 5-year survival rate is 70%. These numbers will be higher for patients with typical carcinoids and lower for those with atypical carcinoids.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Many of these patients live much longer than 5 years after diagnosis, and 5-year rates are used to produce a standard way of discussing prognosis. Five-year *relative* survival rates exclude from the calculations patients dying of other diseases and are considered to be a more accurate way to describe the prognosis for patients with a particular type and stage of cancer. Of course, 5-year survival rates are based on patients diagnosed and initially treated more than 5 years ago. Improvements in treatment often result in a more favorable outlook for recently diagnosed patients.

What Are the Risk Factors for Lung Carcinoid Tumor?

A *risk factor* is anything that increases your chance of getting a disease such as of cancer. For example, smoking is responsible for about 80% of cases of *lung carcinoma* (the usual and more serious type of lung cancer). In contrast, very little is known about why lung carcinoid tumors develop in some people but not in others.

Chemical exposure: Lung carcinoid tumors are not associated with smoking or with any known chemicals in the environment or workplace.

Gender: Carcinoids occur equally in men and women.

Age: These tumors are usually found in people between 45 and 55 years old. Children are rarely affected.

Family History: A genetic tendency to develop lung carcinoid tumors can be inherited. Rare families have been described in which several members have been diagnosed with this cancer. Also, in general children of parents with this disease have a higher chance of developing carcinoid. Still, because this cancer is so uncommon, that risk is still low. And, most people with carcinoid tumors do not have a parent with this form of cancer.

Do We Know What Causes Lung Carcinoid Tumor?

Very little is known about the causes of lung carcinoid tumors. Researchers have learned a lot about how certain risk factors like cancer-causing chemicals or radiation cause lung cells to become carcinomas, the usual type of lung cancer. But, similar studies of lung carcinoid tumors have not found any risk factors.

Sometimes, tiny clusters of neuroendocrine cells that are similar to those seen in lung carcinoid tumors are seen under the microscope as an unexpected finding in lung biopsies done to treat or diagnose other conditions. These lesions, termed *carcinoid tumorlets,* develop in small airways. Under the microscope, tumorlets have a striking resemblance to peripheral carcinoid tumors, except that they are usually much smaller (¼ inch).

Central carcinoid tumors are believed to develop from the glands under the surface of the large air passages. Researchers still do not understand how carcinoid tumorlets develop from lung neuroendocrine cells or why some tumorlets may eventually grow to become carcinoid tumors.

Can Lung Carcinoid Tumors Be Prevented?

Research has not found any avoidable risk factors yet, so there is no way to prevent carcinoid tumors.

Can Lung Carcinoid Tumors Be Found Early?

Because carcinoid tumors usually grow and spread slowly, most are found at an early or localized stage. Most patients with peripheral carcinoid tumors or with small central carcinoid tumors have no symptoms. Carcinoids that do not cause symptoms often are found when you have a chest x-ray during a routine examination or to look into unrelated medical problems, such as some heart diseases.

How Are Lung Carcinoid Tumors Diagnosed?

Signs and Symptoms

Some patients with central carcinoid tumors may have a cough, may cough up bloody sputum, or may have wheezing symptoms like asthma. When a large carcinoid causes partial or complete blockage of a large air passage, the patient may develop a lung infection called *post-obstructive pneumonia.* Sometimes your doctor may suspect a tumor only after treatment with antibiotics fails to cure the pneumonia.

Some carcinoid tumors can produce hormone-like substances that are released into the bloodstream. Lung carcinoids do this far less often (10% to 20% of the time) than gastrointestinal carcinoid tumors. The *carcinoid syndrome* results from the effect of these substances. Symptoms include facial *flushing* (redness and warm feeling that may last hours to days), sweating, diarrhea, and a fast heartbeat. Some carcinoid tumors may produce adrenocorticotrophic hormone (ACTH), a hormone that stimulates your adrenal gland to produce excessive amounts of cortisol and related hormones. Symptoms of excessive amounts of these hormones include weight gain, weakness, secondary diabetes, and increased body and facial hair.

If there is a reason to suspect you may have a lung carcinoid tumor, your doctor will use one or more methods to find out if the disease is really present. About two-thirds of the time, this suspicion is based on your symptoms. If you have one or more symptoms that suggest this type of tumor, your doctor will ask about other symptoms such as:

- Cough
- Chest pain
- Wheezing

- Asthma
- Blood-tinged sputum
- Pneumonia that is not cured by antibiotics
- Recent weight gain
- Facial flushing (redness)
- Diarrhea

A thorough physical exam will provide information about signs of carcinoid tumor, such as the carcinoid syndrome, and other health problems.

Imaging Tests

Imaging tests produce pictures or images of the inside of the body. Imaging tests such as chest x-rays, computed tomography (CT) scans, octreoscans, and MIBG scans are useful in finding carcinoid tumors and determining how far they have spread.

Chest x-rays will be taken to look for a lung tumor. However, some carcinoids that are small or in locations where they are covered by other organs in the chest may not show up on a chest x-ray. If your doctor is still suspicious or if a vague abnormality appears on the chest x-ray, a CT scan may be ordered.

Computed tomography (CT): The CT scan is an X-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, as does a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine will take pictures of multiple slices of the part of your body that is being studied.

CT scans are often used to find small lung tumors. The CT scan can help to determine if surgery is a good treatment option.

This test can help tell if your cancer has spread into your liver or other organs. Often after the first set of pictures is taken you will receive an intravenous injection of a "dye" or *radiocontrast agent* that helps better outline structures in your body. A second set of pictures is then taken.

CT scans can also be used to guide a biopsy needle into a suspected tumor or metastasis. For this procedure, called a *CT-guided needle biopsy,* the patient remains on the CT scanning table, while a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½ inch long and less than 1/8 inch in diameter) is removed and examined under a microscope.

CT scans are more tedious than regular x-rays because they take longer and you need to lie still on a table while they are being done. But just like other computerized devices, they are getting faster and your stay might be pleasantly short. Also, you might feel a bit confined by the ring you lie within when the pictures are being taken.

You will have an IV (intravenous) line through which the contrast "dye" is injected. The injection can also cause some flushing. Some people are allergic and get hives or rarely more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

Somatostatin Receptor Scintography: This is a scan technique that uses radioactive octreotide. A small amount of this radioactive hormone-like substance (octreotide is a hormone that attaches to carcinoid tumors) is injected into a vein. This material is attracted to carcinoid tumors. A special radioactivity-detecting camera is used to show where the radioactivity accumulates. This test is useful in detecting spread of lung carcinoid tumors to other areas of the body.

A similar test uses radioactive *meta-iodobenzylguanidine (MIBG).* MIBG is a chemical that is taken up by carcinoid tumors. The MIBG is attached to radioactive iodine and injected into the bloodstream. If there is a carcinoid tumor, the radioactivity will go there and the scanner will detect it.

About one-third of carcinoids are diagnosed by accident, in people without any symptoms to suggest a carcinoid. In these cases, a chest x-ray done to evaluate an unrelated medical problem finds a lung mass.

Even if imaging tests such as a chest x-ray and/or CT scan find a mass, these imaging tests cannot tell if the mass is a carcinoid tumor, a lung carcinoma, or a localized infection. The only way to tell is to remove cells from the tumor and examine them under a microscope. This procedure is called a *biopsy.*

Biopsy

There are several ways to take a sample from a lung tumor. Tumors of large airways, such as central carcinoids, can be sampled by *bronchoscopic biopsy.* The doctor passes a long, lighted tube called a *bronchoscope* down the throat to look at the lining of the lung's main airways. You will be sedated for this. When a tumor is found, the doctor can take a small sample of the tumor through the tube.

The advantage of this approach is that no surgical incision is needed, no hospital stay is needed, and the patient is ready to return home within hours. One disadvantage is that a bronchial biopsy may not always be able to remove enough tissue to be certain the tumor is a carcinoid. But, thanks to recent advances in laboratory testing of lung tumors, doctors can usually make a more accurate diagnosis even with very small samples.

Bleeding after a biopsy from a carcinoid tumor is a rare but it can be a serious problem. If bleeding becomes a problem, doctors can inject drugs through the bronchoscope into the tumor to narrow its blood vessels, or they can seal off the bleeding vessels with a laser beam aimed through the bronchoscope.

Doctors can also take a *brushing* sample through the bronchoscope. They wipe a tiny brush over the surface of the tumor. The cells removed by the brush are smeared onto a microscope slide and examined in the lab. Brushing samples are sometimes a helpful addition to the bronchial biopsy but are not as helpful with diagnosing carcinoids as they are with lung carcinomas.

Tumors that are not near the large airways are often sampled by needle biopsy. A long needle is passed between the ribs into the lung. CT scan images are used to guide the needle into the tumor so that a small tissue sample can be removed for examination under the microscope. This procedure is also done without a surgical incision or overnight hospital stay. Some patients may experience a collapse of one lung, called *pneumothorax,* after this procedure. But, this complication can be treated by temporarily placing a suction tube into the chest.

In some cases, neither a bronchoscopic biopsy nor a needle biopsy can provide enough tissue to identify the type of tumor, and a *thoracotomy* (surgically opening in the chest cavity) is needed. In other cases, when the doctors strongly suspect a carcinoid or some other type of lung cancer, they may do a thoracotomy and remove the entire mass without first doing a bronchoscopic biopsy or needle biopsy.

Other Tests

Because the carcinoid tumor sometimes secretes chemicals into the blood like the ones that cause the carcinoid syndrome, it can often be detected by urine tests. These abnormal substances are excreted in the urine and can be found by simple laboratory tests. Sometimes, blood tests may be done to detect some of the hormone-like substances produced by carcinoids, particularly if the patient has symptoms of the *carcinoid syndrome,* caused by excessive levels of these substances in the blood.

How Are Lung Carcinoid Tumors Staged?

Staging is a process of finding out how localized or widespread the lung carcinoid tumor is. It will show if the tumor has spread and how far. The treatment and *prognosis* (the outlook for chances of survival) for a lung carcinoid tumor depend, to a large extent, on its stage. Because carcinoid tumors are uncommon, there is no official stage system for these tumors. Generally, the staging system that most doctors use for lung carcinoid tumors is the same one used to stage non-small cell lung cancer.

The system most often used to describe the growth and spread of carcinoids and of non-small cell lung cancers is the **TNM** staging system, also known as the American Joint Committee on Cancer (AJCC) system.

T stands for tumor (its size and how far it has spread within the lung and to nearby organs).

N stands for spread to lymph nodes.
M is for spread to distant organs *(metastasis).*

In TNM staging, information about the tumor, lymph nodes, and metastasis is combined, and a stage is assigned to specific TNM groupings. The grouped stage is described using the number 0 and Roman numerals from I to IV.

T Stages

T1: The cancer is no larger than 3 cm (slightly less than 1¼ inches), has not spread to the membranes that surround the lungs (visceral pleura), and does not affect the main branches of the bronchi.

T2: The cancer has one or more of the following features:
- It is larger than 3 cm.
- It involves a main bronchus but is not closer than 2 cm (about ¾ inch) to the point where the windpipe (trachea) branches into the left and right main bronchi.
- It has spread to the visceral pleura.
- The cancer may partially clog the airways, but this has not caused the entire lung to collapse or develop pneumonia.

T3: The cancer has one or more of the following features:
- It has spread to the chest wall, the breathing muscle that separates the chest from the abdomen (diaphragm), the membranes surrounding the space between the two lungs (mediastinal pleura), or membranes of the sac surrounding the heart (parietal pericardium).
- It involves a main bronchus and is closer than 2 cm (about ¾ inch) to the point where the windpipe (trachea) branches into the left and right main bronchi, but does not involve this area.
- It has grown into the airways enough to cause one lung to entirely collapse or to cause pneumonia of the entire lung.

T4: The cancer has one or more of the following features:
- It has spread to the space behind the chest bone and in front of the heart (mediastinum), the heart, the windpipe, the tube connecting the throat to the stomach (esophagus), the backbone, or the point where the windpipe branches into the left and right main bronchi.
- Two or more separate tumor nodules are present in the same lobe.
- There is a fluid containing cancer cells in the space surrounding the lung).

N Stages

N0: The cancer has not spread to lymph nodes.

N1: The cancer has spread to lymph nodes within the lung, hilar lymph nodes (located around the area where the bronchus enters the lung). The cancer has metastasized only to lymph nodes on the same side as the cancerous lung.

N2: The cancer has spread to lymph nodes around the point where the windpipe branches into the left and right bronchi or to lymph nodes in the *mediastinum* (space behind the chest bone and in front of the heart). The lymph nodes on the same side of the cancerous lung are affected.

N3: The cancer has spread to lymph nodes near the collarbone on either side, to hilar or mediastinal lymph nodes on the side opposite the cancerous lung.

M Stages

M0: The cancer has not spread to distant sites.

M1: The cancer has spread to distant sites such as other lobes of the lungs, lymph nodes farther than those mentioned in N stages, and other organs or tissues such as the liver, bones, or brain.

Stage Grouping

Once the T, N, and M categories have been assigned, this information is combined (stage grouping) to assign an overall stage of I, II, III, or IV. Patients with lower stage numbers have a more favorable outlook for survival.

Overall Stage T Stage N Stage M Stage

Stage IA T1 N0 M0
Stage IB T2 N0 M0
Stage IIA T1 N1 M0
Stage IIB T2 N1 M0
T3 N0 M0
Stage IIIA T1 N2 M0
T2 N2 M0
T3 N1 M0
T3 N2 M0
Stage IIIB Any T N3 M0
T4 Any N M0
Stage IV Any T Any N M1

How Are Lung Carcinoid Tumors Treated?

After the tumor is found and staged, your cancer care team will suggest one or more treatment plans. This is an important decision, and you should take the time to think about all of the choices.

The main factors in selecting treatment options for lung carcinoid tumors are the size and location of the tumor, whether it has spread to lymph nodes or other organs, and if you have any other serious medical conditions. Seeking a second opinion is often a good idea. A second opinion may provide more information and help you feel more certain about the treatment plan that is chosen.

Surgery

Most lung carcinoid tumors are cured by surgery alone. You should be referred to a thoracic or cardiothoracic surgeon who will discuss the surgical options. The type of operation will depend on a number of factors, including the size and location of the tumor and whether you have any other lung problems or serious diseases.

Several types of operations are used to treat people with lung carcinoid tumors. It is usually necessary to remove some normal lung tissue along with the tumor, but surgeons try not to remove any more normal tissue than they need to.

To treat central carcinoids of a large airway, the surgeon may do a *sleeve resection.* If you think of the large airway with a tumor as similar to the sleeve of a shirt with a stain an inch or two above the wrist, the sleeve resection would be like cutting across the sleeve above and below the stain and sewing the cuff back into the shortened sleeve.

If it is not possible to do a sleeve resection because of the size of the tumor and its exact location in a large airway, the surgeon will usually do a *lobectomy* (remove an entire lobe). Less often, it may be necessary to remove two lobes or, rarely, remove the entire left or right lung (this operation is called a *pneumonectomy*).

Carcinoids found at the edges of the lungs away from the large airways, called *peripheral carcinoids,* are usually treated by lobectomy. If the tumor is very small, the surgeon may remove a wedge-shaped piece of the lung in an operation called a *wedge resection*.

In most cases, the surgeon will also remove some lymph nodes near the lungs. This is important because about 10% of typical carcinoids and 30% to 50% of atypical carcinoids will have spread to lymph nodes by the time they are diagnosed. Not removing these nodes might increase the risk of the carcinoid tumor spreading even farther, to other organs. At this point, you can no longer be cured by surgery. Removing the lymph nodes also provides some indication of your risk of having the cancer come back.

If you also have lung diseases, such as severe emphysema or chronic bronchitis, you may not be able to have your carcinoid treated

surgically, because removing some normal lung tissue along with the cancer would cause you severe shortness of breath. If you have other medical problems, such as severe heart disease, you also may not be able to have curative surgery.

If this is the case, palliative procedures, such as removing most of the tumor through a bronchoscope or vaporizing most of it with a laser, can be helpful. These treatments can relieve symptoms caused by blockage of airways, but they cannot cure the cancer and are recommended only if you cannot have surgery to completely remove the tumor. Patients who are treated with these procedures often also have external radiation or radiation given through the bronchus (see our document on radiation therapy).

Recently, a less invasive procedure for treating early stage lung cancer has been developed. This is called video-assisted thoracic surgery. A tiny video camera can be placed inside the chest cavity to help the surgeon see the tumor. Only small incisions are needed so there is a little less pain after the surgery. Most experts recommend that only tumors smaller than 4 to 5 cm (about 2 inches) be treated with this method. The cure rate after this surgery seems to be the same as with older techniques. It is important, though, that the surgeon performing this procedure be experienced since it requires more technical skill than the standard surgery.

Chemotherapy

Chemotherapy uses anticancer drugs that are injected into a vein or a muscle or taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment useful for some types of lung cancer that have spread or metastasized to organs beyond the lungs. Unfortunately, carcinoid tumors are not usually sensitive to chemotherapy.

Chemotherapy is generally used only for carcinoid tumors that have spread to other organs, are causing severe symptoms, and have not responded to other medications. Some of the chemotherapy drugs used in this situation include streptozotocin, etoposide, cisplatin, cyclophosphamide, 5-fluorouracil, doxorubicin (Adriamycin), and dacarbazine. Several chemotherapeutic drugs are sometimes used together to treat metastatic carcinoid tumor, often in combination with other types of medications.

Chemotherapy drugs kill some cancer cells but can also affect some of the normal, healthy cells in your body, causing side effects. Rapidly growing cells, such as the blood-producing cells of bone marrow, cells of hair follicles, and cells lining the mouth, are particularly sensitive to chemotherapy. Possible side effects include:

- Nausea, vomiting, and decrease in appetite
- Temporary loss of hair
- Mouth sores
- Increased risk of infections (because of low white blood cell counts) or bleeding (because of low blood platelet counts)
- Fatigue

If you have side effects, your cancer care team can suggest steps to ease them. For example, drugs are available to help prevent or control nausea and vomiting. Sometimes changing the dosage or the time of day at which you take your medications can reduce side effects. Fortunately, most side effects will disappear when your course of treatment ends.

Chemotherapy is only occasionally effective in shrinking carcinoid tumors. Patients should discuss with their doctors whether the side effects they experience are worth the small chance that they will get better.

Other Drugs for Treating Carcinoid Tumors

Several medications are available for controlling symptoms of carcinoid syndrome (problems arising from release of substances produced by some of these tumors and recognized through blood and urine tests) in patients with metastatic carcinoid tumors.

- *Octreotide* is a drug chemically related to a natural hormone, somatostatin. It is very helpful in treating the flushing (skin redness and feeling hot), diarrhea, and wheezing from carcinoid syndrome. It is given by *subcutaneous* (under the skin) injection. Sometimes octreotide can temporarily shrink carcinoid tumors, but it does not cure them. The medication's side effects include pain at the site of its injection, and, rarely, stomach cramps, nausea, vomiting, headaches, dizziness, and fatigue.
- *Lanreotide* is a drug similar to octreotide but has the advantage of being longer acting. Octreotide must be given at least twice daily while lanreotide can be given every 10 days.
- There is also a long-acting version of octreotide called Sandostatin LAR that can be given monthly.
- *Interferons* are substances that activate the body's immune system. Alpha-interferon is helpful in shrinking some metastatic carcinoid tumors and improving symptoms of carcinoid syndrome.

Other medications are also available for controlling specific *syndromes.* Ask your doctor about them, or describe your symptoms to your doctor and ask about medications to control them.

Radiation Therapy

Radiation therapy uses high-energy radiation to kill cancer cells. Although most cases of carcinoid tumor are cured by surgery alone, if for some reason the patient is unable to have surgery, radiotherapy may be an option.

External beam radiation therapy is the type of radiation used most often for lung cancer. It is like having a regular x-ray except it lasts a little longer. Patients typically have treatments for 5 days a week for several weeks. Radiation therapy is not usually very effective against most lung carcinoid tumors and is seldom used.

The main side effects of lung radiation therapy are fatigue (tiredness) and mild temporary, sunburn-like skin changes. If high doses are given, radiation damage to normal lung tissue can cause scar tissue formation, trouble with breathing, and increased susceptibility to infection.

A radioactive drug has been useful in treated widespread carcinoid tumors. The drug meta-iodobenzylguanidine, or MIBG, is taken up by carcinoid cells. When a radioactive iodine molecule is attached to MIBG, this compound can kill carcinoid cells. Doctors have used this drug effectively in patients who have advanced carcinoid tumors, and about half the patients showed improvement.

Complementary and Alternative Therapies

If you are considering any unproven alternative or complementary treatments, it is best to discuss this openly with your cancer care team and request information from the American Cancer Society or the National Cancer Institute. Some unproven treatments can interfere with standard medical treatments or may cause serious side effects.

Clinical Trials

The purpose of clinical trials: Studies of promising new or experimental treatments in patients are known as clinical trials. A clinical trial is only done when there is some reason to believe that the treatment being studied may be valuable to the patient. Treatments used in clinical trials are often found to have real benefits. Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment helpful?
- How does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are the side effects greater or less than the standard treatment?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Types of clinical trials: A treatment is studied in 3 clinical trials phases before it is eligible for approval by the FDA (Food and Drug Administration).

Phase I clinical trials: The purpose of a phase I study with a new drug is to find the best way to give a new treatment and how much of it can be given safely. Doctors watch patients carefully for any harmful side effects. The treatment has been well tested in laboratory and animal studies, but the side effects in patients are not completely known. Doctors conducting the clinical trial will start by giving very low doses of the drug to the first patients and increasing the dose for later groups of patients until side effects appear. Although doctors are hoping to help patients, the main purpose of a phase I study is to test the safety of the drug. Some phase I clinical trials are designed to fine-tune a regimen such as combining two well known drugs before going into phase III studies, and although the safety is being established, such studies usually utilize drug doses that have already been shown to be at least partially effective.

Phase II clinical trials: These are designed to see if the drug works. Patients are given the highest dose that doesn't cause severe side effects (determined from the phase I study) and closely observed for an effect on the cancer. The doctors will also look for side

effects.

Phase III clinical trials: Phase III studies involve large numbers of patients. Some clinical trials may enroll thousands of patients. One group (the control group) will receive the standard (most accepted) treatment. The other groups will receive the new treatment. Usually doctors study only 1 new treatment to see if it works better than the standard treatment, but sometimes they will test 2 or 3. All patients in phase III studies are closely watched. The study will be stopped if the side effects of the new treatment are too severe or if one group has had much better results than the others.

If you are in a clinical trial, you will receive excellent care. You will have a team of experts looking at you and monitoring your progress very carefully. The study is especially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to discover. While most side effects will disappear in time, some can be permanent or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enroll in a clinical trial.

Deciding to enter a clinical trial: Enrollment in any clinical trial is completely up to you. Your doctors and nurses will explain the study to you in detail and will give you a form to read and sign indicating your desire to take part. This process is known as giving your informed consent. Even after signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in the study will not prevent you from getting other medical care you may need.

To find out more about clinical trials, ask your cancer care team. Among the questions you should ask are:

- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do?
- What is likely to happen in my case with, or without, this new research treatment?
- What are my other choices and their advantages and disadvantages?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to be hospitalized? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can gain access to this service through the ACS cancer information center (1-800-ACS-2345) or our Web site (www.cancer.org) Based on the information you provide about your cancer type, stage, and previous treatments, our computer will compile a list of clinical trials that match your medical needs. In finding a center most convenient for you, the service can also take into account where you live and whether you are willing to travel.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER or visiting the NCI clinical trials Web site www. cancer.gov/clinical_ trials/.

Treatment of Lung Carcinoid by Stage

Localized carcinoid: Surgery is the main treatment if you have localized carcinoid. The surgery should remove the cancer and any nearby lymph nodes. There is no value in adding radiation therapy or chemotherapy in most cases.

Metastatic carcinoid: The treatment of this stage depends on where the cancer is and whether you have symptoms of the carcinoid syndrome. In general, it is a slow-growing cancer, and chemotherapy has not proven very successful. If you have only a small number of tumors that can be removed, surgery is your best option. Another option, if the carcinoid involves only your liver, would be liver transplantation. This is still an experimental procedure that is performed at only a few centers.

If the carcinoid is in your liver and is causing symptoms, 2 kinds of treatment have been tried and have been successful. The first is

placing small particles of materials like gelfoam into the arteries that run into the liver and the cancer. This deprives the cancer of nourishment and causes many of the cells to die. A second approach is to tie off the arteries leading to the liver and the cancer.

Both are temporarily effective, although these procedures can cause serious side effects as the cancer cells and liver cells die. You might experience liver pain , fever, and severe weakness. These usually pass but have sometimes been fatal. It is important that your doctor have experience with these procedures.

If your liver cannot be treated directly, or the carcinoid has spread to other parts of your body, then drugs can be useful. The most useful are octreotide or lanreotide, which can stop the secretion of the chemicals that cause the carcinoid syndrome and also can sometimes actually shrink the cancers. Another drug, alpha-interferon, can act the same way. Sometimes these 2 drugs are given together. Adding chemotherapy may also help reduce symptoms. It seldom causes much tumor shrinkage.

Other possible treatments are radiation therapy for localized tumors and radioactive MIBG for more widespread disease.

What Should You Ask Your Doctor About Lung Carcinoid Tumor?

It is important to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial you might think they are. For instance, consider these questions:

- What kind of carcinoid tumor do I have?
- Has my carcinoid tumor spread beyond the lungs?
- What is the stage of my carcinoid tumor and what does that mean in my case?
- What treatment choices do I have?
- What do you recommend and why?
- Based on what you've learned about my carcinoid tumor, how long do you think I'll survive?
- What risks or side effects are there to the treatments you suggest?
- What are the chances of recurrence of my carcinoid tumor with these treatment plans?
- What should I do to be ready for treatment?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan your work schedule. Or you may want to ask about second opinions or about clinical trials for which you may qualify.

What Happens After Treatment For Lung Carcinoid Tumor?

After treatment, you will be asked to return to the doctor for regular physical exams and, in some cases, x-rays and blood tests. These exams and tests will help find any recurrences of the tumor as early as possible.

It is important for you to report any new symptoms to your doctor right away. They might be signs of the tumor's recurrence or of side effects from treatment.

If you smoke, it is very important to quit. Quitting improves your heart and lungs. After surgery to remove some lung tissue, some people have breathing problems and feel weak. Smoking makes this situation worse.

Once you have recovered from surgery, ask your doctors and nurses about physical activity. A good exercise plan may help you recover faster, regain your energy level, and reduce shortness of breath.

What's New In Lung Carcinoid Tumor Research And Treatment?

Research is ongoing in the field of lung cancer. Scientists are looking for causes and ways to prevent carcinoid tumors. Present and current carcinoid tumor research is focused on identifying causes and improving diagnosis and treatment of metastatic tumors.

Genetics: Researchers have made great progress in understanding how certain changes in DNA can cause normal cells to become cancerous. DNA is the molecule that carries the instructions for nearly everything our cells do. We usually resemble our parents because they are the source of our DNA.

However, DNA affects more than our outward appearance. Some *genes* (parts of our DNA) contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes.* Others that slow down cell division or cause cells to die at the appropriate time are called *tumor-suppressor genes.* It is known that cancers can be caused by DNA *mutations* (defects) that turn on oncogenes or turn off tumor-suppressor genes. Researchers have characterized many of the DNA changes in lung carcinoids in the past few years.

We expect that continued research in understanding these changes will lead to new tests for earlier diagnosis and new drugs for more effective treatment.

Diagnosis: Because the outlook and treatment of lung carcinoids and lung carcinomas are very different, accurate diagnosis is important. Researchers have made great progress in developing tests that can detect specific substances found in the cells of carcinoid tumors but not lung cancers. Other substances may be found in both carcinoids and carcinomas, but higher levels are found in one type. Most of these tests involve treating tissue samples with special antibodies produced in the laboratory. The antibodies are designed to recognize specific substances in certain types of tumors.

Imaging tests: Researchers are testing indium-111-DTPA-octreotide scintigraphy scan (octreoscan) and other nuclear medicine methods to detect carcinoid tumors earlier.

Treatment: New chemotherapy agents are being tested to find treatments that are active against carcinoids. One such agent is a chemical called 7-hydroxytryptophan. This chemical, which is similar to naturally occurring ones, can be toxic to carcinoid tumor cells in test tube experiments. This agent hasn't been studied in clinical trials yet.

Additional Resources

Other National Organizations and Web Sites

In addition to the American Cancer Society, other sources of patient information and support include*:

Alliance for Lung Cancer Advocacy, Support & Education (ALCASE)
1601 Lincoln Avenue
Vancouver, Washington 98660
Telephone: 1-800-298-2436 or 360-696-2436
Internet Address: www.alcase.com

American Lung Association
1740 Broadway
New York, New York 10019
Telephone: 1-800-586-4872 or (212) 315-8700
Internet Address: www.lungusa.org

The Carcinoid Cancer Foundation, Inc.
171 York Avenue
New York, NY 10128
Telephone: 1-212-722-3132
Internet Address: www.carcinoid.org

National Cancer Institute
International Cancer Information Center
Telephone: 1-800-4-CANCER
Internet Addresses: www.nci.nih.gov and cancernet.nci.nih.gov

**Inclusion on this list does not imply endorsement by the American Cancer Society*

American Cancer Society Publications

After Diagnosis: A Guide for Patients and Families (Booklet; Code #9440)

Caring for the Patient with Cancer at Home (Booklet; Code #4545)

Questions About Smoking, Tobacco, and Health (Booklet; Code #2023)

Questions and Answers About Pain Control (Booklet; Code #4518)

Books
American Cancer Society's Guide to Pain Control (Book; Code #9438)

Cancer in the Family: Helping Children Cope with a Parent's Illness (Book; Code #9435)

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home (Book; Code #9422)

Coming to Terms with Cancer: A Glossary of Cancer-Related Terms (Book: Code #9505)

Consumers Guide to Cancer Drugs (Book; Code #9436)

Informed Decisions, Second Edition: The Complete Book of Cancer Diagnosis, Treatment, and Recovery (Book; Code #9449.02)

Other Publications*

Capossela C, Warnock S. *Share the Care: How to Organize a Group for Someone Who Is Seriously Ill.* New York: Simon and Schuster; 1995.

Hoffman B, ed, National Coalition for Cancer Survivorship. *A Cancer Survivor's Almanac: Charting Your Journey.* Minnetonka, Minn: Chronimed Publishing; 1996.

Holland, Jimmie C, and Sheldon Lewis. *The Human Side of Cancer.* New York: HarperCollins Publishers, 2000.

Morra M, Potts E. *Choices.* New York: Avon Books; 1994.

**Inclusion on this list does not imply endorsement by the American Cancer Society*

References

Caplin ME, Buscombe JR, Hilson AJ, et al. Carcinoid tumor. *Lancet.* 1998;352:799-805.

Jensen RT, Doherty GM. Carcinoid tumors and the carcinoid syndrome. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology.* Philadelphia, Pa: Lippincott Williams & Wilkins; 2001:1813-1833.

Kulke MH, Mayer RJ. Carcinoid tumors. *New Engl J Med.* 1999;340:858-868.

Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. *Cancer.* 997;79:813-829.

Revised: 11/04/2002 12:00:00 AM

For additional assistance please contact your American Cancer Society
1 · 800 · ACS·2345 or www.cancer.org