Overcoming Side Effects:
Department of Internal Medicine Specialties Finds Ways to Continue Critical Treatments

by Beth Notzon

Most of their work is conducted behind the scenes, away from the glow of the public limelight. Their laboratory: every clinic and hospital bed, every physician examining room. Their discoveries may not make the evening news, but when cancer treatments bring patients to the edge of what their bodies can tolerate, it is the efforts of the physicians in the Department of Internal Medicine Specialties that enable patients with cancer to continue potentially lifesaving therapies.

Working hand-in-hand with oncologists at The University of Texas M. D. Anderson Cancer Center, Robert F. Gagel, M.D., and his staff in the Department of Internal Medicine Specialties study and treat the side effects of cancer and cancer treatments. Because M. D. Anderson has the largest centralized outpatient chemotherapy unit in the world,
Dr. Gagel and his colleagues have a very large patient population in which to study side effects and their prevention and treatment. Physicians and researchers at M. D. Anderson also encounter large populations of patients who have rare types of cancer.

This proved to be an important advantage for the department in a recent experience with an experimental chemotherapeutic agent called Targetin. Targetin was designed to treat various cancers, including cutaneous T-cell lymphoma, a very rare lymphoma that affects four in 1,000,000 people annually. In clinical trials with Targetin, described in a recent article in The New England Journal of Medicine, Steven I. Sherman, M.D., other members of the Section of Endocrine Neoplasia and Hormonal Disorders, and members of the Section of Dermatology, headed by Madeleine Duvcic, M.D., observed that some patients developed an unusual form of hypothyroidism.

Dr. Sherman and his colleagues monitored the thyroid function of all patients being started on Targetin therapy and conducted studies to determine the etiology of the dysfunction. These studies revealed that the hypothyroidism was caused by “a unique suppression of the pituitary that then suppressed thyroid hormone production,” said Dr. Sherman. The studies also showed that thyroid hormone replacement therapy could both reverse and prevent the hypothyroidism.

Thanks in part to these findings, Targetin is now one step closer to its clinical debut. Of even more far-reaching consequence, Dr. Sherman noted that researchers have targeted the Targetin class of agents for potential use in the treatment of diabetes and tamoxifen-resistant breast cancer.

The physicians in the Department of Internal Medicine Specialties have either general internal medicine training or subspecialty training and focus on internal medicine problems associated with cancer. The specialties include cardiology, pulmonary medicine, infectious diseases, gynecologic and medical therapeutics, endocrine neoplasia and hormonal disorders, dermatology, and infection control.

In an ongoing effort initiated in the Section of Cardiology over a decade ago, Harry R. Gibbs, M.D., and Michael S. Ewer, M.D., have studied strategies to prevent cardiomyopathy, a particularly troublesome side effect that can occur in patients who receive doxorubicin. Doxorubicin has the widest spectrum of antitumor activity of any chemotherapeutic agent, but the cardiomyopathy it can produce is both serious and irreversible. Dr. Gagel explained that Drs. Gibbs and Ewer and their colleagues were “instrumental in first defining the toxicity of these compounds and then developing strategies for their safe use—specifically, alternative ways of administering the drugs.” This involved working very closely with the Department of Breast Medical Oncology, the Department of Melanoma/Sarcoma Medical Oncology, and the Division of Pediatrics.

Dr. Steven I. Sherman’s research into a side effect associated with Targetin has brought the experimental chemotherapy drug closer to clinical use.

Members of the Section of Infectious Diseases, headed by Kenneth Rolston, M.D., and members of the Section of General Internal Medicine studied whether some patients who develop neutropenia in response to chemotherapy and who acquire infections could be treated on an outpatient basis. Dr. Rolston explained that in addition to being more comfortable, patients treated at home would be less likely to be exposed to hospital-borne infections. Dr. Rolston and his colleagues found that, in fact, there are patients with neutropenia-induced infections who can be safely managed on an outpatient basis. These findings have served as a basis for universal guidelines for treatment of neutropenia-induced infection.

This sort of analysis is now being extended by other members of General Internal Medicine to the possible outpatient treatment of other side effects including diarrhea and mucositis, the gastrointestinal epithelial cell injury associated with chemotherapy.

A weakened immune system is an important side effect of chemotherapy that increases the risk of infection in cancer patients. Issam I. Raad, M.D., who heads the Section of Infection Control, has been instrumental in the development of an antibiotic-impregnated central venous catheter that prevents catheter-related infection, a potentially serious problem in patients with cancer. Dr. Raad noted that in a recent multi-institutional trial (described in The New England Journal of Medicine), the catheter he developed in collaboration with Rabih Darouiche, M.D., at Baylor College of Medicine proved to be 12 times more effective in preventing infection than an antiseptic-impregnated catheter already on the market. The antimicrobial activity in the catheter developed by Drs. Raad and Darouiche also lasted considerably longer than that of the other catheter. The technology used in the development of the new catheter is now being applied to heart valves, urinary catheters, and percutaneous catheters.

Another important role of the department is diagnosing the side effects of cancer treatment. Armando J. Huaringa, M.D., and his collaborators in the Section of Pulmonary Medicine focused on a diagnostic method to determine the cause of pulmonary edema. Pulmonary edema can result from cardiac failure or from direct lung injury, and the management of each type of edema is different. However, until recently there was no reliable test that could
Side Effects of Cancer and Cancer Treatments Are the Subject of Clinical Investigations

Clinical trials in progress at The University of Texas M. D. Anderson Cancer Center include the following for patients experiencing side effects from cancer or cancer treatments.

- A randomized trial of outpatient antibiotic therapy for the treatment of febrile episodes in neutropenic patients with lymphoma or breast cancer undergoing high-dose chemotherapy followed by autologous bone marrow transplantation or peripheral blood progenitor support (DM97-161). **Physician: Kenneth V.I. Roelston, M.D.**

Patients in the treatment arm of this study will receive intravenous antibiotics at home. To participate, the patient must live or stay within 30 miles of the study site and have a telephone in his or her home and a caregiver who is willing and able to provide care and transportation during the first 72 hours of the study. Parents who have had previous anaphylactic reactions or are hypersensitive to meropenem, nafcillin sodium, cefazidine, or any penicillin-related agent are not eligible. Adequate blood pressure, respiratory rate, and renal function are required. Patients with uncontrolled hypercalcemia, hyponatremia, or abnormal transaminase levels may not participate. Patients with infections caused by bacteria known to be resistant to the study drugs as well as patients with mycobacterial, fungal, viral, rickettsial, chlamydial, or protozoal infections are ineligible. Participants must be older than 16 years and cannot be pregnant. Uncontrolled nausea and vomiting, grade 4 mucositis, and prosthetic valve endocarditis are also criteria for exclusion.

- A study of the compassionate use of SR29142 for prevention or treatment of hyperuricemia at multiple centers in the United States and Canada (P99-025). **Physician: Sima Jeha, M.D.**

Cancer patients of any age who have or are at risk of developing acute hyperuricemia will receive both inpatient and outpatient treatment. The length and frequency of hospitalization will be determined by the patient's clinical course and need for supportive care. Patients who have received prior treatment with SR29142 will return for evaluation 15-30 days after the first.

(Continued on next page)
Advances in Control of Nausea, Vomiting Aim to Reduce ‘Misery Quotient’

by Dawn Chalaire

Despite improved methods of control, chemotherapy-induced nausea and vomiting remain among the most common—and most dreaded—side effects experienced by patients with cancer. "Sometimes what our patients worry about and what we worry about are different," said Cynthia Hodges, R.N., an Oncology Nurse Specialist in the Department of Melanoma/Sarcoma Medical Oncology. "We’re more concerned about major toxicities that might be life-threatening or cause serious complications. They’re more concerned with the ‘misery quotient’: the nausea, vomiting, aching, and fatigue. Those kinds of symptoms are, for patients, more problematic because those are the things that make them feel unwell."

In addition to diminishing a patient’s quality of life, nausea and vomiting also have been associated with degeneration of self-care and functional ability, wound dehiscence, esophageal tears, and, in extreme cases, the discontinuation of potentially curative treatments. While there have been no studies conducted recently on the effects of chemotherapy-induced nausea and vomiting in large groups of patients, it is clear that nausea and vomiting still cause patients emotional distress and can lead to malnutrition and dehydration. With that in mind, researchers and clinicians at The University of Texas M. D. Anderson Cancer Center are taking a closer look at standard antiemetic guidelines, investigating new antiemetic compounds, and developing more effective strategies for treating individual patients.

The incidence of chemotherapy-induced nausea and vomiting varies according to the type and dosage of chemotherapy a patient receives. For example, a recent study found that vinblastine or fluorouracil experience emesis, while, despite the use of current antiemetics, over 20% of patients treated with cisplatin, carboplatin, cyclophosphamide, or doxorubicin have at least one episode of vomiting. Chemotherapy agents can cause different types of nausea and vomiting, including acute (less than 24 hours after chemotherapy), delayed (more than 24 hours after chemotherapy), and anticipatory.

Chemotherapy-induced nausea and vomiting are believed to be caused by the stimulation of neurotransmitter receptors, which in turn trigger a response in the brain’s vomiting center. For acute nausea and vomiting, the most effective antiemetic drugs in use are the 5-hydroxytryptamine-3 (5-HT3) receptor, or serotonin, antagonists. These medications block activation of the neuromuscular receptor serotonin. Some chemotherapy agents (particularly cisplatin, cyclophosphamide, and doxorubicin) cause delayed nausea and vomiting. While the underlying mechanism is not completely understood, neurotransmitters are again believed to play a role; however, 5-HT antagonists are not as effective at preventing delayed nausea and vomiting.

One solution to this problem is being sought by Edward B. Rubenstein, M.D., an associate professor in the Department of Anesthesiology and principal investigator of a study designed to test the effectiveness of a neurokinin (NK1) inhibitor compound in preventing
"... there is less science and more artistry in finding out what really works best for a particular patient..."

Amy Wood, Pharm.D., visits with a patient. Dr. Wood is studying the effectiveness of current antiemetic guidelines used to treat chemotherapy-induced nausea and vomiting in patients with lymphoma.

delayed nausea and vomiting. The compound, which belongs to a family of peptides called tachykinins, works deep in the brain to inhibit the release of nausea and vomiting signals from the neurotransmitter substance P.

The multicenter study aims to recruit 900 patients from over 40 centers in North America (12-16 from M. D. Anderson) who are receiving cisplatin-based chemotherapy for the first time and have had no previous etiologic therapy. Participants will be randomized into three groups: one group will receive standard antiemetic therapy with a 5-HT3 receptor antagonist plus dexamethasone and a placebo, and the other two groups will receive different dosages of the NK1 inhibitor compound combined with a 5-HT3 receptor antagonist and dexamethasone.

"There were two trials published earlier this year in which NK1 inhibitors given in combination with standard drugs showed promise," Dr. Rubenstein said, "so we are excited about this trial."

Some chemotherapy regimens, such as those administered to lymphoma patients, can cause both acute and delayed nausea. The antiemetic drugs are prescribed to these patients based on guidelines that are tailored to fit the unique sets of patients and chemotherapy regimens at M. D. Anderson, said Amy M. Wood, Pharm.D.

"There are a lot of antiemetic guidelines produced on the national level and within individual institutions," Dr. Wood said. "Unfortunately, there have not been any studies done to show the outcomes associated with these guidelines."

In response to that need, Dr. Wood recently surveyed 100 lymphoma patients who were receiving chemotherapy and antiemetic medication at M. D. Anderson. Some of the questions on the outcomes survey included the number of times a patient vomited or experienced nausea, how the nausea and vomiting affected daily activities, the patient's overall satisfaction with their nausea and vomiting control, and the patient's assessment of the severity of their nausea.

Dr. Rubenstein is working with Dr. Wood to analyze the data from the survey. Once they are finished, Dr. Wood said, the results will be presented to M. D. Anderson's guidelines task force, and, she hopes, the outcome studies will be expanded to other services and to outpatients.

"Using the information obtained from large numbers of patients in these outcome studies, we can decide if we need to readjust our guidelines," Dr. Wood said.

Because each patient responds uniquely to chemotherapy and antiemetic drugs, the most efficacious antiemetic guidelines for a particular chemotherapy regimen don't always work for every patient. Thus, Dr. Wood said, modifying an antiemetic combination to treat patients experiencing breakthrough emesis requires a knowledge of the literature on different combinations, clinical experience, and some trial and error.

"That's where there is less science and more artistry in finding out what really works best for a particular patient and drawing on different types of agents that work in different ways," Dr. Wood said.

According to the National Cancer Institute, 10% to 44% of patients who experience nausea and vomiting with an initial course of chemotherapy will develop anticipatory emesis, which is a conditioned response to a smell, taste, sight, or sound (as in the case of one of Cynthia Hodges' patients whose vomiting was triggered by the sound of an approaching utility cart). Since anticipatory nausea is directly linked to an earlier unpleasant experience with chemotherapy, the best way to prevent it is to prevent the initial nausea by aggressively treating patients for it up front.

"Lymphoma is a curable disease," Dr. Wood said, "so we don't want to compromise the intensity of the chemotherapy. Therefore, we very aggressively employ all the different antiemetic medications that are out there in whatever combination we can to get the patient through the chemotherapy as comfortably as possible."

For more information, contact Dr. Rubenstein at (713) 794-4319 or Dr. Wood at (713) 792-6954.
During a recent Anderson Network Partners in Knowledge, News in Cancer (P.I.K.N.I.C.) session, presenter Rena Sellin, M.D., a professor in the Department of Internal Medicine Specialties at The University of Texas M.D. Anderson Cancer Center, surprised some of the 25 or so people in attendance by walking to the front of the room and promptly sitting down.

Dr. Sellin, a frequent P.I.K.N.I.C. presenter, sees the sessions as an opportunity to encourage interaction between physicians and patients, so she began talking to her audience in a conversational tone—inviting questions, welcoming comments, and tailoring her presentation on "The Role Chemotherapy and Radiation Play in the Onset of Osteoporosis" to what those attending wanted to know.

"I think it's important for us to have informal sessions where patients can have direct access to doctors and have the opportunity to ask questions about their healthcare outside of their formal clinic visits," said Dr. Sellin.

Led by physicians and other staff members at M. D. Anderson (and, occasionally, by speakers outside the institution), the free, weekly P.I.K.N.I.C. sessions give patients, caregivers, and family members what they crave most from physicians—time, information, and accessibility.

The program started out of the voice of the patients. This was something that they asked for and we saw a need for," said Felicia Gonzalez, whose responsibilities as Special Programs Coordinator for the Anderson Network include the P.I.K.N.I.C. program.

P.I.K.N.I.C. is one of many projects run by the Anderson Network, a patient-to-patient support program composed of current and former M. D. Anderson patients. Since its launch in 1993, Gonzalez said, the goal of P.I.K.N.I.C. has been "to provide information to patients, put it in their terms, and empower them. It gives them the tools and resources that they need to be able to talk with their doctors."

Past P.I.K.N.I.C. topics have included breast reconstruction options, stereotactic radiosurgery, soft tissue sarcoma, endostatin trials, and gene therapy. Some of the most-requested topics—which are repeated several times a year—include nutrition, fatigue, depression, coping with the fear of recurrence, and communicating with your doctor. Most of the suggestions for P.I.K.N.I.C. topics come from patients, who are asked to fill out a questionnaire after each presentation. Suggestions also come from faculty and staff.

"I think people should be knowledgeable about what is being done to them," Dr. Sellin said. "The more informed they are, the more successfully they go through a disease."

Gonzalez said that the information presented during P.I.K.N.I.C. sessions is often technical, and patients appreciate a simple, straightforward presentation without glossing over the information or making it too elementary.

"Nothing pleases the patients more than having a doctor take the time to speak on a topic and answer questions," she said. "That means so much to the patients."

Mary Hughes, an advanced practice nurse in the Department of Psychiatry, talks about "Coping with the Fear of Recurrence" during a recent P.I.K.N.I.C. session.

"For more information about P.I.K.N.I.C., contact the Anderson Network at (713) 792-2553."
You have cancer.” Anyone who has ever heard those words knows that they have the power to change lives. Once the initial shock has worn off, patients often respond to the news of a cancer diagnosis with an almost endless list of questions: What caused my cancer? Will I be okay? What do I do now? What are my treatment options? How can I take care of my family?

None of these questions have simple answers, but for patients and their families, taking the first step toward getting the information they need to cope with cancer can be as easy as dialing a telephone.

Make the call

The Cancer Information Service (CIS), launched in 1976 by the National Cancer Institute (NCI), is a nationwide information and education program composed of 14 regions throughout the United States. One simple phone number, 1-800-4-CANCER, links callers across America to comprehensive information about different types of cancer, ongoing research, treatment options, financial resources, and psychological and social support.

Although there is only one phone number, calls are usually answered by the office in the region where the call originated. For example, a caller from Houston will be connected to a CIS information specialist in the South Central Region. The information specialist can give the caller up-to-date information about hospitals, clinics, and research studies, as well as information about support groups and other resources provided by local agencies and organizations and by local chapters of national organizations such as the American Cancer Society.

Choose a source

Callers who dial 1-800-4-CANCER have the option to: 1) talk to an information specialist, 2) order printed information, or 3) hear a recorded message about a particular topic. Information Specialists receive two months of initial training through the NCI and are certified to answer questions using NCI resources. They can also send callers printed literature produced by the NCI or refer callers to another agency or organization that offers support services.

Don’t be afraid to ask

Most of the calls received by the CIS fall into one of three categories: clinical trials, treatment options, and financial assistance and psychological and social support.

Clinical Trials

Patients can get up-to-date information about the clinical trials being conducted at locations near them. The information specialist can describe the enrollment criteria but cannot verify that the patient is eligible. The database includes information about trials investigating various cancer treatments as well as early-detection and prevention studies.

Treatment Options

In some cases, there is more than one way to treat a particular type of cancer. The information specialist can provide a brief description of some of the options and will forward written information to the caller.

Financial Assistance and Support

Many patients have urgent concerns that aren’t directly related to their cancer care: How am I going to make my rent payment this month? While I’m taking chemotherapy, who will watch my children? Is there someone out there who’s been through this that I can talk to? Information specialists have access to a wealth of information about agencies and organizations that provide financial, psychological, social, and other types of support.

After you hang up …

Information received from the CIS is intended to enhance, not replace, the communication between patients and their personal physicians. Information specialists always refer patients back to their personal physicians and encourage them to share the information they have received with their doctors.

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

(800) 392-1611 within the United States, or

(713) 792-5161 in Houston and outside the United States.

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Finding Meaning in Stories of Pain and Suffering

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Survivors of cancer are forever changed by their disease. The pain, disfigurement, and alienation that are often experienced by patients can cause their entire worlds—their perceptions of self, their social realities, and their relationships with others—to unravel. For many, particularly those with metastatic disease, the experience of pain makes it difficult to continue to find meaning in their lives. Culture, ethnicity, and class issues can also increase survivors’ feelings of pain and suffering.

Because pain is inherently subjective, a patient’s own report is the most important assessment tool. The information gathered from the patient usually focuses on frequency, location, severity, and type of pain and on factors that exacerbate or relieve pain. There is evidence, however, that many patients with cancer do not report their pain to their physicians. In addition, research has shown that minority patients with cancer are less likely to receive adequate analgesia and other treatments for cancer-related pain. For these and other reasons, clinical assessments of pain and suffering often fail to adequately capture the damage caused by illness or convey the survivors’ attempts to articulate their experiences. There is a need for methodological approaches that can assess the individual pain and suffering of patients within the cultural, historical, and biological contexts of their lives.

To improve understanding of cancer patients’ experiences with pain and suffering, I led a pilot study to investigate cultural and gender differences in African-American and white patients’ experiences with head and neck and lung cancer. Using qualitative methods, including narrative analysis, I found that helping patients construct stories from their experiences of illness can, in turn, help patients create a sense of meaning out of those experiences. If patients are able to construct narratives, some of their suffering may be alleviated, and their life experiences may once again have coherence and continuity. Thus, rather than seeing themselves as passive victims caught in a terminal web of disease progression, they become authors of their own experiences.

No narrative is fixed; every narrative of the self in pain and the self that suffers is open to interpretation. By telling stories, patients can attempt to make sense of their experiences and remake their shattered worlds, thereby enhancing their communication with clinicians. By listening to the narrative experiences of patients and incorporating these in the treatment of pain, researchers may better understand the meaning of cancer pain and improve their ability to alleviate pain and suffering.