



Oncology

Options for Malignant Pleural Mesothelioma

Early, definitive treatment is essential for this notorious disease type.

By John LeBas

Malignant pleural mesothelioma (MPM) is a disease often misdiagnosed or mistreated at the outset. Almost universally caused by inhaled asbestos fibers embedded deep in the lungs, MPM takes decades to develop after initial exposure—and as a result may occur in patients with no obvious cancer risks. And while later-stage disease produces a painful, rind-like growth that can choke off the lungs or blood vessels, earlier-stage MPM may not appear to be cancer at all.

“When patients are referred to us, they often have been diagnostic dilemmas,” said Anne S. Tsao, M.D., director of the Mesothelioma Program at The University of Texas M. D. Anderson Cancer Center. “Often, several months have passed since the onset of symptoms, and many of these patients have not yet been diagnosed with cancer. And too often, by the



Dr. Anne S. Tsao (left) and physician assistant Vikki J. DeVito review imaging results for a patient with malignant pleural mesothelioma (MPM). Because disease extent is a major determinant of prognosis, all MPM patients at M. D. Anderson undergo a series of imaging, biopsy, and endoscopy procedures.

time the cancer is finally diagnosed, they are no longer candidates for surgery, which offers the best hope for a cure.”

A cure? The notion may seem odd, given the generally poor prognosis of MPM and its widespread reputation as incurable. But in fact, while curing MPM happens very rarely, it is possible, and newer therapies are extending useful life even for patients with unresectable disease.

Many challenges

MPM is notoriously difficult to diagnose in its early stages, particularly if it is a slow-growing variety. It can appear to be adenocarcinoma, even on histologic evaluation, which can prompt therapy for the wrong disease type. Or, MPM may cause a pleural effusion, which

(Continued on page 2)

Malignant Pleural Mesothelioma

(Continued from page 1)

can occur even before a tumor is detectable on imaging, leading to therapies aimed at curing the symptom but not the cause. Such difficult circumstances can have tragic implications for the patient, as delaying effective treatment can shorten the patient's survival considerably.

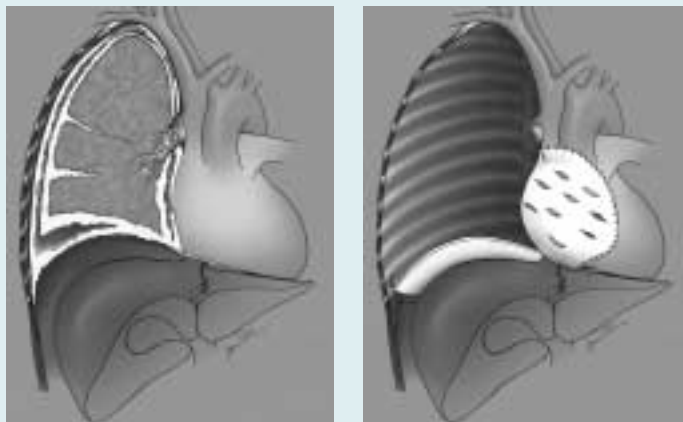
Even when a diagnosis of MPM has been confirmed, the disease's long-standing reputation as incurable or even untreatable sometimes leads to clinical decisions aimed prematurely at palliation, Dr. Tsao said. For example, one common palliative approach, talc pleurodesis, is sometimes used when potentially life-extending surgery might still be an option. MPM is thus a disease best treated at a major cancer center that sees many cases, Dr. Tsao said. Physicians in the Mesothelioma Program at M. D. Anderson evaluate and treat more than 100 patients a year.

Surgical treatment

The only potentially curative treatment for MPM includes extrapleural pneumonectomy (EPP), an extensive surgery that removes the entire lung with the tumor, the pleura, the diaphragm, and the pericardium. The diaphragm and pericardium are reconstructed during the procedure. "If the disease has not spread outside the chest, to the lymph nodes, or into the chest wall and if we determine that the patient can tolerate EPP, then EPP is the best option," said Dr. Reza Mehran, M.D., a professor in the Department of Thoracic and Cardiovascular Surgery and co-director of the Mesothelioma Program.

Determining whether the disease has spread requires careful evaluation; all MPM patients undergo imaging studies with positron emission tomography-computed tomography (PET-CT); endobronchial ultrasound biopsy of mediastinal lymph nodes; mediastinoscopy; and

Surgery for Malignant Pleural Mesothelioma



Extrapleural pneumonectomy (EPP) is the only potentially curative treatment for malignant pleural mesothelioma. At left, the tumor is seen wrapping around the lung throughout the pleural space. At right, the extent of resection in EPP is shown. The surgery involves removal of the tumor, lung, pleura, diaphragm, and pericardium plus reconstruction of the diaphragm and pericardium. Illustrations courtesy of David Rice, M.D., an associate professor in the Department of Thoracic and Cardiovascular Surgery.

diagnostic laparoscopy of regions that might harbor very small metastases. To undergo EPP, patients must have sufficient pulmonary reserve—that is, they must be able to have a good quality of life with their remaining lung. Their tumor must be resectable (for example, not involving a major blood vessel or other anatomical structure that would preclude surgery), and they also must be able to tolerate the 5-hour procedure and a recovery period that can last several months. And, of course, EPP can be performed only if MPM affects just one lung.

Despite the demands of the surgery itself, postoperative management often is the most difficult part of EPP, Dr. Mehran said. Complications occur in 40% of patients, and 8% die within 30 days of the surgery (including those who die during the procedure). The most dangerous complications are a lack of pulmonary sufficiency, which can be underestimated during the preoperative evaluation or compromised by some unforeseen event during or after the surgery, and pulmonary embolism.

A surgical approach to primary treatment that is less favored at M. D. Anderson, according to Dr. Mehran,

is pleurectomy/decortication (P/D), in which the surgeons peel away the pleura but leave the lung in place. P/D offers limited local control and, by itself, little chance of a cure because the lung itself is likely involved. If EPP is not an option but the patient is otherwise a surgical candidate, then M. D. Anderson surgeons will consider performing P/D, but only in combination with chemotherapy or radiation therapy to maximize disease control.

In fact, said Dr. Mehran, "Surgery by itself, whether EPP or P/D, is not sufficient to cure the disease. You need to have surgery in combination with chemotherapy or radiation therapy to achieve the best results."

Radiation therapy

The radiation therapy technique used at M. D. Anderson for MPM is a relatively new method called intensity-modulated radiation therapy (IMRT). IMRT, which uses multiple beams of radiation guided with imaging to deliver cancer-killing doses in the shape of the tumor, is particularly helpful in treating MPM because the disease occurs adjacent to the liver and other radiation-sensitive organs. Owing to its high level of precision, IMRT can kill residual tumor cells that cannot be removed surgically, and its efficacy in MPM has been shown by the changing patterns in disease recurrence.

"Before we had IMRT, there was no option for postoperative local control of MPM. Traditional, 2-dimensional radiation therapy techniques are not appropriate because of the risk to surrounding tissues, and therefore most patients would experience local disease recurrence after surgery," said Zhongxing Liao, M.D., an associate professor in the Division of Radiation Oncology and co-director of the Mesothelioma Program. "Now, distant metastases are more commonly where the disease recurs first. So that means IMRT has been effective at

providing local control.” IMRT is not yet considered a standard of care for MPM; the technology has been commercially available for only about a decade and is still not widely used. But Dr. Liao, who helped develop IMRT for MPM therapy, is confident that will soon change. “IMRT is going to be so critical in treating this disease that it can’t be missed,” she said. “It will likely be almost as important as surgery in controlling the primary tumor and hopefully curing it.”

Dr. Mehran agreed. “We have shown that when EPP is combined with IMRT, we can control the disease locally very well. But patients often come back with distant metastases. That tells us we still need more effective postoperative systemic chemotherapy, which would help reduce the chance of distant recurrence.”

Chemotherapy

Among available chemotherapy regimens, a combination of pemetrexed (Alimta) and cisplatin has yielded the best tumor response rates—around 40%. This combination is commonly given to patients who are not surgical candidates, as it provides symptom palliation and is associated with a median overall survival duration of 12 months.

As Dr. Mehran said, postoperative systemic chemotherapy has not been proven to be effective at preventing distant metastases or to improve overall survival, but it remains under clinical investigation. Preoperative cisplatin-pemetrexed also has been studied in a large, multi-institutional phase II trial in which M. D. Anderson participated; radiation therapy was given postoperatively. Unfortunately, the median overall survival duration among trial participants was only 16.6 months.

A drawback with preoperative systemic chemotherapy is that patients often have disease progression or develop toxicities that make them ineligible for later surgery. Therefore, the use of neoadjuvant chemotherapy is limited and is recommended only in clinical trial settings, Dr. Tsao said.

Clinical trials of novel targeted agents hold the best hope for more effective therapy. One such trial under

way at M. D. Anderson uses dasatinib, a tyrosine kinase inhibitor, for both induction and maintenance therapy. Dasatinib, which was effective against MPM cells in the laboratory, interferes with the actions of the Src kinase family, which researchers believe has a role in regulating MPM. In the trial, patients receive 4 weeks’ treatment with dasatinib, followed by EPP or P/D (and sometimes radiation therapy). If imaging and histologic analysis show that the tumor responded to the dasatinib, participants can receive up to another 2 years’ treatment with the drug after definitive surgery.

According to Dr. Tsao, dasatinib, an oral pill with limited side effects, is ideal to explore as a maintenance therapy for MPM—all other available chemotherapies are too toxic for long-term administration. Also, this trial is the first to test both initial and long-term response to dasatinib. In addition, researchers are collecting blood, tumor tissue, effusion samples, and platelets at two crucial times—before and after initial therapy—in hopes of identifying new therapeutic targets, such as proteins that cause drug resistance, or markers that predict response to treatment. (*Please see “Clinical Trials in Malignant Pleural Mesothelioma,” page 8.*)

“In many ways, this trial holds significant promise for the future, as it will be the first clinical trial in patients with MPM to attempt neoadjuvant therapy using an oral targeted agent and it sets up a new infrastructure of specimen collection to conduct MPM research in the neoadjuvant setting,” Dr. Tsao said.

Another experimental strategy in attacking MPM with chemotherapy is to make the tumor more susceptible to cytotoxic agents by first interfering with proteins that regulate cancer cells’ function or growth. For example, researchers have found that imatinib mesylate (Gleevec), which targets platelet-derived growth factor receptors, can induce increased uptake of cytotoxic chemotherapeutic agents. Imatinib mesylate is now being tested in conjunction with various agents as a front-line therapy for unresectable MPM. While results are preliminary, some patients with very aggressive

After 9/11, Could Another Peak Be Looming?

Before the September 11, 2001, terrorist attack on the World Trade Center, MPM incidence in the United States was expected to peak around 2005. However, because the collapsing buildings spewed asbestos insulation fibers across New York, some MPM specialists fear a second peak may occur in 15–20 years.

MPM usually takes 20–40 years to develop after initial exposure to asbestos, and no cases of MPM have been definitively linked to post-collapse asbestos exposure near the World Trade Center site. The amount of asbestos released—and the risk of exposure to that asbestos—has been controversial. However, various other lung diseases have been documented among some of the thousands of people exposed to toxins present in the post-collapse dust clouds.

To monitor such health effects, New York created the WTC Health Registry (<http://nyc.gov/html/doh/wtc/html/registry/about.shtml>). Registry findings will be shared with physicians who treat patients whose health may have been affected by the collapse. Because thousands of workers and volunteers from outside New York who could be affected arrived immediately after the attack—and because many people who lived in or near New York at the time have since moved—possible victims are spread across the nation. Therefore, physicians nationwide are asked to be vigilant in assessing patients who may have been exposed to health risks after the buildings’ collapse.

tumors have experienced significant disease stabilization with regimens that include imatinib mesylate, Dr. Tsao said. AZD2171, another agent that may increase cytotoxic chemotherapy uptake and may also interfere with the tumor’s blood supply, will be tested in a multicenter Southwest Oncology Group trial that will open next year.

Palliative treatment

Unfortunately, because of the nature of MPM, many patients do require palliative care in lieu of definitive treatment or when primary treatment fails. P/D is

(Continued on page 8)

Intermediate-Stage Bladder Cancer

Deciding on Preoperative Chemotherapy and Urinary Diversion

By **Sunni Hosemann**

Introduction

When bladder cancer is suspected, an in-office cystoscopy is usually done to detect and document the presence of lesions. If lesions are found, the patient then undergoes a transurethral resection (TUR), which is a cystoscopic procedure usually done under general anesthesia. During a TUR, the surgeon examines the bladder wall, removes all possible tumor for pathologic study, and takes biopsy samples from any other suspicious areas.

The bladder neck, areas around the openings of both ureters, and the urethra are examined. A TUR also includes a bimanual examination of the bladder (rectal exam in men, rectovaginal exam in women) to detect palpable tumor masses. Imaging studies are done (computed tomography or magnetic resonance imaging of the abdominal and pelvic areas, depending on the pathologic findings from the TUR). Imaging should determine whether the ureters are dilated (hydronephrosis). Hydronephrosis caused by tumor obstruction is clinically very significant.

Clinical staging of bladder cancer is important for treatment decisions. Standard treatment for early cancers (sometimes considered “superficial” lesions) does not usually include systemic therapy, whereas systemic therapy is standard for advanced (deeply invasive) cancers. But for intermediate (or minimally invasive) cancers, whether systemic therapy should be used is a question that has not been resolved by clinical studies.

Early bladder cancers—those that have not penetrated beyond the subepithelium—are most often treated by resection of the lesion by TUR. For carcinomas in situ and some non-invasive papillary cancers (specifically, those with multiple or recurrent tumors or those that cannot be completely excised), intravesical therapy is added as a prophylaxis against recurrence. Intravesical therapy involves administering a drug into the bladder via a urinary catheter, usually weekly over a period of weeks. Bacille Calmette-Guérin (BCG) is the most commonly administered agent. Tumors that invade the subepithelial tissue without invading deep muscle can be treated with BCG if repeat resection indicates no evidence of residual invasive tumor.

Advanced tumors are those that have macroscopically invaded the bladder wall or nearby organs (prostate, uterus, or vagina) or have spread to the abdominal or pelvic wall. Standard treatment for advanced tumors includes radical cystectomy and systemic chemotherapy.

Intermediate bladder cancers are those that have microscopically invaded the bladder muscle or have begun to penetrate perivesical tissue. Radical cystectomy with concomitant urinary diversion is the standard treatment for these cancers, either alone or with preoperative (neoadjuvant) chemotherapy. Based on pathologic analysis of the resected bladder, postoperative (adjuvant) chemotherapy is sometimes recommended.

Two questions arise in the treatment of intermediate-stage bladder cancer. The first is, which patients should receive neoadjuvant chemotherapy? The second is, which option for urinary diversion after cystectomy is best?

Whether to give neoadjuvant chemotherapy

Because the potential for benefit must be weighed against the risk of adding toxic chemotherapy to a major surgical operation, experts have not agreed on whether all patients with intermediate-stage bladder cancer should receive systemic chemotherapy prior to radical cystectomy. Fifty percent of patients with muscle-invasive tumors experience a recurrence, commonly at distant sites. However, recent large studies and meta-analyses demonstrated only a modest survival benefit in groups that received neoadjuvant chemotherapy, and most accepted guidelines today list cystectomy with neoadjuvant systemic therapy and cystectomy without neoadjuvant systemic therapy as equivalent standards of care.

However, bladder cancer specialists at M. D. Anderson do not view the two approaches as equivalent, because the large studies and meta-analyses so far have considered the group of patients with intermediate cancers to be homogeneous. “But in fact, this group is not homogeneous,” said Randall E. Millikan, M.D., Ph.D., an associate professor in the Department of Genitourinary Medical Oncology. “We believe an identifiable subset of this group are at a higher risk of recurrence than the average and can benefit from neoadjuvant therapy, an idea that has been supported by smaller studies at M. D. Anderson.” Based on his experience and the studies done at M. D. Anderson, Dr. Millikan believes strongly that when larger studies are done in which the higher-risk subset is separated from the overall group, the benefit for some patients will be proven and a new standard will emerge. What is concerning is that some patients may be getting chemotherapy unnecessarily, while others who need it are not. “The size of the group at high risk—those who benefit from neoadjuvant therapy—is hard to know for sure,” Dr. Millikan said. “It may be 20%–30%.”

According to H. Barton Grossman, M.D., deputy chairman of the Department of Urology and a professor in the Departments of Urology and Cancer Biology, patients who have a greater chance of being cured if they receive neoadjuvant therapy (and a higher risk of death if they do not) have adverse characteristics that indicate a higher risk of occult disease. The chief characteristics used by M. D. Anderson (and recommended that colleagues in the community use) to identify this group are:

- Tumors found to have a 3-dimensional mass on examination under general anesthesia
- Tumors that obstruct the ureteral openings (hydronephrosis)
- Tumors for which a biopsy shows microscopic invasion of lymph or vascular spaces

Aggressive pathologic features

“Bladder cancers with such characteristics are considered to have a high risk of lymph node involvement,” Dr. Millikan said. Thus, at M. D. Anderson, patients with such cancers receive neoadjuvant chemotherapy. However, Dr. Millikan points out that patients who do not have the characteristics listed above have been shown to be cured 80% of the time with surgery alone, and therefore chemotherapy has a different risk-benefit ratio for them. “There is no chemotherapy so non-toxic that it can be ethically given to patients with an 80% chance of cure from surgery alone—in essence, you’d be treating many people to help a few, which is unacceptable,” he said, underscoring the fact that both groups benefit from proper staging of their tumors. For the lower-risk group, receiving chemotherapy may have an additional downside: unnecessarily delaying surgery, in some cases by as many as 12 weeks.

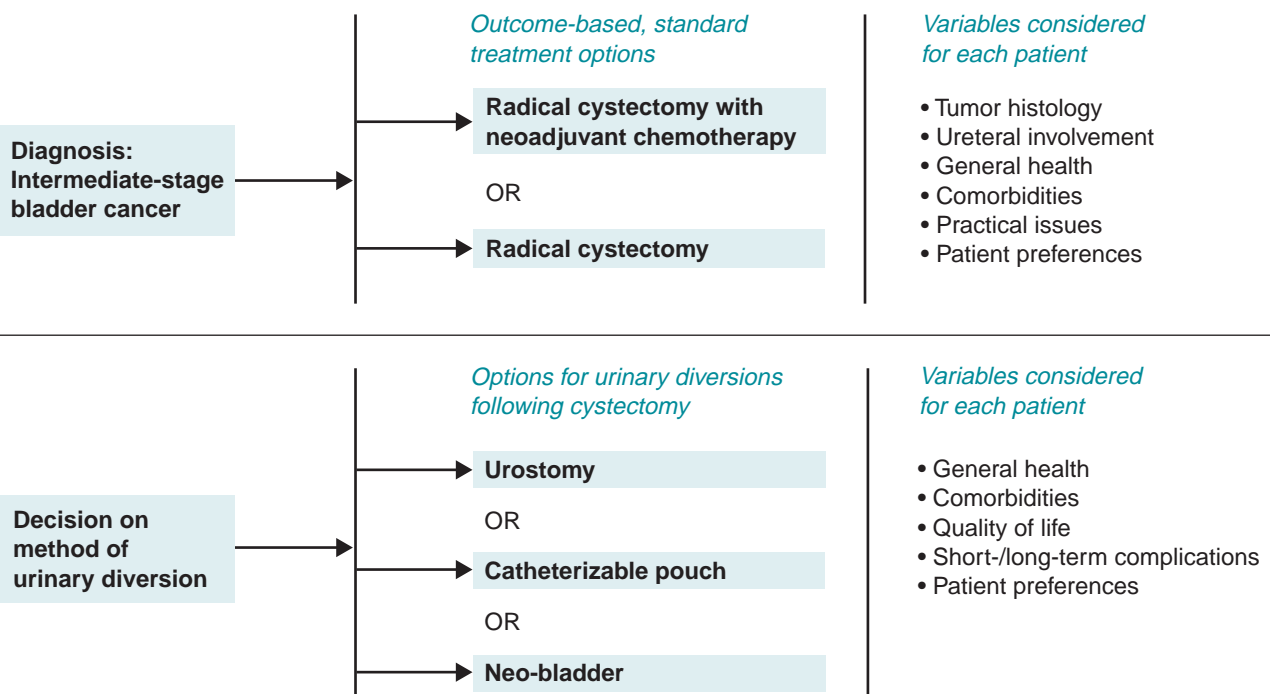
Choosing urinary diversion after radical cystectomy

When the bladder is removed, the urinary flow must be rerouted. According to Colin P. N. Dinney, M.D., chairman of the Department of Urology and a professor in the Departments of Urology and Cancer Biology, there are basically three types of diversions, each with advantages for particular patients:

- **Urostomy.** This is most commonly an ileal conduit created using a segment of the small intestine to connect the ureters to an external stoma on the abdomen, where urine drains into a collection bag. Urostomy is the simplest and shortest of the urinary diversion surgeries. It is not considered a continent diversion, as urine drains into a collection bag as it forms (i.e., continuously), and the patient empties the bag as necessary.
- **Indiana pouch.** In this continent cutaneous diversion, urine collects in an internal pouch created from pieces of the ileum and colon. A thin catheter inserted through the abdominal stoma allows the pouch to be emptied periodically. The pouch is positioned to prevent backflow to the kidneys, and a valve is created between the pouch and the catheterizable channel to prevent leakage. The Indiana pouch requires a longer and more involved surgery than a simple ileal conduit, and the patient must learn to use the catheter to empty urine.
- **Neo-bladder.** In this continent diversion, an internal pouch is created from intestine and is connected to the urethra. As patients learn to use different muscles to retain urine and to void, continence is achieved approximately 90% of the time during the day and about 70% of the time at night. A neo-bladder requires the longest and most involved surgery of the three diversions, and it also requires

(Continued on page 6)

Intermediate-Stage Bladder Cancer: Primary Treatment and Reconstruction Options



bladder training to master control and continence; however, it most closely approximates the “normal” way of voiding. According to Dr. Dinney, patients who have neo-bladders benefit greatly from the assistance of support groups and specialized nursing.

Treatment decisions

Primary treatment

The decision about whether to use neoadjuvant chemotherapy is largely a medical one. It is strongly recommended for the subset of patients who by identified criteria more likely harbor occult disease and therefore are at a high risk for recurrence. “For those patients, it’s a major determinant of survival,” said Dr. Millikan.

For patients who do not have adverse indicators, neoadjuvant therapy can still be considered by the physician and patient. Some patients and physicians prefer to use chemotherapy along with surgery to minimize risk of recurrence. When a patient’s physiologic reserve is adequate to tolerate both approaches, this is a reasonable decision. “Because chemotherapy provides a small advantage, it must be weighed against the side effects,” said Dr. Grossman. “This is significant therapy, and chemotherapy and surgery back-to-back can be quite intensive, so comorbidities are a significant factor.” If the patient is expected to tolerate only one of the two treatments well, surgery alone should be chosen, as it offers the best chance of cure.

Another approach for some patients is to proceed with the surgery and decide afterward about adjuvant chemotherapy, based on the operative findings and postoperative pathologic examination of the bladder. However, response to chemotherapy—often a strong prognostic indicator—cannot be observed if the chemotherapy is given after the bladder and tumor are removed.

According to Dr. Grossman, bladder cancer is a very lethal disease when it becomes advanced, so it is crucial to undertake treatment with a view to minimizing that possibility. Where there are treatment choices to be made, it is important to help patients understand all of their risks and options, to help them arrive at the best choice for their individual situation.

Urinary diversion

The surgeon discusses all options for diversion with the patient preoperatively and learns the patient’s preferences. While patient preferences can usually be met, the final decision is usually made intraoperatively by the surgeon, based on the extent of surgery necessary to remove the cancer. “For example, the creation of a neo-bladder is not among the options for patients in whom we’re not able to spare the urethra,” Dr. Dinney said.

According to Ouida Lenaine Westney, M.D., a reconstructive surgeon and an associate professor in the Department of Urology, other medical factors may also preclude the creation of a neo-bladder. Renal insufficiency and compromised liver function are two contraindications because the

neo-bladder is constructed from intestine, which (unlike bladder tissue) reabsorbs toxins such as creatinine. Likewise, the bowel segment that will be used must be healthy, and therefore patients with extensive bowel disease such as celiac disease or inflammatory bowel disease may not be able to have a neo-bladder or Indiana pouch.

Beyond medical considerations, Dr. Westney said the patient’s lifestyle and desires play a big part in the diversion decision as well. For example, many patients do not want to deal with urostomy’s external urine collection bag, which can be embarrassing for them. On the other hand, some patients are very averse to the idea of a catheter, which is the method of emptying an Indiana pouch (4–6 times per day) and which may have to be used on occasion with neo-bladders, especially in the early months. Some degree of hand-eye coordination and manual dexterity are required to handle a catheter, and Dr. Westney suggests that such capacities be assessed preoperatively. For both types of continent diversion, patients must be able to catheterize and irrigate the internal pouch to prevent mucus buildup and stone formation. Neo-bladders may not be the best option for patients who feel unable (or do not want) to undertake bladder training, which is necessary for continence and normal voiding with neo-bladders. Patients who have significant comorbidities or physical limitations are examples.

According to Dr. Millikan, an important consideration regarding radical cystectomy and urinary diversion is the available surgical experience. Ultimately, the patient will benefit most if such an operation is performed by a surgeon with a great deal of experience doing it. Even though bladder cancer is relatively common (the U.S. National Cancer Institute estimates more than 68,000 new cases and 14,000 deaths in 2008), invasive tumors are rare, so the surgery is uncommon outside of major cities and treatment centers. ●

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Saying No to Smoking: When You Need More than Willpower

If you smoke, quitting is one of the most important things you can do. Smoking greatly increases your risk of cancer, emphysema, stroke, heart disease, and other ailments that can ruin your health and shorten your life.

Of course, you probably already know that smoking is bad for you. But what you may not know is that there are more medicines than ever to help you quit. While overcoming a smoking addiction is never easy, you may not have to rely on willpower alone.

Here is a look at your options for medication.

Nicotine replacement therapies

These quitting aids include the well-known patches, gums, and lozenges that slowly wean you off tobacco. They are called nicotine replacement therapies because they provide controlled doses of nicotine, which is the substance that keeps you physically addicted to smoking. Nicotine replacement therapies are considered relatively safe because they don't contain the cancer-causing chemicals and other harmful compounds found in tobacco.

Nicotine replacement therapies allow you to lower the nicotine dose over time, which should help reduce both your cravings for smoking and the symptoms of physical withdrawal. Multiple studies have shown that nicotine replacement therapy can double your chance of quitting smoking.

Over-the-counter aids such as patches, gum, and lozenges are widely available at



Nicotine patches, gums, and lozenges let you lower the nicotine dose over time.

drug stores, general merchandisers, and grocery stores. You can also ask your doctor about a prescription for other types of nicotine replacement therapy, including nasal sprays and inhalers.

One drawback of nicotine replacement therapies is that they do contain nicotine, which can cause side effects in some people. Pregnant women and some other patients should not use nicotine replacement therapies without a doctor's supervision.

Non-nicotine drugs

Your doctor may recommend a non-nicotine-based medication instead. In recent years, two medications have been introduced that reduce nicotine cravings and withdrawal symptoms without the use of nicotine. As with nicotine replacement therapies, studies have shown that smokers who take non-nicotine drugs are more likely to quit than those who don't take any medicine. You need a prescription to obtain these drugs, which should be taken daily for several months as directed by your doctor.

Bupropion (Zyban) can help reduce cravings and withdrawal symptoms for smokers (although doctors aren't quite sure how the drug works). Bupropion is also marketed as an anti-depressant under the name "Wellbutrin." Patients taking bupropion for depression reported a decreased urge to smoke, leading to its use today as an anti-smoking aid. Side effects may include dry mouth and trouble sleeping. Patients who are pregnant, have seizures, have an eating disorder, or

drink alcohol heavily should not use bupropion.

Another prescription medication, varenicline (Chantix), also helps smokers quit by reducing the urge to light up. This drug limits the pleasurable effects of smoking by interfering with the nicotine receptors in the body. Side effects may include nausea and vivid dreams. Patients who are pregnant or have kidney problems should not take varenicline. Also, because mood swings, depression, and suicidal thoughts have been reported rarely in patients taking varenicline, your doctor should carefully monitor its use.

Final thoughts

Talk to your doctor before trying to quit smoking and especially before using any of the medicines described here. Since not all medicines are right for all people, your doctor can assess any risks you might have and will recommend your best option.

With any quitting aid, it is important to follow the directions fully. Also, remember that these drugs are not a "magic pill"—quitting still requires that you commit to changing the habits that trigger your tobacco use. Support from loved ones or former smokers who understand the challenges of quitting can also help you break the addiction. ●



Prescription medications reduce nicotine cravings and withdrawal symptoms without the use of nicotine.

Sources: www.smokefree.gov, www.surgeongeneral.gov/tobacco

For more information, talk to your physician, or

- visit www.mdanderson.org/smoking
- call askMDAnderson at 1-877-632-6789

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J. LeBas

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Clinical Trials in Malignant Pleural Mesothelioma

A Phase I Study of Induction Dasatinib Therapy in Patients with Resectable Malignant Pleural Mesothelioma (2006-0935). Principal investigator (PI): Anne S. Tsao, M.D. The goal of this trial is to evaluate the effect of neoadjuvant dasatinib against Src kinase Tyr419, a biomarker in MPM, and to correlate the levels of this marker with survival and clinical outcome. Dasatinib is an oral tyrosine kinase inhibitor.

A Phase I Trial of Cisplatin, Pemetrexed, and Imatinib Mesylate in Unresectable or Metastatic Malignant Mesothelioma (2005-0288). PI: Anne S. Tsao, M.D. In this dose-determination study, investigators hope that inhibition of platelet-derived growth factor receptors by imatinib mesylate (Gleevec) will increase tumor cell uptake of the chemotherapeutic agents cisplatin and pemetrexed (Alimta).

A Multicenter Phase I/II Trial of Cisplatin, Pemetrexed, and AZD2171 in Patients with Unresectable Malignant Pleural Mesothelioma (SWOG 0905). PI: Anne S. Tsao, M.D. This Southwest Oncology Group trial will test the oral tyrosine kinase inhibitor AZD2171, which targets platelet-derived growth factor receptors and vascular endothelial growth factor receptors, in combination with the chemotherapeutic agents cisplatin and pemetrexed. (Activation pending.)

A Phase IB, Open-Label, Multicenter Study to Investigate the Effect of Oral LBH589 on Dextromethorphan, a CYP2D6 Substrate, and to Assess the Efficacy and Safety of Oral LBH589 in Patients with Advanced Solid Tumors 2007-0644). PI: Vali Papadimitrakopoulou, M.D. LBH589 is a histone deacetylase inhibitor that may have some activity in mesothelioma. ●

Malignant Pleural Mesothelioma (Continued from page 3)

commonly used for palliation of tumor bulk—removing tumor tissue reduces pain and shortness of breath, which commonly result from MPM. Other palliative options include talc pleurodesis, in which an infusion of talc into the pleura initiates a foreign-body reaction that closes off the cavity, preventing fluid accumulation; and the installation of a permanent chest drain.

Still, Dr. Tsao stresses that such techniques should be used as a last resort and that careful staging and evaluation of patients for potentially curative surgical options should be made at facilities that

are familiar with treating MPM. “Many people don’t know that there are effective therapies for MPM, and so some patients who may benefit from curative treatment don’t receive those therapies,” Dr. Tsao said. “All MPM patients should know about the best treatments that we have available today and should consider enrolling in clinical trials that hold the best hope for the future.” ●

For more information, call Dr. Tsao at 713-792-6363 or visit <http://www.mdanderson.org/diseases/mesothelioma>.

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