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A Cunning Predator

BY KATY HUMAN

Therapies improve for asbestos-caused cancer.

When Klaus Brauch began experiencing chest pain six years ago, he assumed it was his heart. He was working a high-stress job and his blood pressure had been off the charts. Doctors eventually diagnosed him with congestive heart failure and the software company manager prepared for life with a diseased heart—not cancer. Certainly not a rare cancer called mesothelioma. “Misdiagnosis is how it starts for so many people,” says Brauch, now 56, of Huntington Beach, California. “It becomes a wild goose chase.” Six months after Brauch experienced his first symptoms, doctors confirmed a diagnosis of mesothelioma.

About 3,000 Americans will be diagnosed with mesothelioma in 2006, and the rising incidence of mesothelioma outside the United States isn’t expected to peak for another 10 to 20 years. While lung cancer affects the airways of the lung itself, pleural mesothelioma affects the tissues lining the lung and the chest and accounts for the majority of mesothelioma patients. Mesothelioma can also grow across the thin mesothelial tissue that lines the abdomen (peritoneum) or, rarely, the heart or testicles.

Mesothelioma is unusual in that it’s tightly linked with an environmental cause—asbestos exposure, which accounts for more than 80 percent of cases. A variety of migration mechanisms have been proposed to explain how inhaled asbestos fibers reach the pleural surface, but none have been proven. While inhaled asbestos fibers can lead to pleural mesothelioma, it’s believed that peritoneal mesothelioma develops from asbestos fibers that are swallowed and become lodged in the digestive tract. If a person has been exposed to asbestos, smoking greatly increases his or her risk of asbestos-related lung cancer, though smoking does not appear to affect pleural mesothelioma risk. Research also points to a possible connection between asbestos and laryngeal cancer.

[View Illustration: Mesothelioma: Cause & Effect](#)

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Most mesothelioma patients worked or lived in a place where they were exposed to asbestos. Brauch handled asbestos-containing materials as a teenager during a summer contractor job, and later while refinishing a house.

Researchers believe asbestos triggers cancer in several ways, says Harvey Pass, MD, a leading mesothelioma expert and chief of thoracic surgery and thoracic oncology at New York University Medical Center. The mineral's microscopic fibers may physically injure cells during replication, causing genetic changes that lead to cancer. Asbestos fibers may also contain elements that chemically interact with cells, damaging genetic material and thus leading to cancer. Finally, the fibers may trigger immune system changes that lead to cancer.

Making the Diagnosis

Typical mesothelioma patients worked in shipyards or as miners, but Brauch's story isn't unusual, says Jill Dyken, PhD, an environmental health scientist with the federal Agency for Toxic Substances and Disease Registry. Family members of miners and defense workers have also developed the disease—many with relatively little exposure. “We don't know what level of exposure is enough to cause mesothelioma,” says Dr. Dyken.

Such epidemiological questions are vexing in part because mesothelioma tends to appear 30 to 50 years after asbestos exposure. That can also foil diagnosis, says Dr. Pass. Doctors often confuse the earliest symptoms, including shortness of breath, with heart disease or a sign of aging, so months often pass before a patient is correctly diagnosed. Delayed diagnosis is just one of several factors that makes mesothelioma a devastatingly effective killer, says Dr. Pass. It's hard to remove surgically and is resistant to radiation and chemotherapy. Overall, fewer than 10 percent of patients survive five years after diagnosis.

Until recently, many doctors advised patients to forego grueling treatments and just live the rest of their lives as comfortably as possible. But Dr. Pass says they're making progress. New combinations of chemotherapy agents have been found to shrink tumors up to 40 percent of the time, and surgeons are perfecting techniques for removing diseased tissue. Selective use of radiation can even delay recurrence for some patients. “Treatments are better now,” says Dr. Pass. “There is no excuse for a doctor to say, ‘There's nothing to do.’ ” Researchers are finding ways to diagnose and track the disease, and they're uncovering the cancer's cellular quirks to better design new therapies.

Treatment Evolution

Beginning in 1998, one of Danielle Rosinski's lungs kept filling up with fluid. “Every year I had it drained and nothing showed up,” says Rosinski, a 66-year-old mesothelioma patient from Westland, Michigan. In 2003, her pulmonologist suggested pleurodesis—sprinkling talc into the space between her chest and lungs to keep fluid from accumulating. That's when he saw the cancer. “When he told me I could live a year, well, that was a big blow,” says Rosinski, noting she's

reached nearly three years now.

Brauch, who has also survived beyond the norm, says he concentrates on the fight. “I do have moments where I despair, but I don’t allow myself to stay there,” he says. Aggressive treatment appears to be the key to improving survival, Dr. Pass says. Rosinski and Brauch, both of whom have pleural mesothelioma, went through a punishing combination of chemotherapy, surgery and radiation.

Mesothelioma care may eventually evolve away from “big” surgeries as the standard, just as the standard for breast cancer developed as the disease was better understood.

In 2001, Brauch participated in a clinical trial at Brigham and Women’s Hospital in Boston. In a surgical procedure called an extrapleural pneumonectomy, or EPP, doctors removed Brauch’s right lung and its lining as well as the lining of his heart and diaphragm followed by chemotherapy and radiation. Many doctors consider EPP the greatest chance for survival, but it can have serious side effects, such as internal bleeding, respiratory failure and deep vein thrombosis. Rosinski had the less aggressive surgery known as a pleurectomy, in which surgeons remove the tumor, the lining of the lung and chest wall and possibly the lining of the heart and diaphragm if affected.

The choice between the two surgical options depends on a surgeon’s experience and the patient’s health, says Robert Cameron, MD, director of thoracic oncology at the University of California, Los Angeles Medical Center. He says the more extensive surgery doesn’t necessarily remove more cancer tissue. Dr. Cameron suspects mesothelioma care may eventually evolve away from “big” surgeries as the standard, just as the standard for breast cancer developed as the disease was better understood. “We went from radical mastectomy to partial mastectomy to lumpectomy,” he says. “I think we’ll find we shouldn’t be doing any surgery with mesothelioma.”

As for chemotherapy, Alimta (pemetrexed) plus cisplatin is the current treatment of choice for pleural and peritoneal mesothelioma because of its proven ability to improve survival. Alimta acts by inhibiting cellular proteins that stimulate cancerous cells to grow. Approved in 2004, it is the first and only drug currently approved for the treatment of malignant mesothelioma.

Clinical studies of Tomudex (raltitrexed), a drug in the same class as Alimta, also have shown improved response rates and survival times when given with cisplatin compared with cisplatin alone. Other promising agents in testing include Gemzar (gemcitabine) plus cisplatin and newer agents such as Zolanza (vorinostat), the preliminary studies of which suggest an improvement in the survival of patients who did not respond to other drugs. Antiangiogenic agents, such as Avastin® (bevacizumab), may also be effective in treating mesothelioma.

Dr. Pass and others are also searching for biomarkers in the blood that could signal the arrival or return of cancer. Mesothelioma cells overproduce certain proteins, and tracking those could help doctors diagnose the disease earlier and better monitor patients after treatment.

What's Next?

Scientists think they have found a link between mesothelioma and a DNA virus called simian virus 40 (SV40), which contaminated polio vaccines during the 1950s and 1960s. “Tens of millions of Americans were exposed,” says Adi Gazdar, MD, a pathologist and cancer specialist at the University of Texas Southwestern Medical Center in Dallas. He was skeptical when researchers first suggested people with SV40 might be particularly vulnerable to mesothelioma, but Dr. Gazdar says subsequent research—including his own—has been compelling. “We all agree that the major cause is asbestos, but perhaps SV40 makes some contribution,” he says, adding that a better understanding of the role the virus plays could possibly lead to new treatments.

Brauch keeps an eye on all ongoing clinical trials and research. One year after his surgery, a routine monitoring protocol showed a “hot spot” in his chest. By April 2006, it was the size of an orange and had wrapped around his esophagus next to his heart. Today, Brauch is recovering from another experimental treatment—surgical resection followed by brachytherapy. Surgeons removed as much of the tumor as possible and covered the rest with a tiny blanket of material seeded with radioactive iodine.

Brauch misses “that sense of freedom that you have when you’re expecting to live a long, healthy life.” But by his measure, aggressive treatment has already worked, giving him a longer life than many expected, and despite residual pain, the ability to play an occasional game of golf and shop with his wife of 35 years.

Editor’s Note: Klaus Brauch passed away on May 2, 2007. CURE is proud to honor his memory.