

Malignant Mesothelioma

What is malignant mesothelioma?

Malignant mesothelioma is a cancer that starts in cells in the linings of certain parts of the body, especially in the linings of the chest or abdomen.

Cancer starts when cells start to grow out of control. Cells in nearly any part of the body can become cancer. To learn more about how cancers start and spread, see *What Is Cancer?*

The mesothelium

A layer of specialized cells called *mesothelial cells* lines the inside of the chest, the abdomen, and the space around your heart. These cells also cover the outer surface of most of your internal organs. The lining formed by these cells is called the *mesothelium*.

The mesothelium helps protect your organs by making a special lubricating fluid that allows organs to move against each other. For example, this fluid makes it easier for your lungs to move (expand and contract) inside the chest when you breathe. The mesothelium has different names in different parts of the body:

- The *pleura* coats the lungs and the space in the chest containing the lungs.
- The *peritoneum* lines the inside of the abdomen and many of the organs in the abdomen.
- The *pericardium* covers the heart and creates the space that holds the heart in the chest.
- The *tunica vaginalis* lines the testicles.

Mesothelial tumors can start in any of these linings. These tumors can be non-cancerous (benign) or cancerous (malignant).

Malignant mesothelioma

A cancerous tumor of the mesothelium is called a *malignant mesotheliuma*, although this is often shortened to just mesotheliuma. Mesotheliumas can start in 4 main areas in the body.

- **Pleural mesotheliomas** start in the chest. About 3 out of 4 mesotheliomas are pleural mesotheliomas.
- **Peritoneal mesotheliomas** begin in the abdomen. They make up most of the remaining cases.
- Pericardial mesotheliomas start in the covering around the heart and are very rare.
- Mesotheliomas of the tunica vaginalis are very rare tumors that start in the covering layer of the testicles.

Malignant mesotheliomas can also be classified into 3 main types based on how the cancer cells are arranged:

- About half of mesotheliomas are **epithelioid**. This type tends to have a better outlook (prognosis) than the other types.
- About 10% of mesotheliomas are **sarcomatoid** (**fibrous**).
- **Mixed (biphasic)** mesotheliomas have both epithelioid and sarcomatoid areas. They make up the remaining 30% to 40% of mesotheliomas.

Benign tumors of the mesothelium

Benign (non-cancerous) tumors can also start in the mesothelium. These tumors are typically removed by surgery, and there is often no need for additional treatment.

Localized fibrous tumor of the pleura

This type of benign tumor can form in the pleura surrounding the lungs. It used to be called *benign fibrous mesothelioma*, but doctors now know that this tumor actually does not start in mesothelial cells. This disease is usually benign, but about 1 in 10 are cancerous. A similar condition that starts in the peritoneum is called *solitary fibrous tumor of the peritoneum*.

Adenomatoid mesothelioma

This benign tumor can develop in the mesothelium of certain reproductive organs. In men, it often starts in the epididymis (ducts that carry sperm cells out of the testicle). In women, this tumor can begin in the fallopian tubes (tubes that carry eggs from the ovaries to the uterus).

Benign cystic mesothelioma

This rare non-cancerous tumor often begins in the peritoneum.

Only malignant mesothelioma will be discussed further in this document.

What are the key statistics about malignant mesothelioma?

Mesothelioma is fairly rare in the United States, with about 3,000 new cases being diagnosed each year.

The rate of mesotheliomas in the United States increased from the 1970s to the early 1990s, but since then it has leveled off and even gone down slightly. These changes have largely been seen in men, and are probably related to changes over time in workplace exposures to asbestos. (See "What are the risk factors for malignant mesothelioma?") The rate of mesothelioma is lower in women and has been fairly steady for some time. In many other countries, the rate of mesothelioma is still increasing.

Mesothelioma is more common in whites and Hispanics/Latinos than in African Americans or Asian Americans.

Mesotheliomas are much more common in older people than younger people. The average age at the time of diagnosis for pleural mesothelioma (mesothelioma in the chest) is 69.

Information on survival rates can be found in the section "Survival statistics for mesothelioma."

What are the risk factors for malignant mesothelioma?

A risk factor is anything that affects your chance of getting a disease such as 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 known risk factor, or even several, does not mean that you will get the disease. And some people who get the disease may have few or no known risk factors.

Researchers have found some factors that increase a person's risk of mesothelioma.

Asbestos

The main risk factor for pleural mesothelioma is exposure to asbestos. In fact, most cases of pleural mesothelioma have been linked to asbestos exposure, usually from high levels of exposure in the workplace.

Asbestos is a group of minerals that occur naturally as bundles of tiny fibers. These fibers are found in soil and rocks in many parts of the world.

When asbestos fibers in the air are inhaled, they can get into the lungs. Fibers that stay in the lungs can travel to the ends of the small airways and enter the pleural lining of the lung and chest wall. These fibers can then injure the cells of the pleura, and eventually cause mesothelioma. Asbestos fibers can also damage cells of the lung and result in *asbestosis* (scar tissue in the lung) and/or lung cancer.

Peritoneal mesothelioma, which forms in the abdomen, can result from coughing up and swallowing inhaled asbestos fibers.

Many people are exposed to very low levels of naturally occurring asbestos in outdoor air in dust that comes from rocks and soil containing asbestos. This is more likely to happen in areas where rocks have higher asbestos content. In some areas, asbestos can be found in the water supply as well as in the air.

In the past, asbestos was used in many products because of its heat and fire-resistant properties. The link between asbestos and mesothelioma is now well known, so its use in the United States has gone down dramatically. Most use stopped several decades ago, but it is still used in some products.

Still, millions of Americans may already have been exposed to asbestos. People at risk for asbestos exposure in the workplace include some miners, factory workers, insulation manufacturers and installers, railroad and automotive workers, ship builders, gas mask manufacturers, plumbers, and construction workers. Family members of people exposed to asbestos at work can also be exposed because the workers can carry home asbestos fibers on their clothes.

Asbestos was also used to insulate many older homes, as well as commercial and public buildings around the country, including some schools. Because these particles are contained within the building materials, they are not likely to be found in the air in large numbers. The risk of exposure is likely to be very low unless the particles somehow escape into the air, such as when building materials begin to decompose over time, or during remodeling or removal.

The risk of developing mesothelioma is loosely related to how much asbestos a person is exposed to and how long this lasts. People exposed at an early age, for a long time, and at higher levels are more likely to develop this cancer. Still, most people exposed to asbestos, even in large amounts, do not get mesothelioma. Other factors, such as a person's genes, may make them more likely to develop mesothelioma when exposed to asbestos.

Mesotheliomas related to asbestos exposure take a long time to develop. The time between first exposure to asbestos and diagnosis of mesothelioma is usually between 20 and 50 years. Unfortunately, the risk of mesothelioma does not go down over time after the exposure to asbestos stops. The risk appears to be lifelong.

For more detailed information on asbestos, see Asbestos.

Zeolites

Zeolites are minerals chemically related to asbestos. An example is erionite, which is common in the rocks and soil in parts of Turkey. High mesothelioma rates in these areas are believed to be caused by exposure to this mineral.

Radiation

There have been a few published reports of mesotheliomas that developed after people were exposed to high doses of radiation to the chest or abdomen as treatment for another cancer. Although the risk of mesothelioma is higher in patients who have been treated with radiation, this cancer is still rare in these patients.

There have also been reports linking mesothelioma to injections of thorium dioxide (Thorotrast). This radioactive material was used by doctors for certain x-ray tests until the 1950s. Thorotrast was found to cause cancers, so it has not been used for many decades.

SV40 virus

Some studies have raised the possibility that infection with simian virus 40 (SV40) might increase the risk of developing mesothelioma. Some injectable polio vaccines given between 1955 and 1963 were contaminated with SV40. As many as 30 million people in the United States may have been exposed to this virus.

Some lab studies have suggested that SV40 infection might cause mesothelioma. For example, infecting some lab animals like hamsters with SV40 causes mesotheliomas to develop. Researchers also have noticed that SV40 can cause mouse cells grown in lab dishes to become cancerous, and that asbestos increases the cancer-causing effect of SV40 on these cells. Other researchers have found SV40 DNA in some biopsy specimens of human mesotheliomas. But fragments of SV40 DNA can also be found in some non-cancerous human tissues.

So far, the largest studies looking at this issue in humans have not found an increased risk for mesothelioma or other cancers among people who received the contaminated vaccines as children. But the peak age range for diagnosis of mesothelioma is 50 to 70 years. Some researchers have pointed out that this issue may remain unresolved until more of the people accidentally exposed to SV40 between 1955 and 1963 reach that age range.

Most experts have concluded that at this time we still don't know if SV40 is responsible for some mesotheliomas. This important topic is still being researched.

Age

The risk of mesothelioma increases with age. Mesothelioma can occur in young people (even children), but it is rare in people under age 45. About 2 out of 3 people with mesothelioma of the chest are 65 or older.

Gender

Mesothelioma is much more common in men than in women. This is probably because men have been more likely to work in jobs with heavy exposure to asbestos.

Do we know what causes malignant mesothelioma?

Researchers have found several factors that increase a person's risk of mesothelioma, but it's not yet clear exactly how all of these factors might cause this cancer.

Cancers, including mesotheliomas, occur when cells in the body suffer damage to their DNA. DNA is the chemical in each of our cells that makes up our *genes* – the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look. Some genes control when cells in the body grow, divide into new cells, and die at the right time. Changes in these genes may cause cells to grow out of control, which can lead to cancer.

Asbestos exposure is the main cause of pleural mesothelioma. When asbestos fibers are breathed in, they travel to the ends of small air passages and reach the pleura, where they can cause inflammation and scarring. This may damage cells' DNA and cause changes that result in uncontrolled cell growth. If swallowed, these fibers can reach the abdominal lining, where they can have a role in causing peritoneal mesothelioma.

But most people exposed to asbestos, even in large amounts, do not get mesothelioma. Other factors, such as a person's genes, may make them more likely to develop mesothelioma when exposed to asbestos. For example, researchers have found that some people who seem to be at high risk have changes in *BAP1*, a gene that normally helps keep cell growth under control. Other genes are probably important as well.

Radiation treatments for other cancers have been linked to mesothelioma in some studies. Radiation can damage the cells' DNA, leading to out-of-control cell growth.

It is still not known if infection with the SV40 virus increases the risk of mesothelioma, or exactly how it might do so. In lab studies, researchers have found that the virus can affect certain genes that have been linked with cancer, but further research in this area is needed.

Can malignant mesothelioma be prevented?

Being exposed to asbestos is by far the biggest risk factor for mesothelioma, so the best way to reduce your risk is to limit your exposure to asbestos at home, in public buildings, and at work.

People who might be exposed to high levels of asbestos at work include some miners, factory workers, insulation manufacturers and installers, railroad and automotive workers, ship builders, gas mask manufacturers, plumbers, and construction workers. If

there is a chance of on-the-job exposure, such as during the renovation of old buildings, you should use all protective equipment and safety procedures designed for working around asbestos.

Older homes may have insulation containing asbestos or other materials. A knowledgeable expert can check your home to find out if there is any asbestos and whether it poses any risk of exposure. This may mean testing the air for asbestos levels. Just because asbestos exists in a home does not necessarily mean that it needs to be removed. As long as the material is not damaged or disturbed, for example by drilling or remodeling, the fibers will not be released into the air. If asbestos needs to be removed from your home, you should hire a qualified contractor to do this to avoid contaminating your home or causing any exposure to your family or to the workers. You should not attempt to remove asbestos-containing material yourself.

Asbestos can also be found in some commercial and public buildings (including some schools), where the same basic principles apply. Intact, undisturbed materials containing asbestos generally do not pose a health risk. They may pose a risk if they are damaged, are disturbed in some way, or deteriorate over time and release asbestos fibers into the air. By federal law, all schools are required to inspect materials with asbestos regularly and to have a plan in place for managing them.

Can malignant mesothelioma be found early?

Mesothelioma is uncommon, and there are no widely recommended screening tests for this cancer in people who are not at increased risk. (Screening is testing for cancer in people who don't have any symptoms.)

For people with known exposure to asbestos, some doctors recommend imaging tests such as chest x-rays or computed tomography (CT) scans to look for changes in the lungs that might be signs of mesothelioma or lung cancer. But it is not clear how useful these tests are in finding mesotheliomas early.

In recent years, doctors have found that people with mesothelioma often have high levels of certain substances in their blood, including *osteopontin* and *soluble mesothelin-related peptides* (SMRPs). Blood tests for these substances may one day be useful in finding mesotheliomas early, as well as for monitoring the course of the disease in people who have mesothelioma.

Most mesotheliomas are found when a person goes to a doctor because of symptoms. People who have been exposed to asbestos should know the possible signs and symptoms of mesothelioma. Many of these symptoms are more likely to be caused by something other than mesothelioma, but it's important to report any new symptoms to your doctor right away so that the cause can be found and treated, if needed.

Signs and symptoms of mesothelioma

Many of the early symptoms of mesothelioma are more likely to be caused by other conditions, so at first people may ignore them or mistake them for common, minor ailments. Most people with mesothelioma have symptoms for at least a few months before they are diagnosed.

Symptoms of pleural mesothelioma (mesothelioma of the chest) can include:

- Pain in the side of the chest or lower back
- Shortness of breath
- Cough
- Fever
- Excessive sweating
- Fatigue
- Weight loss (without trying)
- Trouble swallowing (feeling like food gets stuck)
- Hoarseness
- Swelling of the face and arms

Symptoms of peritoneal mesothelioma can include:

- Abdominal (belly) pain
- Swelling or fluid in the abdomen
- Weight loss (without trying)
- Nausea and vomiting
- Constipation

These symptoms can be caused by mesothelioma, but more often they are caused by other conditions. Still, if you have any of these problems (especially if you have been exposed to asbestos), it's important to see your doctor right away so the cause can be found and treated, if needed.

How is malignant mesothelioma diagnosed?

Mesothelioma is most often diagnosed after a person goes to a doctor because of symptoms they are having. If there is a reason to suspect you might have mesothelioma, your doctor will examine you and use one or more tests to find out. Symptoms might

suggest that the problem could be mesothelioma, but tests will be needed to confirm the diagnosis.

Medical history and physical exam

If you have any signs or symptoms that suggest you might have mesothelioma, your doctor will want to get your medical history to learn about your symptoms and possible risk factors, especially asbestos exposure.

A physical exam can provide information about possible signs of mesothelioma and other health problems. Pleural mesothelioma can cause fluid to build up around the lungs in the chest (called a *pleural effusion*). In cases of peritoneal mesothelioma, fluid can build up in the abdomen (called *ascites*). In pericardial mesothelioma, fluid builds up in the sac around the heart (called a *pericardial effusion*). Rarely, mesothelioma can develop in the groin and look like a hernia. All of these might be found during a physical exam, such as when the doctor listens to these areas with a stethoscope or taps on the chest or abdomen.

If mesothelioma is a possibility, tests will be needed to make sure. These might include imaging tests, blood tests, and other procedures.

Imaging tests

Imaging tests use x-rays, radioactive particles, sound waves, or magnetic fields to create pictures of the inside of your body. Imaging tests might be done for a number of reasons, such as:

- To look at suspicious areas that might be cancer
- To learn how far cancer has spread
- To help determine if treatment is working

People thought to have mesothelioma may have one or more of these tests.

Chest x-ray

This is often the first test done if someone has symptoms such as a constant cough or shortness of breath. Findings that might suggest mesothelioma include an abnormal thickening of the pleura, calcium deposits on the pleura, fluid in the space between the lungs and the chest wall, or changes in the lungs themselves as a result of asbestos exposure.

Computed tomography (CT) scan

The CT scan uses x-rays to make detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you are lying on a narrow table. A computer then combines these into images of slices of the body.

CT scans are often used to help look for mesothelioma and to determine the exact location of the cancer. They can also help determine the stage (extent) of the cancer. For example, they can show if the cancer has spread to other organs. This can help determine if surgery might be a treatment option. Finally, CT scans can also be used to learn if treatment such as chemotherapy is shrinking or slowing the growth of the cancer.

A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken.

Before the test, you might have to drink a liquid called *oral contrast*. This helps outline the intestine so that certain areas are not mistaken for tumors. You might also need an IV (intravenous) line through which a different kind of contrast is injected. This helps better outline structures in your body. The injection can cause some flushing (redness and warm feeling). 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 any allergies (especially to iodine or shellfish) or have ever had a reaction to any contrast material used for x-rays.

Echocardiogram

This test uses sound waves to look at the heart. It may be done if your doctor suspects that you have fluid around your heart (a pericardial effusion). This test can also tell how well the heart is working. For the most common version of this test, you lie on a table while a technician moves an instrument called a *transducer* over the skin on your chest. A gel is often put on the skin first.

Positron emission tomography (PET) scan

For a PET scan, a radioactive substance (usually a type of sugar related to glucose, known as *FDG*) is injected into the blood. The amount of radioactivity used is very low. Because cancer cells grow quickly, they absorb more of the sugar than most other cells. After waiting about an hour, you lie on a table in the PET scanner for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body.

The picture from a PET scan is not as detailed as a CT or MRI scan, but it can provide helpful information about whether abnormal areas seen on these tests are likely to be cancerous or not. For example, it can give the doctor a better idea of whether a thickening of the pleura or peritoneum seen on a CT scan is more likely cancer or merely scar tissue. If you have been diagnosed with mesothelioma, your doctor may use this test to see if the cancer has spread to lymph nodes or other parts of the body. A PET scan can also be useful if your doctor thinks the cancer may have spread but doesn't know where.

Some machines can do both a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans make detailed images of the body's soft tissues. But MRI scans use radio waves and strong magnets instead of x-rays. A contrast material called *gadolinium* is often injected into a vein before the scan to better show details. This contrast is different than the one used for CT scans, so being allergic to one doesn't mean you are allergic to the other.

MRI scans can sometimes help show the exact location and extent of a tumor since they provide very detailed images of soft tissues. For mesotheliomas, they may be useful in looking at the diaphragm (the thin band of muscle below the lungs that helps us breathe), a possible site of cancer spread.

MRI scans take longer than CT scans – often up to an hour. You may have to lie inside a narrow tube, which can upset people with a fear of enclosed spaces. Special, more open MRI machines may be an option in some cases. The MRI machine makes buzzing and clicking noises that you might find disturbing. Some places will give you earplugs to help block this out.

Blood tests

Blood levels of certain substances are often higher in people with mesothelioma:

- Osteopontin
- Soluble mesothelin-related peptides (SMRPs), detected with the MesoMark® test

Mesothelioma can't be diagnosed with these blood tests alone, but high levels of these substances can make the diagnosis more likely. These tests are not routinely used in most doctors' offices because of their limited value.

Tests of fluid and tissue samples

Symptoms and test results may strongly suggest that a person has mesothelioma, but the actual diagnosis is made by removing cells from an abnormal area and looking at them under a microscope. This is known as a *biopsy*. It can be done in different ways, depending on the situation.

Removing fluid for testing

If there is a buildup of fluid in part of the body that might be due to mesothelioma, a sample of this fluid can be removed by inserting a thin, hollow needle through the skin and into the fluid. Numbing medicine is used on the skin before the needle is inserted. This may be done in a doctor's office or in the hospital. Sometimes ultrasound (or an echocardiogram) is used to guide the needle. These tests use sound waves to see inside the body.

This procedure has different names depending on where the fluid is:

- Thoracentesis removes fluid from the chest.
- Paracentesis removes fluid from the abdomen.
- Pericardiocentesis removes fluid from the sac around the heart.

The fluid is then tested for its chemical makeup and is looked at under a microscope to see if it contains cancer cells. If cancer cells are found, special tests might be done to see if the cancer is a mesothelioma, a lung cancer, or another type of cancer.

Even if no cancer cells are found in the fluid, a person might still have cancer. In many cases, doctors need to get an actual sample of the mesothelium (the pleura, peritoneum, or pericardium) to determine if a person has mesothelioma.

Needle biopsies

Suspected tumors in the chest are sometimes sampled by needle biopsy. A long, hollow needle is passed through the skin in the chest between the ribs and into the pleura. Imaging tests such as CT scans are used to guide the needle into the tumor so that small samples can be removed to be looked at under the microscope. This is often done using just numbing medicine.

Needle biopsy can also be used to get samples of the lymph nodes in the space between the lungs to see if the cancer has spread there (see "Endobronchial ultrasound needle biopsy").

Needle biopsies do not require a surgical incision or overnight hospital stay. But the downside is that sometimes the samples removed are not big enough to make an accurate diagnosis. This is especially true for mesothelioma. A more invasive biopsy method may be needed.

There is a slight chance that the needle could put a small hole in the lung during the biopsy. This can cause air to build up in the space between the lung and the chest wall (known as a *pneumothorax*). A small pneumothorax might not cause any symptoms. It may only be seen on an x-ray done after the biopsy, and it will often go away on its own. But a larger pneumothorax can make part of a lung collapse and might need to be treated. The treatment is placement of a small tube (a catheter) through the skin and into the space between the lungs. The tube is used to suck the air out in order to re-expand the lung and is left in place for a short time.

Endoscopic biopsies

Endoscopic biopsy is commonly used to diagnose mesothelioma. An endoscope is a thin, tube-like instrument used to look inside the body. It has a light and a lens (or tiny video camera) on the end for viewing and often has a tool to remove tissue samples. Endoscopes have different names depending on the part of the body where they're used.

Thoracoscopy: This procedure uses an endoscope called a *thoracoscope* to look at areas inside the chest. It can be used to look at the pleura and take tissue samples for biopsies.

Thoracoscopy is done in the operating room while you are under general anesthesia (in a deep sleep). The doctor inserts the thoracoscope through one or more small cuts made in the chest wall to look at the space between the lungs and the chest wall. This lets the doctor see possible areas of cancer and remove small pieces of tissue to look at under the microscope. The doctor can also sample lymph nodes and fluid and see if a tumor is growing into nearby tissues or organs.

Thoracoscopy can also be used as part of a procedure to keep fluid from building up in the chest. This is called *pleurodesis* and is discussed in the section "Palliative procedures used for malignant mesothelioma."

Laparoscopy: For this test, the doctor uses an endoscope called a *laparoscope* to look inside the abdomen and biopsy any peritoneal tumors. This is done in the operating room while you are under general anesthesia (in a deep sleep). The laparoscope is inserted into the abdomen through small cuts on the front of the abdomen.

Mediastinoscopy: If imaging tests such as a CT scan suggest that the cancer might have spread to the lymph nodes between the lungs, the doctor may want to sample some of them to see if they really contain cancer. The area between the lungs is called the *mediastinum*, and looking at it with an endoscope is called *mediastinoscopy*. This is done in an operating room while you are under general anesthesia (in a deep sleep).

A small cut is made in the front of the neck above the breastbone (sternum) and a thin, hollow, lighted tube (called a *mediastinoscope*) is inserted behind the sternum. Special instruments can be passed through this tube to take tissue samples from the lymph nodes along the windpipe and the major bronchial tube areas.

Lung cancers often spread to lymph nodes, but mesotheliomas do this less often. Testing the lymph nodes can help show whether a cancer is still localized or if it has started to spread, which might affect treatment options. It can also sometimes help tell lung cancers from mesotheliomas.

Endobronchial ultrasound needle biopsy: For this test, a bronchoscope (a long, thin, flexible, fiber-optic tube) with an ultrasound device at its tip is passed down the throat and into the windpipe. The ultrasound lets the doctor see the nearby lymph nodes. A hollow needle is then passed down the bronchoscope and through the airway wall into the nodes to take biopsy samples. This procedure may be done with either general anesthesia (where you are asleep), or with numbing medicine (local anesthesia) and light sedation.

Open surgical biopsy

Sometimes, endoscopic biopsies aren't enough to make a diagnosis, so more invasive procedures are needed. By making an incision in the chest (thoracotomy) or an incision in the abdomen (laparotomy) the surgeon can remove a larger sample of tumor or, sometimes, remove the entire tumor.

Testing the samples in the lab

No matter how they're obtained, all biopsy and fluid samples are sent to the pathology lab. There, a doctor will look at them under a microscope and test them to find out if they contain cancer cells (and if so, what type of cancer it is).

It's often hard to diagnose mesothelioma by looking at cells from fluid samples. It can even be hard to diagnose mesothelioma with tissue from small needle biopsies. Under the microscope, mesothelioma can often look like other types of cancer. For example, pleural mesothelioma can resemble some types of lung cancer, and peritoneal mesothelioma in women may look like some cancers of the ovaries.

For this reason, special lab tests are often done to help tell mesothelioma from some other cancers. To learn about some of the tests that might be done on tissue samples, see *Testing Biopsy and Cytology Specimens for Cancer*.

If mesothelioma is diagnosed, the doctor will also determine what type of mesothelioma it is, based on the patterns of cells seen in the microscope. Most mesotheliomas are classified as either epithelioid, sarcomatoid, or mixed/biphasic.

Pulmonary function tests

If mesothelioma has been diagnosed, pulmonary function tests (PFTs) may be done to see how well your lungs are working. This is especially important if surgery might be an option to treat the cancer. Surgery often requires removing part or all of a lung, so it's important to know how well the lungs are working to start with. These tests can give the surgeon an idea of whether surgery may be an option, and if so, how much lung can safely be removed safely.

There are a few different types of PFTs, but they all basically have you breathe in and out through a tube connected to a machine that measures your lung function.

How is malignant mesothelioma staged?

The stage of a cancer is a standard way for doctors to sum up how far the cancer has spread. Your treatment and prognosis (outlook) depend, to a large extent, on the cancer's stage.

The stage of a mesothelioma is based on the results of physical exams, biopsies, and imaging tests (CT scan, PET scan, etc.), which are described in the section "How is malignant mesothelioma diagnosed?"

Pleural mesothelioma, the most common type, is the only mesothelioma for which a formal staging system exists.

The TNM staging system

The system most often used to describe the growth and spread of pleural mesothelioma is the American Joint Committee on Cancer (AJCC) **TNM** staging system. The TNM system is based on 3 key pieces of information:

- T sums up the extent of spread of the main (primary) tumor.
- N describes the spread of cancer to nearby (regional) lymph **nodes**. Lymph nodes are small bean-shaped collections of immune system cells to which cancers often spread first.
- M indicates whether the cancer has spread (**metastasized**) to other organs of the body. (The most common sites are the pleura on the other side of the body, the lungs, and the peritoneum.)

Numbers or letters appear after T, N, and M to provide more details about each of these factors. Higher numbers mean the cancer is more advanced.

T groups

TX: The main tumor can't be assessed for some reason.

T0: There is no evidence of a main tumor (the cancer is found elsewhere instead).

T1: Mesothelioma is in the pleura lining the chest wall on one side of the chest. It may or may not also affect the pleura lining the diaphragm (the thin breathing muscle below the lungs) or the mediastinum (the space between the lungs). It may also have spread to the pleura covering the lung.

T2: Mesothelioma is in the pleura lining the chest wall on one side of the chest. It is also in the pleura coating the diaphragm, the mediastinum, and the lung. It also has grown into at least one of the following:

- The diaphragm
- The lung itself

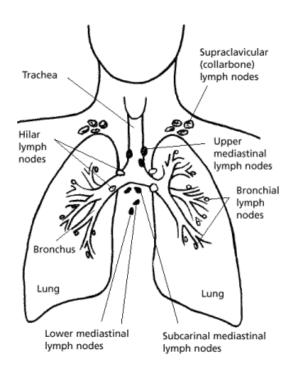
T3: The mesothelioma has grown further but may still possibly be removed with surgery. The tumor is in the pleura lining the chest wall on one side of the chest, as well as the pleura coating the lung, the diaphragm, and the mediastinum. It also has grown into at least one of the following:

- The first layer of the chest wall (called the *endothoracic fascia*)
- The fatty tissue in the mediastinum
- A single place in the deeper layers of the chest wall
- The surface of the pericardium (outer covering layer of the heart)

T4: The mesothelioma has grown too far to be removed completely with surgery. The tumor has grown into the pleura lining the chest wall on one side of the chest, as well as the pleura coating the lung, diaphragm, and mediastinum on the same side. It also has grown into at least one of the following:

- More than one place in the deeper layers of the chest wall, including the muscle or ribs
- Through the diaphragm and into the peritoneum
- Any organ in the mediastinum (esophagus, trachea, thymus, blood vessels)
- The spine
- Across to the pleura on the other side of the chest
- Through the heart lining (pericardium) or into the heart itself

N groups



NX: The nearby lymph nodes can't be assessed.

N0: No spread to nearby lymph nodes.

N1: Spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (called *hilar* or *bronchial* lymph nodes) on the same side as the main tumor.

N2: Spread to other lymph nodes on the same side as the main tumor, such as the *subcarinal* (around the point where the windpipe branches into the left and right bronchi) and the *mediastinal* lymph nodes. Also includes spread to the lymph nodes in the space just behind the breastbone (called *internal mammary* lymph nodes) and those near the diaphragm (called *peridiaphragmatic*).

N3: Spread to lymph nodes near the collarbone on either side (*supraclavicular* lymph nodes), and/or spread to hilar or mediastinal lymph nodes on the side opposite the main tumor.

M groups

M0: No spread to distant organs or areas.

M1: The cancer has spread to distant sites. This can be to distant lymph nodes or to other organs.

Stage grouping for pleural mesothelioma

Once the T, N, and M categories have been assigned, this information is combined in a process called *stage grouping* to assign an overall stage of I, II, III, or IV. Patients with lower stage numbers tend to have a better prognosis.

Stage I

T1, N0, M0: Mesothelioma has grown into the pleura lining the chest wall on one side of the chest. It might or might not also affect the pleura lining the diaphragm (the breathing muscle) or the mediastinum (the space between the lungs). It may also have spread to the pleura covering the lung (T1). It has not spread to the lymph nodes (N0) or to distant sites (M0).

Stage II

T2, N0, M0: Mesothelioma has grown into the pleura lining the chest wall on one side of the chest. It also is in the pleura coating the diaphragm, the mediastinum, and the lung. The cancer has also grown into the diaphragm or the lung itself (T2). It has not spread to the lymph nodes (N0) or to distant sites (M0).

Stage III

Either of the following:

T1 or T2, N1 or N2, M0: Mesothelioma has grown into the pleura lining the chest on one side, and might or might not have grown into the pleura lining the lung, the diaphragm, or the mediastinum. It might also have grown into the muscle of the diaphragm or the lung itself (T1 or T2). It has spread to lymph nodes in the chest on the same side as the main tumor (N1 or N2). It has not spread to distant sites (M0).

OR

T3, N0 to N2, M0: Mesothelioma is in the pleura lining the chest on one side, and has grown into the first layer of the chest wall, the fatty tissue in the mediastinum, a single place in the deeper layers of the chest wall, or the outer covering layer of the heart (T3). It might or might not have spread to lymph nodes in the chest on the same side as the tumor, but it has not spread to lymph nodes near the collarbone or on the opposite side of the chest (N0, N1, or N2). It has not spread to distant sites (M0).

Stage IV

Any of the following:

T4, any N, M0: Mesothelioma has grown into the pleura lining the chest on one side and has grown into more than one place in the deeper layers of the chest wall (including the muscle or ribs), through the diaphragm and into the peritoneum, into any organ in the mediastinum, into the spine, across to the pleura on the other side of the chest, and/or through the heart lining or into the heart itself (T4). It might or might not have spread to lymph nodes (any N). It has not spread to distant sites (M0).

OR

Any T, N3, M0: The tumor may or may not have grown into nearby tissues (any T). It has spread to lymph nodes near the collarbone on either side and/or to hilar or mediastinal lymph nodes on the side opposite the main tumor (N3). It has not spread to distant sites (M0).

OR

Any T, any N, M1: The mesothelioma might or might not have grown into nearby tissues (any T). It might or might not have spread to the lymph nodes (any N). It has spread to distant sites (M1).

Resectable versus unresectable cancer

The TNM system divides mesotheliomas into several stages that help give doctors an idea about a person's prognosis (outlook). But for treatment purposes, doctors often use a simpler system based on whether the cancer is likely to be resectable (where all visible tumor can be removed by surgery) or unresectable.

In general terms, most stage I, II, and III mesotheliomas are potentially resectable, but there are exceptions. Whether or not the cancer can be removed depends not only on how far the tumor has grown, but also on its subtype (most doctors believe only epithelioid and mixed/biphasic tumors are potentially resectable), where it is located, and if the patient is healthy enough to have surgery.

Even for resectable mesotheliomas, in most cases cancer cells that can't be seen are left behind after surgery. For this reason, many doctors use other forms of treatment (radiation therapy and/or chemotherapy) along with surgery when possible.

Other prognostic factors

Stage is an important factor in predicting a person's prognosis (outlook), but other factors also play a role. Some factors linked to longer survival times include:

- Good performance status (being able to carry out normal tasks of daily life)
- Younger age
- Female gender
- Epithelioid subtype
- Not having chest pain
- No significant weight loss
- Normal levels of a substance in the blood called LDH
- Normal red blood cell counts, white blood cell counts, and blood platelet counts

Survival statistics for mesothelioma

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some people want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or might not even want to know them. If you don't want to read about the survival statistics for mesothelioma, stop reading here.

To get survival rates, doctors have to look at people who were treated at least several years ago. Although the numbers below are among the most current we have available, improvements in treatment since then could result in a better outcome for people now being diagnosed with mesothelioma.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they can't predict what will happen in any person's case. Knowing the type and the stage of a cancer is important in estimating outcome. But many other factors can affect survival, such as a person's age and overall health, the treatment received, and how well the cancer responds to treatment. Even taking these other factors into account, survival rates are at best rough estimates. Your doctor can tell you if the numbers below apply, as he or she is familiar with your situation.

Mesothelioma is a serious disease. By the time the symptoms appear and cancer is diagnosed, the disease is often advanced. Regardless of the extent of the cancer, mesothelioma can be very hard to treat.

5-year survival rate

When discussing cancer survival statistics, doctors often use a number called the *5-year survival rate*. The 5-year survival rate is the percentage of people who live *at least* 5 years after their cancer is diagnosed. Of course, some people live longer than 5 years.

Relative 5-year survival takes the proportion of people with cancer that have survived 5 years and compares it to the survival expected in a similar group of people without the cancer. This helps adjust for deaths from causes other than the cancer. Based on data from the National Cancer Institute's SEER program, the relative 5-year survival rate for mesothelioma is between 5% and 10%. People diagnosed at a younger age tend to survive longer.

Median survival times

The numbers in the table below are from a large international study that looked at the median survival time of patients with *pleural* mesothelioma who were treated with surgery between 1995 and 2009. Median survival is the length of time it took for half the people in a certain group (like those with a certain type and stage of cancer) to die. It is kind of like an average – half the patients in the group live longer than that and half the patients don't.

Stage	Median Survival
I	21 months
II	19 months
III	16 months
IV	12 months

As a general rule, survival times are likely to be longer for people with mesotheliomas that can be operated on than for those with cancers that have spread too far to be removed. Other prognostic factors, such as those listed in the section "How is malignant mesothelioma staged?" can also affect survival.

How is malignant mesothelioma treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options. If you have mesothelioma, your cancer care team will recommend one or more treatment options for you to consider. This is an important decision and you should take time to think about all of your choices.

Making treatment decisions

After the cancer is found and staged, your cancer care team will discuss your treatment options with you. The main factors in selecting treatment for mesotheliomas are the location and extent of the tumor, whether it has spread to lymph nodes or other organs, and your health and personal preferences. Based on these factors, your treatment options may include:

- Surgery
- Radiation therapy
- Chemotherapy

More than one of these treatments may be used in many cases. To learn about the most common approaches to treating mesothelioma, see "Treatment of mesothelioma based on the extent of the cancer."

Mesothelioma can be hard to treat because it typically does not grow as a single tumor mass. It tends to spread along nearby surfaces, nerves, and blood vessels. This often makes it very hard to get rid of the cancer completely with surgery and/or radiation. For some people, palliative procedures might be used to help treat some symptoms of mesothelioma.

Because mesothelioma is a rare cancer, it has been hard for doctors to compare the value of different treatments. Only a few large clinical trials of treatments for mesothelioma have been done. In addition, many doctors have very little experience treating this disease. They usually refer patients to specialists who treat large numbers of mesothelioma patients at major medical centers.

You might have different types of doctors on your treatment team, depending on the stage of your cancer and your treatment options. These doctors may include:

- A thoracic surgeon: a doctor who treats diseases of the lungs and chest with surgery
- A **surgical oncologist**: a doctor who treats cancer with surgery
- A radiation oncologist: a doctor who treats cancer with radiation therapy.
- A **medical oncologist**: a doctor who treats cancer with medicines such as chemotherapy

• A **pulmonologist**: a doctor who specializes in medical treatment of diseases of the lungs

Many other specialists might be part of your treatment team as well, including other doctors, physician assistants (PAs), nurse practitioners (NPs), nurses, respiratory therapists, social workers, and other health professionals. See <u>Health Professionals</u>

Associated With Cancer Care for more on this.

Before deciding on a treatment plan, it's very important to have an idea of its likely benefits and possible risks. You will probably have many questions about the treatment options suggested. You can also find some other questions to ask in the section "What should you ask your doctor about malignant mesothelioma?"

Mesotheliomas are rare, so if time allows it's often a good idea to get a second opinion from a doctor who has a lot of experience in treating people with these cancers. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

Surgery for malignant mesothelioma

Surgery for mesothelioma may be done for 2 reasons:

- To try to cure the cancer (potentially curative surgery)
- To relieve pain and other symptoms caused by the tumor (palliative surgery)

Potentially curative surgery may be an option if you are in otherwise good health and the cancer has not spread too far to be removed completely. Unfortunately, even when the surgeon can remove all of the cancer that can be seen, some cancer cells are often left behind. These cells can grow and divide, causing the cancer to come back after surgery. Because of this, not all doctors agree on the exact role of surgery. In most cases it's not likely to cure you, but it may help you live longer. Still, potentially curative surgery is being done in some major cancer centers, and a small number of people who have had the surgery have had long remissions of their disease.

Palliative surgery may be an option if the tumor has already spread beyond where it started and would be hard to remove completely, or if you are too ill for a more extensive operation. The goal of this surgery is to relieve or prevent symptoms, as opposed to trying to cure the cancer.

Surgery for pleural mesothelioma

Surgery for pleural mesothelioma can be done either to help prevent or relieve symptoms or to try to remove all of the cancer. Unfortunately, these tumors often have spread too far to be removed completely. Sometimes, the surgeon might not be able to tell the full extent of the cancer – and therefore which type of surgery might be best – until the operation has started.

Extrapleural pneumonectomy (EPP): This is an extensive operation, but it may offer the best chance to remove all of the cancer for many patients. It's most often used when the surgeon thinks a cure is possible – typically in patients with resectable epithelioid mesothelioma that has not spread to the lymph nodes.

In this operation, the surgeon removes the lung on the side of the cancer along with the pleura lining the chest wall on that side, the diaphragm on that side, the pericardium (the sac around the heart), and nearby lymph nodes. The diaphragm and the pericardium are then reconstructed with man-made materials.

This is a difficult operation that is done only by experienced surgeons in large medical centers. You must be in good overall health with good lung function and no other serious illnesses to withstand this surgery. Several tests must be done beforehand to be sure you're healthy enough for this surgery. Major complications can occur in as many as 1 in 3 people who have this operation.

Pleurectomy/decortication (P/D): This is a less extensive operation in which all of the pleura lining the chest wall (on the side with the cancer) is removed, along with the pleura coating the lung on that same side. The pleura coating the mediastinum and the diaphragm is also removed. The lung and diaphragm are not removed.

In a slightly more extensive version of this operation (known as a radical or extended P/D), the diaphragm and/or pericardium are removed as well.

This surgery can be used to try to cure some early cancers, but it can also be used as a palliative procedure to relieve symptoms if the entire tumor can't be removed. It can help control the buildup of fluid, improve breathing, and lessen pain caused by the cancer.

Debulking (partial pleurectomy): The goal of this surgery is to remove as much of the mesothelioma as possible. In general, less tissue is removed in this operation than in a P/D procedure.

Possible side effects of surgery

The operations used to treat mesothelioma can have serious risks and side effects, although these depend on the extent of the surgery and the person's health beforehand. Serious complications of EPP can include bleeding, blood clots, wound infections, changes in heart rhythm, pneumonia, fluid buildup in the chest, and loss of lung function. Most of these are less common with less extensive operations.

Because the surgeon must often spread the ribs during surgery, the incision will hurt for some time afterward. Your activity will be limited for at least a month or two.

Surgery for peritoneal mesothelioma

Surgical treatment of peritoneal mesothelioma can be done either to help relieve symptoms or to remove the tumor from the wall of the abdomen and digestive organs. As is the case with pleural mesothelioma, these tumors often have spread too far to be removed completely.

Debulking: The goal of this surgery is to remove as much of the mesothelioma as possible. Sometimes this means removing pieces of the intestine as well.

After the cancer is debulked (but before the operation is finished), chemotherapy may be given into the abdomen. This is called *intraoperative chemotherapy*. If the chemotherapy drugs are heated, it is called *heated intraoperative* (or intraperitoneal) chemotherapy or *HIPEC*. In either treatment, the drugs are left in for a short time, and the incision is closed after they are removed.

Omentectomy: The omentum is an apron-like layer of fatty tissue that drapes over the organs inside the abdomen. Cancers in the peritoneum often spread to this tissue, so it may be removed as part of surgery for peritoneal mesothelioma.

Surgery for pericardial mesothelioma

Surgery can remove a mesothelioma from the pericardium (the sac around the heart).

Surgery for mesothelioma of the tunica vaginalis

Surgery for mesothelioma of the tunica vaginalis, which covers the testicles, rarely cures this cancer. Most of the time surgery is done when the tumor is mistaken for a hernia. The surgeon attempts to treat a suspected hernia and only realizes the diagnosis after the surgery has begun. This kind of mesothelioma typically can't be removed entirely.

For more on surgery as a treatment for cancer, see our document *A Guide to Cancer Surgery*.

Palliative procedures for malignant mesothelioma

Mesotheliomas can often be hard to remove or destroy completely. Still, treatments can often help keep the cancer under control for a time or relieve symptoms from it. For example, some types of surgery or radiation therapy might help keep the cancer in check. Chemotherapy might also be helpful.

If the mesothelioma is causing fluid to build up in the body, it can often cause trouble breathing or other problems. Procedures can sometimes be used to remove the fluid or help keep it from coming back.

Removal of fluid

Procedures such as thoracentesis, paracentesis, and pericardiocentesis can be used to remove fluid that has built up and is causing symptoms such as trouble breathing. In these procedures, a doctor uses a long, hollow needle to remove the fluid. These procedures are described in the section "How is malignant mesothelioma diagnosed?" The major drawback to these techniques is that the fluid often builds up again, so they might need to be repeated.

Pleurodesis

This procedure may be done to try to prevent fluid from building up in the chest. A small cut is made in the skin of the chest wall, and a hollow tube (called a *chest tube*) is placed into the chest so that the fluid can drain out. Then the doctor uses the tube to put a substance into the chest, such as talc mixed in a fluid (talc slurry), the antibiotic doxycycline, or the chemotherapy drug bleomycin. This irritates the linings of the lung (visceral pleura) and chest wall (parietal pleura) so that they stick together, sealing the space and preventing further fluid buildup. The tube is generally left in for a day or two to drain any new fluid. Pleurodesis can also be done during a thoracoscopy.

Shunt placement

A shunt is a device that allows fluid to move from one part of the body to another. For example, a pleuro-peritoneal shunt lets excess fluid in the chest move into the abdomen, where it is more likely to be absorbed by the body. This may be used if pleurodesis or other techniques are not effective.

The shunt is a long, thin, flexible tube with a small pump in the middle. In the operating room, the doctor inserts one end of the shunt into the chest space and the other end into the abdomen. (The pump part stays just under the skin over the ribs.) Once the shunt is in place, the patient pushes down on the pump several times to move the fluid from the chest to the abdomen. This is typically done a few times each day.

Catheter placement

This is another approach sometimes used to control fluid buildup. One end of the catheter (a thin, flexible tube) is placed in the chest or abdomen through a small cut in the skin, and the other end is left outside the body. This is done in a doctor's office or hospital. Once in place, the catheter can be attached to a special bottle or other device to drain fluid out on a regular basis.

Radiation therapy for malignant mesothelioma

Radiation therapy uses high-energy x-rays or particles to kill cancer cells. Mesotheliomas are often hard to treat with radiation therapy. They don't usually grow as single, distinct tumors, so it can be hard to aim radiation at them while avoiding nearby normal tissues. But new radiation therapy techniques may make this form of treatment more useful.

Uses of radiation therapy

Radiation therapy can be used in different ways to treat mesothelioma:

• It can be used after surgery to try to kill any small areas of cancer that couldn't be seen and removed during surgery. This is called *adjuvant radiation therapy*.

• It can be used as a palliative procedure to ease symptoms of mesothelioma such as shortness of breath, pain, bleeding, or trouble swallowing.

Types of radiation therapy

Two main types of radiation therapy can be used to treat mesothelioma:

External beam radiation therapy (EBRT): This type of radiation therapy uses x-rays from a machine outside the body to kill cancer cells. It is the most common form of radiation therapy for mesothelioma.

Before your treatments start, the medical team will take careful measurements to find the correct angles for aiming the radiation beams and the proper dose of radiation. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer. The treatment is much like getting an x-ray, but the radiation is much stronger. The procedure itself is painless. Most often, radiation treatments are given 5 days a week for several weeks.

With newer techniques, doctors can treat mesotheliomas more accurately while reducing the radiation reaching nearby healthy tissues such as the lungs. This might offer a better chance of increasing the success rate and reducing side effects.

For example, *intensity-modulated radiation therapy (IMRT)* is an advanced form of 3-dimensional radiation therapy. It uses a computer-driven machine that moves around the patient as it delivers radiation. It shapes the radiation beams to fit the tumor and aims them at the tumor from several angles, as well as adjusting the intensity (strength) of the beams to limit the dose reaching nearby normal tissues.

Brachytherapy: For this type of radiation therapy, a radiation source is put inside the body, in or near the cancer. The radiation given off travels only a very short distance, which limits the possible damage to nearby healthy tissues. Brachytherapy is seldom used for this type of cancer.

Possible side effects

Side effects of external radiation therapy can include fatigue and sunburn-like skin problems and hair loss where the radiation enters the body. These usually go away once treatment is finished. Chest radiation therapy can damage the lungs over time and lead to trouble breathing and shortness of breath. Abdominal radiation therapy may cause nausea, vomiting, diarrhea, and loss of appetite.

If radiation therapy is used together with chemotherapy, the side effects are often worse.

If you are having any side effects from radiation therapy, talk with your doctor. There are often ways to help control these symptoms.

For more on radiation therapy, see *Understanding Radiation Therapy: A Guide for Patients and Families*.

Chemotherapy for malignant mesothelioma

Chemotherapy (chemo) is treatment with anti-cancer drugs.

Uses of chemotherapy

For mesotheliomas that can be treated with surgery, chemo may be given before surgery to try to shrink the cancer and lower the risk of spread. This is called *neoadjuvant* therapy.

Chemo can also be given after surgery to try to kill any cancer cells that were left behind. This type of treatment, called *adjuvant therapy*, may help delay or prevent the cancer growing back.

For cancers that can't be removed with surgery, chemo may be the main treatment (alone or along with radiation therapy). Chemo may shrink the cancer or slow its growth, but it is very unlikely to make it go away completely.

How chemotherapy is given

Doctors usually give chemo in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Chemo cycles generally last about 3 to 4 weeks. Chemo is often not recommended for patients in poor health, but advanced age by itself is not a barrier to getting it.

There are 2 main ways chemo can be given to treat mesothelioma.

In *systemic* therapy, chemo is injected into a vein. The drug enters the bloodstream and travels throughout the body to reach and destroy the cancer cells wherever they may be.

Chemo drugs can also be placed directly into the body space where the cancer is – either *intrapleurally* (directly into the chest) or *intraperitoneally* (into the abdomen). This is done with a small catheter (tube) placed through a small cut in the chest or abdominal wall. Chemo drugs given this way are still absorbed into the bloodstream, but the highest concentrations of the drugs go directly to where the cancer cells are.

For intrapleural or intraperitoneal chemo, the drugs are sometimes heated before they are put directly into a body space (called *hyperthermic chemotherapy*), which may help them work better. Sometimes this treatment is given as a single dose in the operating room, right after surgery to remove the cancer. This approach is called *heated intraoperative chemotherapy*. It is more often used to treat peritoneal cancers, in which case it may be called *heated intraperitoneal chemotherapy* or HIPEC.

Chemotherapy drugs used for mesothelioma

Several chemo drugs can be used to treat mesothelioma, including:

• Pemetrexed (Alimta[®])

- Cisplatin
- Carboplatin
- Gemcitabine (Gemzar®)
- Methotrexate
- Vinorelbine
- Mitomycin
- Doxorubicin (Adriamycin®)

These may be given as combinations of 2 drugs, but single drugs can be used in people who may not be able to tolerate more than one drug.

When 2 drugs are used, most doctors give pemetrexed and cisplatin. Pemetrexed lowers levels of folic acid and vitamin B12 in the body, so patients get these as well to help avoid certain side effects. Other possible combinations include pemetrexed with carboplatin, or cisplatin with gemcitabine.

For HIPEC, either mitomycin or the combination of cisplatin plus doxorubicin is most often used.

Possible side effects

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cell are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemo, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs given and how long they are used for. Common side effects include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

These side effects usually go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about medicines to help reduce side effects, and let him or her know if you have side effects, so they can be managed effectively.

Some drugs can have other side effects. For example, cisplatin and carboplatin can damage nerves (called *neuropathy*). This can sometimes lead to hearing loss or symptoms in the hands and feet such as pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. This usually goes away once treatment is stopped, but it can last a long time in some people.

Be sure to report any side effects or changes you notice while getting chemo to your medical team so that you can get them treated promptly. In some cases, the doses of the drugs may need to be reduced or treatment may need to be delayed or stopped to keep the effects from getting worse.

To learn more about chemotherapy, see A Guide to Chemotherapy.

Clinical trials for malignant mesothelioma

You have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to learn more about promising new treatments or procedures.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get some newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of studies that might meet your needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute (NCI) toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

You must meet certain requirements to take part in any clinical trial, but if you qualify, it will be up to you whether or not to enter (enroll in) it.

To learn more about clinical trials, see Clinical Trials: What You Need to Know.

Complementary and alternative therapies for malignant mesothelioma

You might hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to social media groups and websites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help a person feel better. Some methods that are used along with regular treatment are: meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not be helpful, and a few have even been found to be harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delaying or interrupting your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It's easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country? Also be sure to talk to your cancer care team about any method you are thinking about using.

You can find more tips on what to look for and how to make these decisions in the "Complementary and Alternative Medicine" section of our website.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment of mesothelioma based on the extent of the cancer

The stage (extent) of a mesothelioma is an important factor in determining treatment options. But other factors, such as whether the doctor feels the cancer is resectable (all visible cancer can be removed by surgery), as well as a person's general health and preferences, also play a role.

Mesotheliomas can be hard to treat, whether the cancer is resectable or not. It's very important that you understand the goal of treatment before it starts – whether it is to try to cure the cancer or to help relieve symptoms – as well as the possible benefits and risks. This can help you make an informed decision when looking at your treatment options.

Resectable mesotheliomas

In general, most stage I and some stage II and III pleural mesotheliomas are potentially resectable, but there are exceptions. Whether a tumor is resectable is also based on the subtype (most doctors don't believe that sarcomatoid tumors are helped by resection), where it is in the body, how far it has grown into nearby tissues, and if the person is healthy enough to have surgery.

Many people with resectable pleural mesothelioma have their cancer removed by either pleurectomy/decortication (P/D) or extrapleural pneumonectomy (EPP). Surgery is more likely to result in long-term benefit in early stage cancers, where there is a better chance that most or all of the cancer can be removed. EPP might offer the best chance to remove the cancer, but it is a complex and extensive operation that is more likely to result in complications, and not all patients can tolerate it.

Patients with early-stage peritoneal mesotheliomas might also benefit from surgery that removes as much of the cancer as possible. This may be combined with heated intraperitoneal chemotherapy (HIPEC). Some patients have long remissions after this treatment. Surgery may also be helpful for some later-stage cancers, but the benefits are more likely to last only a short time.

Sometimes, the surgeon may think the cancer is resectable based on imaging tests (such as CT scans) done before surgery, but once the operation starts it becomes clear that not all of the cancer can be removed. In these cases the surgeon may switch to a less extensive operation like P/D (which is easier to tolerate) or even stop the surgery

altogether if it's not likely to be helpful. Treatment would then be the same as for unresectable mesotheliomas (see below).

Doctors are still studying whether giving chemotherapy (chemo) before surgery (neoadjuvant therapy) or giving chemo or radiation therapy after surgery (adjuvant therapy) is helpful, but not all doctors agree on the best course of treatment. Some doctors prefer to give chemo, either before or after surgery. Radiation therapy might be used after surgery, either alone or along with chemo.

If you are not healthy enough to have a major operation, you will be treated for unresectable mesothelioma (discussed below).

If you have symptoms because of fluid buildup in the chest or abdomen, other approaches such as thoracentesis/paracentesis or pleurodesis (described in the section on palliative procedures) may be helpful.

Because these cancers can be hard to treat, taking part in a clinical trial of a newer form of treatment may be a reasonable option. These types of studies are usually done in large medical centers.

Unresectable mesotheliomas

Stage IV mesotheliomas, as well as many earlier-stage mesotheliomas, can't be removed completely by surgery. This can be because of the extent or subtype of the cancer or because a person may not be healthy enough for an operation.

Chemo is the main treatment for these cancers. It may improve symptoms and shrink or slow the growth of the cancer for a time. Although chemo may help people live longer, it's very unlikely to cure these cancers. Before starting treatment, the goals of treatment should be clear to you and your family.

In people with early-stage mesotheliomas that are likely to grow slowly and aren't causing any symptoms, watching them closely at first may be a reasonable option. Treatment can then be started if there are signs that the cancer is growing quickly or if it starts to cause symptoms.

Because these cancers can be hard to treat, taking part in a clinical trial of a newer form of treatment may be a reasonable option.

In many cases, treatment aimed at relieving symptoms and making you more comfortable may be a good choice. This could include treatments that prevent or reduce fluid buildup in the body, such as thoracentesis/paracentesis or pleurodesis (described in the section on palliative procedures). Sometimes pleurectomy/decortication can help with breathing and pain in the chest.

Pain management is another important aspect of care for these cancers. Some minor operations and types of radiation therapy can help relieve pain if needed. Doctors can also prescribe strong pain-relieving drugs. Some people with cancer are worried about taking opioid drugs (such as morphine) for fear of being sleepy all the time or becoming addicted to them. But many people get very effective pain relief from these medicines

without serious side effects. It's very important to let your cancer care team know if you are having pain so that it can be treated effectively.

Recurrent mesotheliomas

Cancer is called *recurrent* when it come backs after treatment. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the brain or liver). Mesotheliomas often come back after the initial treatment. If this happens, further treatment options depend on where the cancer is, what treatments have already been used, and a person's general health.

In most cases the options will be similar to those listed above for unresectable mesotheliomas. For example, chemo or radiation therapy may be used to try to shrink or slow the growth of the cancer and to relieve any symptoms. Because recurrent cancers can often be hard to treat, clinical trials of new types of treatment may be a good option. For more information on dealing with a recurrence, see *When Your Cancer Comes Back: Cancer Recurrence*.

What should you ask your doctor about malignant mesothelioma?

It's important to have honest, open discussions with your cancer care team. You should feel free to ask any question, no matter how small it might seem. Here are some questions you might want to ask:

- What kind of mesothelioma do I have?
- Has my cancer spread beyond where it started?
- What is the stage (extent) of the cancer, and what does that mean?
- Is my cancer likely to be resectable (removable by surgery)?
- Do I need other tests before we can decide on treatment?
- Do I need to see any other types of doctors?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion? Can you recommend someone?
- What are my treatment options?
- What is the goal of treatment?
- What do you recommend and why?
- How quickly do we need to decide on treatment?

- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- What risks or side effects are there to the treatments you suggest?
- How will treatment affect my daily activities?
- What will we do if the treatment doesn't work or if the cancer recurs?
- What type of follow-up might I need after treatment?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times. Or you may want to ask if you qualify for any clinical trials.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, can answer some of your questions. To find out more about speaking with your health care team, see *Talking With Your Doctor*.

What happens after treatment for malignant mesothelioma?

For some people with mesothelioma, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about the cancer coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are leading full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* talks more about this.

For many people, the mesothelioma may never go away completely. These people may get regular treatments with chemotherapy, radiation therapy, or other therapies to help keep the cancer under control and help relieve symptoms from it. Learning to live with cancer that doesn't go away can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

If you have completed treatment, your doctors will still want to watch you closely. It's very important to keep all follow-up appointments. During these visits, your doctors will ask about symptoms, examine you, and may order blood tests (such as the osteopontin or MesoMark tests) or imaging tests such as CT scans or PET scans. There is no widely agreed upon follow-up schedule for people with mesothelioma. Your doctor will most

likely want to see you fairly often (at least every few months or so) at first. The time between visits may be extended if there are no problems.

Follow-up is needed to check for signs of cancer recurrence or spread, as well as possible side effects of certain treatments. This is a good time for you to ask your health care team any questions you might have and to discuss any concerns.

Almost any cancer treatment can have side effects. Some can last for weeks or months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

If the cancer does come back, further treatment will depend on where the cancer is, what treatments you've had before, and your health. For more on how recurrent cancer is treated, see the section "Treatment of mesothelioma based on the extent of the cancer." For more general information on dealing with a recurrence, see *When Your Cancer Comes Back: Cancer Recurrence*.

Seeing a new doctor

At some point after your treatment, you may be seeing a new doctor who doesn't know anything about your medical history. It's important to be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have the following information handy (and always keep copies for yourself):

- A copy of your pathology report(s) from any biopsies or surgeries
- Copies of imaging tests (such as x-rays or CT or MRI scans), which can usually be stored digitally (on a DVD, etc.)
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that the doctor wrote when you were sent home
- If you had radiation therapy, a summary of the type and dose of radiation and when and where it was given
- If you had chemotherapy, a list of your drugs, drug doses, and when you took them
- The names and contact information of the doctors who treated your cancer

It's also very important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen. For more information about health insurance, see *Health Insurance and Financial Assistance for the Person With Cancer*.

Lifestyle changes after malignant mesothelioma

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Make healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they might not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment causes weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits. For more about this, see *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Ouestions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a bone-weary exhaustion that often doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them

to be active and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it's normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. If you haven't been active in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new activity program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to learn to balance activity with rest. It's OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more on dealing with fatigue, see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it can help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

Getting regular physical activity also plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

Can I lower my risk of the cancer progressing or coming back?

Most people want to know if there they can make certain lifestyle changes to reduce their risk of cancer growing or coming back. Unfortunately, for most cancers there isn't much solid evidence to guide people. This doesn't mean that nothing will help — it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or preventing it from coming back.

At this time, not enough is known about mesothelioma to say for sure if there are things you can do that will be helpful. Adopting healthy behaviors such as not smoking, eating well, and staying at a healthy weight might help, but no one knows for sure. However, we do know that these types of changes can have positive effects on your health that can extend beyond your risk of cancer.

So far, no dietary supplements have been shown to clearly help lower the risk of mesothelioma progressing or coming back. Again, this doesn't mean that none will help, but it's important to know that none have been proven to do so.

How might having malignant mesothelioma affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationships with those around you. Unexpected issues may also cause concern. For instance, you might be stressed by financial concerns resulting from your treatment. You might also see your health care team less often after treatment and have more time on your hands. These changes can make some people anxious.

Almost everyone who is going through or has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, religious or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It's not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you don't include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You may also want to read our booklet *Distress in People with Cancer* or in the Emotional Side Effects section of our website.

If treatment of malignant mesothelioma stops working

If cancer keeps growing or comes back after one kind of treatment, it may be possible to try another treatment plan that might still cure the cancer, or at least keep it under control enough to help you live longer and feel better. Clinical trials also might offer chances to try newer treatments that could be helpful. But when many different treatments have been

tried and the cancer is still growing, even newer treatments might no longer be helpful. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides, including treatment side effects. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer – when you have been through many treatments and nothing's working anymore. Your doctor might offer you new options, but at some point you need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. Your doctor can estimate how likely it is the cancer will respond to treatment you're considering. For instance, the doctor may say that more treatment might have about a 1 in 100 chance of working. Some people are still tempted to try this. But it's important to have realistic expectations if you do choose this plan.

Palliative care

No matter what you decide to do, it's important that you feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but it's not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose – the main goal of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation or chemo might be used to help relieve pain caused by the cancer. But this is not the same as treatment to try to cure the cancer.

Hospice care

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. To learn more about hospice, see *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends – times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've

always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

You can learn more about the changes that occur when curative treatment stops working, and about planning ahead for yourself and your family, see *Nearing the End of Life* and *Advance Directives*.

What's new in malignant mesothelioma research and treatment?

There is always research going on in the area of mesothelioma. Scientists are looking for better ways to prevent, diagnose, and treat mesothelioma. Despite recent progress, much remains to be learned about the best way to treat these cancers.

Causes and prevention

Some research is focused on learning exactly how asbestos changes mesothelial cells and their DNA to cause these cancers. Understanding how these fibers produce cancer might help us develop ways to prevent those changes.

The role of asbestos in increasing the risk of mesothelioma is a definite public health concern. Researchers are learning more about which asbestos fibers can cause cancer, how they cause it, and what levels of exposure might be considered safe. Now that the dangers of asbestos are known, we can limit or stop exposure in homes, public buildings, and the workplace. Unfortunately, regulations protecting workers from asbestos exposure are much less stringent in some countries than in others.

Research is also under way to clarify the role (if any) of SV40, a virus that has been linked to mesothelioma in some studies.

Treatment

Mesothelioma remains a difficult cancer to treat, and doctors are constantly trying to improve on current approaches. The exact roles of surgery, radiation therapy, and chemotherapy in the treatment of mesothelioma are still being studied. Combinations of these treatments are now being tested and may provide the most promising option for some patients. Newer types of treatment now being studied may give patients and their doctors even more options.

Chemotherapy

Some chemotherapy drugs can shrink or slow the growth of mesotheliomas, but in most cases the effects last for a limited time. Studies are underway to test newer chemotherapy drugs.

Photodynamic therapy

Another technique now being studied is photodynamic therapy (PDT). For this treatment, a light-activated drug is injected into a vein. The drug spreads throughout the body and tends to collect in cancer cells. A few days later (usually in the operating room, just after surgery), a special red light on the end of a tube is placed into the chest. The light causes a chemical change that activates the drug and kills the cancer cells. Since the drug is only active in the areas exposed to the special light, this approach might cause fewer side effects than using drugs that spread throughout the body. Several clinical trials are now studying the use of PDT for mesothelioma. To find out more about PDT, see *Photodynamic Therapy*.

Targeted drugs

In general, chemo drugs have a limited effect against mesothelioma. As researchers have learned more about the changes in cells that cause cancer, they have developed newer drugs that target these changes. Targeted drugs work differently from standard chemo drugs. They sometimes work when chemo drugs don't, and they often have different (and less severe) side effects.

Sunitinib (Sutent) is an example of a targeted drug that has shown promise in some studies.

Other new drugs have different targets. For example, some new drugs target mesothelin, a protein found in high levels in mesothelioma cells. To learn more about targeted therapy drugs, see *Targeted Therapy*.

Other newer forms of treatment

Because standard treatments often have limited usefulness against mesothelioma, researchers are studying other new types of treatment as well.

Gene therapy: A newer type of treatment being tested on mesothelioma is *gene therapy*, which attempts to add new genes to cancer cells to make them easier to kill. One approach to gene therapy uses special viruses that have been modified in the lab. The virus is injected into the pleural space and infects the mesothelioma cells. When this infection occurs, the virus injects the desired gene into the cells. In one version of this approach, the virus carries a gene that helps turn on the immune system to attack the cancer cells. Early studies of this approach have found it may shrink or slow the growth of mesothelioma in some people, but more research is needed to confirm this.

Immunotherapy: Other new treatments called *cancer vaccines* are also aimed at getting the immune system to attack the cancer. In one approach, immune cells are removed from a patient's blood and treated in the lab to get them to react to tumor cells. The immune cells are then given back to the patient as blood transfusions, where it is hoped they will cause the body's immune system to attack the cancer. This approach is now being studied in clinical trials.

Another form of immunotherapy being studied is a drug called tremelimumab, which targets a certain immune cells and takes the brakes off the immune system.

To learn more, see Cancer Immunotherapy.

Virus therapies: Researchers are also studying the use of specially designed viruses to treat mesothelioma. These viruses can be put into the pleural space, where the hope is that they can either infect and kill the cancer cells directly, or cause the immune system to attack the cancer cells. These approaches are still in the early phases of clinical trials.

Additional resources for malignant mesothelioma

More information from your American Cancer Society

Here is more information you might find helpful. You can read them online or order free copies of our documents from our toll-free number, 1-800-227-2345.

Dealing with diagnosis and treatment

Health Professionals Associated With Cancer Care

<u>Talking With Your Doctor</u> (also in Spanish)

After Diagnosis: A Guide for Patients and Families (also in Spanish)

Coping With Cancer in Everyday Life (also in Spanish)

Living with cancer

Distress in People With Cancer

Anxiety, Fear, and Depression

Nutrition for the Person With Cancer: A Guide for Patients and Families (also in Spanish)

Living With Uncertainty: The Fear of Cancer Recurrence

When Cancer Doesn't Go Away

When Your Cancer Comes Back: Cancer Recurrence

Guide to Controlling Cancer Pain (also in Spanish)

Understanding cancer treatments

A Guide to Cancer Surgery (also available in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Their Families (also available in Spanish)

A Guide to Chemotherapy (also available in Spanish)

Clinical Trials: What You Need to Know (also available in Spanish)

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

What It Takes to Be a Caregiver

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also available in Spanish)

Helping Children When a Family Member Has Cancer: Dealing With Diagnosis (also available in Spanish)

Work, insurance, and finances

In Treatment: Financial Guidance for Cancer Survivors and Their Families (also in Spanish)

Health Insurance and Financial Assistance for the Cancer Patient

Returning to Work After Cancer Treatment

Working During Cancer Treatment

Carcinogens and cancer

Asbestos (also available in Spanish)

If treatment stops working

Nearing the End of Life

Advance Directives

Hospice Care

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

Information on asbestos

Agency for Toxic Substances and Disease Registry

Toll-free number: 1-800-232-4636 Website: www.atsdr.cdc.gov

Offers information on toxic substances, including a special section on asbestos with fact sheets and video information

Environmental Protection Agency

Phone number: 1-202-272-0167

Website: www.epa.gov

Has information about asbestos at www2.epa.gov/asbestos

Occupational Safety and Health Administration

Toll-free number: 1-800-321-6742 (1-800-321-OSHA)

Website: www.osha.gov

Addresses safety and health at work; contains a fact sheet on asbestos at www.osha.gov/Publications/OSHA3507.html; also has an entire section on asbestos at www.osha.gov/SLTC/asbestos

Information on mesothelioma and cancer in general

Mesothelioma Applied Research Foundation

Toll-free number: 1-877-363-6376 (1-877-END-MESO)

Website: www.curemeso.org

Has information on mesothelioma, peer support via other patients and families dealing with mesothelioma, and referrals to clinical trials and doctors who specialize in mesothelioma

National Cancer Institute

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)

Website: www.cancer.gov

Part of the US National Institutes of Health, the NCI provides information on all types of cancer, living with cancer, support information for families of people with cancer, research, and more

National Comprehensive Cancer Network (NCCN)

Website: www.nccn.org

Made up of experts from many of the nation's leading cancer centers, the NCCN develops guidelines for doctors to use when treating patients. Some of these guidelines, including one on pleural mesothelioma, are available in versions for patients as well.

National Coalition for Cancer Survivorship

Toll-free number: 1-888-650-9127

1-877-NCCS-YES (622-7937) for some publications and Cancer Survivor Toolbox®

orders

Website: www.canceradvocacy.org

Offers information on work, health insurance, and more. The Cancer Survival Toolbox is a free, self-learning audio program to help cancer survivors and caregivers develop practical tools needed to deal with the diagnosis, treatment and challenges of cancer. Listen online or order CDs. Also in Spanish and Chinese

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

References: Malignant mesothelioma detailed guide

Alexander HR Jr, Bartlett DL, Pingpank JF, et al. Treatment factors associated with long-term survival after cytoreductive surgery and regional chemotherapy for patients with malignant peritoneal mesothelioma. *Surgery*. 2013;153:779-786.

American Joint Committee on Cancer. Pleural mesothelioma. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010: 271-274.

Arrieta Ó, Medina LA, Estrada-Lobato E, et al. First-line chemotherapy with liposomal doxorubicin plus cisplatin for patients with advanced malignant pleural mesothelioma: phase II trial. *Br J Cancer*. 2012;106:1027-1032.

Calabrò L, Morra A, Fonsatti E, et al. Tremelimumab for patients with chemotherapy-resistant advanced malignant mesothelioma: An open-label, single-arm, phase 2 trial. *Lancet Oncol*. 2013;14:1104-1111.

Haithcock BE, Zagar TM, Zhang L, Stinchcombe TE. Chapter 73: Diseases of the pleura and mediastinum. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Hegmans JP, Veltman JD, Lambers ME, et al. Consolidative dendritic cell-based immunotherapy elicits cytotoxicity against malignant mesothelioma. *Am J Respir Crit Care Med*. 2010;181:1383-1390.

Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER web site, April 2014.

Mirarabshahii P, Pillai K, Chua TC, Pourgholami MH, Morris DL. Diffuse malignant peritoneal mesothelioma--an update on treatment. *Cancer Treat Rev.* 2012;38:605-612.

^{*}Inclusion on this list does not imply endorsement by the American Cancer Society.

National Cancer Institute. Physician Data Query (PDQ). Malignant Mesothelioma: Treatment. 2014. Accessed at

www.cancer.gov/cancertopics/pdq/treatment/malignantmesothelioma/HealthProfessional on March 4, 2015.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Malignant Pleural Mesothelioma. V.1.2015. Accessed at www.nccn.org/professionals/physician_gls/pdf/mpm.pdf on March 4, 2015.

Nowak AK, Millward MJ, Creaney J, et ak. A phase II study of intermittent sunitinib malate as second-line therapy in progressive malignant pleural mesothelioma. *J Thorac Oncol.* 2012;7:1449-1456.

Pan X, Day W, Wang W, et al. Residential proximity to naturally occurring asbestos and mesothelioma risk in California. *Am J Resp Crit Care*. 2005;172:1019-1025.

Pass HI, Carbone M, Krung LM, Rosenzweig KE. Chapter 114: Benign and malignant mesothelioma. 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.

Price B, Ware A. Mesothelioma trends in the United States: An update based on Surveillance Epidemiology and End Results program date for 1973-2003. *Am J Epidemiol*. 2004;159:107-112.

Robinson BWS, Lake RA. Advances in malignant mesothelioma. *N Engl J Med*. 2005;353:1591-1603.

Rusch VW, Giroux D, Kennedy C, et al; IASLC Staging Committee. Initial analysis of the international association for the study of lung cancer mesothelioma database. *J Thorac Oncol.* 2012;7:1631-1639.

Sterman DH, Haas A, Moon E, et al. A trial of intrapleural adenoviral-mediated interferon-α2b gene transfer for malignant pleural mesothelioma. *Am J Respir Crit Care Med.* 2011;184:1395-1399.

Testa JR, Cheung M, Pei J, et al. Germline BAP1 mutations predispose to malignant mesothelioma. *Nat Genet*. 2011;43:1022-1025.

Tsao AS, Wistuba I, Roth JA, Kindler HL. Malignant pleural mesothelioma. *J Clin Oncol*. 2009;27:2081-2090.

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