

A Patient's Guide to Mesothelioma



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MESOTHELIOMA IS A RARE CANCER, with 2,000 to 3,000 new cases diagnosed each year, and understanding the disease is important in making decisions about care and treatment.

MESOTHELIOMA FORMS in the mesothelium, a protective membrane covering internal organs, such as the lungs and heart. The mesothelium is made up of two layers—one surrounding the organ itself and the other forming an outer sac. Between the layers is a lubricating fluid that lessens friction between the membranes and permits the organs to glide smoothly against each other. This is particularly important to the heart and lungs, because they produce significant movement as they function.

Mesothelioma is defined by the site of the primary tumor. Pleural mesothelioma, in which cancer cells surround the lungs and/or the chest wall, accounts for about 85 percent of malignant mesotheliomas. Mesothelioma can also grow across the thin mesothelial tissue that lines the abdomen (peritoneum) or, rarely, the heart or testicles.

Mesothelioma is different from other cancers because it's tightly linked with an environmental cause—**asbestos exposure**, which accounts for the majority of cases. Most mesothelioma patients worked or lived in a place where they were exposed to asbestos. Typical mesothelioma patients

worked in shipyards or as miners and are men age 60 and older, but family members of these workers have also developed the disease—many with relatively little direct exposure. Also, because mesothelioma can take decades to develop, most patients are older at diagnosis.

The geographic distribution of this disease is not uniform across the United States, with the highest death rates appearing in the Northeastern states, along the Pacific Coast, and in Illinois, Florida, Wyoming, and Colorado. As with the demographic imbalance, the geographic distribution can also be explained by asbestos exposure—the regions with the highest death rates are (or were) home to either factories that manufactured asbestos-containing products or shipbuilding facilities (asbestos materials were commonly used as insulation in ships).

Although the average patient survives only four to 18 months after diagnosis, and only 10 percent of patients survive at least five years, there have been reports of long-term survivors who have no evidence of disease many years following treatment.



Causes & Risk Factors

ASBESTOS EXPOSURE IS THE MOST COMMON cause of mesothelioma. The term “asbestos” actually refers to several minerals with shared properties: long, flexible fibers that are resistant to stretching, heat, and corrosion. It’s because of these properties that asbestos was used in products such as insulation, roofing, floor and ceiling tiles, and brake pads.

Though the asbestos industry launched in the late 1800s, scientists didn’t link the mineral to mesothelioma until the 1950s. In the United States, asbestos continued to be mined and used—particularly for insulation—until the 1980s.

Of the various types of asbestos, the fibers most commonly used in the United States are chrysotile (white asbestos), crocidolite (blue asbestos), and amosite (brown asbestos). Chrysotile is most widely used because its fibers are curled, a property that makes it less likely to fragment than the other types of asbestos. Crocidolite and amosite are typically used in limited, specialized applications because their needle-like structure makes them highly susceptible to fragmenting. This is important because if asbestos is easily crushed, it remains airborne longer, which increases the likelihood of inhaling the fibers that cause mesothelioma.

Generally, it takes 20 to 40 years or more for mesothelioma to develop following asbestos exposure. The exact means by which asbestos causes cancer has not yet been fully determined, but it is known when asbestos is inhaled, about two-thirds of the fibers are eliminated from the body by coughing or swallowing. The remaining fibers travel through the airways, and some may reach the alveoli, the tiny air sacs in the lungs. Although the

method by which asbestos fibers arrive at the mesothelium is not certain, it is likely that this journey takes years, a belief that fits with the extended period of time necessary to develop mesothelioma.

It has never been established if there are any “safe” levels of asbestos exposure. However, there is at least circumstantial evidence that even low environmental levels of asbestos exposure can increase the risk of mesothelioma.

Interestingly, smoking is not a risk factor for mesothelioma. However, smoking does increase the risk of lung cancer, which is frequent in people with asbestos exposure. Thus, people with both a history of smoking and asbestos exposure have an elevated risk of developing lung cancer—approximately 60-fold higher than nonsmokers with no asbestos exposure.

While asbestos is the most common cause of mesothelioma, certain characteristics of the disease suggest that asbestos exposure is not the only cause. Other suspects include:

SIMIAN VIRUS 40

Due to conflicting research, perhaps the most controversial link to mesothelioma is exposure to simian virus 40 (SV40), a virus that contaminated polio vaccines during the 1950s and 1960s. In the '50s, monkeys were used to develop a vaccine against polio, but in 1961, it was discovered that these monkeys were infected with SV40, which meant the polio vaccines were likely contaminated. Shortly thereafter, animal studies showed that SV40 was capable of causing cancer, producing significant alarm regarding the cancer-causing potential of the contaminated polio vaccines.

Who's at Risk?

Some research supports the possibility that SV40 and asbestos may work together to cause mesothelioma. For instance, cells with chromosomal abnormalities (such as those caused by asbestos exposure) can gain cancer-like characteristics more easily when infected with SV40 compared to cells with normal chromosomes.

ERIONITE

Erionite is a non-asbestos mineral fiber that is similar in physical characteristics to crocidolite. Erionite has been identified as a cause of mesothelioma based on studies of mesothelioma rates among residents of Cappadocia, Turkey, where erionite has been used in building materials. Of 141 deaths in four villages during a four-year period, 24 percent were due to mesothelioma. Erionite deposits can be found throughout the western United States, primarily in areas with a low population density. To date, however, there have been no cases of mesothelioma attributed to erionite exposure in the United States.

GENETIC PREDISPOSITION

Further examination of the link between erionite exposure in Turkey and the high mesothelioma death rate produced evidence that genetic predisposition might also be a factor in development of the disease. Although all homes in that region contained similar amounts of erionite, mesothelioma occurred in some homes and not in others. In addition, mesothelioma development followed a dominant genetic inheritance pattern, in which half of the children of parents with mesothelioma also developed mesothelioma. This pattern is consistent with a single genetic mutation from one

CANCER patients often wonder why they got the disease.

Most cases of mesothelioma involve asbestos exposure, but you may be unsure when, or even how, your exposure occurred. Although minute levels of asbestos exist in the air, water, and soil, most people do not develop mesothelioma from this type of exposure. People who develop the disease generally have regular asbestos exposure, such as from a job.

In the 1970s, legislation was enacted to protect workers from asbestos exposure, but prior to that, workers in certain industries may have had regular exposure to asbestos. Some of these occupations are:

- Insulation work in buildings and other structures
- Demolition work, especially in older buildings
- Drywall workers
- Firefighters
- Automobile mechanics
- Steel mill workers
- Shipyard and shipbuilding trades
- Navy veterans

Family members of asbestos-exposed workers may develop mesothelioma because of regular exposure to the fibers brought home on clothing, shoes, and hair. Regular exposure may have occurred from tasks such as washing work clothes that contained asbestos fibers.

of the parents causing the disease. While these observations cannot be considered conclusive evidence for a genetic predisposition to mesothelioma, they do provide reason to further study the role of genetics as a risk factor.



Diagnosis & Staging

DIAGNOSING MESOTHELIOMA can be a complicated process. Symptoms do not typically arise until the disease has reached the late stages, and when they do arise, most are nonspecific, including weight loss, fatigue, and night sweats.

Depending on the type of mesothelioma, organ-specific symptoms may be present. For instance, most patients with pleural mesothelioma experience lung-related symptoms, such as consistent chest pain and progressively worsening shortness of breath. The pain is typically caused by invasion of cancer into the chest wall, and shortness of breath is often caused by pleural effusion (excess fluid in the pleural linings of the lungs). The presence of cough, or coughing up blood, can occasionally occur with pleural mesothelioma.

Proper diagnosis requires a combination of physical, radiological, and pathological examinations, as well as an accurate patient history, including potential asbestos exposure.

For patients with pleural effusions, a sample of the fluid is examined for the presence of malignant cells. In most cases, even when a pleural fluid sample is available, a biopsy of the pleural tissue is required to make a diagnosis. Examination of the biopsy samples includes immunohistochemistry (IHC) tests, in which the samples are processed in a way that allows the pathologist to look for specific signs, called markers, of mesothelioma. There are no known markers that correspond to mesothelioma alone, so in order to diagnose mesothelioma, the pathologist generally evaluates the presence or absence of several markers.

Radiological analysis using contrast-enhanced computed tomography (CT) scan provides a three-dimensional view of the entire pleural surface. It can help determine the extent of disease and can aid the physician in finding the desired tissue for biopsy. Magnetic resonance imaging (MRI) and positron emission tomography (PET) scans may also be used to diagnose mesothelioma.

Once the diagnosis is made, the disease stage is evaluated. As with any type of cancer, determining the extent of the disease is used to predict a patient's outcome and to determine the best course of treatment.

In stage 1, the disease is confined to the mesothelium and has not spread to the lymph nodes or any other organs. Stage 1A refers to a tumor in the outer layer of the mesothelium, whereas stage 1B refers to a tumor that has reached both the outer and inner layer. Stage 1 is the most treatable, and patients with this stage disease have the best prognosis (expected outcome).

Stage 2 disease is characterized by the spread of cancer beyond the mesothelium and into the lung tissue and/or diaphragm, but not yet into the lymph nodes. Patients with stage 2 mesothelioma may be candidates for surgical removal of the tumor.

For stage 3 mesothelioma, the cancer has spread into the fatty part of the mediastinum (the space behind the breastbone and between the lungs) and/or to the lymph nodes within the thorax.

Stage 4 is metastatic disease, where the cancer has spread to other organs, such as the heart or opposite lung. The cancer may also have spread into the peritoneum, to the lymph nodes, or into the spine.



Finding a Specialist

BECAUSE MESOTHELIOMA IS A RARE CANCER, it requires disease-specific expertise.

Here are some places you can go to find a mesothelioma specialist:

- Local hospital referral services
- Your nearest National Cancer Institute-designated cancer center (search by state at www.cancer.gov/cancertopics/factsheet/NCI/cancer-centers)
- American Board of Medical Specialties at www.abms.org
- American Medical Association's DoctorFinder at webapps.ama-assn.org/doctorfinder/home.jsp
- American Society of Clinical Oncology's patient site at www.cancer.net
- American College of Surgeons at www.facs.org/patienteducation
- Mesothelioma Applied Research Foundation at www.marf.org

Once you have found several doctors who seem like a good fit, call and ask a few questions—does the doctor take your insurance, is he or she board certified—before scheduling an appointment to meet and interview the doctor/surgeon.

You may also want to get a second opinion. Most oncologists expect their patients to seek second opinions, and many suggest it themselves. If your doctor doesn't recommend a specialist, you can use the resources listed to find a doctor who can offer a second opinion.

Nurse coordinators at large medical centers can be particularly helpful in finding physicians who give second opinions. Support groups and other cancer survivors may also be good sources for recommending

Questions to Ask

PREPARE for your appointment by formulating a list of questions to ask. You may want to divide questions into two categories:

WHAT TO ASK THE DOCTOR

- Do you have experience treating mesothelioma?
- How long have you been in practice, and how many cases of mesothelioma have you treated?
- What types of treatment do you usually recommend?
- How many times have you performed the surgery I need, and what's your success rate?
- Are you involved in clinical trials and research?
- Who else will be on my health care team, and what are their qualifications?

WHAT TO ASK YOURSELF

- Did the doctor give you a chance to ask questions?
- Did you feel like the doctor was listening to you?
- Did the doctor seem comfortable answering your questions?
- Did the doctor talk to you in a way you could understand?
- Do you feel the doctor respected you?
- Did the doctor ask your preferences for treatment?

oncologists and specialists. Keep in mind that these consultations can be expensive and may not be covered by insurance.

For some insurance plans, second opinions are covered or even required before the plan approves payment for treatment, but you may be limited to certain physicians or hospitals.

After you weigh your options, you must choose your medical team. The comfort level, treatment options proposed, and medical expertise should all be evaluated when making a decision.



Treatment Options

IMPROVEMENTS IN TREATMENT have been made in recent years, giving mesothelioma patients hope. An overview of current and investigational therapies are detailed here.

SURGERY

Although complete surgical removal of the tumor is desired, this is rarely achievable for most patients because microscopic tumor tissue is generally left behind. However, surgery is still used to treat patients with the goal of removing the vast bulk of the tumor and thus alleviating symptoms. The surgical procedures include:

■ **Video-assisted thoracoscopic (VATS) talc pleurodesis** is primarily used to treat pleural effusions, but a biopsy can be obtained at the same time for diagnostic purposes. With VATS talc pleurodesis, a camera is inserted into the pleura through a small incision in the chest, and surgical instruments are inserted through two other incisions. The camera allows the surgeon to maneuver instruments into the pleural space, where the surgeon first drains the excess fluid and then blows talc (similar to common talcum powder, but sterilized), causing an inflammatory reaction that literally glues the lung to the inner surface of the rib cage. Eventually, scar tissue forms, creating permanent bonds that eliminate the space in which fluid can develop. This procedure should relieve the shortness of breath that accompanies pleural effusions.

■ **Pleurectomy/decortication (P/D)** is performed with the goal of removing as much of the tumor as possible by removing part of the pleura as well as the fibrous covering of the lungs, which may restrict lung expansion.

This procedure, which can be performed by VATS or through a larger incision on the side of the chest, is associated with a number of postoperative complications, including air leak, bleeding, and pus formation. Conflicting evidence exists regarding the impact of P/D, with some studies suggesting it prolongs life and others indicating it does not.

■ **Extrapleural pneumectomy (EPP)**, the most aggressive surgical treatment for malignant mesothelioma, involves the removal of both layers of the pleura along with the involved lung, some of the lymph nodes, the diaphragm, and the pericardium (the latter two are reconstructed with synthetic materials). Although EPP has inherent dangers, it permits the use of radiation therapy following surgery since the involved lung has been removed. Evidence suggests radiation after surgery may reduce recurrence at the original tumor site and prolong survival in patients with early-stage disease. Chemotherapy is now often incorporated into the treatment plan as well, either before or after surgery. However, because of the morbidity and mortality associated with this procedure, EPP is only performed on patients with early-stage disease, good cardiac health, no history of certain cardiac or lung surgeries, no significant kidney or liver disease, and little, if any, chest pain.

RADIATION THERAPY

Radiation therapy is generally used to treat localized patches of tumor recurrence or small areas of tumor left behind after surgery. There is no evidence to suggest radiation alone improves survival, but it does

alleviate pain for approximately half of the patients receiving it.

CHEMOTHERAPY

The goals of current chemotherapy regimens are to prolong the survival of mesothelioma patients and improve their quality of life by relieving disease-related symptoms.

The approval of Alimta (pemetrexed) in 2004 has led to the largest improvement in patient outcomes. When added to cisplatin, Alimta, which works by inhibiting cellular proteins that stimulate cancerous cells to grow, was shown in a clinical study to prolong average survival by almost three months. Alimta also relieved pain and shortness of breath, and improved lung function in some patients. Alimta plus cisplatin given intravenously once every three weeks has become standard therapy for newly diagnosed mesothelioma. (Clinical studies of Tomudex [raltitrexed], a drug in the same class as Alimta, have also shown improved response rates and survival times when given with cisplatin compared with cisplatin alone.)

Premedication with folic acid and vitamin B12 is necessary when taking Alimta in order to reduce the frequency of side effects, which can include fatigue, nausea, vomiting, anorexia (loss of appetite), constipation, mouth sores, and low blood cell counts. More severe side effects, including renal failure and hearing loss, occur in rare instances.

INVESTIGATIONAL THERAPIES

A number of important mesothelioma studies were presented at the 2009 annual meeting of the American Society of Clinical Oncology. A phase III trial comparing Adriamycin (doxorubicin) with or without the

experimental drug Onconase (ranpirnase), showed the average survival of both groups was nearly identical: 10.7 months for the Onconase group versus 11.1 months for patients receiving Adriamycin alone. However, when investigators looked only at patients who had already received one course of chemotherapy, they found that those patients survived longer, on average, when Onconase was added to treatment: 10.5 months for the Onconase group versus nine months for patients receiving Adriamycin alone.

Also presented at ASCO's annual meeting were results from studies with the targeted agents cediranib and NGR-hTNF, both of which target the tumor's blood supply. Cediranib and NGR-hTNF were examined as single agents, and both demonstrated the ability to slow disease progression in patients with relapsed mesothelioma. As a result of these findings, new clinical trials are being planned.

An ongoing phase III trial is investigating Zolinza (vorinostat), which is already approved for a rare type of lymphoma, to see if it improves survival of patients with mesothelioma. In this trial, patients whose disease progressed after treatment with Alimta will be given either Zolinza or placebo.

New treatments in phase II development include drugs approved by the Food and Drug Administration for other cancers—Sprycel (dasatinib), Velcade (bortezomib), Sutent (sunitinib), Afinitor (everolimus), and Eloxatin (oxaliplatin)—as well as investigational drugs that are not approved (pazopanib, vandetanib, and vatalanib).

Find ongoing mesothelioma clinical trials at www.curetoday.com/trialcheck.



Legal Issues

COMPANIES INVOLVED IN THE MANUFACTURE and distribution of products containing asbestos can be held liable for the development of mesothelioma in workers exposed to asbestos.

Statutes of limitations vary from state to state and may limit the time in which you can file a lawsuit after diagnosis. The limitation period can be as short as one year or as long as three years or more, but the sooner you start the legal process, the sooner you will receive compensation to help with medical bills and other expenses. Your case may be expedited depending on your symptoms and the stage of the disease.

The most common types of lawsuits include:

- **Personal injury:** These lawsuits are filed for personal suffering and pain associated with the illness, which can occur from direct or secondhand exposure to asbestos. Compensation is based on the degree of incapacity, loss of income, and quality of life related to mesothelioma symptoms and treatment. Damages are awarded for medical expenses, lost wages, lost prospects, travel expenses for treatment, pain, and suffering.
- **Wrongful death:** This type of lawsuit is filed on behalf of the family after the patient's death. The damages awarded are for payment of mesothelioma-related medical bills, lost income, counseling related to the patient's death, legal advice, personal loss, and other illness-related services.

Choosing an attorney is a personal decision, just as when choosing a medical team. You should feel comfortable with the answers you receive to your questions, the way you are treated by the attorney and staff, the level of experience and positive

outcomes the law firm has had with other mesothelioma and asbestos-related cases, and the firm's reputation. A word of caution: An attorney should never promise you a specific amount of compensation. There are no guarantees; each case is unique.

Legal advice and the process of filing a lawsuit is an expensive undertaking. Most attorneys accept a case based on a contingency fee, meaning you will have no out-of-pocket expenses and the attorney will receive a percentage of your settlement money as payment. The contingency fee pays for legal work done on your behalf, court filing fees, expert witness fees, and legal representation in court. If an award is not granted, you may be responsible for some expenses depending on the contingency fee agreement.

Once you decide to hire an attorney, you will meet with the legal staff to provide information about your work history and personal history to determine the type and degree of asbestos exposure you sustained. Authorizations will be obtained to get copies of your medical records, and you should not have to undergo any further medical testing for the purposes of the lawsuit.

Next, you will be asked to give a deposition (getting your testimony on tape) in case you are not able to appear in court. Some attorneys also have a videographer follow you for a day to document what a typical day with mesothelioma is like for you. This can be shown in court to support your case.

Many patients worry that with a lengthy litigation process, they may die before the case is settled. If you pass away, your loved ones can continue to litigate in your place if you have designated an executor of your estate and beneficiaries in your will.



Preparing for End of Life

END OF LIFE CARE FOCUSES on patients' comfort and symptom relief, while incorporating spiritual and psychological counseling to help prepare for a good death.

Preparing for death also involves drawing up legal documents, such as a health care power of attorney and living will. With a health care power of attorney, you will want to choose a person to make medical decisions and initiate your care plan when you are no longer able to speak for yourself. Sometimes close family members are not able to separate emotions from logic and may have difficulty carrying out your wishes, so discuss your wishes with your appointee to verify his/her cooperation and comfort with serving as your health care power of attorney.

A living will, sometimes referred to as an advance directive, defines what, if any, extraordinary measures a person would want to be taken to prolong his or her life. Many of the documents you'll need can be found at www.caringinfo.org, a website run by the National Hospice and Palliative Care Organization.

Hospice services are designed to provide symptom relief, pain management, and support to patients and their families. A person is referred to hospice services when life expectancy is less than six months. Most hospice services take place in patients' homes, assisted living facilities, or nursing homes.

Depending on where you live, you may have multiple options when choosing a hospice provider. Just as carefully as you chose the health care team to treat your mesothelioma, you will want to do the same in selecting a hospice provider. Set up an interview and

start by asking the following questions:

- Does the provider serve the area in which you live?
 - How long has the provider been in operation?
 - Does Medicare certify the provider?
 - Does the provider accept Medicaid?
 - Does your insurance cover the provider?
 - Is the provider licensed by the state?
 - What additional services does the provider cover, such as follow-up phone calls, mailings, support groups, and retreats or activities for families?
 - What services, if any, are not provided?
 - Is participation in care by a family member required for enrollment in services?
 - What is expected from the family caregiver?
 - What, if any, out-of-pocket charges can be expected?
 - How flexible is the schedule of visits?
 - Who provides the on-call coverage?
 - Does the provider have a residential facility?
 - What types of services are provided for funeral arrangement support?
 - How are bereavement services managed, and how long do they last?
- After answering your questions, if you are still uncertain whether the provider is right for you, you can request an evaluation visit. This will give you the chance to interact with the staff in a comfortable environment and get a better idea of how the services will work. You may also want to research the reputation of the agency by asking your doctor, a chaplain, other health care professionals, and families of previous patients for advice and information.



Resources

Asbestos Disease Awareness Organization

www.asbestosdiseaseawareness.org
Provides education and advocacy on behalf of asbestos victims.

Cancer Legal Resource Center

213-THE-CLRC (743-2572)
www.disabilityrightslegalcenter.org/about/cancerlegalresource.cfm
Provides information on cancer-related legal issues for cancer patients and their families.

Hospice Foundation of America

800-854-3402
www.hospicefoundation.org
Offers practical information about coping with death and grief, a blog, and teleconferences.

Mesothelioma Applied Research Foundation

877-363-6376
www.marf.org
Provides education, support, and advocacy for mesothelioma patients. MARF also funds research and has established a grant program to help newly diagnosed patients travel to consult with an expert.

National Association of Hospital Hospitality Houses

800-542-9730
www.nahhh.org
Provides accommodations for patients receiving medical treatment away from home.

National Hospice and Palliative Care Organization

800-658-8898
www.caringinfo.org
The NHPCO is an association of programs that provide hospice and palliative care.

For additional resources, visit www.curetoday.com/toolbox.



Glossary

Asbestos > A group of minerals that take the form of tiny fibers. Loose asbestos fibers breathed into the lungs can cause lung cancer and malignant mesothelioma.

Malignant mesothelioma > A rare type of cancer in which malignant cells are found in the lining of the chest or abdomen.

Mesothelium > A membrane that covers and protects most of the internal organs. The mesothelium produces a lubricating fluid that allows moving organs to glide easily against adjacent structures. The mesothelium has different names, depending on its location in the body.

Pericardium > The thin layer of tissue that forms a sac surrounding the heart.

Peritoneum > The tissue that lines the abdominal wall and covers most of the organs in the abdomen.

Pleura > A thin layer of tissue that covers the lungs and lines the interior wall of the chest cavity.

SOURCE: National Cancer Institute

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