OncoLog
MD ANDERSON'S REPORT TO PHYSICIANS ■ Nov./Dec. 2011 Vol. 56, No. 11/12

# Transoral Laser Microsurgery for Laryngeal and Oropharyngeal Tumors

By Sarah Bronson

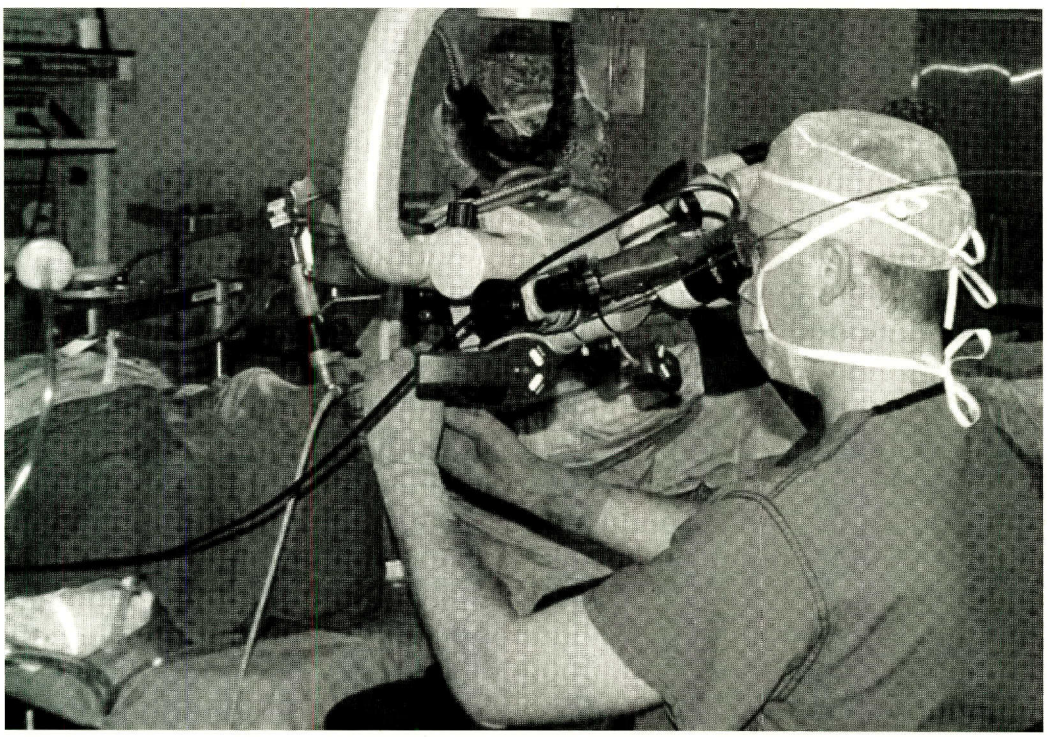
**A minimally invasive surgery for treating cancers of the larynx and oropharynx has cure rates similar to those of open surgery and radiation therapy in selected patients.**

For much of the past century, cancers of the larynx and pharynx have required radical surgical approaches such as total laryngectomy, which results in a stoma, or vertical partial laryngectomy, which preserves part of the functioning larynx but results in severe dysphonia.

As a result, more than 20 years ago, the standard treatment for these lesions shifted to radiation therapy, which is sometimes combined with chemotherapy. Compared with open surgery, radiation therapy may offer patients a better chance to preserve native speech and swallowing.

Today, transoral laser microsurgery can achieve a cure rate similar to that of radiation therapy while offering better organ preservation and fewer adverse sequelae for selected patients with early- or intermediate-stage laryngeal or oropharyngeal cancers that are amenable to resection.

Many of the patients selected for transoral laser microsurgery have stage I or II laryngeal cancer. Because the larynx is integral to speech, swallowing, and respiration, the effectiveness and aggressiveness of



***Dr. Chris Holsinger*** *performs transoral laser microsurgery to remove a laryngeal tumor.*



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therapy can greatly affect long-term quality of life and options for future therapies. For patients with early-stage disease, transoral laser microsurgery can provide both curative treatment and organ preservation.

### Transoral approach

In traditional open surgery for laryngeal cancer, the surgeon resects not only the larynx and surrounding tissues but also the involved vocal cords and supporting structures such as cartilage, which must then be reconstructed.

Open surgery is associated with pain, loss of normal function, and long recovery times. Its potential to adversely affect speech, breathing, and swallowing is a major concern in patients with poor pulmonary function.

In contrast to open surgery, in transoral laser microsurgery, the surgeon accesses the tumor through the mouth with the aid of an endoscope. "You're not disassembling the neck," said Chris Holsinger, M.D., an associate professor in the Department of Head and Neck Surgery at The University of Texas MD Anderson Cancer Center. "You're going through the mouth as a natural orifice and causing as little collateral damage as possible."

A transoral approach gives the surgeon direct access to and magnified, high-resolution views of laryngeal tumors without the need for external incisions. After the patient has been put under general anesthesia and intubated, an endoscope is inserted through the patient's mouth and pharynx and centered over the tumor. An operative microscope is then aligned with the endoscope, and a carbon dioxide laser is coupled to the microscope so that the view through the microscope aligns and moves in accordance with the path of the laser beam. In many patients, the tumor can be reached with a line-of-sight beam; in patients with more out-of-the-way tumors, a highly reflective optical fiber can be used to bend the beam and increase the variety of possible cutting angles.

**Transoral laser surgery allows some patients to avoid the side effects of radiation therapy.**

The goal of transoral laser microsurgery is to resect laryngeal and oropharyngeal tumors with minimal damage to normal tissues and maximal preservation of organ function. Therefore, the tumor is resected with as narrow a surgical margin as possible.

Halsted's principle of removing a tumor en bloc does not always apply in transoral laser microscopy. In fact, dividing the tumor and removing it one piece at a time is not only possible but also often necessary for the complete excision of some larger tumors. Dividing the tumor also enables the surgeon to better assess how far the tumor extends into the surrounding tissue; some "iceberg" lesions may invade to depths that cannot be identified with preoperative laryngoscopy. Also, dividing the tumor is sometimes necessary if the whole tumor is too large to be retracted and ultimately removed by the endoscope.

The extent of normal tissue conservation warranted in patients with head and neck cancers requires the precision of a laser, especially when the surgical site is in the confined space of the upper aerodigestive tract. The laser beam vaporizes a small number of cells at a time and cauterizes adjacent surfaces. The standard carbon dioxide laser's high coefficient of absorption in water limits the beam's penetration, allowing precision in cutting soft tissue with minimal collateral thermal damage to surrounding nerves.

A single laser beam can serve as many different tools. The shape, size, and depth of the laser's penetration can be configured to meet different needs as they arise during surgery. Broadening the beam—retaining the same energy over a larger area—creates a tool for coagulating small blood vessels; narrowing the beam to increase its focus and power creates a cutting tool. Multiple passes of the laser can be made in quick succession to cut through multiple layers of tissue in one location, or each pass can be made independently to cut through smaller amounts of tissue.

Because the heat of the laser cauterizes the edges of the wound the laser creates, no further action is needed to close or cover the area after the tumor has been removed; the wound heals by secondary intention. In fact, tissue heals more quickly after laser surgery than after robotic or traditional open surgery. Transoral laser microsurgery is associated with postoperative complication rates well below 5%.

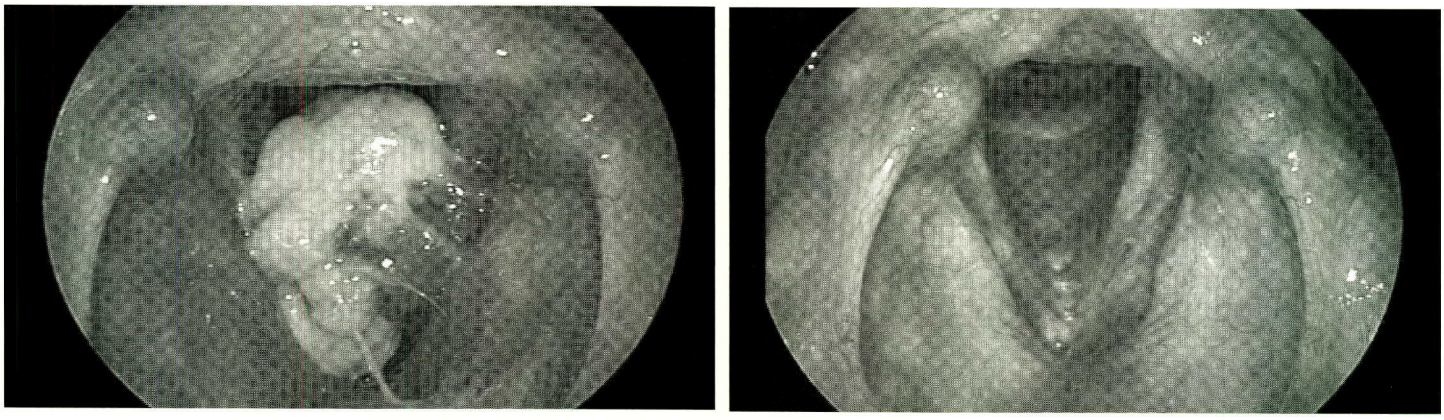
Often, patients spend only a day or two in the hospital and resume their normal activities within a week. Patients with stage III or IV cancers, some of whom receive adjuvant radiation therapy, generally leave the hospital less than a week after undergoing transoral laser microsurgery.

### Outcomes of different modalities

Radiation therapy is a well-established first-line therapy for early-stage laryngeal cancer and has high cure rates. Furthermore, radiation therapy with or without chemotherapy can preserve the structure and function of the larynx while delivering curative treatment in many patients with early- or late-stage laryngeal cancer.

However, these aggressive treatments often cause adverse effects, such as soft-tissue fibrosis, dry mouth, swallowing problems, or loss of sense of taste. Diminished sensory function of the laryngopharynx may predispose patients to aspiration and subsequent pneumonia.

"In selected patients—especially younger patients, who are at higher risk for the cumulative long-term side effects of radiation therapy—transoral



*Endoscopic images show a stage II laryngeal squamous cell carcinoma before surgery (left) and the larynx after the tumor was removed by transoral laser microsurgery.*

laser surgery can spare the need for radiation and eliminate these side effects," Dr. Holsinger said.

Transoral laser microsurgery for early laryngeal cancer yields treatment outcomes similar to those of radiation therapy and achieves a level of tumor control approximately equal to that of radiation or chemoradiation therapy. For example, the survival rates of patients with T2 cancers treated with transoral laser microsurgery tend to be similar to those of patients with T2 cancers treated with radiation therapy.

Dr. Holsinger emphasized that radiation therapy plays a critical role in the treatment of head and neck cancers; for many patients, particularly those whose tumors are no longer at early stages, radiation therapy is the most effective option. However, the routine use of radiation therapy as an initial treatment may limit its use later as a treatment option for persistent, recurrent, or second primary disease. Radiation therapy generally cannot be repeated for curative purposes, so if the tumor recurs, radical surgery will likely be needed. For patients undergoing salvage surgery, previous radiation therapy or chemotherapy can also increase postoperative complications and limit options for conservation surgery.

In contrast, transoral laser microsurgery does not preclude additional therapy of any type. In fact, postoperative adjuvant radiation therapy may be required in patients with intermediate- or advanced-stage cancer.

## Patient selection

Transoral laser microsurgery is an effective curative treatment for early-stage laryngeal cancer. The technique is an established modality for early T1 cancers and is considered safe for T2 cancers.

Transoral laser microsurgery can sometimes be used to remove advanced laryngeal cancer while preserving speech and swallowing functions; however, its effectiveness as a treatment for advanced cancers is not established and warrants further study. Transoral laser microsurgery can also be used as salvage surgery in some patients with recurrent laryngeal cancer.

To determine whether transoral laser microsurgery will be effective, surgeons examine the affected tissues of the laryngopharynx by palpation, endoscopy, computed tomography, and/or videostroboscopy to evaluate the extent of the tumor's invasion and the potential for cure by conservation surgery. Videostroboscopy in particular provides dynamic images that show laryngeal function in detail. Still, the tumor and surrounding tissues are best visualized during surgery, and the surgeon must sometimes adapt the procedure to unexpected findings.

Some large, invasive tumors in the upper aerodigestive tract cannot be cured with transoral laser microsurgery; these cases necessitate radiation therapy. Another contraindication to transoral laser microsurgery is the inability of the surgeon to visualize the tumor or expose the site of the tumor for surgery because of conditions such as trismus, a large tongue base, or prominent dentition.

Transoral laser microsurgery can be an effective alternative to radiation therapy and other more invasive modalities in cancers of the laryngopharynx for which aggressive treatment is not indicated. The stage and depth of invasion of the cancer, the age and treatment history of the patient, and even the amount of free time the patient has can influence the decision.

"If transoral laser surgery can preserve function and achieve tumor control, then this innovative approach should be considered," Dr. Holsinger said. ■

### FOR MORE INFORMATION

*Dr. Chris Holsinger.....713-792-4726*

### FURTHER READING

*For a more comprehensive discussion of radiation therapy and surgery in patients with laryngeal tumors, please see: Hosemann S. Compass: Early-Stage Laryngeal Cancer.* OncoLog. *January 2009. http://www2.mdanderson.org/depts/oncolog/articles/09/1-jan/1-09-compass.html*

# Exploring Causes of and Treatments for Neur

By Zach Bohannan and Bryan Tutt

**Among the most troubling side effects of cancer treatment in some patients is chronic chemotherapy neuropathy syndrome, in which tingling, numbness, and pain in the hands and feet persist long after the completion of treatment.**

Researchers at The University of Texas MD Anderson Cancer Center are conducting clinical and preclinical studies to explore the specific causes of and treatments for this debilitating syndrome.

Charles Cleeland, Ph.D., a professor in and chair of the Department of Symptom Research at MD Anderson, said, "If we can understand the mechanism underlying this pain, we may be able to replace the opioid drugs used for its treatment with more targeted therapies."

## The scope of the problem

Chronic chemotherapy neuropathy syndrome is defined as neuropathy that persists at least 3 months after the completion of therapy. "So far, our studies have only followed patients for 1 year after treatment, but chronic neuropathy can be permanent," said Patrick Dougherty, Ph.D., a professor in the Department of Pain Medicine.

Dr. Dougherty said his department's prospective studies have shown that 60% of patients undergoing chemotherapy develop at least some tingling and numbness during their first 3 rounds of treatment. Of those 60%, about half develop pain as well, and about half of these develop persistent pain. "So around 15% of patients undergoing chemotherapy will have chronic pain," he said.

Taxanes, platinum drugs, and proteasome inhibitors are the agents most likely to cause chronic neuropathy, and they all cause similar neuropathy. Dr. Dougherty said patients describe the pain as an intense burning sensation in the fingers and toes that decreases to numbness or tingling in the palms of the hands and soles of the feet and stops at the wrists and ankles.

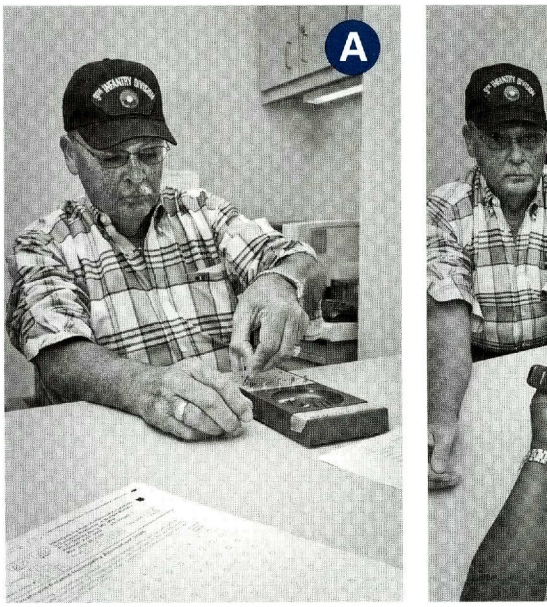
Neuropathy of the hands and feet may also be accompanied by carotenosis of the nail beds, split nails, clubbing of the fingers or toes, or even gangrene. Patients with chronic neuropathy tend to have subnormal skin temperatures (about 30°C) in the painful areas. "This suggests there might be a microvascular component to the pain," Dr. Dougherty said.

## Possible causes

Skin temperature is one of many measures being taken at baseline, during therapy, and after completion of therapy in prospective studies to characterize the psychophysical properties of neuropathy. Other assessments include patient questionnaires, manual dexterity tests, and quantitative sensory testing (QST).

QST is used to assess which types of nerve fibers are affected by neuropathy. Von Frey filaments of varying thickness are used to assess the patient's sense of touch, a reduction in which would indicate damage to Aβ nerve fibers. Blunted needles and weights are used to measure changes in the patient's ability to sense sharp pain, which would indicate damage to Aδ fibers. And measurements of the patient's ability to sense heat or cold assess damage to C fibers.

QST findings have shown a relationship between chronic, cancer-related pain and changes in nerve function. "Patients with chronic pain in the hands and feet also have impaired nerve function that results in a sensory loss," Dr. Dougherty said. To further understand this relationship, prospective studies have been done on skin

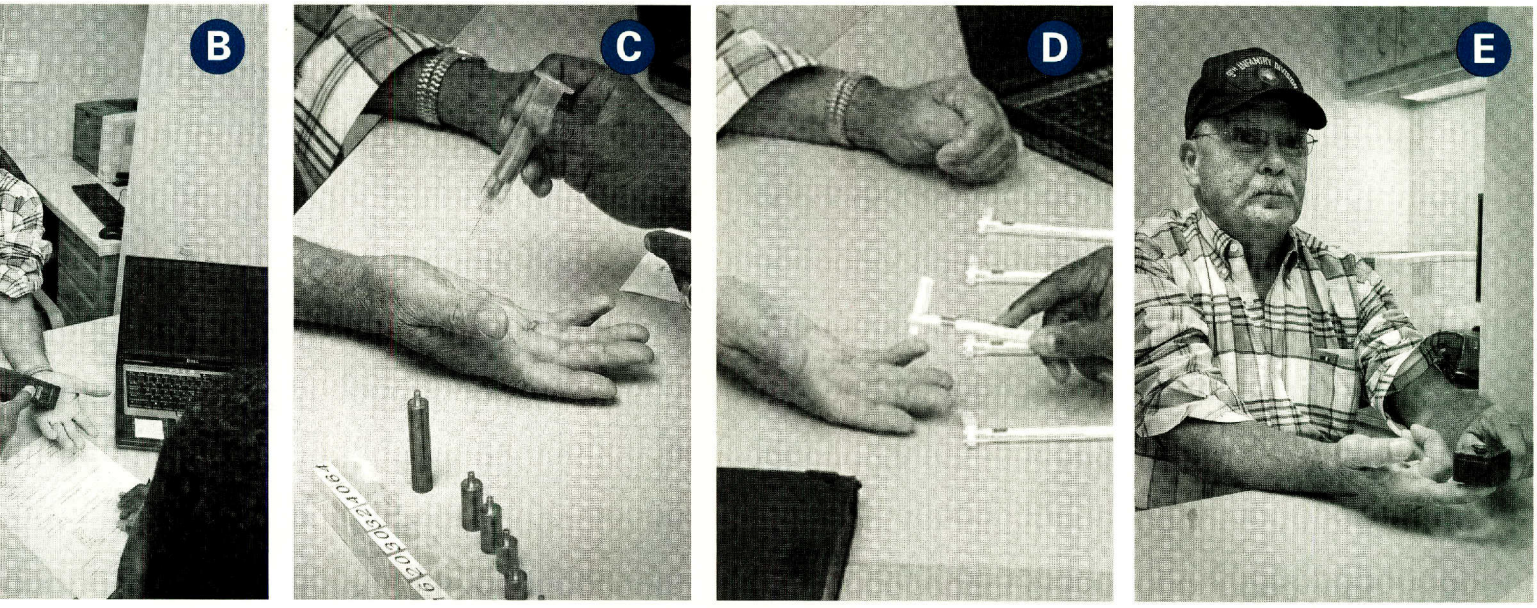



biopsy samples taken before, during, and after cancer treatment. These biopsies revealed a loss of nerve fibers in the epidermis in the areas where patients experienced neuropathy.

Dr. Dougherty said that these studies have also found varying quantities of nerve fibers in baseline samples. "Not only do folks walk in with different baseline nerve counts, but the disease process itself seems to drive neuropathy," he said. Patients who have low nerve fiber counts before therapy tend to have neuropathy during and after treatment, and studies are being planned to determine the predictive value of nerve fiber counts. "It's intriguing that we may be able to prospectively determine who is at risk for neuropathy by counting these nerve fibers," Dr. Dougherty said.

In preclinical studies, researchers are attempting to identify the specific drivers of fiber loss. "My suspicion is that there is an inflammatory response in the dorsal root ganglion that changes the behavior of the fibers—it's not so much that they retract their endings as they fail to re-extend their endings when new layers of skin are formed," Dr. Dougherty said. "We've seen that the interactions between neurons in the dorsal root ganglion change during chemotherapy. We're still trying

# opathy in Cancer Patients




*Hervy Myers, whose multiple myeloma has been in remission since February 2011, is tested for neuropathy during a follow-up visit. Mr. Myers had tests for manual dexterity* **(A)** *and skin temperature* **(B)**. *He then underwent quantitative sensory tests with a blunted needle and various weights to measure the response to sharp pain* **(C)**, *with Von Frey filaments to assess the sense of touch* **(D)**, *and with a thermal stimulator to measure the ability to sense temperature changes* **(E)**.

to understand whether this is related to the failure to re-extend nerve fibers."

## Managing neuropathy

The standard treatments for chronic neuropathy include physical and occupational therapy, analgesic creams, nonsteroidal antiinflammatory drugs, and opioids such as morphine, oxycodone, and fentanyl. Although these alleviate symptoms to some degree, no treatment is currently known to reverse or prevent neuropathy.

Ongoing clinical studies at MD Anderson are testing the use of minocycline to protect nerve fibers during chemotherapy, radiation therapy, or both. According to Dr. Dougherty, MD Anderson is the only institution studying minocycline, but other institutions are studying antioxidants and other compounds that target the inflammation process in different ways to mitigate the side effects of chemotherapy.

Besides neuropathy, inflammation is known to be involved in other symptoms such as depression and fatigue. Therefore, research into the causes of and treatment for one symptom could shed light on other symptoms of cancer and its treatment.

"We know how to treat some symptoms, but the goal of symptom researchers is to one day treat the underlying biology," Dr. Cleeland said. Working toward that goal, he and other physicians at MD Anderson are exploring the creation of a cross-disciplinary center to manage toxicities and symptoms that result from cancer treatment or from the disease itself. ■

### FOR MORE INFORMATION

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*Dr. Patrick Dougherty.....713-745-0438*

## CLINICAL TRIALS: Treatment-Related Symptoms

**Minocycline for reduction of radiation therapy treatment-related symptom burden in oropharynx cancer: a randomized study (2010-0096).** Principal investigator (PI): Gary B. Gunn, M.D. The aim of this study is to learn if minocycline can reduce the symptoms reported by patients with oropharynx cancer who receive radiation therapy.

**A pilot study of minocycline and armodafinil for reducing the symptom burden produced by chemoradiation treatment for non–small cell lung cancer (2010-0872).** PI: Zhongxing Liao, M.D. The goal of this study is to compare armodafinil and minocycline when given alone or in combination to learn which is better for controlling symptoms and side effects of chemoradiation in patients with lung cancer.

**A phase II study of minocycline versus placebo to prevent treatment-induced neuropathy in multiple myeloma (2006-0022).** PI: Sheeba K. Thomas, M.D. The goal of this study is to see if minocycline can help control nerve damage that causes neuropathy in patients receiving thalidomide and/or bortezomib.

### FOR MORE INFORMATION

*Visit www.clinicaltrials.org.*

# Prostate Cancer Screening

## Patients should understand the purpose and limitations of the prostate-specific antigen test

**The U.S. Preventive Services Task Force recommendation against prostate-specific antigen (PSA)–based screening for prostate cancer in men with no symptoms of the disease has led to uncertainty about the appropriate use of the PSA test.**

"The proper use of PSA-based screening is a very nuanced issue that has been interpreted by the media as two extreme choices, which are no use of PSA-based screening or widespread use of PSA-based screening in uninformed populations," said Christopher Logothetis, M.D., a professor in and chair of the Department of Genitourinary Medical Oncology at The University of Texas MD Anderson Cancer Center. "The task force does not advocate either of these choices. The task force is advocating a sophisticated use of the PSA test based on symptoms and on the level of concern shared by the physician and the patient."

The task force's recommendation was made on the basis of two large studies—one in the United States and the other in Europe—showing that PSA-based screening was associated with the overdiagnosis and overtreatment of prostate cancer but did not significantly affect 10-year prostate cancer–specific mortality rates.

However, Dr. Logothetis pointed out that one should not expect a difference in 10-year mortality rates between men who received PSA-based screening and men who did not because most prostate cancers progress slowly. "This disease can take 20 years to result in death, so the timing of these studies is better for detecting excess treatment than for detecting a difference in mortality rates," he said. "The very nature of the disease indicates that the impact of PSA-based screening on mortality is not going to manifest itself for another 10 years."

### Benefits and limitations

While the potential survival benefits of PSA-based prostate cancer screening remain unknown, the potential risk of unnecessary treatment is well documented. "The data are unquestioned that show PSA-based screening has resulted in patients getting treatment who would have done well in the absence of any treatment," Dr. Logothetis said, "and these treatments are not innocuous."

Dr. Logothetis said that many physicians involved in prostate cancer treatment and research have a view that prostate cancer awareness and the widespread use of PSA-based screening have resulted in stage migration—an increasing number of newly diagnosed patients have prostate cancer that is localized and amenable to surgery. "An initial diagnosis of prostate cancer manifested as widespread disease is becoming increasingly unusual," he said. "Because many physicians interpret this as an objective benefit of PSA-based screening, they are reluctant to stop screening."

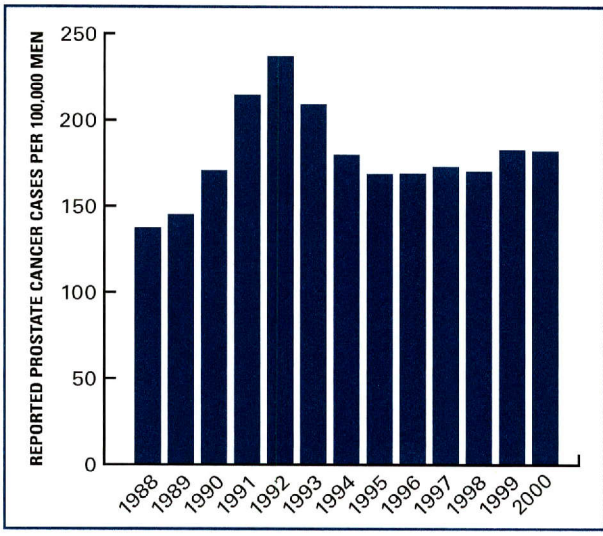
### Informing the patient

The task force did not evaluate the use of the PSA test for disease surveillance after diagnosis or treatment of prostate cancer, nor did it study PSA-based screening as part of a diagnostic strategy in men with symptoms that indicate prostate cancer. "PSA-based screening should be recommended for patients who have symptoms of prostate cancer," Dr. Logothetis said.

MD Anderson recommends that men age 45 years or older with one or more risk factors for prostate cancer discuss screening with their physicians. Risk factors for prostate cancer include African American race or having a first-degree relative who has had prostate cancer. Men age 50 years or older with no symptoms or risk factors for the disease should also discuss screening with their physicians. If screening is desired, men should have annual PSA tests and digital rectal exams.

Dr. Logothetis said that physicians should make sure patients understand that even if PSA levels are elevated and prostate cancer is confirmed by a biopsy, it is likely that no treatment will be necessary.

"My interpretation of the task force's recommendation is that widespread PSA-based screening of patients who are not informed about the wise use of this tool should be avoided, but the use of PSA-based screening by physicians who have informed their patients about the significance and consequences of an elevated PSA level should be continued," Dr. Logothetis said. "If we think of it in those terms, we can reduce the risk of overtreatment." ■




**Prostate Cancer Incidence in the United States (1988–2000).** *The introduction of the prostate-specific antigen test, which was approved in 1992 by the U.S. Food and Drug Administration for prostate cancer screening, corresponded with a higher number of reported prostate cancer cases. Source: National Cancer Institute. Surveillance, Epidemiology, and End Results Program. http://www.seer.cancer.gov.*

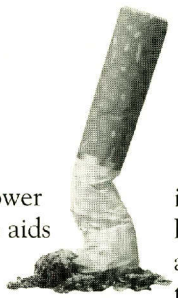
**FOR MORE INFORMATION**

*Dr. Christopher Logothetis...713-563-7210*

# Smoking Cessation

## Medications may help smokers quit

HOUSE·CALL PATIENT INFORMATION SHEET





**You probably already know that smoking is the leading cause of lung cancer. And you may also know that smoking contributes to heart disease, stroke, and lung diseases such as emphysema.** But did you know that even patients who have been diagnosed with these diseases greatly benefit from kicking the smoking habit? And if you're trying to quit smoking, did you know that over-the-counter aids and prescription medicines are available to help you?

### Benefits of quitting

Quitting smoking has both short-term and long-term benefits. Within a few months of quitting, most former smokers have improved blood circulation and lung function as well as less coughing.

As a group, former smokers who have not smoked for 1 year have just half the risk of heart disease as that of smokers. Those who have not smoked for 5 years have half the risk of cancers of the mouth, throat, esophagus, and bladder as that of smokers and the same risk of cervical cancer as that of lifelong nonsmokers. Those who quit smoking 15 years ago have the same risk of heart disease as that of lifelong nonsmokers.

Even after a cancer diagnosis, it's not too late to stop smoking. Studies have shown that lung cancer patients who continue smoking while undergoing treatment have more severe side effects, lower rates of response to therapy, lower 5-year survival rates, and a higher risk of lung cancer recurrence than patients who quit.

### Aids to help you quit

Quitting smoking is important but isn't easy. Nicotine, the substance in cigarettes that keeps you physically addicted, is extremely powerful. And the habit of smoking is deeply ingrained in daily life. Overcoming a smoking addiction takes determination, but you don't have to rely on willpower alone. Here are some of the aids available to help you quit.

*Nicotine replacement therapies*

Nicotine replacement therapies slowly wean you from your nicotine addiction by providing controlled doses of nicotine, which you can lower over time. As your body adjusts to lower and lower doses of nicotine, your cravings for cigarettes and your symptoms of withdrawal will decrease. Studies have shown that nicotine replacement therapy can double your chances of successfully quitting smoking. These therapies are considered relatively safe because they don't contain the cancer-causing chemicals and harmful compounds found in tobacco.

Common nicotine replacement therapies such as patches, gum, and lozenges are available without a prescription and can be purchased at pharmacies and grocery stores. The nicotine patch is frequently the best option for heavy smokers because it delivers a steady stream of low-dose nicotine. The gum and lozenges keep your mouth busy without a cigarette and are especially helpful for people who habitually smoke at certain times, such as after dinner or with their morning coffee.

Electronic cigarettes (e-cigarettes) resemble cigarettes but do not contain tobacco. The doses of nicotine and other additives vary among e-cigarette brands. The safety of e-cigarettes has not been established, and e-cigarettes are not approved as a nicotine replacement therapy by the U.S. Food and Drug Administration.

Some nicotine replacement therapies are available by prescription. The nicotine nasal spray is like a nasal spray you might use for a stuffy nose or allergies. It delivers a fast-acting single dose of nicotine and can be used the moment a craving hits. The nicotine inhaler works like an asthma inhaler—you put it in your mouth and breathe deeply. Like the nasal spray, it delivers a fast-acting, measured dose of nicotine at the moment you need it most.

When considering your options for nicotine replacement therapy, keep in mind that—like cigarettes—these agents contain nicotine, which can cause side effects in some people. Talk to your doctor before using any nicotine replacement therapy.

*Non-nicotine medications*

Your doctor may prescribe a non-nicotine medication to be used instead of or along with nicotine replacement therapy. These medications reduce nicotine cravings and withdrawal symptoms, and studies have shown that smokers who use non-nicotine drugs are more likely to quit than those who don't take the medications.

Bupropion (Zyban) and varenicline (Chantix) are the most commonly prescribed non-nicotine drugs. Some people taking these drugs have side effects, such as nausea, sleeplessness, or mood swings. Your doctor or pharmacist will provide details on possible side effects, and your doctor will monitor you closely if you are taking one of these drugs.

Nicotine replacement therapies and non-nicotine medications work best when used in conjunction with a behavioral counseling program. These medications can help reduce your urge to smoke, but quitting is still up to you. You must commit to changing the habits that trigger your smoking. While making a lifestyle change isn't easy, this is one change that could save your life. ■

*– S. Moreau*

**FOR MORE INFORMATION**

*For information about smoking cessation programs, ask your physician, call 713-792-QUIT, or visit www.mdanderson.org/quitnow.*

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# IN BRIEF

## *BRCA2* Mutations in Ovarian Cancers Indicate High Rates of Survival and Treatment Response for Patients

Women with high-grade ovarian cancers that have *BRCA2* gene mutations live longer and respond better to platinum-based chemotherapy than do patients without *BRCA* mutations, researchers from The University of Texas MD Anderson Cancer Center and the Institute for Systems Biology reported in the October 12 issue of the *Journal of the American Medical Association*.

*BRCA2* and *BRCA1* are tumor-suppressing genes involved in DNA repair; women with mutations of either gene are at increased risk for developing breast and/or ovarian cancer.

The researchers reviewed data from The Cancer Genome Atlas for 316 patients with high-grade serous ovarian cancer, the most common form of the disease. The data for each patient included a genetic survey of the surgically resected primary tumor and comprehensive clinical data.

Most patients in the study had stage III or IV disease and histological grade 2 or 3 tumors. *BRCA2* mutations were found in 29 ovarian cancers and *BRCA1* mutations in 37. All patients had undergone surgery followed by platinum-based chemotherapy.

Patients with *BRCA2* mutations in their tumors had a significantly higher 5-year overall survival rate (61%) than did patients without *BRCA* mutations in their tumors (25%). The 3-year progression-free survival rate also was significantly higher for patients whose tumors had *BRCA2* mutations (44%) than for those whose tumors did not have *BRCA* mutations (16%). *BRCA1* mutations in tumors were not significantly associated with survival.

All patients whose ovarian cancers had *BRCA2* mutations responded to platinum-based chemotherapy, compared with 82% of patients whose tumors did not have any *BRCA* mutation and 80% of patients whose tumors had *BRCA1* mutations.

"*BRCA2*-mutated ovarian cancers are more vulnerable to DNA-damaging chemotherapy agents, which is really exciting because a number of drugs now in clinical trials block DNA repair and might prove effective against these tumors, especially in combinations," said Wei Zhang, Ph.D., a professor in the Department of Pathology at MD Anderson and the report's senior author.

The researchers also found that tumors with *BRCA2* mutations had a median 84 mutations per tumor sample compared with 52 mutations per tumor sample for tumors without *BRCA* mutations. Dr. Zhang said additional studies of *BRCA1* and *BRCA2* mutations are needed to better understand and exploit these findings. ■

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