NEAG COMPREHENSIVE CANCER CENTER

Dialogue

Volume 5 Summer 2006

Giving Back

Participating in the ovarian cancer vaccine trial has given Betty Perkins the chance to help others while helping herself

Two years ago, Betty Perkins signed up for an ovarian cancer vaccine trial at the University of Connecticut Health Center. She'd just been diagnosed with the disease and learned about the study from her doctor. The physician explained its purpose was to determine whether a vaccine made from a patient's own tumor could stimulate the immune system and prevent the cancer from recurring.

"I thought if other people hadn't participated in trials in earlier years, I wouldn't have had a chance to survive," says Perkins. "So I felt there was a chance I could possibly help other women, and hopefully help myself, too."

Thus Perkins became one of 55 women to be screened for the clinical trial since August 2003, and one of only eight to receive the vaccine. The vaccine is made from heat shock proteins and contains antigens unique to each patient's tumor.

Heat shock proteins are housekeeping molecules that bind other molecules in normal and tumor cells and move them around, explains Zihai Li, MD, PhD, an associate professor of medicine and tumor immunology and principal investigator for the ovarian cancer vaccine trial.

In the 1980s, Pramod Srivastava, PhD, now a professor of immunology at the Health Center, discovered heat shock protein derived from tumor cells could be used as a vaccine in mice. Since then he and other researchers around the globe have generated positive results in human trials with heat shock protein-based vaccines targeting melanoma, renal cell and other cancers. The premise is the personalized vaccine will trigger the body's immune system to attack the cancer.

"We've completed a study based on the same concept and technology, using patients with chronic myeloid leukemia," says Dr. Li. The heat shock protein vaccine induced a "measurable immune response" in the majority of the 22 leukemia patients treated.

The ovarian cancer vaccine trial has proved equally promising, producing an immune response "in as early as two weeks" in 60 percent to 70 percent of the participants, according to Dr. Li.

"This is cutting-edge research, and we're the only site where it's being done," he says.

But Dr. Li needs more ovarian cancer patients to take part in the trial, which is a two-part study designed for 22 women. Eleven of them will receive a white blood cell stimulator in addition to the vaccine.

"The ultimate hope is that incorporating heat shock vaccines as a standard therapy with ovarian cancer, after completing surgery and chemotherapy, will prevent or limit relapse," Dr. Li says.

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You're Invited to Celebrate Life

Celebrate a special person and support the Neag Cancer Center at the same time through **Celebrate Life**, a new feature that will begin with the next issue of *Dialogue*. Simply send a monetary donation and the pertinent information. We'll publish your message in the Celebrate Life section of a future issue of *Dialogue*. All proceeds will support Cancer Center clinical and research programs.

To celebrate a life important to you, just mail this form along with your name, address, phone number and your check (made payable to the University of Connecticut Health Center) to the address below.

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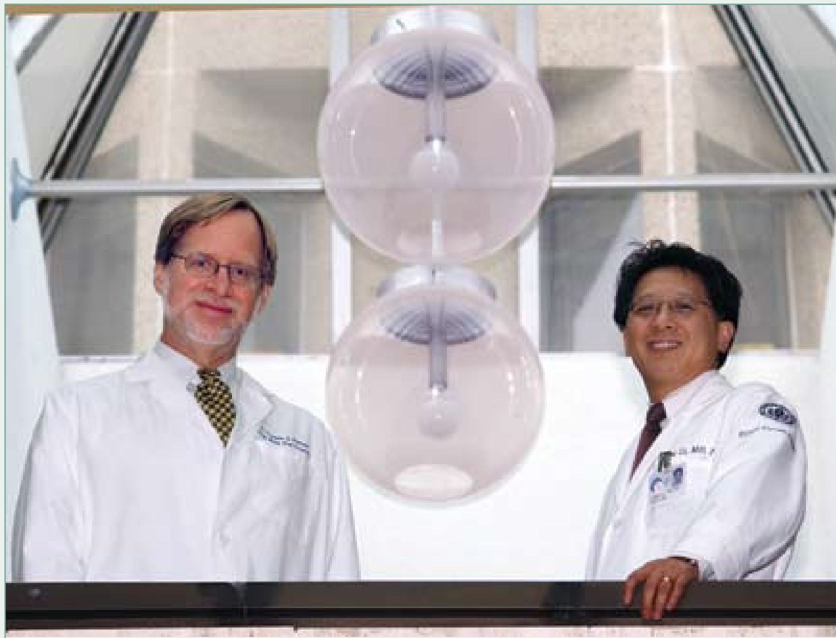
Welcome to the New *Dialogue*



Dr. Douglas Peterson (left) and Dr. Zihai Li.

On behalf of the Neag Comprehensive Cancer Center, we are pleased to present this first issue of our publication. *Dialogue* has been in publication since 2001. Beginning with this edition, we decided to change its content and format to better reflect the exciting advances that have occurred under the leadership of the Cancer Center Director, Carolyn D. Runowicz, MD.

Each issue of *Dialogue* will bring you articles that highlight the Center's unique, leading-edge programs and multidisciplinary approach to preventing and treating cancer. You'll learn how the Center's research activities, advanced technologies and compassionate care benefit patients and families in Connecticut and beyond.

We want *Dialogue* to be a valuable resource for you. A new feature, "Cancer Question," gives you the opportunity to submit questions about cancer. Questions will be answered in subsequent issues by our expert staff. Information on how to submit questions is included in the column on page 5.

As always, our team stands ready to help in any way possible. We would welcome any comments or suggestions you have regarding the new *Dialogue*.

Douglas Peterson, DMD, PhD
Zihai Li, MD, PhD
Medical Editors, Carole and Ray Neag Comprehensive Cancer Center, Dialogue

Team Approach Means Better Care

(l to r) Dr. Robert Dowsett, Dr. Jeffrey Spiro and Dr. Upendra Hegde

The Multidisciplinary Head and Neck Cancer Team helps patients identify the treatment option that's right for them.

For people diagnosed with cancer, the world can often seem like a strange, new place. Dealing with the emotional impact of the diagnosis is challenging enough by itself. But then there are new doctors and other specialists to see, new tests to undergo, a whole new vocabulary to learn and, in many cases, critical decisions to make about which treatment option is best. The decision about treatment is especially challenging when the cancer is located in the mouth, throat, larynx or other places in the head and neck. Fortunately, the Neag Comprehensive Cancer Center's Multidisciplinary Head and Neck Cancer Team stands ready to help patients understand the choices available to them and make informed decisions about their treatment.

Jeffrey Spiro, MD, a surgical oncologist who specializes in head and neck cancers, co-directs the Head and Neck Cancer Team. He and medical oncologist Bernard Greenberg, MD, founded the program in 1989. It is the only one in central and northern Connecticut.

"I started this because it was the right thing to do," says Dr. Spiro. "I trained at Memorial Sloan-Kettering, where they use the same model and found it works best. I wanted to bring the best practices of one of the world's foremost cancer centers to patients right here in Connecticut."

Uncommon Cancer, Unique Problems

Cancers of the head and neck are not very common. In fact, they amount to only a fraction of the number of cases of breast, prostate, lung and colon cancer. But they present unique, complex challenges when it comes to choosing an appropriate treatment.

"Treatment for cancers of the head and neck can have a dramatic impact on a person's appearance and on the ability to eat, swallow and speak," says Dr. Spiro. "The way the cancer is treated initially has profound implications for the patient in these respects. These initial decisions send you down a particular path, and once you've taken that path, there's no turning back."

These critical early decisions, Dr. Spiro says, are best made by combining the perspectives of physicians, dentists and allied health professionals right at the start, before any treatment is begun. This prospective, comprehensive, multidisciplinary approach is what the Head and Neck Cancer Team can offer patients.

In addition to Dr. Spiro, the team includes radiation oncologist Robert Dowsett, MD, and medical oncologist Upendra Hegde, MD, as well as professionals in oral pathology, dentistry, maxillofacial surgery, rehabilitation, nutrition and social work. Specialists in other disciplines, such as neurologic surgery, plastic surgery and dermatological surgery are brought in as necessary.

"A great deal of thought has to go into treatment planning," says Dr. Spiro. "It's complicated, because the problems are always unusual. Treatment needs to be customized to each individual patient. All patients want their cancer cured, but each has different priorities. Some are willing to undergo certain treatments, others are not. For this type of cancer, it's essential that all of this be thought out carefully before anything is done. The best way to do this is to have everyone involved up front."

The average person might not think there could be multiple treatment choices for one cancer. But Dr. Spiro offers as an example a patient who may have cancer in the portion of the larynx above the vocal cords. One treatment would be to surgically remove that portion of the larynx, sparing the vocal cords. But the recovery is long and difficult, requiring extensive rehabilitation therapy. Other possibilities would be to treat the cancer with radiation, or with a combination of radiation and chemotherapy. But these also have long-term side effects. It's important that the patient understand what each treatment involves, so he or she can make an informed decision.

The Patient's Experience

The team typically sees patients who recently have been diagnosed with head or neck cancer and have not yet received any treatment. Usually the diagnosis has been made by an ear, nose and throat physician or an oral surgeon in collaboration with an oral pathologist. The team meets on

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Dr. Ellen Eisenberg

Unlocking The Secrets of Cells

At the University of Connecticut Health Center, the state's only Oral Pathology Biopsy Service plays a vital role in diagnosing and treating cancers and other diseases of the mouth and jaw.

Achieving the best health outcomes for patients begins with an accurate diagnosis of their disease. Helping physicians, oral surgeons and other dental specialists reach that definitive diagnosis is the specialty of the University of Connecticut Health Center's Oral Pathology Biopsy Service. As the only one of its kind in the state, the service provides an invaluable resource to practitioners and patients throughout the Northeast. It is one of the features that make UConn's Neag Comprehensive Cancer Center unique.

Detectives with Microscopes

Ellen Eisenberg, DMD, is an experienced oral pathologist who directs UConn's Oral Pathology Biopsy Service. She heads the Health Center's Division of Oral and Maxillofacial Pathology and serves on the faculty of both the School of Dental Medicine and the School of Medicine. Dr. Eisenberg likens the pathologist's job to that of a detective.

"The pathologist's task is to solve medical whodunits by using the microscope as a kind of magnifying glass to discover the defining clues that answer the fundamental question, 'What disease is this?'"

Abnormalities of the oral cavity can be extremely difficult to diagnose, even for experienced clinicians and anatomic pathologists. That's why it's so important to patients' health for medical and dental professionals to have access to an Oral Pathology Biopsy Service.

"Oral pathologists are the experts in diagnosing, under the microscope, lesions that come from the mouth and jaws," explains Dr. Eisenberg.

That expertise is developed, in part, through extensive, specialty training. After completing dental school, an aspiring oral pathologist must pursue postgraduate education, serve a residency, and pass a rigorous, comprehensive examination leading to certification by the American Board of Oral and Maxillofacial Pathology. Maintaining board certification requires ongoing study, practice, and annual continuing education and competency testing. With only 300 or so board-certified oral pathologists in the country, these diagnostic experts are relatively few and far between.

Connecticut is especially fortunate to have Dr. Eisenberg, who has both impressive educational credentials and the incomparable advantage of extensive experience. Each year, UConn's Oral Pathology Biopsy Service analyzes approximately 4,500 specimens, and Dr. Eisenberg has been with the service for 28 years. In addition to her diagnostic laboratory work and teaching dental and medical students, she sees patients and collaborates with other practitioners in their care.

"Clinical experience makes a big difference," Dr. Eisenberg says. "Working with patients, solving problems and looking at slides over so many years, you gain a certain amount of expertise just from the sheer exposure to a variety of problems, in addition to the good training."

Is It Cancer?

Diverse conditions can cause abnormalities in the mouth. They include common inflammatory irritants; microbial infections; autoimmune diseases; skin diseases, such as lichen planus, which can affect the mucous membranes; benign tumors; and, of course, oral cancer, technically known as squamous cell carcinoma.

As diagnostic specialists, Dr. Eisenberg and her faculty colleague, Easwar Natarajan, BDS, DMSc, apply clinical knowledge and microscopic analysis of tissue samples to distinguish among the various diagnostic possibilities and make definitive diagnoses for each and every case they

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encounter. It is not unusual for Drs. Eisenberg and Natarajan to see patients who have had a condition for some time but have yet to receive a correct diagnosis and, therefore, appropriate treatment.

"Sometimes things that affect the mouth, if allowed to run their course, will also affect other parts of the body adversely," notes Dr. Eisenberg. "We make an important contribution when we are able to diagnose things early and prevent complications."

Because accurate diagnosis is so critical, the service makes it easy for practitioners outside the Health Center to submit specimens. It has a courier service that will pick up specimens at providers' offices. The service also provides specimen bottles, forms and postage-paid packaging that providers can use to mail in samples. The service receives samples from practitioners across Connecticut, as well as from those in the other New England states and New York.

"Many of the contributors were trained here at UConn or did their residencies here," says Dr. Eisenberg. "They continue to use the service because they trust it. And others learn about it by word of mouth."

Practitioners who submit tissue samples can count on a fast, thorough response. The service typically reports the results of the biopsy to the contributing practitioner within 24 hours of receiving the sample. If the biopsy reveals that the patient has a cancerous, precancerous or other serious condition, Dr. Eisenberg calls the doctor immediately. She is also available to answer questions and discuss treatment options.

"If it turns out to be oral cancer, we'll recommend that the patient be seen by the Health Center's Head and Neck Cancer team, which usually includes representation from UConn's Oral/Maxillofacial Surgery group," Dr. Eisenberg says. "I also follow these patients long term, since they are at risk for second primary lesions or recurrences of their precancerous lesions or cancerous tumors."

Dr. Eisenberg works closely with Jeffrey Spiro, MD, and his colleagues on the Head and Neck Cancer Team (see related article). She often takes part in the team's multidisciplinary tumor board, which considers factors such as location and size of the tumor and whether it has spread to distant sites, the patient's overall health and his or her family situation, and then recommends the best course of treatment for the patient.

"The treatment option for oral cancer is usually surgical, first and foremost, but also may include radiation therapy or chemotherapy or a combination of all three modalities," says Dr. Eisenberg. "There are some promising new protocols available for treating this disease, and our Head and Neck Cancer Team actively pursues all of them."

For more information about the Oral Pathology Biopsy Service, call (860) 679-3333.

—Noreen S. Kirk

Cancer Question

Carolyn D. Runowicz, MD
Director, Neag Comprehensive Cancer Center
President, American Cancer Society

Cancer Question, a brand-new feature of *Dialogue*, gives you the opportunity to ask questions and learn more about the exciting initiatives under way at the Neag Comprehensive Cancer Center. We invite you to write or e-mail us with questions about cancer research, treatment or prevention. Our team of cancer experts will answer your questions in this section in future issues.

Simply e-mail your question to cancerquestion@uchc.edu or mail it to Cancer Question, The Carole & Ray Neag Comprehensive Cancer Center, University of Connecticut Health Center, 263 Farmington Ave., Farmington, CT 06030-1614.

Q: *I have heard a lot about the development of a "Navigator Program" for the Cancer Center. Can you please describe this program for me and tell me how I can learn more about it?*

A: The Navigator Care Program is a service to help women who are newly diagnosed with breast cancer. The program pairs patients with trained volunteers who literally "navigate" them throughout their care. Volunteers accompany women to medical appointments, chemotherapy treatments, radiation, surgery, support groups and more. It is an optional program designed to complement the Neag Comprehensive Cancer Center's compassionate team of doctors, nurses, social workers and other care givers. Our goal is to help every patient reach her full potential for recovery. For more information regarding the Navigator Program, please do not hesitate to contact our Cancer Center offices at (860) 679-2100 or you can send e-mail to cancerquestion@uchc.edu.

—Nancy Baccaro, APRN

Preventing Colon Cancer at the Cellular Level with Powerful New Technologies

Dr. Daniel Rosenberg (left) and Dr. Joel Levine

Ten years ago George Williams began experiencing health problems that he should have regarded as a warning sign. But Williams, like too many Americans, ignored the warning.

"He never went in for a check-up," says his sister, Shirley Osle, assistant town manager of Plainville. "He always took his health for granted."

By the time Williams sought help it was too late. When he died of colon cancer, Williams was just 50, the age at which physicians generally recommend their patients first undergo a colonoscopy.

One of the most common forms of cancer, colon cancer afflicts nearly 45 of every 100,000 Americans annually, but it's highly treatable if detected early. Even more important, it is increasingly preventable. And with breakthrough research being conducted at the Neag Comprehensive Cancer Center, doctors are optimistic about making it more preventable still.

Emphasizing Prevention

As researchers learn more about the causes of colon cancer, the emphasis in healthcare is increasingly on prevention, says Joel Levine, MD, professor of medicine and co-director of the Health Center's Colon Cancer Prevention Program.

Cancer begins with genetic damage and a wide range of lifestyle factors, such as smoking, obesity, lack of exercise, excessive consumption of red meat and fats, that can contribute to the development of the disease. But even people whose lifestyles do not include these elements may be at risk. That's because colon cancer may also be related to one's heredity, ethnicity and cultural background.

"To prevent cancer, you must think about all of those factors," says Dr. Levine. Indeed, preventing cancer, a superior alternative to treating it once it has occurred, is the idea upon which the Colon Cancer Prevention Program was founded last year. The more information doctors and researchers can gather about factors that predispose one to developing cancer, Dr. Levine believes, the more successful they will be at identifying people most at risk and helping them to avoid George Williams' fate.

At the Colon Cancer Prevention Program, efforts to identify people at risk involve careful screening of patients based on the risk factors noted above. But they also involve the use of cutting edge technology that offers the possibility of detecting microscopic changes in the cells of the colon—changes that may be the precursors of cancer.

Beyond Colonoscopy

Ten years ago, cancer biologist Daniel Rosenberg, PhD, who co-directs the Colon Cancer Prevention Program, began studying colon cells called aberrant crypt foci, or ACF. Since 2000, he has collaborated with Levine. Operating on the understanding that the earlier cancer can be detected, the better the outcome is likely to be for patients, Drs. Rosenberg and Levine aim to develop a way to detect precancerous cells in the colon as early as possible.

ACFs are not cancer cells, but they are often found in the colons of people with cancer and experts believe there is a relationship. Clarifying that relationship has become a mission for Drs. Levine and Rosenberg. Their research illustrates the importance of work being done at the Neag Comprehensive Cancer Center.

Increased use of colonoscopies has unquestionably saved thousands of lives. But while a conventional colonoscope can reveal tumors and polyps, it's a limited tool, completely inadequate for detecting the kinds of aberrations, Drs. Levine and Rosenberg seek.

For that task they use a prototype close-focus colonoscope, provided through a partnership with Olympus Corp., that

…continued on next page

allows them to see colon tissue at the cellular level. Using microarray analysis, they can simultaneously evaluate thousands of cells, monitoring their roles in the development of cancer.

Since 2003, Levine and Rosenberg have gathered the largest human ACF collection anywhere, over 300 samples of abnormal cells. This invaluable resource is being analyzed by UConn researchers employing many different research projects with a common objective: finding out what, precisely, triggers development of ACFs and which ACFs are most likely to become cancerous. Some of those projects have already generated promising results.

In the past year, Levine has augmented the close-focus technology with narrow-band imaging. This shortened light wavelength makes it possible to more clearly study ACFs on the surface of the colon and boosts the speed and efficiency with which small variations in ACFs can be detected. One of the greatest advantages of this enhancement is the ability to clearly observe tiny blood vessels in order to study the relationship between ACF development and blood supply that feeds tumors as they grow.

This year the Program's technology will be utilized in a study linking 10 hospitals nationwide. Spearheaded by the Mayo Clinic, the study will explore the impact of three different medicines, all of which have shown promise in reducing ACFs.

Better Health Care

These powerful technologies, coupled with intensive screening of Neag Comprehensive Cancer Center patients and individualized programs to help them manage their risks, amounts to state-of–the-art colon cancer prevention. But patients and their individual experiences are also important for the Center's researchers.

"The more we know about the many factors that cause colon cancer, the more likely we are to find effective ways to combat this disease," says Levine. "We learn from our patients."

Just ask Shirley Osle. After her brother's death, she underwent a colonoscopy at the Health Center during which Dr. Levine removed several polyps. Last year, when she returned for a follow-up, it was to the Neag Comprehensive Cancer Center. And the experience, she says, was strikingly different.

"Ten years ago I underwent a routine test," she recalls. "This time I received a lot more literature. There were intensive surveys to be completed and informative videos to watch. I had the clear impression that the experience wasn't just valuable for me, but that it was valuable to the Center, as well."

—James Smith

Giving Back *continued from page 1*

Ovarian cancer is particularly insidious. Often well advanced when detected, the cancer recurs in as many as 80 percent of patients.

"Once it comes back, it comes back with a vengeance, so this vaccine could be a viable option for preventing recurrence," says Jennifer Bendiske, PhD, director of clinical and translational research at the Carole and Ray Neag Neag Comprehensive Cancer Center, which is overseeing the study.

Participants in the ovarian cancer vaccine trial must be diagnosed with Stage III or Stage IV ovarian cancer and agree that tissue removed at the time of their surgery be frozen while they undergo chemotherapy (usually carboplatin and taxol) and further testing to assure they have no evidence of disease or have remained stable, without disease progression, for at least two months.

At that point, if they still meet the study criteria, Bei Liu, MD, a research associate working with Dr. Li, produces a vaccine from the patient's tumor.

"We purify it, then check for toxicity and sterility," Dr. Liu says. "The tumor has a lot of heat shock protein and contains the tumor antigen, which stimulates the immune response in the patient."

Perkins, who retired from her position at Westminster School in Simsbury to battle her ovarian cancer, says she feels "very fortunate" to have been among the few women chosen to receive the vaccine. She completed the eight-week series of weekly injections in 2004.

"I didn't have any side effects," she says.

"The vaccine is very well tolerated," agrees Diahann Wilcox, APRN, a nurse practitioner who was the ovarian cancer vaccine trial's study coordinator until March 2006 and still monitors the women every three months. They'll be tracked for five years, for relapse and longevity, with testing including blood work and CAT scans.

So far, participants range in age from their early 40s to late 60s, live in the Hartford area and include wives, mothers, workers and an artist who completed the trial but then died of breast cancer.

"She [the artist] made my daughter's christening outfit from my grandmother's wedding dress," Wilcox says.

Six of the eight ovarian cancer vaccine recipients were still alive (as of May 5, 2006) but "only two are disease free," Wilcox says.

These days, Perkins, now 63 years old, enjoys spending time with her children and grandchildren and caring for her husband's parents, who share their Newington home.

"I feel good, and I think I have a pretty positive attitude, which helps in a lot of ways," she says.

Though her most recent CAT scan showed "no sign of recurrence" and she wasn't undergoing any treatment (in early May 2006), Perkins' blood still has a slightly elevated CA125, which is a biomarker for ovarian cancer.

"I'm kind of on the fence," she says. "You don't hear a lot of good news about ovarian cancer, but there are people who have gone on a long time."

Perkins has no regrets about her treatment, including her decision to be injected with the experimental vaccine.

"I'd like to think it has helped," she says.

Dr. Li would like to expand the geographical range of trial participants far beyond the Hartford area.

"For the leukemia study, we recruited patients from all over the U.S., England and Canada," he says, adding he hopes women with ovarian cancer living in these places, and elsewhere, will follow Perkins' lead and enroll in the study.

For more information on the ovarian cancer vaccine trial, call the Neag Comprehensive Cancer Center at 860-679-3066.

—Karen Singer

Nancy Baccaro, APRN

"Team Approach" *continued from page 3*

two Friday mornings each month to see patients. Each patient is made comfortable in an exam room where he or she will remain for the morning. Team members visit each room in turn, examining and talking with each patient. The group then gathers in a conference room to discuss each case and outline what they think they can offer in terms of a treatment plan. The physicians then go back to each patient and explain the various treatment options. If appropriate, they will recommend the one they believe is most advisable.

"Curing the cancer is the top priority," says Dr. Spiro. "The more advanced the cancer is when we first see the patient, the greater the likelihood that the patient will have functional problems down the line. Our job is to figure out how to cure the disease, but leave the person with the best possible functional and aesthetic outcome."

Patients leave the Health Center that Friday with the information they need to talk things over with their family or friends over the weekend. Then they can come back to the team with a decision about which way they want to go. Very often, patients choose to have their treatment at UConn. Dr. Spiro says that people often comment on how much they appreciated the team's clear explanations and patient-centered approach. Referring physicians have also mentioned how impressed they were with the assistance the team gave their patients.

The UConn Factor

There are a number of reasons why the University of Connecticut Health Center is able to offer this prospective, interdisciplinary approach to developing treatments plans for cancers of the head and neck. One is its medical school, with its critical mass of faculty in a variety of disciplines. Another is the fact that it also has a dental school. Treating head and neck cancers frequently calls for the expertise of general dentists, as well as dentistry specialists such as oral surgeons, prosthodontists and oral pathologists. Experts in these areas are readily available at the Health Center.

Dr. Spiro himself is another reason the program exists. He is the only ear, nose and throat physician in the area with advanced, specialized training in surgical treatment of head and neck cancers.

But the most important point is that patients with these types of cancers receive the best medical advice and treatment available anywhere when they come to UConn's Neag Comprehensive Cancer Center. And their prospects are good.

"Survival and cure rates from head and neck cancer are better than those from some other smoking-related cancers," says Dr. Spiro. "We have some notable successes. And that's why, after 18 years, I'm still committed to this work."

For more information about the Multidisciplinary Head and Neck Cancer Team at the Carole and Ray Neag Comprehensive Cancer Center, call (860) 679-2100 or (800) 579-7822 or e-mail us at cancer@uchc.edu.

—Noreen S. Kirk

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