

MD Anderson Oncolog

Cancer patients receiving medical treatment at other centers now eligible for mental health services at M. D. Anderson

Psychiatry at M. D. Anderson: Helping patients learn to live with cancer

Patient care

Survival is the principal goal of cancer patients. People with cancer become immersed in a complex world of medical decisions and choices, all aimed at fighting their tumors and prolonging their lives. Their days are filled with a bewildering array of diagnostic and therapeutic procedures, the rest of their time with an interminable wait for the results. And when the news is good, they often face a new set of problems as they try to resume the lives they had before cancer. At the same time, family members and loved ones juggle their own needs with the needs of the patient and the demands of everyday life.

Patients, survivors, family members—what all have in common when touched by cancer are mental stress and emotional extremes. Their mental health is threatened by the anxiety, anger, frustration, and sadness they feel as they cope with the disease. To promote the emotional balance that leads to healing, The University of Texas M. D. Anderson Cancer Center is offering a newly expanded program of mental health services.

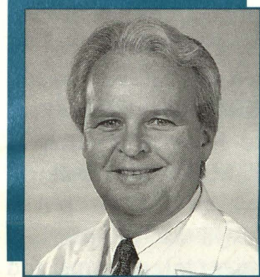
“Because survival has long been the focus of cancer medicine,” said Walter F. Baile, M.D., chief of Psychiatry in the Department of Neuro-Oncology, “the patient’s mental health has sometimes been overlooked. More and more, however, cancer patients are concerned not just with the duration of their lives but with the quality of their lives during and after treatment. Increasingly vocal cancer patient advocacy groups are demanding attention for quality-of-life issues. We believe that a cornerstone of a quality life for these patients is learning to adjust to their disease, to manage the negative feelings they have.” Because of this shift, mental health services are expected to become increasingly important in cancer centers.

Emotional problems often undetected

Baile noted that although not all patients experience emotional difficulties in adjusting to their disease, “most have some sort of emotional reaction, which is usually negative, at least at first. There’s nothing wrong with these feelings, but many patients need help coming to terms with the disease. They often go without this help, however, because of their unwillingness to admit emotional difficulties.” Many patients are reluctant to bring up their sadness or depression with their doctors because they fear the stigma. “Patients take personal responsibility if they are not coping well,” said Baile. “Some fear that if they tell the doctor, they will be labeled ‘crazy.’ Others don’t want to bother the doctor.” Although most physicians treating cancer patients are sensitive to these feelings, the patients’ reluctance is hard to overcome. Unrelieved, these emotional difficulties can worsen over time and may interfere with a patient’s recovery.

Baile sees this changing, however. He believes that the best way to encourage patients to acknowledge their feelings is to educate them about the kinds of feelings they might have, validate those feelings, and inform patients of the resources available to help them cope. “While patients and their caregivers learn about taking physical care of the patient after discharge, they should also be learning to care for their mental health,” he said. Baile and his colleagues are developing workshops on coping skills for patients and their families. Said Baile, “We’re going to be more and more proactive in helping the cancer patient cope and in helping the family adjust and support the patient.”

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Walter F. Baile is chief of Psychiatry, Department of Neuro-Oncology

“Regardless of where they are receiving medical treatment, cancer patients can receive mental health counseling or therapy at M. D. Anderson.”

M. D. Anderson part of “wellness” movement

This activity is not isolated to M. D. Anderson. Baile cited the growing “wellness” movement in cancer care, referring to facilities within cancer centers whose focus is the psychological rehabilitation of the patient and family. The American Society for Psychiatry in Oncology and AIDS, a group Baile is active in, is part of a task force that is developing a mental health fact sheet for cancer patients. He cited another group, the Center for Advancement in Health in Washington, DC, whose mission is to create awareness of psychosocial issues in cancer.

Education is just one way patients are helped in their adjustment. Because the kinds of emotional problems most cancer patients have are mild or temporary, they respond well to short-term treatment, reported Baile. “We usually don’t see patients who are as severely disabled as patients who might be treated in psychiatric hospitals.” These patients are also helped by counseling, by support from loved ones, and by participation in support groups or by talking with another cancer patient. All of these services are available at M. D. Anderson. Patients’ family members can also receive individual therapy. “The importance of the patient and family members communicating their feelings to each other can not be underestimated in helping all family members cope with the disease,” said Baile.

Because of the success of these services within M. D. Anderson, the Psychiatry section recently began offering them on an outpatient basis to patients whose cancer is being treated at another institution. Regardless of where they are receiving medical treatment, cancer patients can receive counseling or therapy from Baile and his staff at M. D. Anderson or participate in M. D. Anderson support groups. Physicians in the community who treat cancer patients may refer their patients for this therapy while continuing to manage the patients’ medical treatment. (For more information about referring a patient, see the information at the end of this story.)

Educating clinicians to detect depressive disorder

Education should not be limited only to patients and their families. Baile sees a need for increased professional education on the mental health needs of cancer patients. This training should include how to recognize the anxiety and depressive disorders that affect about 25% of cancer patients (see box). “Not only do we have to educate patients to bring their emotional problems to the physician, we have to educate the physician to recognize the problems, which are often hidden behind somatic complaints. Physicians need to make the distinction between normal sadness and depression that cancer patients feel and depressive disorder, and they need to realize that help is available for both.” This fall, M. D. Anderson will offer an interviewing skills workshop for its physicians in which small groups will use role-playing, videotaping of physician-patient interactions, and peer feedback to encourage physicians to be more aware of mental health problems when talking with patients.

Continued Baile, “It is inappropriate, even dangerous, to consider depression as something that just ‘goes with the territory’ of cancer. We expect patients to feel sad or depressed, but signs of clinical depression, what psychiatrists call depressive disorder, require professional treatment. Because depressive disorders are disabling and are associated with poor medical outcomes, immediate attention is important.”

This attention is available at M. D. Anderson. Said Baile, “The biological revolution in psychiatry has created a class of new and very effective medications for patients with severe emotional problems, such as antidepressants and anti-anxiolytics.” There is some evidence, though, that the depressive disorders of people with physical diseases may be different in some ways than those of people being treated for mental health problems only and not for physical problems. Because research on this question is just beginning, for now the two groups are treated in much the same ways.

Baile's research centers around various techniques for improving the quality of life for both patients and their family caregivers. One aspect of that is improving ways for detecting mental health problems. The standard written instruments for detecting depression, for example, were designed for physically healthy people and include physical symptoms such as low energy and poor appetite that are normal for many cancer patients. Use of these instruments for cancer patients might lead to overdiagnosis of depression in this group. He and his colleagues are also designing studies of the effects of mental health support to cancer patients on their health outcomes.

Regardless of these studies' results, however, Baile and his colleagues at M. D. Anderson have

seen for themselves that the mental health services they provide help patients, survivors, and their families release stress and handle emotions. This in turn helps them keep a positive attitude, solve problems, and maintain relationships. "There is a new repertoire of skills people need to learn when they are affected by cancer," said Baile. "By teaching those skills, we are trying to prepare patients to cope with whatever comes at them."

—KATHRYN L. HALE

REFERRALS. Physicians who have questions or would like to refer a patient may write Dr. Baile at the Department of Neuro-Oncology, Box 100, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, or call the New Patient Referral office at (713) 792-6161 or 1-800-392-1611. ■

DEPRESSIVE DISORDER, as defined in the American Psychiatric Association's Diagnostic and Statistical Manual, 4th edition (popularly known as DSM-4), is not simple sadness or discouragement but a constellation of symptoms ranging from loss of interest in usual activities to thoughts of suicide.

Depressive disorder is most likely to improve if it is diagnosed and treated promptly, and fortunately the signs and symptoms are distinctive. The two primary signs are anhedonia, a loss of the ability to enjoy what once gave pleasure, and repeated complaints of feeling sad or disheartened. Secondary signs include loss of interest in usual activities, changes in sleep pattern, indecisiveness or inability to concentrate, low self-esteem, recurrent thoughts of death or suicide, unexplained somatic complaints (in cancer patients especially, pain out of proportion to disease), increased irritability, tearfulness or sad appearance, and brooding, self-pity, or pessimism. Depressive disorder always includes at least one of the primary signs. In its mild form, patients also have one of two secondary signs; in its moderate form, three or four secondary signs. The severe form encompasses almost all of the signs. The mild or moderate forms are typical of cancer patients struggling with their disease.

Clinicians should maintain a high index of suspicion for depressive disorder in cancer

patients, especially those who have a history of depressive disorder. The best way to gauge the patient's mental state is to include a few simple questions in the usual medical history taking at each visit. For example, asking the patient about loss of interest in usual activities may open the subject. However, because patients may not volunteer this information even when questioned directly, the clinician may want to consult family members or others who spend time with the patient.

Communicating the diagnosis of depressive disorder need not be uncomfortable if the clinician emphasizes the positive. Point out to the patient that the symptoms are real, not imaginary, and that they are not due to progression of the cancer. Depressive disorder can be likened to other diseases characterized by biochemical deficiencies.

Finally, the clinician should assure the patient that most people respond fully to antidepressant medication, especially those with the mild or moderate depression typical of cancer patients. One group of antidepressants in particular—the serotonin re-uptake inhibitors—are useful in cancer patients because they have fewer of the toxic effects that sometimes cause patients to stop taking their antidepressant medication.

Clinic works with patients and their physicians

Second opinion clinic helps patients get the best treatment

Diagnosis

Second opinions are frequently sought by patients and encouraged by physicians when an initial diagnosis is unfavorable or a recommended treatment is complex or risky. Of course, the ideal outcome is that the findings in the second evaluation will be more optimistic; however, even if the second opinion is the same as the first, the patient is usually able to face a challenging situation more confidently after having it confirmed by another experienced professional. Second opinions are particularly helpful in the cancer setting, because innovations in cancer medicine are being introduced continually. In 1994, realizing the value of such a service to both patients and community physicians, The University of Texas M. D. Anderson Cancer Center launched a Second Opinion Clinic to broaden its already active role in evaluating cancer diagnoses.

Clinic a practical setting for second opinions

M. D. Anderson Cancer Center has always been involved in providing second opinions; however, until this clinic opened, the institution did not have a program dedicated solely to this service. In the past, when patients came to M. D. Anderson for evaluation of an initial diagnosis, physicians were pulled together from different specialty areas to consult on the case. Because this happened only sporadically, the physicians and other staff often found themselves subject to conflicting demands. There was a clear need for a more focused, efficient program. According to James Abbruzzese, M.D., chief of General Medical Oncology and director of the Second Opinion Clinic, the new program was developed to centralize the services needed to support this special patient group. "We set up this clinic for the express purpose of providing second opinions. Our greatest resource is the expertise of our physicians. We structured the new clinic to give patients who are new to our system immediate access to M. D. Anderson's multidisciplinary approach, allowing them to benefit from the recommendations of several experienced specialists."

Second opinions: the demand is growing

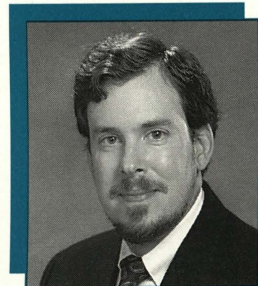
Approximately three to five new patients are seen in the Second Opinion Clinic each week. Sixty percent of the patients are Texas residents; the other 40% come from all parts of the world. Some patients are referred by their primary care physicians, and others are self-referred. In response to concerns about the costs of medical care, some insurance companies are now requiring that patients get second opinions. This trend is expected to continue, said Abbruzzese. "We anticipate that insurance companies will be requesting that patients get second opinions about cancer diagnoses more and more frequently. Likewise, patients who expect their insurance carriers to cover the cost of cancer care will need to get a second opinion." Because of this growing demand, Abbruzzese has overseen development of a streamlined pricing schedule that will incorporate all services associated with a second opinion.

Patients can get answers after one visit

The patient consultation is conducted by one of the physicians of the General Medical Oncology staff. To streamline the process, patients are asked to have their pathology, radiology, and any other records sent to M. D. Anderson before the actual visit. In some instances, additional tests are needed, but usually the tests the patient has already had are sufficient. The records are reviewed by physicians and pathologists from the appropriate specialty area. They either agree or disagree with the initial diagnosis and treatment plan. Abbruzzese or Lenzi will then tell the patient what these specialists recommend. "With our new, more efficient process," explained Abbruzzese, "we can typically consult with the other physicians by telephone. Patients can usually get answers to their questions in a single visit."

Abbruzzese commented that patients benefit from the advanced technology available at M. D. Anderson, such as fine-needle biopsy, ultrasonic testing, comprehensive breast diagnostic testing, and specialized interventional radiography and

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James Abbruzzese is chief of the Section of General Medical Oncology

On the Internet, Oncolog draws readers from around the world

M. D. Anderson Oncolog has been available on the Internet for nearly a year. The Internet is a worldwide network of millions of computers. The contents of each issue of *Oncolog* since January 1994 are posted on M. D. Anderson's Gopher+ and World Wide Web servers.

The response to the online version of the *Oncolog* has been phenomenal. Our log of electronic visitors shows readers from all over the United States and the world. We have received electronic mail from readers in European countries, Brazil, and Mexico asking for information about our stories as well as about M. D. Anderson, our publications, and our activities.

We're reproducing here part of the *Oncolog* title page from the World Wide Web version. From any computer equipped with a modem and

inexpensive "Web browser" software, a few simple keystrokes or clicks on the mouse can take you to M. D. Anderson's "home page," site of several publications and other information about M. D. Anderson.

Gopher clients can access *Oncolog* files by connecting to host `utmdacc.uth.tmc.edu`, port 70. World Wide Web clients can connect to `http://utmdacc.uth.tmc.edu`. Other M. D. Anderson publications that can be viewed include the *Research Report 1992-1993*, *Hereditary Colon Cancer Newsletter*, *Gynecologic Oncology Newsletter*, *Current Issues in Transfusion Medicine*, and *Conquest*.

We welcome your comments on *Oncolog* and our other publications. Send electronic mail to `khale@acadresources.mda.uth.tmc.edu`.

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MD Anderson Oncolog

M. D. Anderson Oncolog is a quarterly publication of The University of Texas M. D. Anderson Cancer Center intended for the physician in general practice. It reports recent developments in cancer patient care, significant diagnostic progress, and current clinical and basic science research activities at M. D. Anderson Cancer Center. For additional information on the electronic and print versions of M. D. Anderson Oncolog, see [publication information](#).

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Gene mapping

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and section head Robert F. Gagel, M.D., recognized that finding and characterizing the PHHI gene would eventually yield extremely important information about insulin secretion and thus diabetes, one of the most prevalent and potentially destructive chronic diseases.

Wanted: gene carriers

Locating a gene requires a source of DNA—usually blood or tissue specimens—from persons who carry the gene. A significant problem in the study of PHHI genetics is the scarcity of patients with the disease. So the researchers' first step was to identify children affected by the disease whose families would agree to help them in their search. By spreading the word to colleagues in Houston and beyond, Cote and Thomas were able to locate a few children with the condition. They then heard from P.M. Mathew, of the Dhahran Health Center in Saudi Arabia, where the prevalence of consanguineous marriage has made PHHI more common than in the United States (1 in 2,675 live births versus 1 in 50,000 live births). (The marriage of two individuals with a common ancestor has a well-known magnifying effect on recessive inherited disorders.) Mathew had been studying the disease for some time and was willing to collaborate on a genetic study of the disease. He identified ten children with PHHI from five Saudi families and sent whole blood samples from these children and their parents and siblings to Houston. (Although Mathew later identified other children affected by PHHI, the original ten were sufficient to complete the genetic study.)

Narrowing down the location

The research group's next step was to get a general idea of the gene's location. They were faced with finding a specific sequence of perhaps 10,000 to 20,000 base pairs of nucleotides (the building blocks of DNA) among the approximately 3 billion base pairs that make up the 23 pairs of chromosomes of the human genome. They used a technique called homozygosity mapping, which takes advantage of the long regions of genetic homozygosity (matching pairs of alleles) unique to the DNA of persons affected by rare recessive diseases. Although it was likely that each affected child would have several regions of homozygosity, only one of these regions, the one containing the disease gene, would be common to all.

The goal was to find that one region. To identify homozygous regions, the DNA was extracted from the blood of the affected children and their immediate families and compared with a purchased library of very short genetic sequences called primer pairs which recognize a single unique chromosomal site whose location is known. These primer pairs were used to identify polymorphisms, genetic sequences that vary in length from person to person. Polymerase chain reaction (PCR) analysis of each person's DNA revealed who carried which polymorphisms. The researchers were looking for a polymorphism that was carried in two different forms by all the family members unaffected by PHHI and in only one form by the children with PHHI. "The polymorphisms allowed us to tell which alleles each child had inherited and which came from the mother and which from the father," explained Cote. "From that, we looked for a pattern of inheritance of these polymorphisms in the affected children."

After carefully recording and comparing this information for all the family members, Cote, Thomas, and their colleagues found the region they were looking for—on the short arm of chromosome 11. Because the location of each polymorphism is known, this analysis allowed the researchers to pinpoint a chromosome and a region where the gene would be found. In a few more steps, using ever more closely spaced markers, they were finally able to narrow this region down to a single 4 million base-pair sequence.

After eight months of work, the researchers had an approximate site for the PHHI gene. Their finding was confirmed by complex statistical calculations called a linkage analysis, which shows how closely the disease gene lies to a specific marker. In this case the linkage analysis, done by Michael Hallman, Ph.D., of The University of Texas School of Public Health, revealed a high probability that this region was the site of PHHI. (This technique is similar to that used for the highly publicized DNA analysis of blood and other tissues in criminal cases.) Finding the site on chromosome 11 was ironic, since the group had begun their search there. As the site of another gene for a related insulin-secretion disorder, chromosome 11 had been a hunch that paid off.

Luck a factor in the discovery

The group's work was not over, however, because a 4 million base-pair region contains somewhere between 50 and 150 genes. "We took a candidate gene approach," said Cote, "looking for nearby known genes that might be related func-

tionally somehow to PHHI or insulin secretion. Only about six genes were known in that region, and no functional connections were apparent." The researchers were at a loss for a starting point.

Then they got lucky. At an endocrinology research seminar at Baylor College of Medicine (BCM), Cote and Thomas heard a presentation by a research group at BCM who were working on the genetics of diabetes. This group had identified the gene that produces the receptor for the drug sulfonylurea, which stimulates insulin production and is used to treat adult-onset diabetes. Cote immediately saw a possible connection between this sulfonylurea receptor and the hypersecretion of insulin seen in PHHI. Thomas approached the BCM researchers, who also saw the connection and agreed to work together to find the PHHI gene. They gave Thomas a probe, which was used to map the sulfonylurea receptor gene by a technique called fluorescence in situ hybridization (FISH); the gene was found within the 4 million base-pair sequence that had been identified for the PHHI gene.

"So we had two things," recalled Cote, "a gene that was definitely involved in insulin secretion and what we call a 'fish localization' showing that the sulfonylurea receptor gene was in the exact same place." This was more than mere coincidence, the group decided, and they focused their attention on the sulfonylurea gene. Genetic studies of that gene

revealed two different mutations for which PHHI-affected children were homozygous, while their parents and unaffected siblings were not. This clearly suggested that the hypersecretion of insulin in PHHI is caused by a mutated form of the sulfonylurea gene. The researchers concluded that the PHHI and sulfonylurea genes are apparently one and the same.

Cote said he still does not know exactly how this finding will be applied clinically. "We have a better understanding of the role of this gene in insulin secretion and metabolism. That's an important first step in understanding insulin regulation disorders." His work on the sulfonylurea gene is now focused on its significance in certain kinds of endocrine cancers called insulinomas, which produce insulin in an unregulated manner. And he hopes to continue collaborating with the BCM group. For Cote, this relationship represents the ideal in interinstitutional collaboration in medical research. "It was a team effort," he said, referring to locating the gene for PHHI. "We couldn't have done it without our collaborators."

—KATHRYN L. HALE

Readers who have questions may write to Dr. Cote, Endocrine Section, Department of Medical Specialties, Box 15, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, or call (713) 792-2840. ■

Second opinions

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nuclear imaging. "State-of-the-art equipment and the expertise of diagnosticians who work with cancer every day means that patients get the most accurate assessment of their condition possible," he said.

Most of the time, M. D. Anderson physicians concur with the original diagnosis. "In about 90% of cases, our recommendations regarding management of a patient's condition echo what the patient has already been told," reported Abbruzzese. "It is actually unusual that we have a big disagreement with an original diagnosis." Because it is a research institution, however, M. D. Anderson is sometimes able to make suggestions for patients interested in experimental therapies. Said Abbruzzese, "It is not the goal of this clinic to promote non-traditional approaches to cancer care; however, some patients come to us in search of such treatments."

Program updates patients, physicians about cancer care

One of the goals of the service is to provide cancer patients and primary care physicians with a general view of the treatments available for their particular types of cancer. "This clinic was developed," Abbruzzese explained, "to educate patients and physicians about developments in cancer care and to reassure them that the best possible actions are being taken to ensure the most effective, cost-conscious patient care."

—VICKIE J. WILLIAMS

REFERRALS. Physicians who would like to refer patients or patients interested in self-referrals may write Dr. Abbruzzese at the Department of Gastrointestinal Oncology and Digestive Diseases (Box 78), The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, or call the New Patient Referral office at (713) 792-6161 or 1-800-392-1611. ■

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Published quarterly by the Department of Scientific Publications, Division of Academic Affairs, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030.

Made possible by a gift from the late Mrs. Harry C. Wiess.

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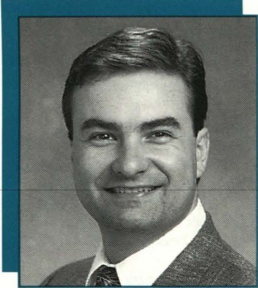
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Newly located gene may be key to insulin dysregulation

Technology and cooperation powerful tools in locating genes

Genetics



Gilbert Cole is assistant professor of medicine, Endocrine section

With the unlocking of the genetic code, fueled by new technologies and by projects such as the Human Genome Project, the discovery of disease-causing genes has become almost commonplace. Many human diseases are now understood to be at least partly regulated by abnormal DNA, and this decade has seen an unprecedented surge in research efforts to identify these abnormalities. Newly discovered genes are reported on a nearly daily basis, many of them heralded as the first step in the development of a cure for the disease process they regulate. Despite this unprecedented rate of discovery, we can expect to hear of more and more of these announcements; there are over 100,000 genes in the human genome. To understand the true significance of these discoveries, it is helpful to first understand how genes are located.

A recent gene discovery by researchers at The University of Texas M. D. Anderson Cancer Center illustrates the process. The search for the gene began when Gilbert Cote, Ph.D., was approached by his colleague Pamela M. Thomas, M.D., both of

the Endocrine section, Department of Medical Specialties, about a rare inherited disease involving dysregulation of insulin secretion. The disease, persistent hyperinsulinemic hypoglycemia of infancy (PHHI)—also called nesidioblastosis—is characterized by overproduction of insulin and severe hypoglycemia. An autosomal recessive disease, PHHI affects only children who have inherited two abnormal copies of the causative gene, one from each parent. Scientists knew there was a gene that caused PHHI, but they didn't know its location or anything about it. Thomas wanted to change that.

Thomas had two reasons for her interest in the PHHI gene. One was to help children with the disease; PHHI is treatable if discovered promptly and the hypoglycemia corrected. Untreated, PHHI can cause serious damage to the child's developing central nervous system. Identification of the genetic abnormality would allow development of a new and simpler test for the disorder. Moreover, she, Cote,

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