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REPORT TO PHYSICIANS

JULY/AUGUST 2004 Vol. 49, No. 7/8

Oncology



Dr. Alfred R. Smith, a professor in the Department of Radiation Physics, stands before M. D. Anderson's new Proton Therapy Center, which is slated to open in the fall of 2006. Dr. Smith is overseeing the design, assembly, installation, and testing of equipment for the 88,000-square-foot, \$125 million facility.

Proton Therapy Comes into Its Own

by Dawn Chalaire

It may come as a surprise to many to learn that patients were first treated with protons more than 50 years ago at the University of California's Cyclotron Laboratory in Berkeley. Beginning in the early 1960s, the Harvard Cyclotron Laboratory in

Cambridge, Massachusetts, in collaboration with Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary in Boston, provided continual proton therapy until it was replaced with a modern facility at Massachusetts General Hospital in 2002. So far, about 36,000 patients worldwide have been treated with proton therapy.

Yet, in the United States, the field has only recently begun to come into its own, with a number of new facilities dedicated to proton therapy scheduled to open in the next few years.

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THE UNIVERSITY OF TEXAS
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CANCER CENTER

Proton Therapy Comes into Its Own

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According to Alfred R. Smith, Ph.D., a professor in the Department of Radiation Physics at The University of Texas M. D. Anderson Cancer Center, the surge in new proton therapy centers in the United States can be attributed to three factors: (1) positive results of clinical studies of proton therapy were published; (2) proton facilities applied for and were granted procedure codes from the American Medical Association, and Medicare and insurance providers set reimbursement rates, which enabled proton therapy providers to be paid; and (3) once it became evident that such centers would be able to charge for their services, more vendors became interested in designing and building proton therapy facilities.

The economic feasibility of proton therapy centers coincided with the development of more precise imaging and proton treatment delivery methods. Although the precision of proton beam therapy has been known for decades, applications were limited to a few anatomic sites because of energy and treatment delivery limitations and the difficulty in precisely defining the tumor volume to be treated.

Beginning in the late 1970s, improved imaging modalities and

improved means of contrast enhancement greatly increased the precision with which tumors could be visualized. These improvements, combined with a better understanding of tumor biology and the power of sophisticated computers for treatment planning, helped to justify the cost and effort required to build clinical proton therapy facilities.

A new \$125 million Proton Therapy Center under construction at M. D. Anderson (see related article on page 3) will join 20 proton therapy facilities worldwide (four in the United States) that are treating patients. A hospital-based center is under construction at the University of Florida at Jacksonville, and at least five other centers are in the initial planning stages.

“So it’s a very exciting period for proton therapy. Those of us who have spent most of our lives in particle therapy are of course very happy about this,” said Dr. Smith.

The advantages of protons

The main advantage of protons over photons has to do with the way their energy is released. Much of the total dose of a photon is deposited before it gets to a tumor, and a photon beam continues to deposit energy after passing

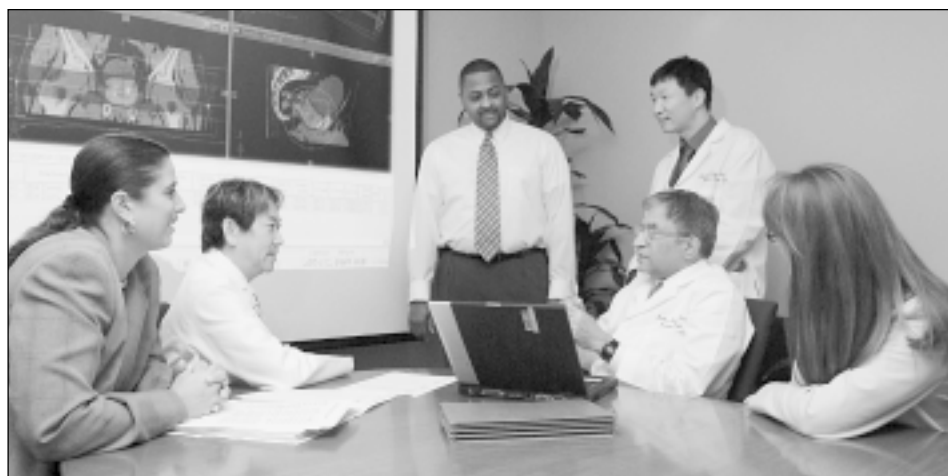
through the tumor. Protons, on the other hand, deposit a much lower dose before arriving at the tumor and can be stopped immediately after exiting the tumor. This results in a much lower dose to normal surrounding tissues while allowing for the delivery of a higher treatment dose to the tumor with fewer side effects. Higher doses delivered to the tumor will result in higher rates of local control and disease-free survival in many tumor sites.

“It is our strong belief that most tumors that are treated with x-rays can receive a more localized dose distribution with protons,” Dr. Smith said. “In those cases where local control is quite good with photons, you can decrease late effects using protons.”

Improving proton therapy

In standard proton therapy, a proton beam entering the treatment delivery nozzle is scattered into a broad, uniform beam and shaped to conform to the tumor. The process of scattering the protons generates neutrons, which could cause late effects, including new tumors years after treatment. These effects are comparable to those caused by radiation therapy using photons, which can be cause for concern. Using computerized treatment planning methods, a team of researchers led by Radhe Mohan, Ph.D., professor and chair of the Department of Radiation Physics, is applying intensity-modulated delivery techniques to proton therapy. This method of treatment delivery will use a pencil-beam scanning nozzle that was designed especially for the M. D. Anderson facility.

With intensity-modulated proton therapy, or IMPT, a single, narrow proton beam about a centimeter in diameter is swept across the tumor from multiple directions, depositing the radiation dose, mostly near the end of the beam’s range. The energy of the proton beam can be changed at any time to penetrate the tumor at varying depths. The technique is also known as pencil-beam scanning, but Dr. Mohan describes the process as using a paintbrush to apply proton energy to the tumor. “Using magnets, we make it sweep across the tumor,” he said, “but



The proton therapy planning system development team discusses a sample treatment plan for a patient with prostate cancer. Sitting from left to right are **Robin Famiglietti**, an administrative director in the Department of Radiation Physics; **Dr. Shiao Woo**, a professor in the Department of Radiation Oncology; **Dr. Radhe Mohan**, professor and chair of the Department of Radiation Physics; and **Beverly Riley**, a medical dosimetrist in the Department of Radiation Oncology. Standing from left to right are **Stephen Bilton**, a clinical supervisor in the Department of Radiation Physics, and **Dr. Xiaodong Zhang**, an instructor in the Department of Radiation Physics.



When the new Proton Therapy Center opens in 2006, it will house four treatment rooms and be equipped to treat 3,400 patients a year.

Building from the Ground Up **A New Proton Therapy Center at M. D. Anderson** **Will Offer Patients the Latest Technology and Practices**

When Alfred R. Smith, Ph.D., a professor in the Department of Radiation Physics, came to The University of Texas M. D. Anderson Cancer Center two years ago, there was only one item on his to-do list: oversee the design, assembly, installation, and testing of literally tons of complicated equipment—and the software needed to operate it—for an 88,000-square-foot, \$125 million Proton Therapy Center.

For someone shouldering such a huge responsibility, Dr. Smith seemed unusually calm, almost serene, as he described the steps involved in such a task. First, Dr. Smith—who came to M. D. Anderson from Massachusetts General Hospital in Boston, where he was involved in the construction and commissioning of the modern proton therapy center there—and his team spent three months writing the specifications for the equipment, which includes three huge gantries that rotate around the patient, enabling the delivery of treatment from 360 degrees, and a high-energy synchrotron, a compact particle accelerator that emits proton beams of different energies. He then wrote the scope of work and,

along with Wayne Newhauser, Ph.D., an assistant professor in the Department of Radiation Physics, and others, began working with Hitachi, a Japanese company, to design the equipment to meet their specifications. Next came more than a dozen intensive design reviews, followed by assembly and testing of the equipment in Japan. The team was joined last summer by Martin Bues, Ph.D., and more recently by George Ciangaru, Ph.D., both instructors in the Department of Radiation Physics.

“We did a complete assembly in the factory and a mechanical test of the gantry,” Dr. Smith said. “It passed with flying colors. I’m just amazed because it is such an engineering feat.”

After passing inspection in Japan, the equipment was shipped to Houston, where it arrived in June. Moving such massive, yet delicate, equipment is a monumental task in and of itself. “The large gantries, which are 190-ton devices that are three floors in height, are broken down into several pieces,” said Dr. Smith. “We can lower the individual pieces through some large hatches in the ceiling [of the Proton Therapy Center]. The synchrotron is

made up of many magnets that can be brought in individually and set up.”

Dr. Smith, Dr. Newhauser, and their team will be on hand to oversee the reassembly of the equipment in Houston and then perform acceptance testing to verify that it meets all of their specifications. If all goes as planned, all four treatment rooms will be operational by the fall of 2006, at which time the center will be equipped to treat about 3,400 patients a year. But the work of Dr. Smith and his colleagues will not be finished.

“We’re thinking about how to improve some of the technology—even before it is installed. We wanted our facility to be on schedule, to be safe and very robust. One makes certain conservative decisions in that process, and having made those decisions, I realize that there is potential to make improvements in the design. Already, we are discussing certain patents that we will hold jointly with Hitachi to develop new technology and techniques in the future,” Dr. Smith said. ●

FOR MORE INFORMATION, contact Dr. Smith at (713) 563-1519.

as it is sweeping, we can also change its energy. In a way, we have a brush that we’re painting the tumor with. We can deposit some dose here, then come from another direction and paint it from a different direction.”

The software needed to plan IMPT treatments for individual patients is being developed by Dr. Mohan and his

colleagues. The treatment planning process involves simulating the treatment on a computer, making adjustments, and calculating the optimum dose. “Treatment planning is a very large part of the whole thing,” Dr. Mohan said. “You have the treatment delivery component, which is what the machine will do, but then you

have to tell the machine what to do.”

In addition, Drs. Mohan and Smith and their teams are developing techniques for respiratory-correlated, image-guided proton therapy, in which movement caused by breathing is incorporated into the treatment-planning model.

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Proton Therapy Comes into Its Own

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Defining proton therapy's potential

All patients treated in M. D. Anderson's new Proton Therapy Center will be entered into protocols. In general, these studies will help clinicians understand how to use proton therapy optimally and quantify the improvements in clinical outcomes that can be achieved with proton therapy. A specific question that the researchers will try to answer is whether proton therapy can be delivered in fewer fractions at higher doses per fraction. Completing treatments during a shorter period of time by delivering fewer fractions would allow for minimal tumor growth, be less expensive, and enable the center to treat more patients. However, clinical studies are needed to determine how much treatments can be shortened without sacrificing efficacy or safety.

Because, on average, protons deliver half the dose to normal tissues that photons deliver, it may be possible to give a more intense regimen of chemotherapy in conjunction with proton therapy, with fewer side effects than can be expected with chemotherapy combined with photon therapy.

Another question about proton therapy that researchers hope to answer has to do with the biological effect of protons. Owing in part to the ability of protons to kill tumor cells in the absence of oxygen, proton therapy produces an elevated biological response in tumor cells. In general, this effect is believed to be about 10% greater than that of photon therapy, but the response appears to vary depending on the type of tumor, the dose, and other factors.

"I think there can be a number of studies done to more clearly define the tissue-, organ-, and tumor-specific biological response. Once we do that, it will enable us to give even better treatment. Instead of using a generalized factor for all tissues and all tumors, we will be able to optimize the treatment even more," Dr. Smith said. ●

FOR MORE INFORMATION, contact Dr. Smith at (713) 563-1519 or Dr. Mohan at (713) 563-2505.

Treating Patients with Cancer

by David Galloway

When a cancer is diagnosed, it is common for all attention to be focused on the tumor, and everything else—including the patient's other medical conditions—tends to fall by the wayside. But if the patient is cured of cancer and dies of a heart attack the following week, the treatment cannot be considered a success.

"It's important to keep comorbid conditions in mind for the sake of the entire patient and not just focus on the cancer," said Ellen F. Manzullo, M.D., F.A.C.P., an associate professor in the Department of General Internal Medicine, Ambulatory Treatment, and Emergency Care at The University of Texas M. D. Anderson Cancer Center, "because the patient can do extremely well as far as their cancer is concerned but subsequently die of coronary artery disease or stroke."

Some comorbid conditions exist before the cancer, and others develop later on. "As survival increases with cancer, we are going to run into patients who have had the time to develop other problems that might not be related to the cancer," said Joseph Swafford, M.D., an associate professor in the Department of Cardiology at M. D. Anderson. "And when they come back for surveillance, we end up picking up on some of those problems."

Comorbidities affect cancer treatment

A patient's other medical conditions can alter the course of cancer treatment. For example, for a patient with a single lung tumor, surgery would normally be the first treatment considered. However, if that patient has severe chronic obstructive pulmonary disease

or coronary artery disease, surgery might prove more deadly than the lung cancer.

As many as 25% of patients whose lung tumors would otherwise be considered resectable cannot undergo surgery because of heart or lung problems, said Ritsuko Komaki, M.D., F.A.C.R., a professor in the Department of Radiation Oncology at M. D. Anderson. "We have to treat those patients with radiation therapy, alone or with chemotherapy," she said. At the same time, internal medicine specialists administer medications or use physical therapy to improve the patient's lung function or cardiac function so that surgery will be an option later.

Of course, there are emergency situations in which there is no choice but to take a patient to surgery. But in most other cases, internists have time to evaluate the patient before surgery and develop strategies to maximize the safety and success of surgical procedures, Dr. Manzullo said.

A patient's comorbid conditions can also interfere with chemotherapy and radiation therapy. In lung cancer, "usually, we go with concurrent treatment, chemotherapy and radiation therapy," Dr. Komaki said. "The chemotherapy will promote the radiation effects to kill more cancer cells. But it also sensitizes the normal cells, and sensitive normal cells will be killed by concurrent chemotherapy and radiation therapy." A patient with compromised lung function or cardiac function might not be able to tolerate that damage, so researchers are searching for the optimal sequential treatment.

Other conditions affecting cancer treatment include hypertension, diabetes, kidney problems, congestive heart failure, and Alzheimer's disease.

Diabetes, for example, complicates cancer treatment by interfering with a patient's healing processes. Concurrent chemotherapy and radiation therapy, commonly used in the treatment of many cancers, lowers a patient's blood count, especially the neutrophils. Patients with diabetes are then left especially vulnerable to infections.

Requires Looking Beyond the Tumor



Dr. Ellen F. Manzullo, an associate professor in the Department of General Internal Medicine, Ambulatory Treatment, and Emergency Care, consults with patient ██████ in the Ambulatory Treatment Center.

Although the connection might not seem obvious, Alzheimer's disease and other cognitive disorders can alter the treatment of lung cancer. In the case of nonmetastatic small cell lung cancer (SCLC), the usual treatment includes prophylactic brain irradiation to counteract that disease's propensity to spread to the brain. However, prophylactic brain irradiation is contraindicated if the patient's mental function is already compromised by Alzheimer's disease, chronic alcoholic brain syndrome, or other mental disorders.

"Sometimes, these patients have medical conditions that they're not even aware of," Dr. Manzullo said. "They come here for their cancer treatment, and then we discover that they have other medical conditions that need to be treated."

Identifying and treating comorbid conditions can significantly affect a patient's overall prognosis. "Sometimes, it can be just as important as the cancer itself as far as determining how well the patient will do," Dr. Manzullo said.

Cancer and treatment affect comorbidities

Other comorbid conditions are caused by cancer or its treatment. SCLC, for example, produces a hormone that can lead to Eaton-Lambert syndrome, leaving a patient with severe muscle weakness. If the SCLC is resected or otherwise successfully treated, the patient's muscle strength will return.

Sometimes, a comorbid condition caused by a cancer will appear before the malignancy is found. Dr. Komaki told of a 70-year-old woman undergoing treatment for SCLC whose cancer was discovered in an attempt to diagnose a sudden mental deterioration. "She was totally confused, and so she was taken to the emergency room, where they did an MRI [magnetic resonance imaging], and there was no cancer or any other abnormality. But her sodium level was very, very low. That was caused by small cell lung cancer, or paraneoplastic syndrome. Now, after two weeks of treatment, her sodium level is up, and she walked to the park and enjoyed the weekend. Her cancer has almost gone, and the cancer-related muscle weakness and the mental confusion have disappeared."

Some common chemotherapeutic agents—paclitaxel, doxorubicin, and trastuzumab, for example—can trigger hypertension or problems with the heart, such as arrhythmias, congestive heart failure, or bradycardia. "There are some, like 5-FU [fluorouracil] and Xeloda [capecitabine], that can cause chest pains, resulting from spasms of the arteries that go to the heart," Dr. Swafford said. Many patients on chemotherapy become anemic, and that can trigger further cardiac complications. Studies now are investigating whether drugs such as angiotensin-converting enzyme inhibitors and beta-blockers, commonly used to treat congestive heart failure, can be used to prevent that condition in patients undergoing chemotherapy.

Other agents affect the kidneys, sometimes to the point of requiring
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Looking Beyond the Tumor

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dialysis. In addition, because many patients on chemotherapy are immunocompromised, pulmonary infections are quite common.

Another treatment-related problem is esophagitis, which is caused by radiation therapy to the chest. "It is very difficult to avoid normal tissue damage right around the tumor," Dr. Komaki said. "And the esophagus is very sensitive to radiation. Esophagitis makes it very painful to swallow food, so we do everything possible to minimize that complication." The best way to minimize toxicity from radiation therapy is to limit the volume of tissue irradiated. Advances in imaging and radiation therapy delivery such as immobilization and respiration gating over the past few years have made it possible to irradiate less normal tissue while still hitting the tumor, and the hope is that fewer radiation-related complications will be seen.

Clinicians are making many efforts to limit the side effects of cancer treatment, including using more focused radiation beams and cytoprotective agents to give normal cells a fighting chance against chemotherapy and radiation therapy. One such cytoprotector is nothing new. Amifostine (WR-2721), which was synthesized at the Walter Reed Army Institute of Research during the Cold War years to protect soldiers from radioactive fallout, is activated by alkaline phosphatase,

Identifying and treating comorbid conditions "can be just as important as the cancer itself as far as determining how well the patient will do."

— Ellen F. Manzullo, M.D., F.A.C.P., associate professor, Department of General Internal Medicine, Ambulatory Treatment, and Emergency Care

an enzyme found in the membranes of normal cells but not (or at greatly reduced levels) in the membranes of tumor cells. Clinical trials have shown that it does protect normal cells, but not tumor cells, during concurrent chemotherapy and radiation therapy.

Managing comorbid conditions on an outpatient basis

Most patients treated at M. D. Anderson are seen as outpatients, and while that arrangement has many benefits for patients, it affords health-care providers fewer opportunities to assess the patient's overall health.

"They usually eat what they want and so on, so we don't have much control," Dr. Komaki said. "But I think they should be treated as outpatients. Cancer patients should function as normally as they can. We should not confine them in a hospital, the way they do in some other countries. When they are outpatients, their spirit is better, and they can be more active, which is very important to maintain their appetite and weight and to reduce the chances of muscle weakness, osteoporosis, deep vein thrombosis, depression, et cetera."

At least one therapy that is normally reserved for inpatients can now be given on an outpatient basis, in the right setting. "An example of that is the use of Natreco [nesiritide] for congestive heart failure," Dr. Swafford said. "We've worked out with the ATC [Ambulatory Treatment Center] that patients can go there and get their Natreco for six to eight hours and see if that will help decrease their need for admissions to the hospital."

On the other hand, if outpatients experience side effects when they are not at the treatment center, "we have to make sure they come to the emergency room very quickly so they don't suffer and die of complications like sepsis," Dr. Komaki said. The key to that, she said, is making sure patients are well informed. ●

FOR MORE INFORMATION, contact Dr. Manzullo at (713) 745-4516, Dr. Swafford at (713) 792-7612, or Dr. Komaki at (713) 563-2300.

Conference Offered on Comorbid Conditions

To give health-care providers a closer look at many comorbid conditions, The University of Texas M. D. Anderson Cancer Center is offering a conference, "Internal Medicine and the Cancer Patient," September 10 – 11, 2004, in the Houston Marriott Medical Center in Houston, Texas. Ellen F. Manzullo, M.D., F.A.C.P., an associate professor in the Department of General Internal Medicine, Ambulatory Treatment, and Emergency Care, will chair the conference.

The goal of the conference is to educate participants to recognize, diagnose, and treat the wide spectrum of comorbid conditions seen in patients with cancer. Participants also will be informed of the unique aspects of some of these medical conditions in cancer patients.

Presentations scheduled for the conference include the following:

- Noninvasive Diagnosis of Cardiac Disease in Cancer Patients
- Rheumatology in the Cancer Patient
- Cancer-Related Fatigue
- Osteoporosis and Other Bone Diseases in Cancer Patients
- Evaluation of Thyroid Nodules
- Psychiatric Issues in Cancer Patients
- Catheter-Related Infections
- Thrombosis/Bleeding in Cancer Patients
- 10 Years of Experience: The Ethics Consult Service at M. D. Anderson
- When the Patient has a Finding Suspicious of Cancer ... What to Do?
- Diabetes in the Cancer Patient
- Hypertension in the Cancer Patient. ●

FOR MORE INFORMATION, call the Office of Continuing Medical Education/Conference Services at (713) 792-2222.



Protecting Yourself Against Skin Cancer

Around the world, the incidence of skin cancer is skyrocketing. More than one million Americans will be diagnosed with skin cancer this year. And the occurrence of the most serious form of skin cancer, malignant melanoma, has more than doubled since 1973, according to the American Cancer Society.

What has caused this dramatic increase in skin cancer incidence? The popularity of suntans, increased recreational time spent outdoors, and thinner material used in today's clothing that allows ultraviolet light to penetrate to the skin have all contributed to the increase in skin cancer cases, as has the continual depletion of the ozone layer, which protects the Earth from ultraviolet light.

Despite these factors, there are many fairly simple changes that all of us can make to protect ourselves from the sun's damaging rays:

- ☀ Apply liberal amounts of sunscreen 20 to 30 minutes before going out-



side. Use a palm-full of sunscreen to cover your arms, legs, neck, and face. Reapply every two hours and right after swimming.

- ☀ Make sure that babies are never exposed to direct sunlight. When they are outside during the day, protective clothing should be used to shield them from the sun. Sunscreen, however, should not be used on infants younger than six months old.
- ☀ Stay out of the sun as much as possible between 10 a.m. and 4 p.m., when the sun's ultraviolet rays are strongest.
- ☀ Use a sunscreen that has a sun protection factor (SPF) of at least 15 and protects against both ultraviolet

A (UVA) and ultraviolet B (UVB) rays (see box). Both types increase your risk of skin cancer. Be aware that the SPF applies only to UVB-blocking ability. Currently, there is no rating system for UVA protection.

- ☀ Be extra vigilant about protecting children from the sun. Melanoma is linked to severe sunburns and intermittent exposure to intense sunlight, mainly before the age of 18. Children should always wear sunscreen when going outside. Regular use of sunscreen during the first 18 years of a child's life could reduce his or her lifetime incidence of skin cancer by 78%, according to M. D. Anderson Cancer Center.
- ☀ Cover up with a broad-brimmed hat, UV-protective sunglasses, clothing made of tightly woven fabrics (preferably long-sleeved shirts and pants), and, of course, sunscreen.
- ☀ Don't use tanning beds. A study published in the *Journal of the National Cancer Institute* in 2002 found that people who used tanning lamps and tanning beds were 1.5 to 2.5 times more likely to develop common kinds of skin cancer than those who did not. If you want your skin to look tanned, try a spray-on tan from a bottle.

Getting the Most out of Sunscreen Lotions

When buying a sunscreen lotion, look for brands that are waterproof or water-resistant and that contain broad-spectrum ingredients. The following ingredients provide protection against both ultraviolet B (UVB) and ultraviolet A (UVA) rays:

- ☀ *Avobenzone (Parsol 1789), oxybenzone, and sulisobenzone.* These organic formulas filter out and absorb UV light.
- ☀ *Titanium dioxide and zinc oxide.* These inorganic pigments physically block nearly all UVA and UVB rays and are not absorbed by the skin. Newer inorganic sunblocks called microfine oxides are less visible and not as messy as older ones, which left thick, hard-to-remove smudges.

People with light-sensitive skin conditions should be aware that neither organic formulas nor inorganic microfine oxides protect against visible light. Inorganic, transparent sunscreens that block visible light are currently available in Europe but not in the United States.

You may notice that a lot of sunscreens say "PABA free." The problem with PABA (*para-amino benzoic acid*), an organic formula that was once very popular, is that it does not provide protection against UVA rays, many people are allergic to it, and it can stain clothing. Worst of all, PABA may actually break down when exposed to UV light and release free radicals, which are atoms or groups of atoms that damage cells and promote aging.

- ☀ Check your skin regularly for changes in moles and birthmarks, and see your physician if you notice any changes. Remember that skin cancer, if detected early, is curable. ●

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

☎ (800) 392-1611, Option 3, within the United States, or

☎ (713) 792-3245 in Houston and outside the United States.

July/August 2004

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DiaLog

Treating Cancer-Related Fatigue

Ellen Manzullo, M.D., F.A.C.P.
Department of General Internal
Medicine, Ambulatory Treatment,
and Emergency Care

Fatigue is the most common and distressing symptom experienced by patients with cancer. Although cancer-related fatigue is usually defined as an unusual and persistent sense of



tiredness that accompanies cancer or cancer treatment, this symptom can also affect cancer survivors who have completed their treatment and have no evidence of malignancy. The condition may affect both physical and mental capacity and is unrelieved by rest. Often, fatigue takes the patient by surprise, and the clinician is at a loss to recommend an effective approach to help alleviate it. Recently, however, an increasing awareness of cancer-related fatigue has led to its acceptance as a diagnosis. In addition, the National Comprehensive Cancer Network has appointed a panel of experts in fatigue to provide guidelines for the evaluation and treatment of patients with this distressing symptom.

There are many possible causes of cancer-related fatigue, which has been observed in patients both before treatment and after chemotherapy, radiation therapy, bone marrow transplantation, or surgery. In addition, many comorbid conditions can contribute to cancer-related fatigue, including anemia, endocrine diseases (such

as hypothyroidism), sleep disorders, pain, and psychiatric illness (such as depression and anxiety). Often a patient's fatigue is due to several factors. Hence, when the clinician encounters a patient experiencing cancer-related fatigue, a thorough and systematic approach is warranted.

Cancer-related fatigue can be challenging to treat. Occasionally, a reversible cause, such as anemia, is discovered, and with treatment the patient experiences significant improvement. However, when several factors account for the fatigue, a multimodality approach is warranted. Often, physicians, nurses, nutritionists, physical therapists, and others are all needed to address the many facets of this symptom. Patients diagnosed with cancer should be offered education about cancer-related fatigue and strategies to help them cope with it. Nonpharmacologic therapies that could be beneficial are exercise and improved nutrition. Pharmacologic therapies include stimulants such as methylphenidate and modafinil, which both appear to be promising agents to combat the severity of cancer-related fatigue. At The University of Texas M. D. Anderson Cancer Center, the Fatigue Clinic was established in 1998 to improve the quality of life of patients with cancer-related fatigue by alleviating the severity of this symptom.

Research in cancer-related fatigue is in its infancy, and well-designed clinical trials are needed to evaluate both pharmacologic and nonpharmacologic treatments. As we obtain a better understanding of the pathophysiologic mechanisms of this symptom, we will be able to develop more effective modalities for its treatment and thus improve the quality of life of our patients.

OncoLog

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