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REPORT TO PHYSICIANS

APRIL 2008 VOL. 53, NO. 4

Oncology

Cancer as a Chronic Disease

While a cure remains elusive, great progress has been made in controlling advanced malignancies over the long term.

By Dianne C. Witter and John LeBas

When [REDACTED] was diagnosed with multiple myeloma more than 6 years ago, he faced a generally incurable malignancy with a 5-year overall survival rate of about 35%. Given this outlook, [REDACTED] knew he might die of his cancer.

But what he didn't expect was that cancer would become a way of life, rather than solely a threat to it.

"I was inevitably surprised at the cyclical nature of the situation," said [REDACTED] describing the long line of stem cell transplantations, radiation, and drug therapies he has received at The University of Texas M. D. Anderson Cancer Center. When one therapy failed, another would become available, enabling a long-term management of his disease that [REDACTED] and his doctors didn't initially think was possible. "Eventually I realized that this was something I would be dealing with for a long time."

During this up-and-down cycle of treatment, [REDACTED] joined a growing subset of patients--those who are living with cancer as a chronic disease. These patients have metastatic disease that cannot be cured but can be controlled over the long term. And they are living months or years longer than did patients with the same types of advanced cancers less than a generation ago. (Continued on page 2)



[REDACTED] and his wife, [REDACTED], take a coffee break at M. D. Anderson, where he is being treated for multiple myeloma.

[REDACTED] disease has been controlled over the long term in a way that was not possible until recently.

THE UNIVERSITY OF TEXAS
MD ANDERSON
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Cancer as a Chronic Disease

(Continued from page 1)

A changing landscape

In fact, many cancers, while still very serious, could become largely manageable chronic diseases with ongoing surveillance and/or treatment—similar to the way heart disease, diabetes, and HIV infection are managed today. While this vision has yet to become a reality for most forms of cancer, the past 10–20 years have seen a marked acceleration in advances toward this goal.

The reasons for this shifting paradigm are as varied and complex as cancer itself, but a few big factors are at play. Improved symptom control along with less toxic and “targeted” therapies have enabled patients to better tolerate systemic treatment. Furthermore, more clinical trials of experimental agents are available today than ever before, offering patients with metastatic cancer more chances at disease control after standard options have been exhausted. Successful trials have, in turn, broadened the field of effective agents available to the wider patient population.

Many cancers for which only a single therapy was available just a few years ago now have second- or even third-line therapies available today. Thus, patients are living longer by using one therapy until its effectiveness wanes, then moving to the next option, and then to the next. Michael Fisch, M.D., an associate professor of gastrointestinal medical oncology and director of M. D. Anderson’s General Oncology Program, describes this as the “hitchhiker model”—buying time for the patient by going from point A to point B, from point B to point C, and so on. The longer a patient lives, the greater the chances are that another effective therapy will be approved, a promising clinical trial will become available, or—perhaps—a cure will be found.

“Cancer treatment today is less likely to follow the traditional model of offering one or two lines of systemic cancer treatments and then focusing on end-of-life care, but physicians and patients often still think of it that way,” Dr. Fisch said. “The goal of therapy is often turning out to be one of maximizing the area under the quality of life-over-time curve—that is, extending life and maintaining and improving quality of life as long as possi-

ble and by whatever means are available in patients who cannot be cured.”

‘Hitchhiker model’ in practice

The concept and practice of long-term cancer management are not new; many low-grade lymphomas and chronic leukemias, for example, have been controllable for years with a combination of watchful waiting and conventional chemotherapies. But the tantalizing idea that this could become the rule for other cancers is gaining momentum, as disease types historically considered among the deadliest join the ranks of manageable cancers.

Multiple myeloma is a prime example, with ██████████ among the beneficiaries. Over the past 6 years, his doctors have sought a lasting abatement of his disease using the hitchhiker model of therapy. When an autologous stem cell transplant was not effective, he underwent a second transplant, this time with cells from a matched donor. The procedure put him into temporary remission, but it also led to both acute and chronic graft-versus-host disease. This complication has had ongoing effects, some of them serious, such as pulmonary problems that cost him the use of one of his lungs.

When ██████████ disease eventually relapsed, his doctor gave him bortezomib, a proteasome inhibitor approved by the U.S. Food and Drug Administration in 2003; this brought about a partial remission. He also received radiation in an attempt to further reduce the number of cancer cells. Most recently, he was having some success with the thalidomide analogue lenalidomide, which studies have shown delays disease progression, until complications leading to a broken clavicle made it necessary to discontinue the therapy. Currently, he and his doctor are reviewing the next options.

The promise of targeted therapies

Agents such as the ones that have helped keep ██████████ disease in check have resulted directly from our rapidly expanding knowledge of cancer’s molecular roots. For example, researchers are identifying abnormal proteins that promote cancer proliferation and developing agents that block those proteins



“We now have first-, second-, and third-line therapies, and this is why people are living longer with metastatic renal cell cancer.”

– Dr. Nizar Tannir

or induce their normal expression. These agents are known as targeted therapies because they interfere with specific molecular pathways to cancer, in contrast to older, broadly cytotoxic chemotherapies. Since they are generally less harmful to the patient and can be administered for greater lengths of time than traditional chemotherapies, targeted therapies are emerging as a crucial component of cancer management, particularly for widespread disease.

One of the first agents developed to target a specific molecular pathway—the tyrosine kinase inhibitor imatinib—has dramatically reduced disease-progression rates for patients with chronic myelogenous leukemia (CML) since clinical trials began in the 1990s. Although imatinib resistance sometimes develops, those patients can now turn to next-line targeted therapies for CML (specifically, dasatinib and nilotinib) that didn’t exist a decade ago.

Exciting results from targeted therapies are also being seen in solid tumors, such as conventional-type (formerly known as clear-cell) renal cell carcinoma. From the early 1980s to 2005, the only agents available for metastatic conventional-type renal cell carcinoma were the cytokines interferon and interleukin-2. About 5% of patients could be

cured with high-dose, bolus interleukin-2 and only 1%–2% with interferon; additionally, these therapies are generally toxic and suitable only for young patients with good performance status and no brain metastasis. The median overall survival after metastasis was about 1 year.

Finally, after years of negligible progress against the disease, three new agents were approved from 2005 to 2007: sorafenib, sunitinib, and temsirolimus. In one large phase III trial at M. D. Anderson and other institutions, temsirolimus was associated with an increase in median overall survival of roughly 50% for patients with advanced renal cell cancer, said Nizar Tannir, an associate professor in the Department of Genitourinary Medical Oncology. Sorafenib and sunitinib have been associated with improved progression-free survival. “We’re not curing these patients, but they are living longer,” Dr. Tannir said, explaining that many patients today are expected to survive about 2 years after the discovery of metastatic renal cell cancer. “I think it’s fair to say that these drugs have changed the paradigm, changed the landscape of renal cell cancer. Renal cancer has pulled away from the pack of those dreaded cancers where, for metastatic disease, there has not been any meaningfully effective therapy.”

Moreover, the newer therapies are appropriate for a wider spectrum of renal cell cancer patients, including those who are older and have a poorer performance status. Also, in addition to these recently approved agents, two or three other agents are expected to gain approval within the next year, giving oncologists the opportunity to offer multiple lines of therapy. “We now have first-, second-, and third-line therapies, and this is why people are living longer,” Dr. Tannir said.

Successes in breast cancer

Some types of metastatic breast cancer have also become manageable over the long term, perhaps most famously with tamoxifen, which can slow or stop malignant cell growth in many women with estrogen-dependent cancer by blocking hormone receptor

sites on tumor cells. And in the past decade, researchers have developed a new class of aromatase inhibitors that target estrogen production, with initial results of clinical trials showing them to provide better results than tamoxifen.

Another important advance has been made in the HER2-positive subtype of metastatic breast cancer, which used to be associated with an overall survival of 1–2 years. But thanks to trastuzumab, a monoclonal antibody that targets the overexpressed HER2 protein in this cancer, many patients with metastatic HER2-positive breast cancer are surpassing the 5-year survival mark.

Francisco J. Esteva, M.D., an associate professor in the Department of Breast Medical Oncology, has seen multiple successes attributable to trastuzumab since its approval more than a decade ago. One patient, for example, was diagnosed with stage II breast cancer in 1995. She underwent a mastectomy to remove the primary tumor and received tamoxifen for 5 years, but pulmonary metastases were discovered in 2000. The patient was then treated with aromatase inhibitors until she developed progressive disease. Because the cancer was HER2-positive, doctors began treating it with trastuzumab as a single-agent



“**Making metastatic solid tumors into chronic diseases is a reasonable short-term goal, but we should strive to find a cure.**”

– Dr. Francisco J. Esteva

therapy—and with very positive results. “The trastuzumab therapy was able to stabilize her metastases for years, and that’s something we had not seen before,” Dr. Esteva said. The patient, who participated in several clinical trials of novel therapeutics at M. D. Anderson, is currently receiving a standard therapy combination of trastuzumab with nanoparticle albumin-bound paclitaxel and is enjoying a relatively normal quality of life.

Future implications

Dr. Esteva sees the unfolding of a watershed period, one that will lead to widespread, effective cancer management as more is learned about the genetic profiles of specific disease types. “I think that what the HER2 story has taught us is that if you find a critical pathway that cancer cells need to survive and if you can target that pathway by blocking even a single protein like HER2, you can make a significant impact on outcome for that patient,” he said. “One of the hopes in the next 10 years is that we will understand the genetic makeup of each tumor, find the pathway driving that tumor, and treat the patient accordingly.”

As genetic profiling improves, clinicians might be able to identify those who could benefit from experimental therapeutics before they undergo cytotoxic chemotherapy, which often makes patients ineligible for trials of new agents. The more patients in clinical trials, the faster the development of next-generation therapeutics can proceed.

While a cure remains the ultimate goal, even for patients with metastatic disease, the chances for long-term cancer control have never been so great.

“Making metastatic solid tumors into chronic diseases, so that patients are stable for a long time, is a reasonable short-term goal, but we should strive to find a cure,” Dr. Esteva said. “I hope to see in my lifetime that we can cure metastatic cancer.” ●

For more information, call Dr. Fisch at 713-563-9905, Dr. Tannir at 713-563-7265, or Dr. Esteva at 713-792-2817, or visit www.mdanderson.org.

Barely Benign

Noncancerous brain tumors can still pose significant risks, and the decision on how—or whether—to treat such lesions is as individual as each patient.

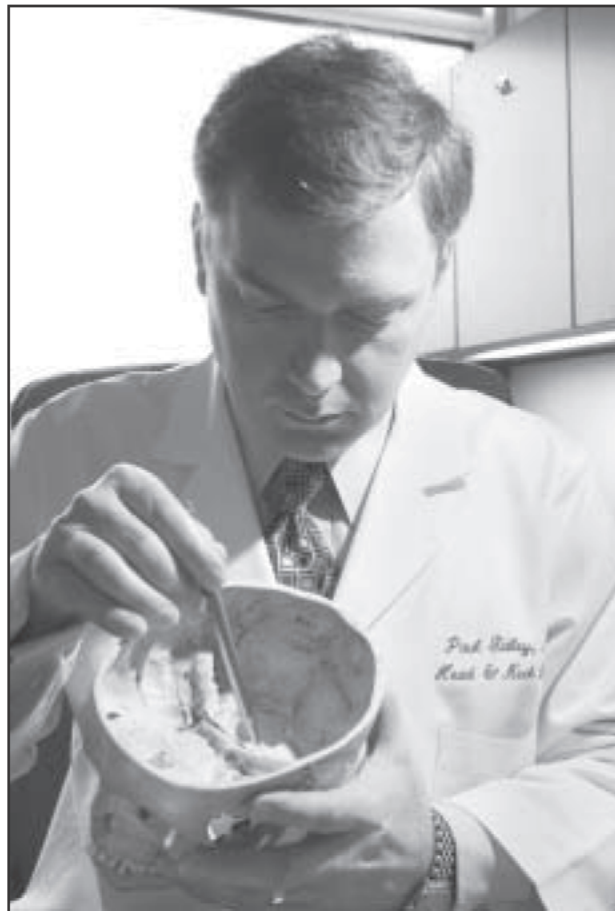
By Sunni Hosemann

Most benign tumors are rather harmless. By definition, they lack the ability to metastasize, and many don't even spread significantly in terms of the space they occupy. Moreover, they are often located in places where they do no damage to neighboring organs or surrounding structures.

But when benign tumors are growing inside the unforgiving confines of the skull, on or near delicate brain tissues, vital vessels, and major nerves, they can do considerable harm. They can even kill. And in these cases, benign tumors must be dealt with to prevent death and disability.

That's why specialists at M. D. Anderson treat just as many, if not more, benign intracranial tumors as malignant brain growths. As many as one-third of all brain tumors are benign, said Franco DeMonte, M.D., a professor in and deputy chair of M. D. Anderson's Department of Neurosurgery, though he treats an even higher percentage since benign tumors are more common in the skull base (his specialty) than other regions of the brain. "Easily half—perhaps two-thirds—of the patients I treat have benign tumors," said Dr. DeMonte, who also serves as medical director of the institution's Brain and Spine Center and co-director of the Skull Base Tumor Program.

The benign brain growths most commonly seen include meningiomas, schwannomas, craniopharyngiomas, and pituitary tumors. Rarer benign intracranial lesions include glomus tumors, choroid plexus papillomas, and hemangioblastomas, all of which are highly vascularized; epidermoid and dermoid cysts, which arise from cutaneous epithe-



Dr. Paul Gidley points to the internal auditory canal, where acoustic neuromas occur. Acoustic neuromas are the most common type of schwannoma, a benign tumor type that accounts for 4%–8% of all intracranial tumors.

lial cells displaced during embryonic development; and a variety of others.

Some of these tumors are discovered incidentally by imaging done for unrelated reasons, which is a relatively common occurrence given the widespread use of magnetic resonance imaging (MRI), Dr. DeMonte said. Other times, patients present with significant symptoms, such as headaches, loss of vision, seizures, or balance problems. Occasionally, deficits accumulate so slowly that a tumor may not be suspected as the cause; for example, gradual hearing loss due to a tumor can become profound but often is attributed to other causes or accepted as part of aging. The same can be true of mental functions that have declined slowly over time

and gradual personality changes.

Imaging alone is usually sufficient to determine that a mass is benign—that it is not a primary or metastatic cancer—and very often imaging is also sufficient to diagnose the tumor type. "MRI is the most important imaging tool in this regard, as its high sensitivity makes it the gold standard for detecting and delineating even very small masses," Dr. DeMonte said. "But computed tomography (CT) scanning plays a very important role as well, because it is superior in showing bony involvement, and that can be an important factor in assessing some intracranial tumors." Being able to assess bony involvement is important because lesions can slowly erode bony portions of the skull over time. A smooth erosion is seen with benign tumors, whereas actual bone destruction is often seen with malignant tumors.

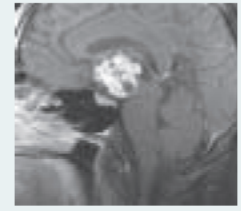
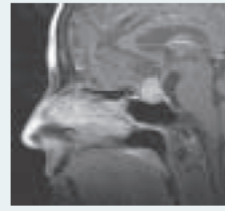
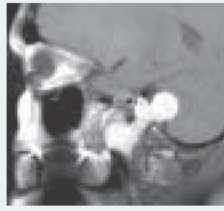
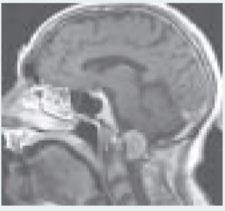
In addition, some tumors, mainly meningiomas, can cause excess bone growth, and some tumors become calcified; these are best evaluated with CT as well.

A conversation begins

When a patient is diagnosed with a cancer, the discussion between the physician and patient usually centers on various options for treatment. It will likely be about removing the tumor, deciding *when*, and perhaps explaining *how*, that will be done, and discussing whether other treatment modalities such as radiation or chemotherapy will be used.

When a tumor is benign, however, the conversation is often about *whether* to remove it surgically, treat it with radi-

Common Benign Brain Tumors



Meningiomas account for approximately 20% of intracranial tumors. Meningiomas arise from leptomeningeal tissue and are usually benign. Approximately 5% of meningiomas are associated with neurofibromatosis type 2. Ionizing radiation is a known cause of meningiomas, and according to Dr. DeMonte, meningiomas that are associated with radiation exposure tend to be more aggressive biologically and have atypical histologies. Meningiomas associated with neurofibromatosis type 2 and radiation exposure are more likely to occur in multiple locations and have a greater tendency to recur than other meningiomas.

Schwannomas are intracranial nerve sheath tumors that account for 4%–8% of intracranial tumors. The most common are vestibular schwannomas, better known as acoustic neuromas, which cause gradual, unilateral hearing loss. Schwannomas can also occur on the trigeminal and facial nerves, and more rarely, on the third, fourth, sixth, and 12th cranial nerves. Jugular schwannomas can take on dumbbell shapes and protrude into or through the jugular foramen, into the posterior fossa, or extracranially, causing specific symptom complexes depending on affected nerves. Most patients present with hoarseness as an initial symptom.

Pituitary adenomas account for about 10% of intracranial tumors. The majority are benign. These tumors are most commonly seen in the third and fourth decades of life, but they are also found in children. As some pituitary tumors secrete hormones, presenting symptoms can be associated with endocrine dysfunction. Problems associated with growth, weight gain, fertility, and menses are common. Larger tumors cause symptoms by compressing the pituitary gland itself as well as nearby structures. The optic nerve is particularly vulnerable because of its adjacent location; vision loss is a hallmark of pituitary tumors.

Craniopharyngiomas, which account for 4% of intracranial tumors, have a wide histopathologic spectrum, and their origins are not precisely known. Some are thought to arise from remnant embryonic cells, while others may represent squamous metaplasia of residual epithelial cells. These tumors occur in adults and children, with incidence peaks at 5–14 years of age and 50–60 years of age. Depending on their anatomic location, craniopharyngiomas can cause distinct clinical symptom complexes, which include headache in most cases, varying types and degrees of endocrine dysfunction, and sight disturbances.

ation, or simply keep a close watch over it. This sort of discussion is therefore more involved, according to Paul Gidley, M.D., an associate professor in M. D. Anderson's Department of Head and Neck Surgery. Dr. Gidley is a neurotologist who brings his unique specialty to bear in the surgical treatment of skull base tumors and tumors that involve the temporal bone and lateral skull base.

"First, we must do no harm," he said of the approach to treating benign tumors. "It does not benefit the patient to treat a benign tumor and leave the patient with more problems than were present at the outset." Thus, the post-diagnosis assessment becomes all-important for these kinds of tumors. This assessment includes a comprehensive history and physical examination, imaging studies, and often, tests to evaluate existing deficits (in hearing, for example).

The size and location of a tumor, its aggressiveness and damage potential, and the symptoms or deficits it is already causing are all important factors that must be weighed against the risk of

intervention. A tumor growing inside the confined space that houses the carotid artery or jugular vein, for example, can be life-threatening and should be removed. If a tumor is not threatening vital processes or is causing minimal symptoms or if the risk of complications from treatment is high, the discussion may focus on monitoring it over time.

"I tend to make a tumor prove that it needs treatment," Dr. DeMonte said. "And therefore, if the tumor is not growing and not causing symptoms, I'm able to tell patients they don't need surgery or other therapy. I have patients that we've been watching for 15 years."

But patient preference is also an important factor. Some patients are very averse to the idea of leaving a tumor in place, even when its effects are minimal. Conversely, even when it's medically evident that a tumor should be treated, some patients have strong biases against surgery and radiation therapy. So, these discussions are very specific and individualized. They are a process—a series of conversations—rather than a simple, one-stop consultation.

Treatment options

Surgery

When a tumor has proven that it needs treatment—when the risks of the growth outweigh the risks of intervention—the first option to consider is usually surgery. "Preserving and optimizing function is the most important factor when we're talking about benign tumors, which often lie on or perilously close to major nerves," Dr. Gidley said. He performs microscopic surgery for these kinds of lesions, using a variety of devices to monitor nerve function as he removes tumor tissue incrementally. Electrodes can be strategically placed on the face to show facial nerve responses. A device can be placed in the larynx to monitor vocal cord function, and hearing can be monitored with an instrument that generates sound in the ear and causes a brainstem response.

These techniques, along with surgeon experience, enhance the safety of these procedures and thus change the risk-benefit equation. Ancillary rehabilitative services available at

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Barely Benign

(Continued from page 5)

M. D. Anderson can also help patients who present with significant nerve deficits caused by these tumors. These can include audiology services; speech, language, and swallowing therapies; neuropsychology and behavioral psychology services; nutrition services; and occupational and physical therapy.

Radiation therapy

For some patients, radiation therapy is a better option than surgery. “A few days ago, I saw two patients who have similar tumors,” Dr. DeMonte said. “One of them is a healthy 38-year-old man, and the other is in his late 50s and represents a higher risk: he’s had bypass surgery and is on aspirin and clopidogrel, an anti-platelet drug. For the higher-risk patient, radiation therapy provides an alternative to surgery. Occasionally, this is also a patient preference.”

Anita Mahajan, M.D., an associate professor in radiation oncology, specializes in radiation treatments and radiosurgery for intracranial tumors. Radiosurgery refers broadly to the use of highly focused radiation beams in a single session. The beams can be shaped and are precisely aimed using computer-calculated, stereotactic, three-dimensional coordinates to destroy tumor tissue with minimal risk to surrounding healthy tissue. Fractionated radiation therapy, given in daily sessions over several weeks, can be delivered with a technique



I tend to make a benign tumor prove that it needs treatment.”

— Dr. Franco DeMonte

known as three-dimensional conformal radiation, which also uses multiple customized beams. Intensity-modulated radiation therapy (IMRT) allows alteration of the beam intensities coming from different directions to produce a truly customized dose.

The radiation oncologist has an array of tools to choose from to treat a given tumor; at M. D. Anderson, linear accelerator-based (photon) and particle beam-based (proton) systems are available. The decisions about which tool to use and whether to deliver treatment in one session or fractionated over a period of days or weeks are based on factors specific to the individual patient. For example, some techniques are better suited to certain tumor shapes than others: IMRT is better suited to treat an irregularly shaped tumor than are other modalities, including proton therapy, which is considered when minimal irradiation of surrounding tissues is crucial—in children, for example.

In all cases, patient factors that might be considered “practical” are an important part of the decision as well. For example, some radiation techniques require patients to be able to tolerate certain positioning requirements, and that may not be feasible for some people.

Not least in the list of considerations is the patient’s ability to visit the facility for treatments, and in some cases, this can affect a decision about whether to deliver the radiation in one session or over a period of 2 to 6 weeks. The latter is generally preferable, as a larger dose can be given over time with less risk to normal tissues.

Radiation therapy is sometimes used as an adjuvant to surgery for intracranial tumors. Because of the incredible density of vital neurovascular structures at the base of the skull, surgeons sometimes must stop short of complete resection of benign tumors to avoid damaging delicate and critical structures. Radiation therapy can be used to control residual tumor if it continues to grow or cause symptoms. For example, hormone hypersecretion, which occasionally continues after incomplete removal of some pituitary tumors, can be treated in this way.



These tumors are challenging because there are so many variables.”

— Dr. Anita Mahajan

Combined therapy

In some cases, the best treatment is a planned combination of surgery and radiation therapy, Dr. Mahajan said. That approach would be used for a patient with a very large meningioma at the skull base or a cavernous sinus meningioma, for instance. In such situations, the surgeon removes the part of the tumor that is compressing the optic nerves or brainstem, and radiation treatments follow to achieve control of the rest. The surgery relieves compression by reducing the bulk of the tumor, and the radiation treats the remainder of the lesion. This approach achieves good results in terms of eradicating the maximum amount of tumor while minimizing risk.

“These tumors are challenging because there are so many options for treatment, and so many patient variables,” said Dr. Mahajan, who, like her surgical colleagues, finds that the physician-patient discussion must include an exploration of various patient constraints, needs, and desires to choose the optimal treatment for an individual patient. Above all, she agrees that benign tumors—unlike their cancerous counterparts—must prove that they can be treated without the patient losing functional ground. ●

For more information, call Dr. DeMonte at 713-563-8705, Dr. Gidley at 713-745-5146, or Dr. Mahajan at 713-563-2350.



Caring for the Caregiver

Taking care of a loved one who has a serious illness or disability is a heroic but stressful undertaking, both physically and mentally. If you are one of these caregivers, you are not alone. There are an estimated 44.4 million unpaid caregivers in the United States.

Too often, caregivers feel that they cannot take the time to care for themselves. But caregivers are at increased risk for depression, infections such as colds and flu, and chronic diseases such as heart problems, diabetes, and cancer, according to the Department of Health and Human Resources Administration on Aging. Depression is twice as common among caregivers as it is in those without this challenging responsibility.

Clearly, caregivers need to find ways to look after themselves. Here are a few suggestions:

■ **Make your own health a priority.**

Get a yearly checkup, a flu shot, and cancer screenings as recommended by your doctor. Tell your doctor if you feel depressed or extremely anxious.

■ **Get enough sleep, eat balanced meals, and exercise regularly.**

Being healthy and well rested improves your physical and emotional strength for caregiving.

■ **Find support from people in the same boat.**

You could join a caregiver support group in the community or the hospital where your loved one is being treated. Or you could share experiences with other caregivers on the Internet. Communicating with others facing similar problems allows you to vent frustrations, exchange solutions, and receive comfort and support.

■ **Ask for help.** You can't do everything yourself, and you don't have to.

Online Resources for Cancer Caregivers

The Anderson Network
www.mdanderson.org/andersonnetwork

Patient and caregiver support program run by M. D. Anderson's Department of Volunteer Services offers a newsletter, a message board, a video for caregivers, an online support group called WarmNet, and information on support groups that meet weekly at M. D. Anderson

Caregiver.com

Offers information, chat rooms, and discussion forums

FamilyCaregiving101.org

Helps caregivers protect their own health

National Family Caregivers Association

www.nfcacares.org

Provides caregiver news and a message board

Make a list of tasks others can do for you, such as run an errand, prepare a meal, or babysit your children while you go to a doctor's appointment. Enlist the help of your family, friends, and neighbors.

■ **Tell someone you trust how you're feeling.**

It's normal to feel overwhelmed by your expanded and sometimes sudden responsibilities or to sometimes feel angry with the patient you're caring for. Talking with a friend, a relative, a clergy member, or another caregiver can help you gain a better perspective and alleviate intense feelings,

such as sadness, guilt, or fear. The Anderson Network, a cancer patient and caregiver support program run by M. D. Anderson's Department of Volunteer Services, has a telephone support line that will make arrangements for another caregiver to call you within 24 to 48 hours. Also, a pediatric caregiver telephone support network has been set up specifically for people taking care of children with cancer. You can reach both support lines at 1-800-345-6324.

■ **Do something for yourself every day.**

Even if it's only taking a short walk, reading a magazine, phoning a friend, pursuing a hobby, or writing in your journal, doing something that is pleasurable to you will restore your strength for the next day. Treat yourself to dinner or a movie with friends. Practicing meditation or regularly breathing deeply can help you relax.

■ **Use resources available through independent and government agencies.**

Home care agencies can often provide medical equipment and a variety of services, such as preparing meals, delivering medication, and helping the patient bathe, eat, or dress. Your state or local health department and the American Cancer Society can help you locate available services. The American Cancer Society also has a volunteer program, Road to Recovery, that transports patients to their treatment appointments.

No matter what you do to stay healthy, always remember that taking care of yourself is as important and medically necessary as taking care of your loved one. ●

For more information, talk to your physician, or:

- call askMDAnderson at 1-877-632-6789
- visit www.mdanderson.org

OncoLog, April 2008
 K. Stuyck

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IN BRIEF

Cancer-Promoting Protein in Ovarian Cancer May Be Stopped with RNA Liposome

The protein interleukin-8 (IL-8) appears to promote the growth of ovarian cancer, but its production can be stopped by a specific bit of RNA, a research team led by scientists at M. D. Anderson reported recently in the *Journal of the National Cancer Institute*.

To examine IL-8's role in ovarian cancer, the team analyzed tumors from 102 patients diagnosed and treated between 1988 and 2006 at M. D. Anderson and the University of Iowa. Of these patients, 43 had tumors with high levels of IL-8. The median overall survival of patients with high IL-8 expression was 1.62 years, compared with 3.79 years for those with low expression. All 43 tumors with high expression of IL-8 were of high grade, and 42 were stage III or IV tumors.

The researchers then identified a specific chain of short interfering RNA (siRNA) that stopped production of IL-8 in laboratory testing. They tested this siRNA against two lines of ovarian cancer in mice by inserting it into a liposome, which served as a vehicle to the tumors.

Among mice receiving injections of the IL-8 siRNA liposome, tumors from the two lines shrank by a median of 32% and 52%. Median tumor weight shrank by 90% and

98% in mice receiving both IL-8 siRNA and the taxane-based chemotherapy drug docetaxel. Mice receiving control siRNA plus docetaxel had reductions in tumor weight of 67% and 84%. IL-8 siRNA alone reduced blood vessel density in tumors by 34% and 39%.

In mice with an ovarian cancer known to be resistant to taxane-based drugs, IL-8 siRNA alone reduced tumor size by 47%. When the IL-8 therapy was combined with docetaxel in these mice, tumor size decreased by 77%, suggesting that the combination re-sensitizes a resistant tumor to taxanes.

IL-8 is overexpressed in many types of cancer and has been shown to promote tumor growth, angiogenesis, and metastasis. "In the long run, this research will have applications in other cancers as well," said Anil Sood, M.D., a professor in the M. D. Anderson Departments of Gynecologic Oncology and Cancer Biology and senior author of the research. The IL-8 siRNA liposome is the third developed by M. D. Anderson researchers as a way to potentially deliver inhibitors to cancer-promoting proteins.

Along with Dr. Sood, the development of these liposome delivery systems is being led by Gabriel Lopez-Berestein, M.D., a professor in the Department of Experimental Therapeutics. A phase I clinical trial of a liposome containing the oncoprotein EphA2 could begin within a year. ●

OncoLog

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