



Communities that have more doctors who practice primary care are likely to have healthier senior citizens, concluded a DMS study published in the *Journal of the American Medical Association*.

Study shows fat chance of attacking tumors

Lipoprotein lipase (LPL), an enzyme that helps tumors grow by providing them with fatty acids, is a tough critter. Or, as DMS endocrinologist William Kinlaw, M.D., puts it, “a very woolly enzyme to work with.” Woolly or not, Kinlaw—with DMS oncologist Nancy Kummerle, Ph.D., D.O., and others—has dug into LPL’s bizarre daily life to explore a new way to attack tumors.

Kinlaw and his team knew, based on a past study, that patients with invasive breast cancer were less likely to have a post-treatment recurrence if they followed a very-low-fat diet. Most researchers were focusing on developing drugs to inhibit fat synthesis. But Kinlaw thought that perhaps cancer cells could “wiggle out” of fat synthesis inhibitor drugs by using LPL to take in dietary fat from the bloodstream.

Particles: LPL is an enzyme that clips fatty acids out of insoluble fat particles. The now-soluble fat, broken down by LPL, is then able to get into tumor cells through a channel called CD-36, a hole in the cell membrane.

Kinlaw’s idea turned out to be right. He found if you use fatty acid synthesis in-

hibitors to prevent cancer cells from synthesizing fat, the cancer cells will then consume dietary fat from the bloodstream, using LPL and CD-36.

Prevalent: Kinlaw and Kummerle then studied 45 different breast cancer cell lines, and cells from breast cancer and liposarcoma tumors, and found that LPL was very prevalent in six of the cell lines and in nearly all of the tumor cells.

“Nancy . . . really got into this whole hog,” says Kinlaw. “With a great deal of tenacity, she pulled off something that is known to be very difficult to do, and that was to generate an antibody against [human LPL].”

“If I choose a peptide from a region of human LPL that isn’t identical to that part of mouse LPL—maybe 70% to 85% identical, but not 100%—the mouse will recognize it as a foreign protein, and it will make antibodies against it,” explains Kummerle. So she then harvested those antibodies and made the mouse anti-human LPL antibody. The idea was to see if the antibody could prevent LPL from providing tumors with fatty acids.

The finding is interesting scientifically, but there’s a problem with making clinical use of it. That’s because, explains Kinlaw, “poisoning LPL is going to deprive the patient of a way of getting rid of circulating fat particles.” Over time, such particles can build up, eventually causing inflammation of the pancreas—a very serious condition. So the long-term inhibition of LPL may not be the best way to attack tumors.

Steps: Still, the finding holds promise. Targeting CD-36 may work better, Kinlaw thinks. The researchers plan next to investigate ways to keep CD-36 from functioning or to prevent the cell from moving it to the surface so fatty acids don’t pass through it. MATTHEW C. WIENCKE

LPL is an enzyme that clips fatty acids out of insoluble fat particles.



JON GILBERT FOX

Kinlaw, shown with his lab manager, Christina Donnelly, discovered how tumor cells use dietary fat.

Diabetes dangers

Diabetes, which affects 11% of Americans over the age of 20, carries all sorts of complications. A recent study by DMS researcher Todd MacKenzie, Ph.D., may have found yet another complication. The study, published in the journal *Cancer*, found that individuals with diabetes were twice as likely to develop bladder cancer as individuals without diabetes. The link grew even stronger over time; people who’d had diabetes for 16 years or more were three and a half times as likely to develop bladder cancer. Diabetics who used oral medications to control their blood sugar rather than just monitoring their diet also had a much higher risk.



In good hands

Good hand hygiene is key to health in everyday life, and it’s critical to patient health in intensive care units. Even seemingly small changes in hand-hygiene procedures, like giving ICU staff a personal hand-sanitizer unit that they can attach to their clothing, can reduce infections among patients. So found a recent study published in the *Journal of Critical Care* by a team of DH anesthesiologists. The incidence of ventilator-associated pneumonia decreased by 50% after the introduction of such dispensers, although the rate of central line catheter-related infections remained the same.





An editorial in *Nature* by DMS's Michael Sporn, M.D., called on clinical oncologists to reexamine the concept of chemoprevention and on regulators to better accommodate chemoprevention trials.

Understanding a breast-feeding bottleneck

For newborns, a balanced diet is overrated. The American Academy of Pediatrics says infants should be fed exclusively breast milk during the first six months of life. But a study by DMS pediatrician Alison Holmes, M.D., found that advice is often disregarded. Even in the first week of life, many U.S. infants are fed a combination of formula and breast milk.

Using data from a survey conducted by the Centers for Disease Control and Prevention, Holmes examined feeding practices for newborns. Of the 6,788 infants in her analysis, 55% were fed only breast milk in the first week of life, while 8% were fed a combination of formula and breast milk; the rest were fed only formula or were started on breast milk but switched to formula only.

Milk: Furthermore, "there are really significant racial and ethnic differences" in the data, Holmes says. Only 7.2% of white infants got a combination of formula and breast milk, compared to 24.4% of Hispanic and 17.9% of black infants.

Holmes also found that women who fed their newborns the combination were more likely to stop breast-feeding entirely by four months. About 65% of infants who were exclusively breast-fed during the first week of life were still breast-feeding at

four months, compared to only 40% of the infants who got the combination during their first week. This link was particularly strong for white infants.

Accrue: Holmes says the health benefits of breast-feeding are strongest when infants are fed only breast milk. Getting some breast milk "is probably a little bit helpful, especially against infectious diseases, but most breast-feeding benefits seem to really accrue when you have exclusive breast-feeding."

In her analysis, 55% were fed only breast milk for the first week.

Further analysis by Holmes found that children fed only breast milk during their first four months were less likely to

be overweight or obese at age two to six than children fed formula and breast milk. One possible explanation, she says, is that mothers who breast-feed may develop a better sense of when their children are full. "When you're breast-feeding, you can't really tell how much your child is feeding," she says. "But you're very attuned to their behavior . . . when they're hungry and when they're full."

Holmes says other research has shown that one reason mothers supplement breast-feeding with formula is they're under the mistaken impression that formula offers benefits not found in breast milk. Another reason, she says, is that hospital staffers may fall back on formula if a mother has trouble breast-feeding. She hopes her study will encourage them to take the time to help the mother and "not to supplement with formula quite so early."

Week: Her study, published in the *Journal of Pediatrics*, makes it clear that promoting a breast-only approach, even if just for the first week of a baby's life, could lead to better lifelong health and perhaps even reduce racial and ethnic health-care disparities. Holmes is now working on a quality improvement initiative to put this knowledge into practice. AMOS ESTY



Even for just a week, breast-only offers benefits.

Too much surgery? Who nose . . .

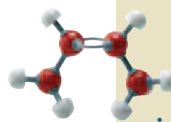
Endoscopic sinus surgery (ESS) is on the rise among the elderly, and the per capita rate of the procedure varies widely from place to place, according to a paper by DH otolaryngologist Giridhar Venkatraman, M.D. "Variability in high-use versus low-use regions seems to be random and independent of climate or the number of beneficiaries diagnosed as having chronic rhinosinusitis," he and his coauthors wrote in *Archives of Otolaryngology*. Per capita ESS rates ranged from 2 to 10 surgeries per 100,000 Medicare beneficiaries. This points to "the need for identifying and adopting more rigorous clinical criteria for ESS," they concluded.



Weight, weight . . . don't tell me

Depression and obesity often go hand in hand in the elderly, Dartmouth's Laura Barre, M.D., has found. She determined that among patients in their sixties, seventies, and eighties, the incidence of depression rises with body mass index. About 17% of elderly people who are obese are depressed, compared with only about 11% of those of normal weight. Barre's study did not prove that obesity causes depression (or vice versa), but it did establish a correlation between the conditions. She presented her findings at the annual meeting of the American Association for Geriatric Psychiatry.





The Dartmouth Immunology COBRE (Center of Biomedical Research Excellence), a cross-disciplinary effort to better understand the immune system, has \$6 million in new funding.

Movie scenes serve as signals to smoke

Smokers who are trying to quit know to avoid people and places likely to remind them of their habit. But now a study in the *Journal of Neuroscience* shows that simply watching actors smoke on-screen may induce an urge to light up, by activating regions of the brain associated with both the reward system and the physical act of smoking.

The study, conducted in the lab of Dartmouth's Todd Heatherton, Ph.D., provides new insights into an area of psychology called cue reactivity; its focus is how people react when exposed to cues associated with a behavior they are trying to regulate, such as smoking or overeating. DMS's James Sargent, M.D., a coauthor of the study, had previously found that the more smoking there is in a movie, the more smokers report craving a cigarette after watching it. Sargent and Heatherton wanted to explore this phenomenon more deeply.

Scenes: To find out what happens in smokers' brains when actors smoke on-screen, Heatherton and graduate student Dylan Wagner designed a study showing scenes from the 2003 movie *Matchstick Men*, which has a lot of smoking in it but not a lot of other potentially confounding actions, such as violence. They measured the brain activity of both smokers and nonsmokers using functional magnetic resonance imaging (fMRI).

The participants did not know that smoking was the subject of the research.

"We thought it was important for the participants not to know what the study was about," says Heatherton, lest that knowledge alter the results.

Area: Compared to nonsmokers, smokers showed greater activity in an area of the brain called the reward region, which is associated with cue reactivity. Smokers also showed greater activity in areas associated with the motor actions of smoking. "This was really interesting and a bit of a surprise," says Heatherton. "You're getting a double whammy—both the reward system that says it would be good to have a cigarette and the motor systems are now active. It's like sharing a cigarette with the actor."

The results have important implications. "One of the things that we know causes problems for people trying to control a behavior, like smoking, is exposure to cues associated with that behavior," says Heatherton. So, if smokers trying to quit were aware that just watching someone smoke in a movie might increase their urge to smoke, they could try to avoid such situations.

Cue: The next step will be linking the brain activity the study showed to real-world behavior. For example, does the degree of someone's cue reactivity predict how successful the person is at giving up smoking? And what brain systems are involved in overriding the cues? Heatherton's group is already seeking answers to these and other questions. LAUREN WARE

Smokers showed greater activity in the brain's reward region.

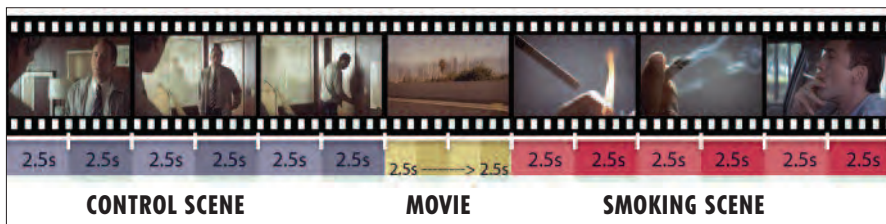
Testimony

A rise in the incidence of pulmonary emboli, blockages in the arteries that carry blood from the heart to the lungs, may be overdiagnosis, says a DMS team. In 1998, a new CT scan was able to better detect such blockages; in succeeding years, their incidence jumped 81%—but the death rate from the condition stayed about the same, and complications associated with treatment rose 71%. "Many assumed this highly sensitive test would improve outcomes," the team wrote in *Archives of Internal Medicine*. But "the increased sensitivity . . . may have a downside: the detection of emboli that are so small as to be clinically insignificant."



Safe sedation

When children need anesthesia, are they safer in the hands of an emergency physician, a pediatrician, an anesthesiologist, or some other specialist? It turns out it doesn't matter who provides sedation, according to a paper coauthored by two DH anesthesiologists. Sedation performed outside versus inside an operating room "is unlikely to yield serious adverse outcomes," they wrote. The study, published in *Pediatrics*, found that there was no greater risk of complications when a child was sedated by one type of clinician over another, as all had similarly low complication rates. ■



These are stills from *Matchstick Men*, which was used in a study analyzing brain activity in smokers.