Tobacco Research and Treatment Program’s Studies Include Ways to Prevent and Treat Nicotine Dependence in Special Populations

by Kerry L. Wright

According to both the Centers for Disease Control and Prevention (CDC) and The Foundation for a Smokefree America, smoking claims the lives of more than 400,000 individuals each year in the United States—more than alcohol, drug abuse, homicide, suicide, fires, car accidents, and AIDS combined. Yet 47 million Americans continue to smoke.

The link between smoking and cancer is irrefutable: 90% of all cases of lung cancer occur in smokers or former smokers, and at The University of Texas M. D. Anderson Cancer Center, approximately one third of all patients have tobacco-related cancers. Therefore, in addition to their efforts to find better treatments for these cancers, researchers at M. D. Anderson are focusing on ways to prevent people from smoking and to help those who already smoke quit. The institution’s Tobacco Research and Treatment Program (TRTP), funded in part by grants from the National Institutes of Health and through funds from the Texas tobacco settlement, is devoted to outreach, education, and research in smoking prevention and treatment for nicotine dependence.

“Prevention and intervention, or treatment, are really what it’s all about,” (Continued on next page)
said Paul Cinciripini, Ph.D., a professor in the Department of Behavioral Science at M. D. Anderson and director of the TRTP. While most studies in tobacco cessation have addressed healthy, white populations, the TRTP’s research includes alternative or smaller populations who may have higher-than-average rates of smoking or smoking-related illnesses or who may find it more difficult to break their addiction to nicotine.

**Racial, Ethnic, and Socioeconomic Factors**

According to the National Center for Chronic Disease Prevention and Health Promotion at the CDC, African-American men are more than 50% more likely than white men to develop lung cancer. This may be partly due to the fact that African-American men have higher smoking rates than do white, Hispanic, or Asian men, and African Americans metabolize nicotine more slowly than do white or Hispanic smokers.

“So we’re attempting to develop some culturally appropriate, culturally specific kinds of treatments for helping African-American smokers quit,” said David Wetter, Ph.D., an associate professor in the Department of Behavioral Science. Specifically, he is planning a smoking cessation study that includes the use of handheld computers in this population.

The handheld computer technology Dr. Wetter works on (see related article on this page) enables the smoker to interact with the computer, which responds to high-risk situations by supplying the user with general information about quitting when prompted. The study will test whether a group of African-American smokers who use the computers in addition to standard care (nicotine patch and counseling) will have better quitting rates and fewer postcessation symptoms than will a group receiving only standard care.

Dr. Wetter is also involved in several projects in collaboration with the Cancer Information Service of the National Cancer Institute to increase smoking cessation services to Spanish-speaking populations. Plans include advertising a Spanish-language cancer information line and then conducting a counseling-based smoking cessation study of smokers who call the line.

In addition to race or ethnicity, socioeconomic status can play a role in one’s decision to start smoking or ability to quit, said Ellen R. Gritz, Ph.D., professor and chair of the Department of Behavioral Science. “In this country, there is a socioeconomic gradient—the lower your income and educational level, the more likely you are to smoke,” she said.

As a result, high-income, educated populations have lower levels of smoking-related illnesses than do the lower socioeconomic groups, said Amy Lazev, Ph.D., an instructor in the Department of Behavioral Science.

**Comorbid Disease**

Quitting smoking can—in a short amount of time—improve circulation, decrease pulse rate and blood pressure, and make it easier to breathe. For patients with cancer, it can also improve the efficacy of treatment and reduce the risk of developing a second malignancy or infections such as pneumonia.

Dr. Lazev is working with Dr. Gritz to study smoking cessation in populations who already have smoking-related illnesses. Dr. Gritz is the principal study coordinator and Dr. Lazev the project manager of a Southwest Oncology Group trial that has recently opened to study smoking cessation in patients with stage I or stage II non-small cell lung cancer.

All patients in the study will be given behavioral therapy and the nicotine patch. In addition, they will be randomly assigned to receive either a placebo or the antidepressant bupropion (Zyban), which the U.S. Food and Drug Administration approved in 1997 as a smoking cessation therapy. Outcome measures will include smoking cessation rates and will also explore second malignancies, survival, and symptom status. Results will be analyzed for the entire group and by sex, since men and women may have different success quitting. Drs. Gritz and Lazev hope to begin recruiting patients to the study within the next few months.

Another group these investigators find important to target for smoking intervention is patients with HIV.

“Those infected or living with HIV have especially high rates of smoking,” said Dr. Gritz. “It’s a population that already needs at least two major health interventions: treatment for HIV and treatment for smoking-related illnesses.”
CD-ROM, and over five sessions, the program collects information from the students and monitors their level of contemplation about starting to smoke or quitting smoking, their motivation to learn or change particular behaviors, and any behavior changes. It then adjusts the information the students receive from the CD-ROM accordingly. Feedback from the pilot testing has been positive so far, Dr. Prokhorov said, and the tool will eventually be evaluated for efficacy.

According to The Foundation for a Smokefree America, 60% of smokers have their first cigarette by the age of 14, and 90% become regular smokers before the age of 19, making high school and college students prime targets for a smoking intervention.

In another study, Dr. Prokhorov is analyzing data from more than 400 students from 15 community colleges in the greater Houston area to determine whether computer-assisted smoking cessation counseling produces higher cessation rates than does standard counseling. In the experimental group, a computer program assists the counselor in determining students' readiness to quit smoking and levels of addiction. Physiologic parameters such as lung age and levels of carbon monoxide in the expired air are also recorded by the computer to motivate participants and reinforce smoking cessation.

Like most smoking cessation therapies, the computer programs used in these studies are available to the participants only intermittently. However, handheld computers are now being designed that can be used by smokers on a daily basis to deliver intervention "in real time in the real world," said David Wetter, Ph.D., an associate professor in the Department of Behavioral Science and principal investigator of several clinical trials of handheld computers.

The computers, which can fit into a pocket or a purse, gather information about when the smokers crave cigarettes, when they light up, and how they feel throughout the day. This information can then be used to discern important factors that may lead to smoking.

About half of all relapse episodes in former smokers or those who are trying to quit are characterized by anger, anxiety, depression, or frustration, said Dr. Wetter, and research has shown that these emotions often occupy a smoker's cognitive workspace, making it difficult to make healthy decisions when confronted with the urge to smoke. Once the handheld computer has enough information about a person's mood and smoking patterns, it can deliver individualized coping strategies when prompted in times of stress.

"The key point is that you want to break the association between environmental cues of smoking and self-administration of nicotine," said Paul Cinciripini, Ph.D., a professor in the Department of Behavioral Science and director of the TRTP.

Research has already shown that smokers who quit on a schedule have better cessation rates than those who gradually quit on their own, said Dr. Cinciripini, who is conducting a study in which the handheld computers assess how often and how much participants smoke and then devise an appropriate quitting schedule. The computer alerts patients when it is time to smoke and requires them to record, within minutes of the alarm, whether or not they are keeping up with the schedule.

Some may argue that computers are too impersonal to be effective tools in smoking intervention strategies, but it may be easier for some people to tell a computer the truth about their smoking behaviors. And it seems that computers—at least some of them—can give pretty good advice.

For more information, contact Dr. Prokhorov at (713) 745-2382, Dr. Wetter at (713) 745-2682, or Dr. Cinciripini at (713) 792-0919.

Women and Smoking

Between 1950 and 1991, the incidence of lung cancer in the United States rose 550% in women compared with 200% in men. And although the rate of smoking in women is slightly lower than that in men, said Dr. Gritz, "There are many reasons to focus on women that are not purely related to smoking prevalence."

In addition to the risk of lung cancer, smoking increases a woman's risks of heart disease and cancers of the oropharynx, bladder, and cervix, among others. Children of smokers also have (Continued on page 4)
more illnesses than do children of nonsmokers, and smoking before or during pregnancy is associated with risks to both the mother and the fetus, including preterm delivery, low birth weight, ectopic pregnancy, spontaneous abortion, and infertility.

Previous research in the TRTP evaluated the use of videotapes to help pregnant smokers kick the habit. In one study, women viewed at home a series of six videotapes that led them through the steps of quitting smoking throughout their pregnancy and postpartum. The researchers found that depression played a big part in the difficulty these women had quitting. According to the 2001 Surgeon General's Report on Women and Smoking, "The association of smoking and depression is particularly important among women because they are even more likely to be diagnosed with depression than are men."

**Depression in Smokers**

Unfortunately, people with major depression are typically excluded from smoking cessation studies, even though they account for about 10% of the smokers who are interested in such studies, said Janice Blalock, Ph.D., an assistant professor in the Department of Behavioral Science.

Because current treatments address only smoking cessation or only depression, Dr. Blalock is interested in developing a psychotherapeutic program that addresses both. She is currently recruiting smokers with major depression or subthreshold depressive disorders for a pilot study of standard smoking cessation (relapse prevention) counseling versus a proven therapy for chronic depression that will be modified to incorporate a smoking cessation aspect.

"The experimental therapy has a problem-solving exercise in it that I think is going to work very well in both the high-risk situations smokers deal with and the typical situations that make people depressed," said Dr. Blalock. The therapy, called the cognitive-behavioral analysis system of psychotherapy, also develops a more supportive relationship between the patient and the therapist than does the standard cessation treatment, and it assesses the interpersonal history of the patient and tailors the treatment accordingly.

Several other researchers in the TRTP are trying to understand what it is about mood that influences people's decisions to start smoking and to continue the habit. For example, many smokers experience negative emotions, such as anxiety and depression, at fairly high levels when they attempt to quit, said Brian Carter, Ph.D., an instructor in the Department of Behavioral Science.

Dr. Carter is collaborating with principal investigator Dr. Cinciripini to study the emotional reactivity of smokers in relation to nicotine. In the study, two groups of smokers—one of which must refrain from smoking for 12 hours prior to participation—are given a dose of nasal nicotine and shown pictures that normally produce positive, negative, or neutral emotions. Their eye-blink responses (startle responses) to the pictures are then measured by electrodes attached to their facial muscles.

Results presented at the 8th Annual Meeting of the Society for Research on Nicotine and Tobacco in February show that nicotine-deprived smokers have a stronger startle response to positive and negative stimuli when given nicotine compared with a placebo than do the nondeprived smokers, suggesting that nicotine helps regulate mood in nicotine-dependent smokers. As part of this study, Drs. Carter and Cinciripini are also testing whether individuals with a genetic predisposition to nicotine dependence have an elevated startle response during nicotine withdrawal when compared with control smokers.

"Our series of studies show that smokers who carry a certain gene, the DRD2 A1 allele, quit less often, are less responsive to antidepressant therapy while quitting, and are more emotionally reactive during nicotine withdrawal than those with the A2 allele," Dr. Cinciripini said. People who have the A1 allele, he added, may have fewer or less-responsive dopamine receptors. (Dopamine is an important neurotransmitter for the experience of pleasure.)

The possibility that some people are genetically predisposed to smoking is but one of several avenues of study being explored by researchers in the TRTP. Said Dr. Carter, "We're trying to figure out why people smoke and why it's so hard for certain people to quit."

**FOR MORE INFORMATION, contact Dr. Cinciripini at (713) 792-0919, Dr. Wetter at (713) 745-2682, Dr. Gritz at (713) 745-3187, Dr. Lazev at (713) 792-0919, Dr. Blalock at (713) 792-0919, or Dr. Carter at (713) 745-4294.**
Emergency Center Provides Specialized Care for M. D. Anderson Patients Experiencing Oncologic Emergencies

by Ann Sutton

Cancer tends to be a progressive disease, and tumors often grow slowly, but there are such things as cancer emergencies. In the Emergency Center at The University of Texas M. D. Anderson Cancer Center, physicians don't deliver babies, and they never treat victims of gunshot wounds or car crashes. Instead, they manage specialized—and often complicated—oncologic emergencies.

Sixty to 70 patients a day are treated for oncologic emergencies in the Emergency Center, a 24-room, 28-bed facility that is part of the Department of General Internal Medicine, Ambulatory Treatment, and Emergency Care, according to Carmelita Escalante, M.D., ad interim chair of the department and medical director of the Emergency and Ambulatory Treatment centers. "There is no sign outside that says 'Emergency Center,' but we are a Level 3 emergency center," she said. The Level 3 designation is given by the Joint Commission on Accreditation of Healthcare Organizations and the Centers for Medicare and Medicaid Services. A Level 3 center provides assessment, resuscitation, stabilization, and triage but is limited in what illnesses it can treat.

"Our emergency center is unique because it is located within a comprehensive cancer center," said Ellen Manzullo, M.D., associate medical director of the Ambulatory Treatment Center. Memorial-Sloan Kettering Cancer Center in New York City houses its own urgent care center, but we are a Level 3 emergency center," she said. The Level 3 designation is given by the Joint Commission on Accreditation of Healthcare Organizations and the Centers for Medicare and Medicaid Services. A Level 3 center provides assessment, resuscitation, stabilization, and triage but is limited in what illnesses it can treat.

"Our emergency center is unique because it is located within a comprehensive cancer center," said Ellen Manzullo, M.D., associate medical director of the Ambulatory Treatment Center. Memory-Sloan Kettering Cancer Center in New York City houses its own urgent care center, but many other cancer hospitals do not, instead using the emergency rooms of nearby hospitals.

Dr. Manzullo added that M. D. Anderson oncologists are notified about any visits their patients make to the Emergency Center. "It's very important for us to facilitate the continuity of a patient's care," she said.

The Emergency Center at M. D. Anderson is staffed by nine physicians who work exclusively in the center and 11 others who also work in other care centers. All of the Emergency Center physicians are internal medicine specialists, rather than oncologists.

"Most cancer emergencies are medical emergencies, as opposed to those seen in other emergency centers where there are trauma and surgical components," said Mary Ann Weiser, M.D., associate professor of General Internal Medicine.

The three most common cancers seen in patients in the Emergency Center are leukemia, gastrointestinal cancer, and breast cancer. The most common oncologic emergencies treated in the center are fever, uncontrolled pain, nausea or vomiting, and dyspnea. Others include bowel obstruction, neurologic conditions, spinal cord compression, hemorrhage, and mucositis.

Fever accounted for 19% of Emergency Center visits in 2000 and is usually caused by an infection. According to Dr. Weiser, infections are not uncommon in patients with cancer, and infections in patients with neutropenia are more difficult to treat and more often lead to complications. As recently as 10 to 12 years ago, the vast majority of patients with neutropenia were admitted to the hospital, Dr. Weiser said. However, as a result of research conducted by the Emergency Center and the Department of Infectious Diseases, Infection Control, and Employee Health, many patients with neutropenic infections are now being treated on an outpatient basis. These patients are initially evaluated in the Emergency Center and return for follow-up visits during their treatment. (Continued on page 6)
Emergency Center Provides Specialized Care
(Continued from page 5)

As part of an institution-wide study of pain management, physicians in the Emergency Center are developing clinical pathways for abdominal pain and chest pain that they hope will expedite patients’ workups.

Dyspnea, which is frequently treated in the Emergency Center, can be caused by several different conditions, including infections, lung malignancies, pulmonary emboli, and chemotherapy- or radiation therapy-induced lung injuries. Often, patients with cancer who require emergency treatment for dyspnea are in the latter stages of their disease. A model developed by Dr. Escalante that predicts whether death is imminent in patients with dyspnea may help physicians choose between supportive care and more aggressive measures in this group of patients.

Members of the department are also collaborating on two outpatient trials that study the use of low-molecular-weight heparin to treat deep venous thrombosis. In the first trial, the investigators are trying to establish whether dalteparin is as effective as warfarin in treating patients with chronic thrombosis. The second trial studies the use of dalteparin in outpatients at M. D. Anderson and 15 other sites.

While the main focus of the center’s physicians is the treatment of oncologic emergencies, they also treat other emergencies that develop in patients, visitors, and employees. However, the center is not always equipped to handle complicated nononcologic emergencies, so it is not uncommon for patients who have heart attacks or strokes, for example, to be transferred to another hospital in the Houston area after being stabilized in the Emergency Center.

Dr. Weiser once researched the rate of hospital admissions from patients seen in traditional emergency centers nationwide and found that it ranged from 6% to 30%. The M. D. Anderson Emergency Center’s admission rate, patients who are newly diagnosed with cancer and those who only suspect they have cancer will come to the Emergency Center seeking initial examination and treatment planning. “We evaluate these patients to make certain they are not having any acute problems, and then we direct them to the appropriate channels to help them get an appointment with the appropriate care center,” said Dr. Manzullo.

“Providing emergency care for non-emergencies] takes resources that could have more appropriately been used for patients who really need the Emergency Center, and it also increases the costs for these patients because their insurance company may reject the claim. The patient may be left to pay for an emergency room visit when it truly wasn’t something that needed to be seen in the Emergency Center,” said Dr. Escalante.

According to Dr. Weiser, fewer patients are treated in the Emergency Center than in a traditional emergency room, but the complexity of each patient’s condition makes up for it. “If you went to another emergency center with a really, really bad headache, it’s as likely to be a bad migraine as anything. In our patient population, it’s just as likely to be a new brain metastasis,” she said.

For more information, contact
Dr. Escalante at (713) 792-2148,
Dr. Manzullo at (713) 745-4527,
or Dr. Weiser at (713) 745-4516.

Correction
In an article about the Selenium and Vitamin E Cancer Prevention Trial (SELECT) in the March 2002 issue of OncoLog, the dose of selenium given to study participants was published as 200 mg. The correct dose is 200 μg.
Depression and Cancer

Sometimes, the struggle with cancer and its aftermath brings a greater sense of clarity to the lives of patients. Finding this peace of mind is not always easy, however, and all patients struggle with fear, anger, anxiety, denial, sadness, or uncertainty at some time during their cancer experience.

Recognizing the difference between a normal emotional reaction to cancer and a more severe depression is important for patients and their families, friends, and caregivers because appropriate treatment can significantly reduce the suffering caused by depression and improve quality of life. Most signs of depression lessen over time as individuals learn to cope with their disease, but according to the National Institute of Mental Health, clinical depression (which requires treatment) occurs in about 25% of patients with cancer, more than double the 10% incidence rate in the general population.

What is clinical depression?

Everyone deals with a diagnosis of cancer differently, and not all patients will become depressed. However, emotional problems that become chronic and interfere with a patient's daily activities (including the ability to follow treatment regimens) may indicate a severe problem requiring treatment (usually medication, psychotherapy, or both).

Physicians recommend that patients receive an evaluation for clinical depression if they have five or more symptoms of the disorder that last for more than two weeks or disrupt a patient's normal day-to-day functioning (please see list above).

Some of these symptoms, such as fatigue and appetite loss, can also arise as a result of treatment for cancer or from the disease itself. According to the National Institute of Mental Health, if symptoms of uncertain origin are present with additional depressive symptoms, they may still indicate clinical depression.

Certain individuals with cancer may be more likely than others to become depressed. Risk factors include a history of depression, alcohol or substance abuse, poorly controlled pain, social isolation, socioeconomic pressure, and advanced-stage cancer. Just because you have these risk factors does not mean that you will become depressed, but being aware of them is important. Dealing with stressors not directly related to your cancer can often help alleviate some of your sadness or anxiety.

Advice for patients

If you or someone you love is having difficulty dealing with cancer or the daily stress of life, it may be time to try something new. Don't be afraid to talk about your feelings with friends and family members and to encourage them to talk about theirs in return. Don't, however, force your loved ones to have these discussions, recommends the American Cancer Society. Just providing reassurance and support can also help.

Seeking private counseling or joining a support group may bring you comfort. Or practice deep-breathing exercises several times a day to relieve tension: close your eyes, breathe in deeply, and breathe out slowly while you concentrate on each body part, one at a time, and relax it; when your whole body is relaxed, think of a pleasant place to be.

If you have tried several of these activities and the depressive symptoms outlined above are still present after several weeks or are still interfering with your daily activities, talk to your health care professional. Treatment for clinical depression has improved greatly over the past 10 to 15 years with the introduction of newer, more effective, and safer antidepressants, and the large majority of patients with clinical depression who are started on medication have a good response. Feeling depressed is certainly not something to be embarrassed about, and seeking help is a great start to feeling better.

For more information, contact your physician or contact the M. D. Anderson Information Line:

☎️ (800) 392-1611 within the United States, or
☎️ (713) 792-6161 in Houston and outside the United States.

May 2002

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M. D. Anderson’s Emergency Center

Carmelita Escalante, M.D.
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The emergency care of patients with cancer is extremely complex. They may require treatment for conditions related to the malignancy (for example, dyspnea secondary to lung cancer), a complication of cancer therapy (including heart failure secondary to doxorubicin-induced cardiomyopathy), or an underlying comorbid condition, such as uncontrolled diabetes mellitus.

Emergency and urgent care for patients at M. D. Anderson Cancer Center is provided through the institution’s own Emergency Center. To ensure that the center’s resources are used in the most efficient manner possible, patients and their physicians are asked to keep the following guidelines in mind.

Patients who are not registered at M. D. Anderson are given a medical screening examination in the Emergency Center to determine if they require emergency or urgent care. If the patient has a stable medical condition, he or she is referred to the institution’s New Patient Referral Office and discharged from the Emergency Center with instructions for further care to be provided by their local physician.

Patients requiring transfer to M. D. Anderson should go through the usual registration procedures via the New Patient Referral Office.

M. D. Anderson patients often return home between cancer treatments, or they may receive treatments at a local health care facility. If emergency or urgent complications develop, we advise these patients to seek care at the nearest emergency care center. We also request that the local emergency center physician call the patient’s cancer specialist at M. D. Anderson to discuss whether the patient should receive further care at the local emergency center or be transferred to M. D. Anderson. Communication is essential in these situations to provide our patients the best and safest venue for continued care.

Patients who call the Emergency Center with urgent or emergency symptoms are advised to seek evaluation at their nearest emergency center, especially if they are far from M. D. Anderson. We do not give medical treatment advice via the telephone. Instead, we request that patients come in for evaluation, and we offer to connect them via telephone with their cancer specialist.

Because they routinely see patients with acute problems, physicians in the Emergency Center are able to rapidly evaluate and treat a multitude of medical problems. The Emergency Center physicians then discuss with the cancer specialists the final disposition and appropriate follow-up schedule for the patient. This teamwork between our Emergency Center staff and the cancer specialists provides our patients with the best possible care—no matter what their emergency.