When a melanoma is found early and properly removed, the outlook is excellent. In fact, patients with early-stage melanoma can have survival rates as high as 95%. But for patients with melanoma that has metastasized, the disease is more deadly: the survival rate for patients with metastatic melanomas involving a major organ is no more than 6%—evidence that today’s clinicians have a challenge in finding ways to better manage advanced forms of the disease.

(Continued on next page)
New Approaches for Advanced Melanoma
(Continued from page 1)

Currently, only two FDA-approved drugs exist for the treatment of metastatic melanoma: dacarbazine and interleukin (IL)-2. Dacarbazine is a conventional cytotoxic chemotherapy agent. According to Kevin Kim, M.D., an assistant professor in the Department of Melanoma Medical Oncology at The University of Texas M. D. Anderson Cancer Center, the rate of response to dacarbazine in metastatic melanoma is only about 10%, and it rarely produces a durable response. And although combination regimens that include dacarbazine have been investigated, none have improved survival more than dacarbazine alone.

On the other hand, IL-2, which works by stimulating killer T-cells to attack melanoma, produces a response in 15% to 20% of patients; in 7% to 8% of patients, the response is durable. “We can essentially cure some patients with advanced disease using IL-2, but only a small minority of patients have this remarkable response. We want to know why,” said Patrick Hwu, M.D., professor and chair of the Department of Melanoma Medical Oncology. Knowing ahead of treatment who is likely to respond to IL-2 would spare the majority of patients with advanced melanoma from undergoing a treatment that can be toxic and must be delivered in the ICU. “Beyond that,” said Dr. Hwu, “if we can understand how it’s working, perhaps we can convert non-responders into responders.”

Clearly, other treatments are also needed for those who are unlikely to respond to either of these two agents, both of which are toxic and costly. To that end, investigators are pursuing several promising avenues.

Ideal candidate for immunotherapy

Dr. Hwu believes that certain factors make melanoma an ideal candidate for therapies based on the immune system. “When you remove a melanoma,” he said, “you find immune cells there already trying to attack it.” On that basis, Dr. Hwu and colleagues at the National Cancer Institute pioneered a treatment approach currently in use, in which adoptive T-cells are harvested from the patient’s tumor, grown in the lab, and reintroduced to attack the tumor in greater numbers. In a current study of this method in patients with advanced or recurrent melanoma, half of the tumors responded.

Vaccine therapy is a second immune-based approach, one that Dr. Hwu expects may be of greatest benefit in preventing recurrence, perhaps in combination with other therapies that attack active disease. “With initial therapy, patients may reach a point where they have no identifiable disease, but we know the cancer might come back, and this is where a vaccine might help keep the disease at bay,” he said. In current trials, vaccine therapy is being used in combination with other kinds of agents to see if this dual approach is helpful.

Another avenue of research focuses on combining targeted therapies to achieve a synergistic response. Although individual targeted agents have failed to improve response rates in melanoma, preclinical data have recently shown that combinations of targeted agents have promise. “One of our focuses is looking at combination strategies that use targeted agents to block receptor proteins in melanoma cells,” Dr. Kim said. Such combinations might include more than one targeted agent or a targeted agent plus a chemotherapy agent.

According to Dr. Kim, gene transfer is yet another promising line of inquiry. As a result of the work of Elizabeth Grimm, Ph.D., a professor in the Department of Experimental Therapeutics and leader of the Melanoma SPORE grant at M. D. Anderson, Dr. Kim is leading a trial in greater number. In a current phase II clinical trial, intratumoral injections of a virus expressing IL-24 are being evaluated in patients with metastatic melanoma who have cutaneous lesions.

Treating “in-transit” disease

A difficulty associated with melanoma is the treatment of “satellite” or “in-transit” disease, which appears as cutaneous or subcutaneous deposits of tumor cells between the primary tumor and the regional lymph node basin. For example, when a primary tumor is on the foot, metastatic lesions between the foot and groin would likely be considered “in-transit.” Some patients, progressing, the cells lose their expression of the IL-24 gene. Further, they have observed that when the IL-24 gene is reintroduced, the melanoma cells undergo apoptosis,” said Dr. Kim. In a current phase II clinical trial, intratumoral injections of a virus expressing IL-24 are being evaluated in patients with metastatic melanoma who have cutaneous lesions.

“Accurate staging is key,” says Dr. Jeffrey E. Gershewald (r), discussing a case with Mary Salazar, a nurse.

We can essentially cure some patients with advanced disease using IL-2, but only a small minority of patients have this remarkable response. We want to know why.”

– Patrick Hwu, M.D.
whose satellite lesions become too numerous or bulky to excise, can undergo perfusion, the regional delivery of chemotherapy after the vasculature of the targeted area, usually a lower limb, has been cannulated and isolated.

In a newer version of this approach, known as “minimally invasive isolated limb perfusion” or “isolated limb infusion,” the chemotherapeutic agents are circulated via catheters placed into the affected arm or leg while a pressure cuff device or tourniquet temporarily stops circulation, effectively isolating that area. “Compared to conventional limb perfusion, this evolving approach involves a lower flow rate and an overall shorter duration of circulation, but it can also have significant toxicity,” said Jeffrey E. Gershenwald, M.D., an associate professor in the Department of Surgical Oncology at M. D. Anderson.

**Advances in staging: sentinel lymph node biopsy**

Accurate staging is critical to the management of melanoma. “One of the recent success stories in this disease is our ability to identify patients with newly diagnosed intermediate- and high-risk melanoma who have no clinical evidence of lymph node involvement but in fact harbor microscopic metastases in their regional lymph nodes,” said Dr. Gershenwald. Combining diagnostic modalities, such as lymphatic mapping and sentinel lymph node biopsy, allows more information to be gathered about the existence and extent of metastases. One such combined approach uses a radioactive tracer injected around the primary tumor site and a blue dye to identify sentinel lymph nodes, the regional nodes most likely to contain evidence of microscopic metastases, which are then removed for pathologic analysis.

According to Dr. Gershenwald, sentinel lymph node biopsy accurately determines the involvement in regional nodal basins, improves regional nodal control, may offer a survival benefit, and has enabled the selection of more stage-appropriate treatments. Specifically, the procedure can identify the 15% to 20% of patients with microscopic stage III disease who need additional or more aggressive treatment, such as a complete lymphadenectomy. These patients are also offered adjuvant therapy or the opportunity to participate in adjuvant therapy trials. Even more, if a biopsied node is negative, the patient is spared a complete lymph node dissection.

A key to further progress against melanoma may lie in the increasingly sophisticated study of tumor biology and pathology. In most current trials, any tissue removed is subjected to intense pathologic scrutiny.

“A unique aspect of the sentinel lymph node biopsy approach is that the surgery is based on the biology of the patient’s own tumor environment. It allows us to identify regional lymph node disease that we might not see even with complete lymph node dissection,” said Dr. Gershenwald. He stresses that the success of a sentinel lymph node biopsy includes the identification and removal of the sentinel lymph nodes from all regional basins at risk and the intense histologic analysis of removed tissues.

Traditionally, pathologists have used similar methods to study the stained slices of lymph nodes removed during either complete or sentinel lymph node dissections. However, newer evidence has led pathologists to examine multiple slices from different “levels” of sentinel nodes and use immunohistochemical analyses. According to Dr. Gershenwald, M. D. Anderson investigators are also looking into the potential prognostic significance of microscopic regional lymph node disease.

**Insights from molecular pathology**

Another key to progress may come from the field of molecular pathology. “We used to think that melanoma was a single entity,” said Victor Prieto, M.D., Ph.D., a professor in the Department of Pathology. “But in the last five years, we have come to realize that isn’t the case at all.”

What investigators have recently realized is that the four major subtypes of melanoma, long-recognized as superficial spreading, nodular, lentigo maligna, and acral lentiginous melanoma, each have a different genetic profile and further, that this genetic profile can be linked to a phenotype. According to Dr. Prieto, this is an important insight because targeted therapies are specific to particular proteins.

For example, imatinib (Gleevec)—the agent used so successfully in chronic myelogenous leukemia—met with limited success in melanoma. But after one patient, whose acral lentiginous melanoma had an alteration in an imatinib-targeted tyrosine kinase

With more sophisticated tumor analysis will come more precisely targeted therapies, says Dr. Victor Prieto.

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pathway and showed a response to imatinib, researchers began examining acral lentiginous and mucosal melanomas for alterations in the same pathway to determine whether patients with these specific phenotypes might also respond to therapy with imatinib. “This is similar to the Herceptin story for breast cancer, where only 25% of patients have HER2/neu receptors, and only those tumors are expected to respond to that specific therapy,” said Dr. Prieto. “It seems clear that as the biological and pathologic analysis of tumors grows more sophisticated, the targets for targeted therapies will also become more precise.”

In addition to leading to more targeted therapies, analyses using molecular pathology can yield more precise prognostic information, an important guide in making treatment decisions. According to Dr. Prieto, “The information allows us to better determine who should receive additional therapy—patients who have a higher risk of recurrence or metastasis, for example—and whether additional therapy will confer a survival benefit.”

Broader implications

Dr. Hwu and his colleagues at M. D. Anderson believe that melanoma research will have broad implications for other cancers, especially because cutaneous melanoma metastases are readily accessible for biopsy and study. This makes it easier for researchers to study key disease characteristics, such as whether a certain kind of tumor responds to certain drugs, whether a therapeutic target was hit, whether a signal pathway was effectively blocked, and whether a particular switch was successfully turned on or off.

By seeking answers to these questions and more, melanoma researchers are going beyond “skin deep,” gaining knowledge that may advance treatment not only in the field of melanoma but in other diseases across the spectrum of cancer.

**For more information**, contact Dr. Hwu and Dr. Kim at (713) 792-2921, Dr. Gershenwald at (713) 792-6936, and Dr. Prieto at (713) 792-3187.

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**CLINICAL TRIALS FOR METASTATIC MELANOMA**

- **Study on the feasibility and bio-equivalence of using a DNP-modified autologous melanoma tumor cell vaccine as therapy in patients with stage III or IV melanoma (“M-Vax,” 2005-0361).** Principal investigator: Jeffrey Lee, M.D.

- **Phase I/II study of combined BAY 43-9006 (sorafenib) and CCI-779 (temsirolimus) in patients with metastatic melanoma (2005-0215).** Inclusion criteria include having metastases involving the skin, superficial lymph nodes, or other organs, which can be easily biopsied by punch, core needle biopsy, or excision. Principal investigator: Kevin Kim, M.D.

- **Phase II study of the biological efficacy of intratumoral INGN 241 (Ad-mds7) in patients with at least three in-transit melanoma (2003-0590).** Principal investigator: Kevin Kim, M.D.

- **Phase I/II study of CR011-vcMMAE in patients with unresectable stage III or IV melanoma (2006-0378).** Eligible patients cannot have active brain metastases and must have failed no more than one prior cytotoxic regimen (no limit on biologic therapies). Principal investigator: Patrick Hwu, M.D.

- **Phase III multicenter randomized study of immunization with the gp100: 209-217 (210M) peptide followed by high-dose IL-2 vs. high dose IL-2 alone in patients with metastatic melanoma (2003-0835).** Principal investigator: Patrick Hwu, M.D.

- **Phase I trial of oral CHIR-265 in patients with locally advanced or metastatic melanoma (2005-0949).** Prior chemotherapy treatments are not an excluding factor. Principal investigator: Kevin Kim, M.D.

- **Lymphodepletion plus adoptive cell transfer with or without dendritic cell immunization in patients with metastatic melanoma and who are HLA-A2+ with a good ECOG performance status score (2004-0069).** Principal investigator: Patrick Hwu, M.D.

- **Phase II study of biochemotherapy with temozolomide, velban, cisplatin, IL-2, interferonα, and thalidomide, with optional preventative CNS treatment (DM03-0218).** Eligible patients are those with inoperable metastatic melanoma who have not had prior chemotherapy, isolation perfusion, or exposure to IL2. Principal investigator: Nicholas Papadopoulos, M.D.

- **Phase I study of combined CC-5013 (lenalidomide) and DTIC (dacarbazine) in patients with metastatic melanoma who have not previously received systemic chemotherapy (2004-0487).** Principal investigator: Agop Bedikian, M.D.

- **Phase I multicenter trial of the efficacy and safety of adding bevacizumab to chemotherapy with carboplatin and paclitaxel to achieve better tumor control in the first-line treatment of patients with stage IV metastatic melanoma (2006-1054).** Principal investigator: Kevin Kim, M.D.

- **Phase II study of temozolomide, thalidomide, and lomustine in patients with metastatic melanoma in the brain who have not previously been exposed to any of these drugs (2004-0595).** Principal investigator: Nicholas Papadopoulos, M.D.

**For more information** and a broader listing of clinical trials currently enrolling at M. D. Anderson, visit www.clinicaltrials.org or call askMDAnderson at (877) MDA-6789.
Helping Patients Stop Smoking

It’s never too late: patients with cancer reap big benefits from kicking the habit, even after diagnosis.

by Karen Stuyck

Even after they’ve been diagnosed with cancer, smokers can benefit greatly from giving up tobacco—so much so that M. D. Anderson has instituted a no-cost program to help its patients do just that.

Started in January 2006, the Tobacco Treatment Program is open to all M. D. Anderson patients who either currently use tobacco or have quit using it within the last 12 months. The program offers free counseling and tobacco-cessation pharmacological treatment as well as relapse-prevention counseling for recent quitters.

Participants receive a psychological assessment, in-person behavioral counseling, follow-up telephone counseling and support, various nicotine-replacement therapies, or tobacco cessation prescription medication. Patients' family members who smoke also can receive free smoking cessation counseling.

M. D. Anderson's Tobacco Treatment Program is supported by State of Texas Tobacco Settlement Funds. “This program puts into practice everything we believe is state of the art in addressing tobacco use in the cancer patient,” said Ellen R. Gritz, Ph.D., professor and chair of M. D. Anderson's Department of Behavioral Science.

Dr. Gritz and her colleagues are spreading the word to their oncologist colleagues that stopping smoking is a significant factor in the effectiveness of treatment and overall outcome for cancer patients. While the harmful effects of smoking are well known, there are additional risks for cancer patients who smoke. Studies show that tobacco use before, during, and after treatment can affect cell growth, cell death, and tumor density, decreasing the efficacy of cancer treatment. Smoking increases the likelihood that the cancer will recur or a second primary tumor will develop. It decreases the cancer patient's survival rate as well as the quality of life. It aggravates treatment side effects and can complicate radiation therapy, chemotherapy, and surgery, according to Dr. Gritz.

Motivation to quit

In an article in the journal Cancer, Dr. Gritz and colleagues concluded that the optimal time to help smoking patients quit is when they are initially diagnosed with cancer. Motivation and interest in smoking cessation increase after patients are diagnosed with cancer, giving health care providers a window of opportunity to intervene and assist patients to give up tobacco, according to Dr. Gritz. Their research determined that using this “teachable moment” can help up to 70% of patients stop smoking, compared to a typical success rate of 20% to 25% in the general population at one year follow-up.

This teachable moment can consist of a brief (3 minutes or less) smoking cessation intervention by the physician, with the discussion tailored to the individual patient. Ideally, Dr. Gritz said, the message needs to be reinforced and delivered multiple times, preferably coming from all health care team members. “The teachable moment has to be heavily emphasized at diagnosis because of all the things that can go wrong during treatment if the patient continues to smoke. But you have to keep repeating the message because smoking is a chronic relapsing disorder—an addiction—and when people start to feel better, smoking sometimes creeps back in.”

To inform physicians, Dr. Gritz, with some of her colleagues, has also written a chapter on “Tobacco Control in the Oncology Setting” for an upcoming American Society of Clinical Oncology (ASCO) Cancer Prevention Curriculum and a chapter called “Tobacco and Smoking Cessation—Focus on Oncology” in the upcoming 8th edition of Principles and Practice of Oncology.

Oncologists who deal with smoking-related tumors, such as in lung or head and neck cancers, are usually well aware that it’s important for their patients to stop using tobacco, but doctors who treat tumors not causally related to smoking are often less aware of the benefits of quitting, Dr. Gritz said. In more than 20 studies conducted using cross-sectional surveys, the respondents, who were mostly general practitioners and family physicians, cited several factors to explain why they did not actively encourage their cancer patients to stop smoking: lack of time to discuss smoking behavior, their belief that such discussions would be ineffective, lack of counseling skills, and concern that they were invading the patient's privacy.

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Helping Patients Stop Smoking
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Guideline for physicians
The U.S. Public Health Service has issued a Clinical Practice Guideline to help health care providers deliver effective smoking cessation treatment. The Guideline recommends documenting every patient’s tobacco use, strongly encouraging each smoker to quit, determining the patient’s willingness to attempt quitting, using counseling and pharmacotherapy to assist in quitting, and scheduling follow-up contact.

M. D. Anderson’s Tobacco Treatment Program uses therapeutic interventions based on these guidelines. As of early March 2007, 543 patients have been treated in the program, according to Janice Blalock, Ph.D., assistant director of the Tobacco Treatment Program and an assistant professor in the Department of Behavioral Science.

The program’s staff includes one psychiatrist, an advanced practice nurse, three Ph.D. clinical and counseling psychologists, one master’s-level psychologist, and one master’s-level social worker, Dr. Blalock said, with counseling staff likely to expand as the number of patients enrolled increases.

The program’s ultimate goal, Dr. Blalock said, is to proactively identify all M. D. Anderson patients who are tobacco users or recent quitters and then contact eligible patients to invite them to participate in the Tobacco Treatment Program.

As part of a pilot program to test this proactive approach, patients in M. D. Anderson’s Head and Neck Clinic fill out a questionnaire in the Patient History Database when they register. The questionnaire identifies and automatically notifies the staff of the Tobacco Treatment Program when a patient is a smoker or a recent quitter. Program staff then contact those patients to make them aware of the program and schedule an appointment for those willing to meet with a clinician. The database eventually will be used in all M. D. Anderson clinics, which will enable the Tobacco Treatment Program to identify eligible patients throughout the institution.

No matter how they are referred, smokers come to the program in various stages of willingness to stop using tobacco, Dr. Blalock said. In their initial assessment, all patients are evaluated for motivation to quit as well as for concurrent psychiatric problems.

“If there are motivational problems, we focus on delivering motivational interventions before we do anything else,” she said. Motivational interviewing is one technique shown to be effective. Such discussions help patients consider the risks and benefits of taking action and let the patients know about available resources, while at the same time demonstrating acceptance of the patients’ feelings, beliefs, and personal goals regarding changing tobacco use. If patients are reluctant to quit immediately, the program’s staff will help them achieve other tobacco-use goals, such as reducing their smoking rates. Many of the medications used in the Tobacco Treatment Program decrease the desire to smoke, which can also help the patients who prefer to make gradual changes.

The program offers, at no cost to patients, all the front-line medications recommended by the Clinical Practice Guideline, Dr. Blalock said. These include various nicotine-replacement products—patch, gum, lozenges—as well as bupropion (Zyban), an antidepressant shown to be effective in helping people quit smoking, and a promising new drug, varenicline (Chantix), which decreases the desire to smoke.

The program also addresses other problems patients might have that could affect their ability to stop smoking. “We know that people who smoke often have concurrent problems, like alcohol abuse, depression, or an anxiety disorder,” Dr. Blalock said. In such cases, the program psychiatrist will assess the patient and possibly prescribe medication. If additional therapy is considered necessary, the patient will be referred to other counseling services.

“Our goal was to create a program that addresses all the barriers individuals may have to stopping smoking,” Dr. Blalock said. Whether that barrier is low motivation to quit, a concurrent psychiatric problem, a spouse or family member who still smokes, or a lack of financial resources to pay for a smoking cessation program, M. D. Anderson’s Tobacco Treatment Program is working to provide solutions.

SMOKING CESSATION PROGRAMS

The Tobacco Treatment Program is available free of charge to M. D. Anderson patients. For a copy of the clinical practice guidelines, “Treating Tobacco Use and Dependence,” developed by the U.S. Department of Health and Human Services, go to www.mdanderson.org/departments/quitnow.

M. D. Anderson smoking cessation studies available to patients and the public include those listed below. Call (713) 792-2265 for more information or go to www.mdanderson.org/topics/smoking.

• Project Baby Steps Smoking cessation treatment addressing the special needs of pregnant smokers.
• Project PRISM Smoking cessation study for those 18 years or older. Participants receive free nicotine patches, counseling, and self-help materials and are paid for their time.
• Project CARE Smoking cessation research study for those 21 years old or older. Participants receive free nicotine patches, and counseling and are paid for their time.
• Project MOM Study to help women stay smoke-free after the birth of a child.
• Project MIND – Group Therapy for Nicotine Dependence Study to evaluate smoking cessation treatment offered in a group setting.
• Project PASS International study to assess the efficacy of dianicline as an aid to smoking cessation.
• Pharmacogenetics, Emotional Reactivity and Smoking Study to assess the effects of antidepressants on changes in emotional reactivity during smoking cessation.
Simple Skin Cancer Prevention

This year, more than one million Americans will be diagnosed with skin cancer, a disease that is almost totally preventable. The most common cancer in the United States, skin cancer is usually a direct result of too much sun exposure.

By adopting a few fairly simple behaviors, you can help yourself and your family avoid the disease.

Enlighten yourself—use sunblock

Ultraviolet (UV) radiation comes from both sunlight and artificial sources, such as tanning booths. So much scientific research confirms that UV rays cause the majority of skin cancers that the U.S. Department of Health and Human Services now classifies UV radiation as a carcinogen—a cancer-causing agent.

Reducing your risk of skin cancer begins with sun protection. Make applying sunscreen a daily part of your routine, said Carol Drucker, M.D., associate professor in M. D. Anderson Cancer Center’s Department of Dermatology. Women can use moisturizer, powder, or makeup that contains sunscreen. Dr. Drucker suggests putting sunscreen on children every morning when they’re getting dressed. Sunscreen should always be applied about 30 minutes before children go outdoors. Babies, however, should never be exposed to direct sunlight.

That sneaky sunlight—exposure adds up

A great deal of sun damage occurs in childhood. According to M. D. Anderson Cancer Center experts, research indicates that the regular use of sunscreen during the first 18 years of life can reduce the lifetime incidence of skin cancer by 78%.

Most of us don’t realize how much sun we’re getting and that you don’t have to go to the beach to get too much sunlight. Studies following people who work indoors found that most had 20 to 30 hours of cumulative sun exposure in one week just by doing their normal, day-to-day activities, Dr. Drucker said. “That’s an amazing amount of sun exposure.”

How to keep those dangerous rays at bay

Choose sunscreen with a minimum sun protection factor (SPF) of 15 that blocks both UV-A and UV-B rays. Although it is UV-B rays that cause sunburn, UV-A rays also increase the risk of skin cancer, and sunscreens with an SPF of at least 15 filter out 93% or more of these rays. “If you’ve had sun damage or pre-cancerous lesions, a sunscreen with an SPF of 30 is recommended for the face,” Dr. Drucker said. Pick a sunscreen that protects you from both UV-A and UV-B rays.

To cover your body, use enough sunscreen to fill a shot glass. According to the American Academy of Dermatology, most people don’t use enough sunscreen to receive the level of protection promised on the package.

Use special sunscreen when you’ll be outside longer than usual. For example, on vacation or on days when you’ll be outdoors much of the day, choose a heavy-duty sunscreen, such as DuraScreen, which stays on all day and binds to the skin, Dr. Drucker said. Another product that offers extra protection is Rit Sun Guard, a laundry additive that washes sunscreen protection into clothing and is especially helpful for loose-weave clothing that lets a lot of light go through the fabric.

Seek shelter between 10 a.m. and 4 p.m. Particularly in the southern United States, it’s a good idea to keep indoors or in the shade during mid-day, when the sun’s UV rays are the strongest. If possible, schedule outdoor activities before or after those hours. And when you’re in the sun, cover up with clothing and sunglasses, in addition to using sunscreen. People with fair skin who freckle or burn in the sun are at high risk of skin cancer and should be especially diligent in following these precautions.

Stay out of tanning beds. If you soak in artificial UV rays of any kind—even if you follow all the other recommendations listed here—you will undermine all your other efforts to prevent skin cancer. “There is no redeeming value to tanning beds,” Dr. Drucker said. “They’re not safe.”

It isn’t difficult to protect yourself from skin cancer, and the effort is worth it.

For more information, talk to your physician, or:
• call askMDAnderson at (877) MDA-6789
• visit www.mdanderson.org.

March 2007

K. Stuck

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Toward Gender Equity in Academic Medicine

Elizabeth Travis, Ph.D.
Associate Vice President,
Women Faculty Programs

The percentage of women graduating with medical and doctorate-level degrees in the biological sciences has been slowly increasing over the past 25 years, and today, women outnumber men in both undergraduate and graduate programs in the sciences. For at least a decade now there has been a rich pipeline of women to staff and lead the ranks of academic medicine. However, the proportions of female faculty and leaders in academic medicine do not reflect this reality.

While men are fairly equally distributed across academic medicine, the distribution of women in the ranks forms a pyramid, with a large assistant professor base (38%) and a small minority (16%) as full professors. Furthermore, women make up only 16% of all tenured faculty and only about 10% of top leadership.

Why is it that at a time when the future prosperity of the United States increasingly depends on training more physicians, scientists, engineers, and mathematicians, we are not capitalizing on this ready pool of talent? Global competition for scientific talent is increasingly fierce; we can’t afford to underutilize women’s potential as leaders in medicine and science any longer.

The barriers are unintentional, but they are deeply rooted in our culture. The practices in academic medicine still assume a traditional family structure, with a non-working spouse upholding family obligations. Today’s reality is often a two-career household with intensive workloads, though family responsibilities still fall primarily to women. Professional structures and expectations often overlook these realities, and in so doing, unwittingly close the doors on rich resources of leadership.

Programs to accommodate the unique needs of women are beneficial but haven’t made substantial progress toward professional gender equity. Rather than developing more programs aimed at “fixing the women,” I think it’s time to concentrate more on “fixing the institutions.”

For example, one of the first initiatives should be increasing the number of women at the leadership tables of academic medicine. Studies show that the dynamics change as three or more women are added to the mix. Second, no program can equal the clear example set by a president, dean, or chair communicating in words and actions the importance of both men and women in leading the organization. When this happens, others notice and the culture begins to change. M. D. Anderson has underscored and reaffirmed its commitment to developing female leadership through the recent appointment of an associate vice president for Women Faculty Programs. I’ve accepted this challenging, but exciting, task.

But this is not only a leadership issue. The subtle practices and assumptions at the root of the problem are often best recognized and changed at the grassroots level—among individuals and workgroups and departments.