

DMS ranks 12th among the 126 U.S. medical schools on the basis of research funding per basic science faculty member, according to the Association of American Medical Colleges.

Bad things come in small packages, too

Tumors of the colon and rectum are the second most common cause of U.S. cancer deaths for men and women combined. During 2005, there were an estimated 145,000 new cases and nearly 55,000 deaths. It has long been known that colorectal cancer can develop from polyps—small growths on the lining of the colon or rectum. But doctors have been less certain just how big a polyp needs to be before it is worrisome. A new study by Dartmouth gastroenterologist Lynn Butterly, M.D.—published in *Clinical Gastroenterology and Hepatology*—has shed light on that question.

Orifice: Polyps can be seen with a colonoscope, a device that's inserted into the colorectal orifice, or with a shorter version called a sigmoidoscope. These instruments also allow doctors to painlessly remove any growths that are found.

One type of polyp, an adenoma, is usually benign at the time of its removal. But over five to 10 years, some adenomatous polyps become cancerous. Colonoscopy is therefore a little different than, for example, mammography, which detects already existing cancers. In colonoscopy, the goal is to find and remove polyps *before* they can develop into cancers. Indeed, there is

strong evidence that removing polyps reduces the incidence and mortality rate of colorectal cancer. Cancer risk has been shown to be related to polyp size, with risk clearly increasing if polyps are larger than 10mm—about half an inch. But what about those under 10mm?

Small polyps are very common. They are found in as many as a fourth to a third of all asymptomatic patients and are often regarded as clinically insignificant. The question of when they become worrisome has assumed even greater importance since the advent of so-called “virtual colonoscopy”—CT colonography (CTC). Butterly, the director of colorectal cancer screening at DHMC, explains that “at present CTC is less able to detect small polyps than colonoscopy. Moreover, CTC does not allow for removal of polyps [during screening]. Therefore, if polyps are seen on CTC, the patient will probably need to have a second procedure—a colonoscopy—to remove them.” So recognizing at what point between 5mm and 10mm adenomatous polyps should be removed is important.

Began: Butterly's study began in 1989 and included 3,291 consecutive colonoscopies that she herself performed. All detected polyps were removed for pathologic examination. About a third of the procedures revealed adenomatous polyps of 10mm or less—a total of almost 2,000 adenomas. Of those, 921 were between 5mm and 10mm; 110 of these showed abnormal tissue, with some already deemed cancerous. The finding—that at least 10% of small adenomas may contain significant pathologic changes, including nearly 1% with clear cancer—provides strong evidence that they should be identified and removed along with larger polyps.

In other words, small packages may contain bad things and so ought to be opened.

ROGER P. SMITH, PH.D.



MARK WASHBURN

Butterly studied 3,291 consecutive colonoscopies.

Call me sometime

Improving cancer-screening rates among minority and low-income women may be just a phone call away. In a study led by DMS's Allen Dietrich, M.D., researchers found that minority and low-income women were more likely to get screened for breast cancer, cervical cancer, and colorectal cancer if they received a phone call encouraging them to do so. Published in the *Annals of Internal Medicine*, the study showed that phone calls boosted screening rates 12 percentage points for mammography, 7 points for Pap tests, and 13 points for colorectal screening.



Compound interest

A compound developed by DMS pharmacologists proved extremely effective, even in small doses, at preventing liver cancer in rats during a recent study conducted at Johns Hopkins. The compound—CDDO-Im—caused an 85% reduction in precancerous lesions at the lowest dose and a 99% reduction at the highest dose.

Dartmouth researcher Michael Sporn, M.D., who has been leading the development of CDDO-Im and related compounds for over a decade, believes CDDO-Im may also be useful in inflammatory bowel disease, hepatitis, and the prevention of liver metastases from colon cancer.





A DMS research team has received a federal grant of almost \$400,000 to develop a simple factual box, like the nutrition information panel on packaged foods, for prescription drugs.

Karagas: Curious about cancer culprit

In 2002, Dartmouth epidemiologist Margaret Karagas, Ph.D., sounded the alarm about the dangers of tanning booths. Now she may have identified another risk factor for skin cancer—human papillomavirus (HPV).

In a study published in the March 15 *Journal of the National Cancer Institute*, Karagas reported that beta HPVs may be a risk factor in developing squamous cell carcinoma—one of the most common kinds of skin cancer. The beta subtype of HPV is linked to skin cancer, while the alpha subtype is associated with cervical cancer.

Long before scientists knew that HPVs cause cervical cancer, they'd identified a link between the virus and skin cancer in people with a rare, inherited disorder called epidermodysplasia verruciformis.

Skin: "Most of their skin tumors contain HPV DNA," Karagas says. But it was unknown "whether HPV is causal or just present because these patients also have diminished immunity." It was also unknown whether there is a link between HPV and skin cancer in the general population. Karagas was determined to find out.



ION GIBERT FOX

Epidemiologist Karagas has confirmed an association between a common virus and skin cancer.

So she assembled a team that included DHMC dermatologist Steven Spencer, M.D., and others; secured funding from the National Institutes of Health; and collaborated with the New Hampshire Society of Dermatology on a population-based study of basal cell and squamous cell carcinomas. She also took advantage of a new technology she had learned about at an international meeting while she was a visiting professor in Italy.

Lab: Her team collected plasma samples from 252 patients with squamous cell carcinoma, 525 patients with basal cell carcinoma, and 461 control subjects. The samples were frozen and sent to a lab in Germany—one she'd heard about at the meeting. There, the samples were tested for beta HPV antibodies. The German scientists had developed a test—based on fluorescent bead technology—that can detect multiple viral antibodies simultaneously. "We were able to test for 16 different HPV types," says Karagas. "And in a week we'd have the data."

The results were statistically significant. HPV antibodies were present more often in patients with squamous cell cancer (though not those with basal cell cancer) than in the control group. Even after taking into account other risk factors—such as smoking, medical history, sun exposure, and sun sensitivity—the team still found an association between beta-type HPV and squamous cell carcinoma.

Karagas stresses that her study shows only an association between HPV and skin cancer. Further research is needed to see if HPV actually *causes* skin cancer. "The next step for us is to look at the tumors themselves" to determine whether they contain HPV, she says. "If it's true that the virus is related to skin cancer . . . it may open up a whole new way of us treating skin cancers and preventing them." LAURA STEPHENSON CARTER

Risk is revised

The risk after an initial melanoma diagnosis of developing a second melanoma—the deadliest form of skin cancer—may be higher than had been previously thought, according to a recent Dartmouth study. Of 354 individuals diagnosed with melanoma, 27 (8%) had a recurrence within two years, and 20 of the 27 had a recurrence within one year. The results "underscore the importance of close surveillance of patients with melanoma," wrote researcher Linda Titus-Ernstoff, Ph.D., and her coauthors in the *Archives of Dermatology*.

Stick 'em up

A typical dose of seasonal flu vaccine could protect five people instead of just one, according to preliminary results of a DHMC study. Kathryn Kirkland, M.D., associate director of infection control, presented the early findings at a meeting of the Society of Healthcare Epidemiology of America. While stretching the supply of seasonal influenza vaccine appears safe and effective, a similar approach probably could not be used in case of a bird-flu vaccine shortage, Kirkland cautioned. To stretch the seasonal supply, the vaccine was injected into skin rather than muscle. A bird-flu vaccine, if and when one is developed, would probably require injection into muscle.



DMS doctoral student David Radley quantified off-label prescription drug use in an *Archives of Internal Medicine* paper that was deemed a "must read" in the May 19 *Medical Economics*.

Women versus men in matters of the heart

A popular treatment for cardiovascular disease is as safe and effective for women as it is for men, found a recent DMS study. Led by cardiologist Craig Thompson, M.D., the study did reveal many differences between male and female patients, but their overall outcomes were similar.

The treatment in question—percutaneous coronary intervention (PCI) with drug-eluting stents—has become the procedure of choice for patients whose only alternative several years ago would have been coronary artery bypass surgery. PCIs are favored over bypass surgery because they're noninvasive and require a much shorter recovery time.

PCI involves feeding a catheter—a tiny flexible tube—through an artery in the abdomen, leg, or arm into a blocked blood vessel on the heart. The tube acts as a tunnel through which cardiologists can insert tools to clean and widen the diseased vessel. Then a mesh tube called a stent is inserted to keep the vessel walls open so blood can flow freely.

Drug-eluting stents (DESs) are coated with a time-release medicine that prevents re-blockage of the vessel. Since coming on the market in 2003, DESs have "completely changed the landscape of in-

terventional cardiology," says Thompson. He and several other cardiologists at DHMC have been tracking how PCI patients have fared since DESs were introduced. Their most recent study, on gender-based differences, was published in December 2005 in *Catheterization and Cardiovascular Interventions*.

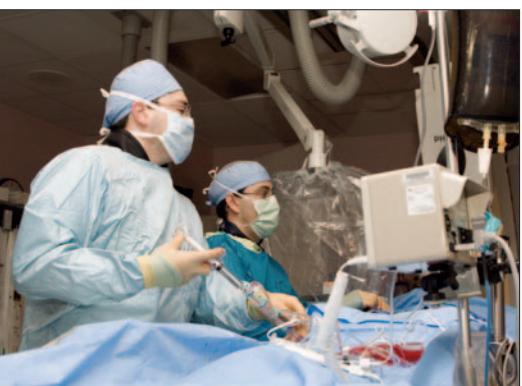
In the gender-based study, Thompson found that "women tend to present with coronary disease later in life than men do, and at that point may have other medical illnesses that track along with it." Among the study's patients, women were more likely to have heart failure and high blood pressure and to be older, obese, and diabetic, whereas men had higher rates of smoking and more obstructed vessels. After Thompson adjusted the results for these differences, the similarities in outcomes for men and women were clear.

The study also found that women on either end of the body mass spectrum—very small or very large—are more susceptible to vascular and renal complications than average-sized women. The complications included swelling or bleeding at the PCI access site and some degree of kidney dysfunction. The correlation between body mass, age, and complications was so strong that Thompson says his team "could predict vascular complications" based on those factors alone.

What do these findings mean for the future of PCI? Thompson says his team plans to "explore different ways to approach catheterization in women," such as performing the procedure from the wrist rather than the leg, using larger or smaller stents, and trying new blood-thinning agents that wear off very quickly.

But "all in all," Thompson concludes, "our ability to get the stents in place [and] to have a technically successful procedure . . . was pretty comparable between men and women."

LAURA EVANICH



CHRIS MILLMAN

Cardiologist Thompson, left, found that overall, women fare as well as men after having a PCI.

Is bypass better?

Heart-bypass surgery trumps catheter-based procedures in patients over 80, concluded a recent seven-center study. The DHMC-based Northern New England Cardiovascular Disease Study Group compared the survival rates of nearly 1,700 patients aged 80 to 89 who underwent either a catheter-based coronary procedure—called percutaneous coronary intervention (PCI)—or heart-bypass surgery. Short-term survival was better among the PCI patients, but after six months heart-bypass surgery took the lead. DHMC surgeon Lawrence Dacey, M.D., was the lead investigator.



Utility notice

Physicians order the test 100,000 times a year, and with good cause it seems. Esophageal manometry (EM)—in which a tube is inserted into the esophagus to measure its muscle action—provides new information for diagnosis 86% to 100% of the time, according to a survey by DHMC gastroenterologist Brian Lacy, M.D., Ph.D. Presenting his findings at an American College of Gastroenterology meeting, Lacy said that information gleaned from EM led to a change in patient management in up to 60% of the cases in his study. That's not bad for a test whose clinical utility had never before been formally evaluated. ■

