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After Diagnosis, Another Hurdle: Cancer Screening for the Cancer Patient

by Jude Richard

Scared, mystified, sometimes both—that's how Therese Bevers, M.D., medical director of the Cancer Prevention Center (CPC) at The University of Texas M. D. Anderson Cancer Center, says many cancer patients feel when they first come for cancer screening.

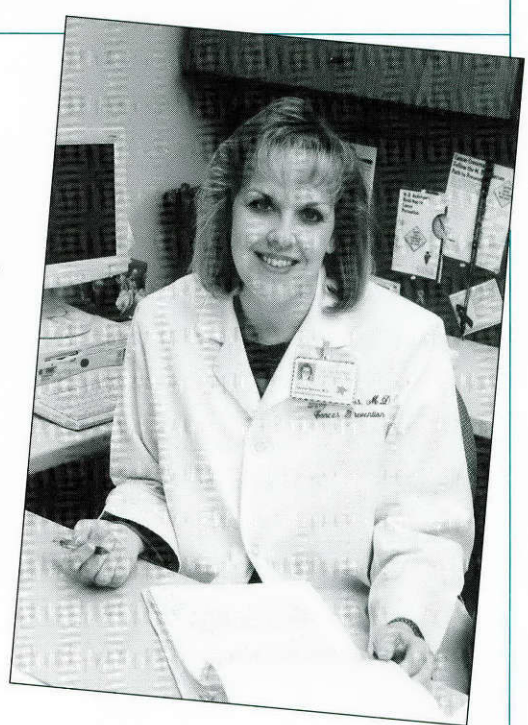
"The occasional patient is so shocked already by the diagnosis of his or her first primary cancer," says nurse practitioner Mervianna Thompson, R.N., C.S., A.N.P., A.O.C.N., who screens patients in the CPC daily, "that they can't handle screening and the possibility that another cancer will be found." But when they leave—after they understand screening's benefits—they're often thinking differently.

"The cancer patient must be reminded," advises Lewis Foxhall, M.D., "that having one cancer may make it more likely he'll have a

(Continued on **next page***)*

"... the patient is more susceptible to other cancers and other illnesses."

– Mervianna Thompson, R.N., C.S., A.N.P., A.O.C.N., nurse practitioner, Cancer Prevention Center



"More and more patients are also asking for genetic screening."

– Therese Bevers, M.D., medical director, Cancer Prevention Center

second primary and that, consequently, the patient needs to stay healthy and have recommended regular screening." Dr. Foxhall, who formerly referred patients to M. D. Anderson from a primary care practice, now is co–medical director of M. D. Anderson's Office of Referral Relations.

Educating the patient is part of the process, Thompson agrees. "We first explain we're looking for other cancers before they become more advanced, which requires more extensive treatment."

The patients' own experience with early detection of a primary cancer can make the search for second primaries palatable, according to Dr. Bevers. "Often, when we establish that a patient has a good chance of survival because the cancer was caught early, we use that example to convince the patient of the need for continued screening," she said.

Furthermore, patients aren't the only ones unsure about screening in cancer patients. Members of the American Society of Clinical Oncology said in a survey reported in 1992 that lack of patients in their practice without cancer and the difficulty of incorporating screening economically into practice were major barriers to putting cancer screening and prevention activities into practice.

For the best patient outcome, primary physician, oncologist, and patient must cooperate in screening efforts. If not performed by the oncologist during workup, screening may be done by the community physician if indicated based on the projected outcome of the cancer treatment.

"Communication between the oncologist and the community physician is key since the community physician often keeps seeing the patient while the patient is being treated over time for the cancer," says Dr. Foxhall.

Treatment, too, is shifting after diagnosis at major centers like M. D. Anderson to treatment near home. "Occasionally, recommended treatment is being done in the community, after centers like ours have done the initial screening and workup," said Thompson. "The community physician is then more involved in screening the patient on a regular basis and sends the patient back to the oncologist for regular checkups."

When the community physician will be performing the screening, Dr. Bevers said the oncologist must make clear to the community physician the outlook for the patient, including "the exact ramifications of the patient's tumor stage and grade, treatment, treatment-related side effects, and expected five-year survival and recurrence rates."

"Certain cancers have certain life expectancies, and at some point, screening for other life-threatening conditions may no longer be of benefit to the patient," she said. "But until that point, the patient should continue being screened."

Once determined necessary, however, screening should be regular.

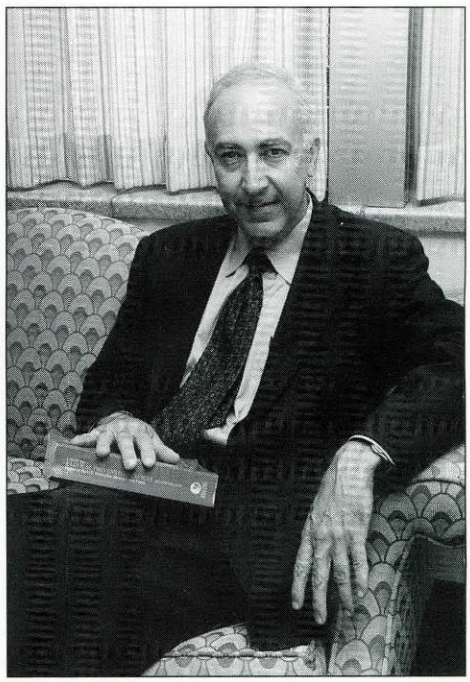
"Wherever the screening is done and whoever does it, vigilance must increase," according to Dr. Foxhall.

"What cancer patient, oncologist, and community physician must all remember is that the patient is more susceptible to other cancers and other illnesses and that concerted primary surveillance and secondary screening is necessary," said Thompson.

Dr. Foxhall said that in his experience, patients often became more willing to be regularly screened after they have had a cancer diagnosed: "The diagnosis of that first primary cancer breaks down the barrier of patient denial and gives the oncologist and community physician a persuasive toehold."

"The community physician . . . can be crucial in reducing cancer mortality."

– Lewis Foxhall, M.D.,
co–medical director, M. D. Anderson's
Office of Referral Relations



"More and more patients are also asking for genetic screening," Dr. Bevers says, despite its high cost and their awareness that the results, even though confidential, can raise new fears and concerns when a genetic marker linked to cancer is found.

"But because it's highly specialized and involves DNA sequencing," Dr. Bevers adds, "most national medical associations recommend that the community physician defer to comprehensive cancer centers for such screening. However, both the patient and the community physician can stay alert to any signs of genetic predisposition to disease." Such a predisposition would include a strong family history of cancer, such as breast, ovarian, colon, or endometrial cancer.

At present, genetic screening can be done for colon, breast, ovarian, and thyroid cancers. M. D. Anderson offers these tests.

But Dr. Bevers points out that community physicians can do a great deal of screening in the office. What they may not be able to do (e.g., sigmoidoscopy), they can order. Results can then be forwarded to the oncologist.

"The community physician," says Dr. Foxhall, "by providing preventive clinical services to try to detect cancer during its asymptomatic phase when treatment can be most effective, can be crucial in reducing cancer mortality."

For the busy community physician who wants to improve his or her screening program, whether for those with a history of cancer or without it, Dr. Foxhall recommends a program developed by the U.S. Public Health Service and now being promoted by major medical associations called "Put Prevention Into Practice," or PPIP.

Through the Agency for Health Care Policy and Research web site (http://www.ahcpr.gov/ppip), community physicians and other primary care providers have access to useful patient health questionnaires, flow charts, patient education materials, reminder postcards, and record-keeping tools meant to organize and streamline screening in a busy practice. PPIP materials are also available through the Texas Department of Public Health.

Thompson points out that patients, too, can lead the early detection effort. "Patients can keep educating themselves and keep reminding their own personal physicians of the need for routine screening," she said. ●

FOR MORE INFORMATION, *contact the Cancer Prevention Center at (713) 745-8040 or Dr. Foxhall at (713) 792-2202. E-mail Dr. Bevers at tbevers@notes.mdacc.tmc.edu and Dr. Foxhall at lfoxhall@mdanderson.org.*

M. D. Anderson Researchers Study Children's School Lunch Habits and Choices

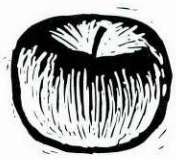
Low scores by the nation's schoolchildren are sending researchers scurrying. But this time it is to the lunchroom, not the classroom.

Dr. Karen Cullen *is leading a study of schoolchildren's lunchtime eating habits.*

Research shows that children consume fewer than 2.5 servings of fruits and vegetables daily, giving them a score below 50% on the test of eating five servings per day. This dismal score so early in life worries cancer prevention experts who say that meeting the standard may reduce the risk of cancer by 30% to 40%.

To get answers, researchers are conducting a pilot study to determine what food choices children make when selecting from an array of sweets, high-fat snacks, fruits, and vegetables as lunch choices.

"If children are given freedom of choice in selecting food for lunch, will their diets change for the worse?" asks Karen Cullen, DrPH, principal investigator for the two-year study funded by the Cancer Research Foundation of America. Dr. Cullen is an assistant professor in the Department of Behavioral Science at The University of Texas M. D. Anderson Cancer Center.



Research shows that children consume fewer than 2.5 servings of fruits and vegetables daily, giving them a score below 50% on the test of eating five servings per day.

As part of the study, 600 students at one middle school and four elementary schools in Texas City are filling out daily food diaries for a week, recording for the researchers what they choose to eat for lunch.

Recent studies show that the National School Lunch Program meals provide a significant amount of fruit and vegetables for third-grade children, says Dr. Cullen. But no research to date has examined what happens to children's diets when they move into middle and junior high schools, where snack bars offer competing foods, such as candy, chips, and soft drinks.

"We know that poor nutrition is a risk factor for colorectal, prostate, and possibly breast cancers," says Dr. Bernard Levin, M. D. Anderson's vice president for cancer prevention. "We ultimately want to reduce the number of cancers by seeing people begin in childhood to practice healthy nutrition habits that last a lifetime," he said.

Investigators also will examine whether children change their eating habits over the course of the school year, perhaps choosing nutritious foods after the novelty of having less healthy foods available has worn off.

"This research will provide important information to enable us to develop and implement middle school nutrition behavior change programs to influence children's choices of fruit, vegetables, and low-fat foods," says Dr. Ellen Gritz, chair of the Department of Behavioral Science.

Results of this study may also enable schools to offer more healthful lunch choices in a manner more acceptable to students, says Dr. Cullen. ●

FOR MORE INFORMATION, *contact Dr. Cullen at (713) 745-2847.*

M. D. Anderson Participates in Multinational Breast Cancer Prevention Trial of Tamoxifen and Raloxifene

by Alison Ruffin and Michael Courtney

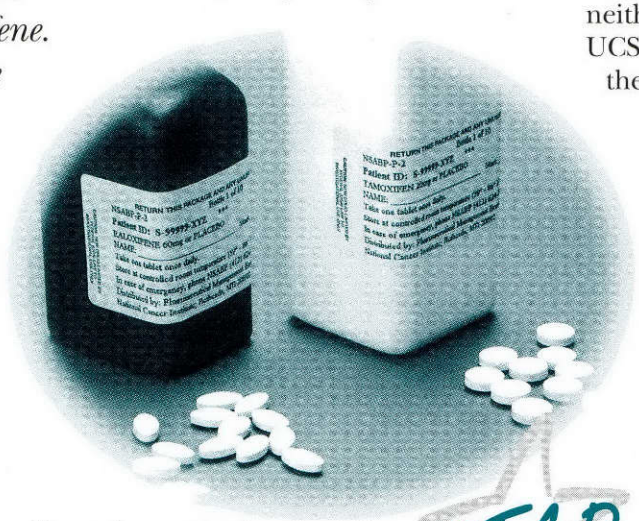
The University of Texas M. D. Anderson Cancer Center is recruiting women for a multinational study meant to further define tamoxifen's role in reducing breast cancer risk by comparing it with raloxifene. The study aims to determine which is more effective in reducing breast cancer risk and which has fewer side effects in postmenopausal women at high risk for breast cancer.

Tamoxifen, used as the control in this National Cancer Institute-supported trial, was found last year in a double-blind study of 13,000 pre- and postmenopausal women to halve the women's risk of breast cancer compared with that of controls. Researchers cut the trial short when tamoxifen's effectiveness became apparent.

The new trial, one of the largest breast cancer prevention studies ever, expects to enroll 22,000 women at more than 400 centers across the United States, Canada, and Puerto Rico. Called the STAR trial (Study of Tamoxifen And Raloxifene), the research is part of the National Surgical Adjuvant Breast and Bowel Project. M. D. Anderson plans to enroll 400 participants. Other study sites in Texas include ones in Lufkin and El Paso.

"We are excited about bringing the STAR trial to the greater Houston metropolitan area," said Dr. Therese Bevers, principal investigator at M. D. Anderson. "Women everywhere are at risk for breast cancer, and we are pleased that Houston-area women will have the chance to participate in this important study."

Side effects are a major safety interest because women who took tamoxifen in the earlier study benefited from having fewer fractures of the hip, wrist, and spine than did controls, but they also experienced increased risk of endometrial cancer, deep vein thrombosis, pulmonary embolism, and possibly stroke.



Researchers comparing the ability of tamoxifen and raloxifene to prevent breast cancer intend to enroll 22,000 postmenopausal women at increased risk.

"Tamoxifen is a medically proven intervention but is not perfect," said Dr. Bevers. "Women who are at increased risk of breast cancer need options for preventing this disease with a minimum of side effects, and STAR is a concerted effort to find one."

Information about the safety of raloxifene is limited, according to Dr. Bevers. Raloxifene was approved in December 1997 by the U.S. Food and Drug Administration (FDA) to prevent osteoporosis and has been in breast cancer clinical trials for about five years. In a three-year study conducted by the University of California, San Francisco (UCSF), raloxifene decreased the risk of breast cancer in postmenopausal women with osteoporosis by 76%. Tamoxifen, approved by the FDA as a breast cancer treatment for more than 20 years, has been in clinical trials for about 30 years.

Women taking raloxifene in studies of osteoporosis have had an increased chance of deep vein thrombosis or pulmonary embolism similar to the risk seen with tamoxifen. But neither in these studies nor in the UCSF study did raloxifene increase the risk of endometrial cancer.

Women who participate in STAR must be postmenopausal, at least age 35, and have an increased risk of breast cancer as determined by their age, family history of breast cancer, personal medical history, age at first menstrual period, and age at birth of their first child.

Once a woman chooses to participate, she will be randomly assigned to receive either 20 mg of tamoxifen or 60 mg of raloxifene daily for five years and will have regular follow-up examinations, including mammograms and gynecologic exams.

Tamoxifen's manufacturer, Zeneca Pharmaceuticals of Wilmington, Delaware, and the maker of raloxifene, Eli Lilly and Company of Indianapolis, Indiana, are providing drugs for the trial without charge. ●

FOR MORE INFORMATION *about STAR, visit M. D. Anderson's web site at http://www.mdanderson.org, the National Surgical Adjuvant Breast and Bowel Project web site at http://www.nsabp.pitt.edu, or the National Cancer Institute's clinical trials web site at http://cancertrials.nci.nih.gov. Additional information is also available by phone from M. D. Anderson's STAR line at (713) 792-8064 or from the Cancer Information Service at (800) 4-CANCER.*

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CLINICAL PRACTICE GUIDELINES
Quarterly Supplement to *OncoLog*
SUMMER 1999, VOL. 1, NO. 2

CLINICAL DISCUSSION: Prostate Cancer

About These Clinical Practice Guidelines

This guideline may assist in the diagnostic evaluation of patients with clinical symptoms or positive screening tests (if such testing exists). The clinician is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care.

M. D. Anderson Cancer Center's Practice Guidelines are continuously updated as new information becomes available and are being expanded to include the entire spectrum of cancer management. New guidelines for screening and diagnosis are currently under development. The most current version of all M. D. Anderson Practice Guidelines can be found on the World Wide Web at http://www.cancermanager.org.

Continuing Medical Education:
An expanded version of these materials with CME category 1 credit is available on the internet at **http://www.cancermanager.org**

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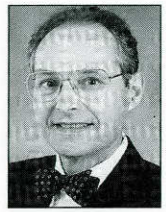

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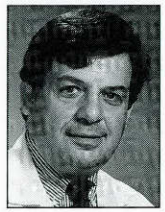

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About This Program

Scope of this Guideline

This guideline addresses clinical decisions in the screening and diagnosis, staging, and management of early, advanced, and recurrent prostate cancer.

Synopsis & Highlights

Screening and initial workup:
It will be noted that "life expectancy" features prominently in clinical decisions in this guideline. In this context, the term is an expression of multiple factors such as co-morbid conditions and the age and general health of the patient. These factors enter into the risk-benefit equation in any disease, but because most (but not all) prostate cancers tend to progress slowly and often asymptomatically, the physician and patient must consider whether the disease will actually shorten the patient's life expectancy. Approximately 75% of patients with localized disease will have local extension within 10 years, so younger patients who are in otherwise good health are more likely to be affected by the disease's natural progression and therefore are most likely to benefit from intervention.

These guidelines begin with the assumptions that

- an initial examination has indicated the need for further investigation based on digital rectal examination (DRE) and/or prostate-specific antigen (PSA) levels and that
- this examination was undertaken in a patient who is a candidate for treatment.

The initial diagnosis is confirmed by core biopsy (preferably ultrasound-guided), and the staging evaluation includes a complete blood count and measurement of serum alkaline phosphatase. A bone scan should be done for patients with T1 or T2 disease whose PSA is ≥ 15 ng/ml or whose Gleason score is ≥ 8. Patients with T3 or T4 disease or who are symptomatic should have a bone scan and CT or MRI scans of pelvic nodes. If disease-positive nodes are found, a fine-needle aspiration biopsy should be done for cytologic examination.

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Pull Out

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Treatment decisions are based on clinical stage, the probability of organ-confined disease, and the presence of symptoms and co-morbid factors influencing the patient's health and life expectancy.

Surgery and radiation therapy are first-line definitive treatment choices for localized (T1-T2) disease. Locally advanced and systemic disease are treated with androgen ablation alone or combined with radiotherapy. Cytotoxic chemotherapy is not a first-line modality in the treatment of prostate cancer, but it is important as a palliative measure in patients who have progressive disease and is specifically indicated in patients with small cell carcinoma of the prostate.

Observation alone is noted as an appropriate option at various stages in the guideline and is undertaken as a risk-benefit analysis based on individual variables, in which treatment options vs. the likelihood of disease progression and its probable impact upon both life expectancy and quality of life are considered. This analysis can pose one of medicine's more challenging clinical dilemmas, particularly when the data are inconclusive or insufficient. Patients with early-stage disease (T1A) are representative of this dilemma, because current information does not enable us to predict whose disease will become significant. A high PSA level or Gleason score in these patients indicates that definitive treatment should be recommended, while observation alone may be an acceptable option in others. Decisions about treatment should take into account that treatment of patients with a low volume of disease is associated with very favorable outcomes.

Surgery

The standard surgical treatment for prostate cancer is radical prostatectomy with pelvic lymph node dissection. According to Dr. Grossman, this surgery, widely and successfully used for the treatment of localized prostate cancer, is best employed for patients in whom the disease is clinically confined within the prostate and whose tumors are well to moderately differentiated. In general, patients with T3-T4 disease are not surgical candidates, although for patients with low-volume stage T3A disease and a Gleason score of < 7, surgery may be considered.

Improvements in surgical techniques have dramatically reduced the morbidity of radical prostatectomy: anesthesia time and blood loss are markedly lower, and convalescence is much shorter. On average, the hospital stay for this procedure is 3 days. Where possible, the Walsh nerve-sparing retropubic approach is used, preserving continence in > 90% of cases and potency in > 60%.

Radiotherapy

Radiotherapy is the other primary definitive modality of prostate cancer treatment. It is used in localized and advanced disease. Dr. Zagars relates that one of the most promising recent developments in the treatment of prostate cancer is the use of conformal 3-D treatment, wherein the beam is guided by CT scan, thus increasing accuracy in focus and so allowing delivery of a high dose to the target area with lower exposure to surrounding tissues. This radiologic technique, preferred at M. D. Anderson, is associated with a low incidence of serious complications and a high success rate: approximately 85%-90% in the most favorable categories (T1-T2, with PSA below 10 ng/ml). Substantial improvements in seed implant techniques have brought greater accuracy in radiation delivery and shortened convalescence for patients given brachytherapy. Brachytherapy is currently used only in very favorable cases (low PSA, disease confined to one half of the prostate, and a low Gleason score).

For patients with locally advanced disease (T3-T4), radiotherapy combined with androgen ablation achieves good results and is the recommended action for patients who are in good physical condition. Approximately 80% of patients given this treatment have sustained disease-free survival. This combination is also used for patients who experience a relapse after radical prostatectomy.

Androgen Ablation

Androgen ablation is the mainstay of therapy for patients who can no longer be treated with local modalities, specifically those patients with regionally advanced disease or detectable distant metastases. One question is whether to start androgen ablation early or to wait for the patient to become symptomatic. According to Dr. Logothetis, accumulating evidence suggests that early treatment is preferable.

A second question has been whether the addition of radiation therapy improves disease control. Current evidence shows that the combination therapy achieves prolonged disease-free and perhaps actual survival for patients with high-volume, localized disease. In addition, combination therapy may enhance disease control, although interpretation of the data that compared radiotherapy alone with the combined modalities but not androgen ablation alone is controversial.

According to Dr. Logothetis, androgen ablation is indicated as a single modality in most patients with obvious bony metastases at initial presentation. The combination of radiotherapy with androgen ablation should be viewed as standard for some patients with a high volume of localized prostate cancer and should also be considered for achieving control of locally advanced disease or localized cancer in patients who are symptomatic but are too infirm to justify aggressive local modalities.

Chemotherapy

In prostate cancer, cytotoxic chemotherapy is not a mainline modality, but when used palliatively in the setting of metastatic disease, it provides significant symptom relief and prolongs pain-free survival for some patients. Patients who have visceral or lytic metastases of the neuroendocrine or small-cell phenotype should be identified by means of biopsy results analysis, as they have been shown to benefit significantly from therapy with cisplatin and etoposide.

Surveillance: Patients under observation for potential treatment should have a digital rectal examination and measurement of PSA level every six months; those patients whose life expectancy is ≤ 10 years do not require specific intervention unless symptoms develop.

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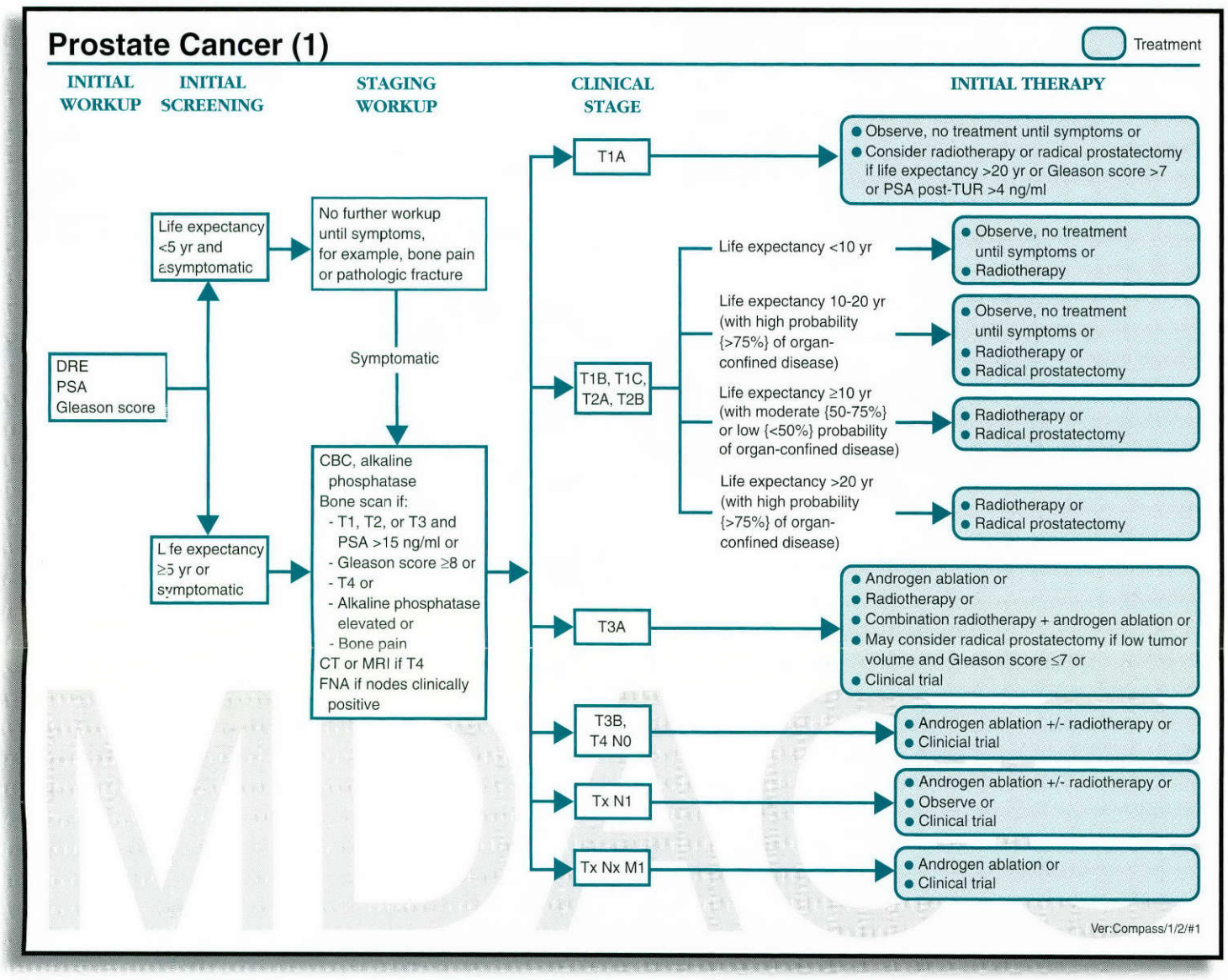

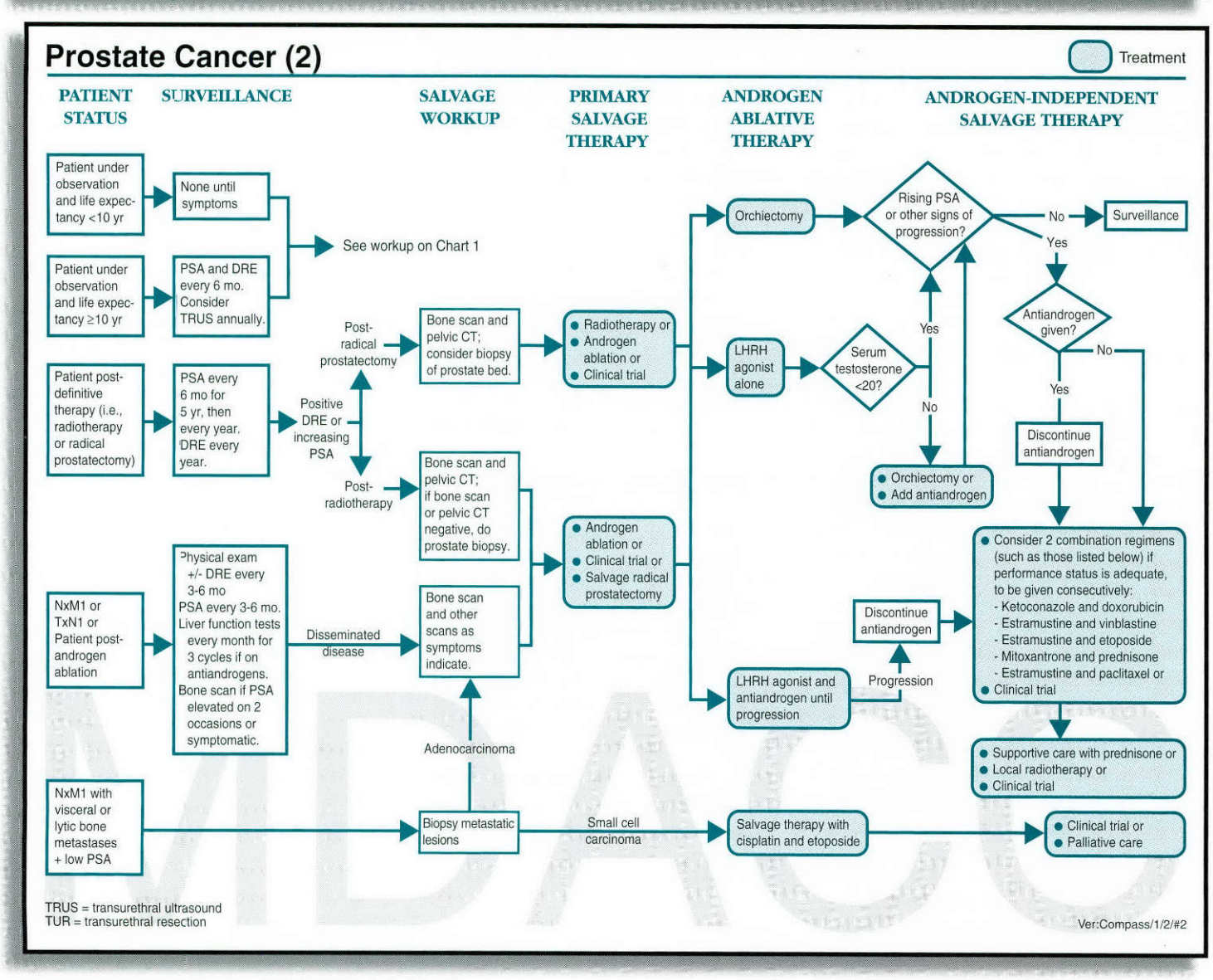

This practice guideline was developed in a collaborative effort between the physicians and nurses at The University of Texas M. D. Anderson Cancer Center and the National Comprehensive Cancer Network. The core development team at M. D. Anderson working on this practice guideline included Dr. H. Barton Grossman, Dr. Christopher J. Logothetis, and Dr. Gunar K. Zagars.

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Patients who have undergone definitive therapy should have serum PSA levels measured every 6 months for 5 years and then yearly thereafter. Patients who have had radical prostatectomy should have no detectable PSA levels. Postradiotherapy patients will continue to have detectable PSA; the level should fall to a low point, after which two consecutive increases indicate possible recurrence.

Surveillance measures for patients with advanced or metastatic disease include: physical exam (including DRE and measurement of PSA level) every 3 months; if the patient is taking antiandrogens, liver studies are indicated monthly for 3 months; a bone scan should be done if the patient is symptomatic or has elevated PSA levels on two occasions.

Salvage: Those patients whose disease recurs, as evidenced by rising PSA levels or abnormal DRE findings, should have a staging workup including biopsy, bone scan, and pelvic CT to evaluate extent of disease.

Those whose recurrence is locally advanced continue to pose a clinical challenge, as management in this setting is not firmly established. For patients whose initial treatment was radical prostatectomy, current treatment recommendations include radiotherapy for those whose staging workup indicates that disease is confined to the pelvis and androgen ablation for those whose disease is metastatic.

For patients whose initial treatment was radiotherapy, it is appropriate to take a biopsy sample from the prostate for histologic and prognostic information. The probable intervention in this scenario and in that of disseminated disease is androgen ablation. While the feasibility of surgical removal of the prostate after radiation therapy has been established, there is limited evidence that it alters the course of the illness. According to Dr. Logothetis, the only absolute indication for surgery in patients with localized disease after hormone or radiation therapy failure is painful or debilitating symptoms.

Management of metastatic disease in those who have exhausted standard therapies includes antiandrogen withdrawal and palliation of symptoms using one or more of the following therapies: glucocorticoids and local radiation to metastatic sites, second-line hormonal therapies, and cytotoxic chemotherapy agents.

Q&A: Authors' Perspectives...

Surgery or Radiotherapy?

In some cases, there are clear clinical reasons to choose one or the other. For example, radiotherapy is chosen over surgery in symptomatic patients who have limited life expectancy because of its overall lower morbidity. But where these two are indicated in the guideline as equivalent options, good long-term data show similar survival rates, so "patients really do have a true choice," says Dr. Zagars. He believes that it is important for patients to have access to both a surgeon and a radiation oncologist to discuss this choice, in consideration of patient preferences for undergoing the respective procedures, quality of life issues, and complication possibilities.

Often, the decision is based on the patient's personal preference. Many come to the situation with a decided bias or fear, often based on the experience of a friend or relative. There are patients who, faced with cancer, voice a distinct desire to have the disease "cut out" in order to feel truly rid of it and others who express a preference to "remain intact."

Screening Recommendations?

Screening to detect early, treatable prostate cancers is recommended. According to all of our experts, it is important to help patients understand that current treatment approaches for localized prostate cancer are very favorable, based on survival data. Patients with early-stage disease have very good prognoses and a choice of treatments with low complication rates, suggesting that detecting early-stage disease is important.

According to Dr. Grossman, physicians at M. D. Anderson endorse the approach of annual screening (DRE and serum PSA) for men between the ages of 50 and 70. Where there is a family history of prostate cancer, screening should begin at age 40. Where there are no symptoms and no other conditions limiting life expectancy, screening is unnecessary.

What's New?

All of our experts agree that it is appropriate to investigate clinical trials for patients with any stage disease. At M. D. Anderson, trials are ongoing in various modalities for all disease stages, and there are several interesting new studies. Dr. Christopher Wood is directing a study in which autologous nerve grafts are employed as a strategy against impotence, and Dr. Curtis Pettaway is investigating the use of hormonal ablation in patients who are identified to be at high risk for disease recurrence after radical prostatectomy. Another of Dr. Pettaway's studies is investigating potential genetic links to prostate cancer in African Americans. More information about clinical trials and current protocols available at M. D. Anderson can be found at http://www.mdanderson.org/research. ●

Compass

Quarterly Supplement to *OncoLog*

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References & Suggested Reading

Millikan R, Logothetis C: Update of the NCCN Guidelines for Treatment of Prostate Cancer. NCCN Proceedings, November 1997. *Oncology* 11(11A):180-193, 1997

Pollack A, Zagars GK: External beam radiotherapy for stage T1/T2 prostate cancer: How does it stack up? *Urology* 51:258-264, 1998

Zagars GK, Pollack A, von Eschenbach AC: Management of unfavorable locoregional prostate carcinoma with radiation and androgen ablation. *Cancer* 80:764-775, 1997

HOUSE•CALL

Reduce Cancer Risk With Regular Cancer Screening

You've heard it many times: early detection of cancer saves lives. By catching the disease at an early stage, treatment is more likely to be successful. But while most of us are aware of the value of regular cancer screening examinations, many of us are confused about how often we should get these checkups.

Cancer-related Checkup

In addition to age- and sex-specific cancer screening examinations done for cancers of the breast, cervix, endometrium, prostate, colon, and rectum, the American Cancer Society recommends that adults between the ages of 20 and 40 years have a cancer-related checkup every three years. Once the person reaches 40, the recommendation is for a yearly checkup. Such an examination should include health counseling and, depending on the person's age and sex, might include examinations for cancers of the thyroid, skin, oral cavity, lymph nodes, testes, and ovaries.

Tests for Women

M. D. Anderson Cancer Center encourages women between the ages of 20 and 39 years to perform breast self-examinations each month and to undergo a breast examination by a health professional every one to three years. For women 40 years and older, experts add an annual mammogram and make the professional breast examination an annual requirement. The examination performed in the clinic should occur near the time of the mammogram. Throughout life, women are encouraged to perform breast self-examinations monthly.

M. D. Anderson also recommends that all women have an annual pap smear to check for cervical cancer. Women who are at high risk for cancer of the uterus should, according to the American Cancer Society, have a sample of their endometrial tissue examined when menopause starts.

Tests for Men

Men age 50 to 70 years should have a prostate-specific antigen blood test and a digital rectal examination by a health professional annually, according to M. D. Anderson Cancer Center recommendations. To detect testicular cancer early, men should perform a monthly testicular self-examination to check for lumps or other changes in their testicles.

Colon and Rectum Examinations

M. D. Anderson recommends that men and women who are 50 years or older should have one of the following combinations of examinations:

- A yearly fecal occult blood test (a sample of stool is examined for blood) and a flexible sigmoidoscopy (an examination of the rectum and lower colon with a slender, lighted instrument) every five years; *or*
- A colonoscopy (an examination of the rectum and entire colon with a lighted instrument) every 10 years; *or*
- A double-contrast barium enema every 5 to 10 years.

A digital rectal examination should be performed at the same time as the sigmoidoscopy, colonoscopy, or double-contrast barium enema. People who are at higher-than-average risk for colorectal cancer should consult their doctor about a recommended testing schedule.

Skin and Oral Cavity Examinations

Skin cancer is the most common cancer, but most cases are highly curable. Melanoma, skin cancer's most serious form, is occurring more frequently: its incidence rate has more than doubled in the last two decades. Experts recommend that adults practice self-examination regularly, and some say yearly examinations by a physician are necessary if risk is higher than average.

Dentists and physicians should check the oral cavity at regular checkups for changes in the lining of the oral cavity.

These various screening examinations can detect cancers of the breast, cervix, colon, rectum, prostate, testes, oral cavity, and skin at the earliest and most treatable stages. These cancers, according to the American Cancer Society, account for about half of all new cancer cases. The five-year relative survival rate for patients with these cancers is about 81%. (A relative survival rate is the survival rate of a group of patients with cancers compared with the rate for a similar group of persons in the general population.) If all Americans participated in regular cancer screenings, the ACS predicts, the rate could increase to more than 95%.

That's a very good reason to make an appointment right now for screening. ●

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

(800) 392-1611 *within the United States, or*

(713) 792-6161 *outside the United States.*

June 1999

Nerve Grafting Attempts to Restore Erectile Function After Prostatectomy

by Dawn Chalaire

Despite advances in surgical techniques and postoperative therapies, the fact remains that for many men with localized prostate cancer the price of a potentially curative radical prostatectomy is permanent sexual dysfunction.

"Sexual functioning is an important part of a man's life," said Christopher G. Wood, M.D., assistant professor of urology and cancer biology at The University of Texas M. D. Anderson Cancer Center. "To suggest to men that they need to give that up in the name of cancer control forces them to make a very difficult and heartbreaking decision. With the sural nerve graft, we're offering an opportunity to maximize cancer control and improve their quality of life."

Dr. Wood is the principal investigator in a phase I study to test the safety and efficacy of using autologous sural nerve grafts to preserve erectile function following radical retropubic prostatectomy. Although this particular study is being conducted exclusively at M. D. Anderson, Baylor College of Medicine Assistant Professor of Urology Edward D. Kim is one of the study's coinvestigators. Dr. Kim, who has a special interest in erectile dysfunction and infertility, and colleagues at Baylor are also performing the procedure.

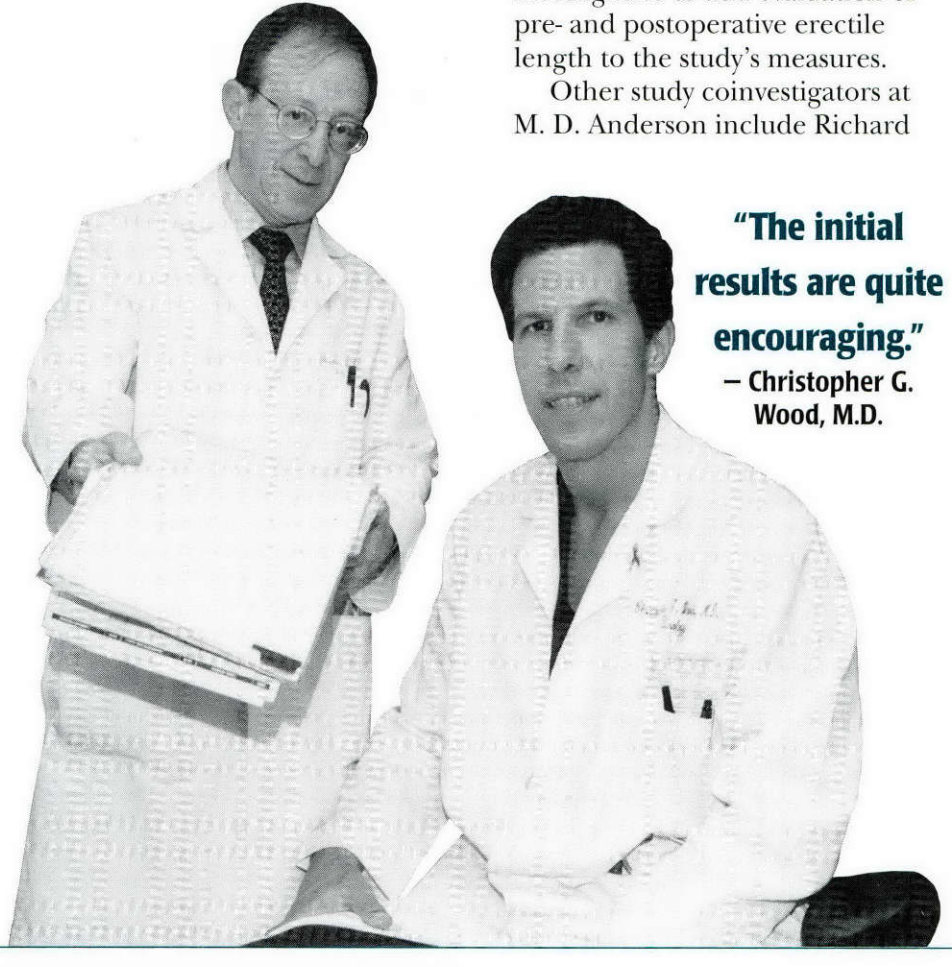
While there may be other causes of erectile dysfunction following radical prostatectomy, removal of the cavernous nerves, located on either side of the prostate gland, is the most common cause of postoperative impotence. The rate of impotence following the removal of both cavernous nerves is essentially 100%.

Depending on the stage, grade, and location of the tumor, one or both of the cavernous nerves are sometimes left intact during prostatectomy. Between 40% and 60% of patients who undergo unilateral nerve-sparing surgery retain the ability to have spontaneous erections. Some evidence suggests, though, that leaving the cavernous nerves intact increases a patient's risk of both positive tumor margins and recurrence. The nerve bundles are a common site of prostate cancer and may even provide a pathway for the cancer to spread outside the prostate, according to Dr. Wood.

"By removing both nerves, you definitely are going to improve cancer control at the expense of impotence after surgery," Dr. Wood said. "So the advantage of sural nerve grafting is to potentially address that problem of impotence while still optimizing cancer control."

To be eligible, patients must be candidates for radical prostatectomy but have clinically localized disease that requires bilateral removal of the cavernous nerves. They must also have normal erectile function before surgery. Dr. Kim conducts pre- and postoperative evaluations. Preoperative evaluation includes a physical examination, completion of a questionnaire about the patient's sexual history, and a determination of baseline erectile functioning. The fairly common patient complaint that penile length decreases following radical prostatectomy prompted investigators to add evaluation of pre- and postoperative erectile length to the study's measures.

Other study coinvestigators at M. D. Anderson include Richard



"The initial results are quite encouraging."
– Christopher G. Wood, M.D.

Dr. Stephen Kroll *(standing), professor of plastic surgery, and* **Dr. Christopher Wood**, *assistant professor of urology and cancer biology, are collaborators who are working to restore erectile function in men after prostatectomy.*

Babaian, M.D., professor of urology, and Drs. Stephen Kroll and David Chang, professors of plastic surgery. One plastic surgeon and one urologist typically work together during the three- to four-hour combined prostatectomy and nerve-grafting procedure.

The plastic surgeon harvests a section of the sural nerve through an incision in the back of the lower right leg. Following the removal of the prostate and surrounding nerve bundles by the urologist, the plastic surgeon cuts the sural nerve in half and grafts it onto the preserved stumps of each cavernous nerve. Surgeons use loupes for magnification during suturing and must take care to avoid tension on the nerve grafts. The only permanent side effect of the sural nerve harvest is numbness in an area about the size of a half dollar on the outside of the ankle.

Four to six weeks after surgery, Dr. Kim initiates erectile dysfunction therapy. Research indicates that beginning therapy as soon as possible after surgery improves a patient's chances of being able to have spontaneous erections. Therapy options include sildenafil (Viagra) taken orally; penile injections of papaverine, prostaglandin E1, and phenotolamine (Trimix); a vacuum erection device; and use of the medicated urethral system for erection (MUSE). MUSE includes the insertion of a pellet of prostaglandin into the urethra through the tip of the penis. Patients return at 3, 6, 12, and 24 months after surgery for assessment of erectile function.

So far, 10 patients have undergone prostatectomy with bilateral nerve grafting at M. D. Anderson, where the enrollment target is 30 patients. None of those patients have completed the 14 months of follow-up investigators think is necessary to determine if the procedure has been successful, but some patients have reported by telephone that they are having erections. At Baylor, Dr. Kim's initial results indicate a success rate of about 60% among the 15 patients who have undergone the surgery and passed the 14-month postoperative evaluation point.

"One of the things that should be emphasized is that this is a research study. While the initial results are quite good, I do believe that it's going to be very much surgeon dependent, on the part of both the plastic surgeon and the urologist involved in the case," Dr. Wood said.

The concept of using autologous nerve grafting to maintain erectile function is not new. In a 1991 laboratory study, the genitofemoral nerve was used to replace the cavernous nerves following radical retropubic prostatectomy in rats, resulting in a significant return of erectile function. But a subsequent attempt to use genitofemoral nerve grafting in humans was not successful, the procedure became controversial, and many urologists abandoned the idea.

"This is not something that everyone has signed on to," Dr. Wood said. "Actually, most people have not, but our approach to it has been: it's an unknown, the initial results are quite encouraging, and it's something we should evaluate."

One of the arguments against the grafting centers around the differences in impulse conduction believed to occur when the sural nerve, which is myelinated, is used to replace the unmyelinated cavernous nerve. Dr. Wood points out that grafted nerves eventually become unmyelinated and serve as a scaffold, rather than a bridge, for nerve fibers at one end to grow back to the other side.

According to Dr. Kroll, it is not that nerve grafting is inappropriate, it is that grafting is complex. He said the difficulty involved with attempting a nerve-grafting procedure so deep within the pelvic cavity might explain why the technique has not been successful before, even though the concept behind it is sound.

"Nerve grafting is a well-accepted procedure that has been done for many years with a high rate of success," he said. "It's not a new idea to repair nerves." He said the procedure is "just a logical extension of traditional plastic surgery to a new area." ●

FOR MORE INFORMATION, *contact Dr. Kroll at (713) 794-1247 or Dr. Wood at (713) 792-3250.*

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Staff Publications in June

Below is a partial list of staff publications appearing this month.

Aboul-Nasr R et al. Comparison of touch imprints with aspirate smears for evaluating bone marrow specimens. *Am J Clin Pathol* 1999;111(6):753–8.

Allgayer H et al. Transcriptional induction of the urokinase receptor gene by a constitutively active Src. Requirement of an upstream motif (-152/-135) bound with Sp1. *J Biol Chem* 1999;274(26):18428–37.

Anderlini P et al. Allogeneic blood progenitor cell collection in normal donors after mobilization with filgrastim: the M.D. Anderson Cancer Center experience. *Transfusion* 1999;39(6):555–60.

Beaupre DM et al. Autocrine interleukin-1-beta production in leukemia: evidence for the involvement of mutated RAS. *Cancer Res* 1999;59(12):2971–80.

Davies MA et al. Regulation of Akt/PKB activity, cellular growth, and apoptosis in prostate carcinoma cells by MMAC/PTEN. *Cancer Res* 1999;59(11):2551–6.

Esmaeli-Gutstein B, Winkelman JZ. Uveitis associated with varicella virus vaccine. *Am J Ophthalmol* 1999;127(6):733–4.

Kardon R et al. Bacterial conjunctivitis in Muc1 null mice. *Invest Ophthalmol Vis Sci* 1999;40(7):1328–35.

Levy DA et al. Transrectal ultrasound-guided intraprostatic injection of absolute ethanol with and without carmustine: a feasibility study in the canine model. *Urology* 1999;53(6):1245–51.

Mitchell DL et.al. Effects of chronic low-dose ultraviolet B radiation on DNA damage and repair in mouse skin. *Cancer Res* 1999;59(12):2875–84.

Molldrem JJ et al. A PR1-human leukocyte antigen-A2 tetramer can be used to isolate low-frequency cytotoxic T lymphocytes from healthy donors that selectively lyse chronic myelogenous leukemia. *Cancer Res* 1999;59(11):2675–81.

Mukhopadhyay A et al. Identification and characterization of a novel cytokine, THANK, a TNF homologue that activates apoptosis, nuclear factor-kappa B, and c-Jun NH2-terminal kinase. *J Biol Chem* 1999;274(23):15978–81.

Ng CS et al. Metastases to the pancreas from renal cell carcinoma: findings on three-phase contrast-enhanced helical CT. *AJR* 1999;172(6):1555–9.

O'Brien S et al. Sequential homoharringtonine and interferon-alpha in the treatment of early chronic phase chronic myelogenous leukemia. *Blood* 1999;93(12):4149–53.

Ravandi-Kashani F et. al. Thrombotic microangiopathy associated with interferon therapy for patients with chronic myelogenous leukemia: coincidence or true side effect? *Cancer* 1999;85(12):2583–8.

Rodriguez J et al. ASHAP: a regimen for cytoreduction of refractory or recurrent Hodgkin's disease. *Blood* 1999;93(11):3632–6.

Shin HJ, Sneige N, Staerkel GA. Utility of punch biopsy for lesions that are hard to aspirate by conventional fine-needle aspiration. *Cancer* 1999;87(3):149–54.

Siddique I et al. Recurrent bleeding from a duodenal plasmacytoma treated successfully with embolization of the gastroduodenal artery. *Am J Gastroenterol* 1999;94(6):1691–2.

Sturgis CD et al. Image analysis of papillary thyroid carcinoma fine-needle aspirates: significant association between aneuploidy and death from disease. *Cancer* 1999;87(3):155–60.

Sun SY et al. Implication of *p53* in growth arrest and apoptosis induced by the synthetic retinoid CD437 in human lung cancer cells. *Cancer Res* 1999;59(12):2829–33.

Thomas JW, Staerkel GA, Whitman GJ. Pulmonary hamartoma. *AJR* 1999;172(6):1643.

Vadlamudi R et al. Transcriptional up-regulation of paxillin expression by heregulin in human breast cancer cells. *Cancer Res* 1999;59(12):2843–6.

Weinkauff R et al. Use of peripheral blood blasts vs. bone marrow blasts for diagnosis of acute leukemia. *Am J Clin Pathol* 1999;111(6):733–40. ●

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