

Dartmouth surgeon Richard Barth identified benefits beyond survival when breast cancers are discovered earlier.

Study finds new benefits from mammography

If the devastating Southeast Asian tsunami hadn't taken over the headlines in late December and early January, the results of a Dartmouth study of mammography might have gotten more press.

The investigation, led by cancer surgeon Richard Barth, M.D., and published in the January issue of the *American Journal of Roentgenology*, confirmed that mammograms are better than physical examinations at detecting breast cancers early and that tumors found by mammography are smaller and less likely to have metastasized. That finding is not surprising, since the benefits of regular mammography—especially for women aged 50 to 69—have long been known. But the study also determined that these smaller cancers are usually treated less aggressively.

Link: “We were one of the first studies to actually link mammography to breast-cancer treatment,” says one of Barth’s coauthors, Patricia Carney, Ph.D. The finding may still attract attention in the medical community, but Barth had hoped it would get coverage in the lay press as well—and it likely would have if it hadn’t been for the timing.

Aggressive surgical treatment of larger tumors can mean breast removal as opposed to more conservative surgery. Chemotherapy is also part of aggressive management of ad-

vanced breast cancers, except in very elderly patients or those with other serious diseases. Even in young, otherwise healthy patients, chemotherapy’s side effects—which occur in a high proportion of patients—include hair loss, nausea and vomiting, increased susceptibility to infections, and memory deficits.

Less toxic: “The take-home message is that there can be benefits other than just a survival benefit from having your breast cancer detected early by using mammography,” says Barth. “These benefits are that if you’re unlucky enough to get the breast cancer, you can have it treated with less toxic therapy. This applies to women across the entire spectrum . . . women of any age who are going to develop breast cancer.”

Barth and his colleagues did a retrospective study of 992 patients with invasive breast cancer who were treated at DHMC over an 11-year period. (In a retrospective study, researchers examine patients’ medical records, looking at what actually happened.)

The breast cancer was detected by physical examination in 532 of the women and by mammography in 460. The tumors detected by mammography were half the size of those found by physical examination (1.5 centimeters, compared to 2.9 centimeters) and were less likely to have metastasized to the

lymph nodes. In addition, patients in the mammography group were much more likely to have undergone breast-conserving surgery, such as lumpectomy, and less likely to have had chemotherapy.

Benefits: In addition, the study identified benefits to mammography for both younger and older women. Experts have long debated whether mammography improves survival for women under 50 or over 70, but Barth’s study showed that regular screenings help women in these age categories, too. For women who were 40 to 49 years old, their chance of receiving chemotherapy more than doubled if the tumor was discovered by physical examination instead of by mammography. And women 70 and older were five times as likely to undergo a mastectomy and four times as likely to receive chemotherapy if their tumor was discovered by physical exam.

“To me, the nice thing about this paper is that it shows that breast cancers detected by mammography are also less likely to result in mastectomy [and] less likely to result in toxic treatment,” says Carney.

It was Barth’s years of caring for women who discovered their cancers too late to take advantage of less aggressive treatments that led him to do this study. “When you see a bunch of people with advanced breast cancer, and you have to take care of them day in and day out, all week long, it’s so obvious that detecting these cancers earlier is better,” he says. “The really frustrating thing is to get people who haven’t been screened and come in with really big cancers. . . . They all have to get really aggressive treatment in an attempt to save them.”

Though experts debate optimal screening rates generally, there’s no question in Barth’s mind how he’d advise women about breast cancer screenings: “Start annual mammography when you are 40, and continue for the rest of your life.” But, he adds, physical examination—by a caregiver or self-administered—shouldn’t be stopped. It does no harm and can detect tumors, albeit not as early as mammography. **ROGER P. SMITH, PH.D.**



Even doctors can misinterpret Latin abbreviations in medical records, research shows. DHMC is part of a national effort to use unambiguous terms like “daily” instead of “Q.D.” (*quaque die*).

Female reproductive tract plays defense

The immune system of the female reproductive tract has a big job to fulfill,” says Dartmouth physiologist Patricia Pioli, Ph.D. That “big job” includes fending off a multitude of invading microorganisms but also knowing which foreign cells *not* to attack, such as sperm and the cells of a developing fetus. So how does the system do that?

Attack: This is one of the questions that Pioli and her colleagues are trying to answer. They study the innate immune response of the female reproductive tract. Innate immunity is the body’s initial response to an invading pathogen. This front-line defense attacks pathogens nonspecifically, without factoring in previous exposure, as acquired immunity does.

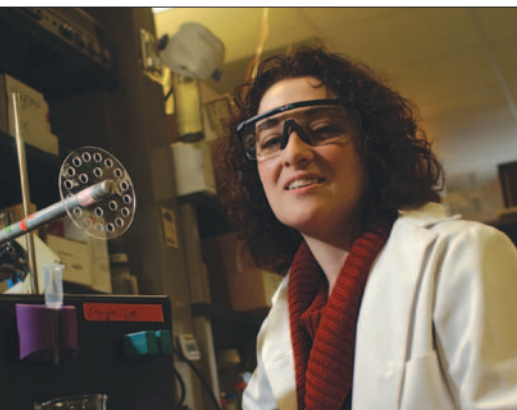
Recent studies have shown that toll-like receptors (TLRs) are important in initiating innate immune responses in several types of human cells. TLRs are molecules found on cell surfaces that act as “watchdogs” for the cells. They recognize invaders and send signals to the inside of the cell, culminating in the production and recruitment of immune cells to combat the infection. Pioli and several colleagues recently published a paper suggesting that TLRs mediate the innate immune response in the human female re-

productive tract. They have been able to show the presence of several types of TLRs throughout the tract.

The team’s latest paper, in the journal *Infection and Immunity*, focuses on two kinds of toll-like receptors—TLR2 and TLR4. Different tissues of the reproductive tract are exposed to different types and amounts of pathogens and must mount a response accordingly. For example, the tissues in the lower part of the tract are exposed to a large number and a wide array of bacteria and viruses, whereas far fewer pathogens make it to the upper part of the tract. TLR2 and TLR4 are able to recognize different types of pathogens, and this paper shows that the two receptors are present in differing levels in the different tissues of the tract.

Levels: An especially interesting finding was that low levels of both TLRs were found in the lowest part of the reproductive tract, where the most pathogens are present. This may seem counterintuitive, but, as Pioli explains, “it’s actually not surprising, because there is a whole host of organisms that are encountered in that part of the tract and you really wouldn’t want to mount an inflammatory response to every single bacteria,” since chronic inflammation of the tract would have many harmful effects.

What’s next for Pioli? “What I’m looking at right now is the influence of estrogen and progesterone on toll-like receptor expression,” she says. The levels of these hormones fluctuate during the menstrual cycle and throughout pregnancy. Recognizing how they regulate TLR levels in the tissues of the reproductive tract may yield insight into how the innate immune system functions at different times during the menstrual cycle and pregnancy—to defend against an array of pathogens and also to provide an environment conducive to reproduction. KRISTEN GARNER



Patricia Pioli is probing the immune system.

Test pattern

Getting an annual Pap smear to screen for cervical cancer is a hard habit to break, even if a woman’s doctor advises otherwise, found a DMS study. A Pap is recommended only every two or three years for women over 30 who’ve had more than three normal Paps, and no screening is advised for elderly women. Of the 360 women aged 40 and older in the study, 75% wanted a Pap at least annually and only 35% planned at some point to stop getting the test. “The strongest predictor of reluctance to reduce the frequency of screening was a belief that cost was the basis of current screening frequency recommendations,” wrote the authors in the *American Journal of Medicine*.

Supplementary evidence

Vitamin E, the most popular supplement in the U.S., isn’t a cure-all and may even be harmful in high doses, said a study in the January 4 *Annals of Internal Medicine*. In an accompanying editorial, DMS epidemiologist Robert Greenberg, M.D., questioned the finding that Vitamin E may be harmful but wrote, “I fully agree with the authors’ conclusion that high-dose vitamin E supplementation is unjustified. . . . Our message to the public must be clear on this point,” he added: “Vitamin E supplements won’t help, and might harm, so save your money.”



Feds examine decision-making à la DHMC

Can helping patients make informed medical decisions save the federal government money? During the coming year, DHMC will be trying to answer this question through a \$5-million demonstration project funded by the Centers for Medicare and Medicaid Services (CMS).

The reasoning behind the project goes like this: Patients who are well educated about their treatment options are more likely to make medical decisions that match their own values instead of their physicians', and that often results in their choosing more conservative, less-expensive treatments. A growing body of research from both the United Kingdom and the United States supports these claims. If they hold true in the demonstration project, CMS may ask health-care providers around the nation to employ some of the practices and procedures already being used at DHMC's Spine Center and Center for Shared Decision-Making (CSDM).

Value: Both centers have been models of integrating decision-making tools into clinical care, according to orthopaedic surgeon James Weinstein, D.O., M.S., who plays a leadership role in both centers and is heading up the demonstration project. But Weinstein and his collaborators hope to go beyond just finding financial savings. They also want to implement decision-making tools elsewhere at DHMC and introduce such tools at two other New Hampshire hospitals in order to demonstrate the value and feasibility of collecting data in an office practice, to show how patient data can improve patient-physician communication, and to develop a process for measuring the quality of decisions that patients make.

That's a tall order, but data collected by the CSDM and the Spine Center over the past several years will help in pursuing these objectives. "Because we are the only center for shared decision-making in the country with a dedicated space and staff," explains Kate Clay, M.A., B.S.N., program director for

the CSDM, "we really are modeling always and trying to capture . . . what we do so that others can do it, wherever they are."

At the CSDM, patients can learn about their conditions and possible treatments through books, videos, interactive Web-based decision aids, and one-on-one counseling. The materials and methods are designed to present the latest information available, in an unbiased context.

Although the CSDM opened in 1999, it wasn't until 2003—when its comprehensive database came online—that the center began measuring how the information it provides affects patients' decisions. Both the database and the center's clientele are growing rapidly; in 2004, the CSDM assisted almost 900 patients.

Clay often hears patients and clinicians from other parts of the country ask, "Why isn't this at my hospital? Why isn't this everywhere?" But the goal "is not for everybody to have a dedicated space . . . in every hospital," she explains. "The goal is to see what's feasible in your place, so that we end up with the ability to make these tools available to patients, add as little work as possible to clinicians, and yet have everybody happy with the process."

Model: Replicating what the CSDM does is a key initiative of the demonstration project. New Hampshire's Concord Hospital and Lakes Region General Hospital will receive \$1.2 million and \$500,000, respectively, of the \$5 million, to implement shared-decision-making services in their clinical settings. They'll use the CSDM's Comprehensive Breast Program as a model. In this program, women diagnosed with early-stage breast cancer learn about their disease and treatment options at the CSDM before consulting with their surgeon. So when a patient and her surgeon sit down together, they don't have to "go over all the information about breast cancer treatment," explains Clay. "This woman already knows quite a lot about



In her role as program director of DHMC's Center for Shared Decision-Making, Kate Clay counsels patients and directs them to decision-making resources.

mastectomy, about lumpectomy, about the risks and benefits of both, about the differences between the two. So they can have a conversation that starts a lot further along than it would have otherwise."

Though the federal demonstration project does not include any long-term follow-up with patients to determine if they have regrets about their medical decisions, the intent is to measure "patients' knowledge, values, and preferences at the time they are making the decision," says Clay. This will help the researchers evaluate the quality of the patients' decisions. In other words, are they basing their decisions on what Clay calls "good knowledge"?

Best interest: It's possible that the demonstration project may not reveal any cost savings from helping patients better understand their health-care choices. But even if that is the case, Clay and Weinstein have no doubt but that shared decision-making is in the best interest of patients. "We believe strongly that our work is showing this is a good tool," says Weinstein. JENNIFER DURGIN



How the brain's auditory cortex stores memories was the focus of a recent Dartmouth study. Published in *Nature*, it measured subjects' brain activity while they listened to familiar songs.

Rise in cancer rate was real, study found

I expected one thing and found something else," says Gilbert Welch, M.D., M.P.H. He's talking about a study he recently published that confirmed the rapid rise of a deadly but very rare cancer, esophageal adenocarcinoma. From 1975 to 2001, the incidence of this glandular cancer increased sixfold in the United States—from 4 to 23 cases per million. This got Welch's attention.

Detect: "Whenever the number of new cancers is growing quite rapidly," says Welch, "I ask the question 'Is there a change in diagnostic practice?'" An internist on the DMS faculty, he is the author of *Should I Be Tested for Cancer? Maybe Not and Here's Why*. His research focuses on problems created by efforts to detect disease early and by expansions in the definition of diseases. Whenever doctors screen more intensively for disease or widen the parameters for defining a disease, they find more of it, he explains. Welch suspected that the rise in esophageal adenocarcinoma was the result of a change in diagnostic capabilities. "In the

last 20 years, the use of endoscopy—that flexible tube that we pass into the mouth, down the esophagus, into the stomach—has grown exponentially," he points out.

To test this hypothesis, Welch and Heiko Pohl, M.D., a gastroenterology fellow, compared the number of new cases of esophageal adenocarcinoma with the number of deaths from the cancer, per million Americans. "If it's real cancer, and it's really increasing," says Welch, "you'd expect death rates to rise." And that's exactly what the research team found. The number of new cases and the number of deaths from the cancer are increasing at nearly the same rate. Between 1975 and 2001, deaths from esophageal adenocarcinoma increased sevenfold, from 2 to 15 deaths per million. "Conclusion: The rising incidence of esophageal adenocarcinoma represents a real increase in disease burden," Pohl and Welch wrote in their article, which was published in the *Journal of the National Cancer Institute*.

Discover: Not knowing what you're going to discover in a study "is what makes research interesting," says Welch. "You may have an idea, and it may be right or it may not be. Here, either answer was interesting to me."

Welch says that he doesn't plan to do any further studies of esophageal adenocarcinoma, but he hopes that others will. It's still a very rare cancer, he emphasizes, but even so "we should be trying to understand why it could possibly be going up so fast."

JENNIFER DURGIN



JON GILBERT FOX

Gil Welch's finding in a recent study was unexpected but interesting.

Inflammatory matter

DMS researchers reported on a molecule that seems to play a key role in diseases of the central nervous system, such as multiple sclerosis (MS), and inflammatory responses in general. Pathologist William Hickey, M.D., and others demonstrated the anti-inflammatory effects of antisecretory factor (ASF). Increased expression of ASF may be "a means of counteracting the pro-inflammatory environment and limiting [the] tissue damage" associated with MS and other inflammatory diseases of the central nervous system, the authors wrote in the *Journal of Leukocyte Biology*.



Brainstorm

A big brain—or, more accurately, a brain with a lot of surface area—has long been associated with higher-order cognitive ability. Researchers at DMS and the University of California discovered one of the genes responsible for brain size. They found that the gene *Id4* regulates the timing, number, and differentiation of cortical neurons, the cells that make up the cerebral cortex. "This study reveals a crucial role for *Id4* in cortical development and identifies the molecular pathways over which its effects are mediated, while suggesting important new areas for future study," they wrote in the journal *Development*.



Assessing a pay-for-performance model

Clinicians can't bill the government for a phone call to a Medicare or Medicaid patient and so have little incentive to use the phone for follow-up. But what if a call encourages a diabetic to stick to his diet, or a patient with heart disease to continue her beta-blocker therapy? Such a phone call might prevent a costly hospitalization, thereby saving the government thousands of dollars—not to mention providing better care to the patient. The Centers for Medicare and Medicaid Services (CMS) are trying to address this flaw in their payment system with a new demonstration project, called the “pay-for-performance” initiative.

The Dartmouth-Hitchcock network was one of 10 physician groups nationwide selected to participate in the three-year trial—the second CMS demonstration project Dartmouth is involved in this year. But unlike the \$5-million project on informed decision-making (see page 5), this CMS trial doesn't come with money up front.

Currently, CMS reimburses physicians, clinics, and hospitals based on the number and complexity of services they provide to Medicare and Medicaid patients. Under the system being tested in this trial, CMS will compare the total cost of care for the 20,000 Medicare patients who primarily use the Dartmouth-Hitchcock physician network to the cost of care for other similar patients in the region. CMS will also assess the quality of care delivered by each participating group, using 32 measures of common chronic illnesses and preventive services.

Bonus: If Dartmouth-Hitchcock provides high-quality care that's less expensive than that of its competitors, CMS will pay the network a bonus based on both the cost savings and the quality of care. In year one, bonuses will be based 70% on cost savings and 30% on quality; in year two, 60% on savings, 40% on quality; and in year three, savings and quality will be equally weighted.

For nonprofit physician groups like Dart-

mouth-Hitchcock, “the thought is that with the extra money that you make, you can invest in your care system to provide those services that you don't get direct reimbursement for,” says Barbara Walters, D.O., senior medical director for DHMC. Such services include information technology, disease registries, and enhanced nursing care.

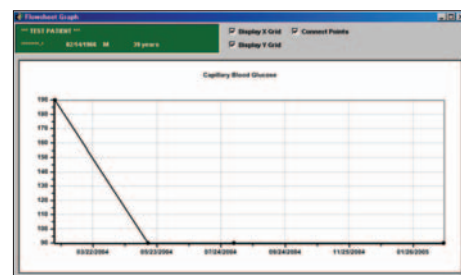
Many physicians are skeptical of the new payment model because of its emphasis on cutting costs. “If the program is focused on quality, one would expect to see a greater percentage of the [payment pool] across all three years based on quality,” said John Armstrong, M.D., a trustee of the American Medical Association (AMA) in an AMA newsletter. “The upfront expense of providing more preventative care has the potential to save money over the long run by avoiding costly treatments years down the road,” the AMA article went on, “but the project's three-year span might not be long enough to register this.”

Yet whether or not the initiative saves money, improving the coordination of care “is the right thing to do clinically,” says Walters. “It's what we should all be attempting to do—all physicians.” The trial, she adds, is “certainly better than the incentives that we have without this kind of a system.”

Leader: Measuring and improving the quality of care has been a focus for DHMC since the late 1970s, when the organization emerged as a leader in medical outcomes research. Now, for the first time, Dartmouth-Hitchcock and the other groups participating in the initiative—such as the Geisinger Health System in Pennsylvania and the University of Michigan Faculty Group Practice—will be compensated by CMS for providing better care, not just more care.

As part of the CMS initiative, Dartmouth-Hitchcock is about to roll out a new software program for managing diabetic patients. It was created by John Butterly, M.D., vice chair of the Department of Medicine; several other clinicians; and Debra Dulac,

Date Charted	02/24/2004	05/05/2004	05/14/2004	07/14/2004
Time Charted	11:01 AM	12:26 PM	2:14 PM	12:51 PM
Type	Type 1 controlled	Type 1 controlled	Type 1 controlled	Type 1 controlled
Date of Diagnosis	02/03/2004	02/03/2004	02/03/2004	02/03/2004
Hemoglobin A1c	8.7	8.0	8.0	8.0
Systolic BP	128	132	128	132
Diastolic BP	80	80	80	80
Weight (kg)	72	72	72	72
Weight (lb)	158	158	158	158
HbA1c (paper)	25.27	28.84	28.84	32.05
Capillary Blood Glucose	80	90	90	100
Comment	pre-procedure			



Dartmouth-Hitchcock is part of a federal project to see if software like this can improve care and save money.

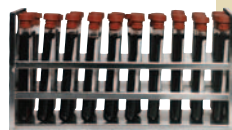
R.N., director of the Clinical Information System (CIS). It puts all the clinical information about a diabetic patient in one location—instead of scattered among a multitude of forms and electronic repositories. The concept sounds simple, but it's actually rare among health-care systems.

Data: “It's extremely unique,” says Dulac, because of the breadth of disease-specific information it contains. The program includes everything from lab-test results to dietary instructions to health goals for the patient. Any data can be graphed and printed so patients can take it home. And, because it runs on CIS, more than 6,000 clinicians at all Dartmouth-Hitchcock locations, not just DHMC in Lebanon, can make use of the tool.

The diabetes initiative jibes nicely with CMS's own description of the pay-for-performance initiative: “Physician groups will use a variety of care-management strategies to improve care under the demonstration. These include increased use of disease-management and case-management services . . . electronic medical records, disease registries, and evidence-based guidelines.”

Determining best practices and spreading those practices in a coordinated way is “what we're really trying to do,” explains Walters. “Best practices decrease variation. Decreased variation decreases waste. Decreased waste saves money.”

JENNIFER DURGIN



A new model for studying a rare disorder caused by abnormal heme production, porphyria cutanea tarda, was reported by Dartmouth biochemist Peter Sinclair, Ph.D., in the journal *Hepatology*.

Why paramedics go for the punch(line)

For most people, there is nothing funny about a motorcycle accident or a heart attack. But for paramedics, and other emergency medical service (EMS) professionals, morbid humor is essential to managing their work-related stress.

"The biggest coping mechanism that we have is dark humor," says Victoria Corum, a flight paramedic for the Dartmouth-Hitchcock Advanced Response Team (DHART), which supplies ground and air medical-transport services all over New England. "I've worked in various states, and it's constant throughout EMS. . . . Everybody does it."

Corum—who has 10 years' experience, seven of them as a flight medic—wanted to know what other, perhaps less obvious, coping strategies were common in her profession. So as part of earning her bachelor's degree in emergency-health services, she conducted a study about ways her colleagues cope with the kind of trauma most people see only in the movies. She surveyed paramedics in New Hampshire and Vermont, as well as members of the National Flight Paramedics Association.

Study: The 608 respondents to Corum's survey ranged in age from 20 to 64 and had an average of 15 years' experience. Almost 90% admitted to using dark humor. Other coping mechanisms respondents listed were talking with colleagues (37%), spending time with family and friends (35%), and exercising (30%).

Corum was not surprised that talking with colleagues ranked second, after dark humor. "If we get back from a really yucky flight, the first thing we do, probably even on the way home, is debrief the flight," she says. "It's usually informal. We start with the crew, and then we have an official debriefing" back at the hangar. Reviewing what went well on a call and what didn't helps the medics learn from each trip.

"You can work for five years and have

the same kind of patient, then one patient will click with you for some reason," Corum says. And what affects one member of the crew often affects the others, given the close confines of their work. "Basically it's just the three of us," a pilot, a nurse, and a medic, she adds, "and we have to rely on each other."

Let go: The nature of their work means EMS workers must be able to focus in intense situations and then just let go. That dichotomy is what makes dark humor a beneficial coping mechanism. "As long as it's done in an atmosphere where no one is offended by it, and it's helping you and your partner to get through your day, then I think it's a positive thing," says Corum. "It may sound crass that you are laughing at someone else's misfortune, but that's the way you have to deal with it."

The key, she says, is to "get through your day so that with your next patient you're thinking about *that* patient and not your previous one. You need to be there for *that* patient." ANNE VILLENEUVE

MARK WASHBURN



Paramedic stress was the focus of a recent study.

Nerve ending

The results are in from an eight-year study on the safety and efficacy of vagus nerve stimulation (VNS), a treatment for epilepsy that can't be controlled with medication or surgery. In the trial, conducted at DHMC and a hospital in Belgium, 7% of VNS patients were free of seizures with impaired consciousness and 50% had their seizure frequency halved.



There were no serious side effects, though 15 of 131 patients experienced hoarseness and gagging. The verdict: "VNS proved to be efficacious and safe," the authors wrote in the *Journal of Clinical Neurophysiology*.

Breath of fresh air

A team of DMS pharmacologists has discovered an enzyme that may help prevent lung cancers, which kill more than 150,000 people a year in the U.S. The enzyme, UBE1L, seems to keep a particular protein, cyclin D1, in check. Since cyclin D1 is often abundant in lung cancers, the finding means that UBE1L may be a good target for chemopreventive strategies. Smoking cessation and prevention will ultimately reduce the number of lung-cancer deaths, the researchers wrote in *Cancer Research*, but in the meantime, "there is a need to understand better how to prevent lung cancers in those [already] at high risk." ■

