



The Milken Institute ranked New Hampshire ninth among the 50 states on its Science and Technology Index, for having assets that are likely to foster high-quality economic growth.

Is breast best even with HIV-infected moms?

Breast is best” is no news flash. It’s now common knowledge that breast-feeding provides superior nourishment for babies and helps them build strong immune systems. Breast-feeding does, however, allow the human immunodeficiency virus (HIV) to pass from an infected mother to her child. In the U.S. and Europe, HIV-infected mothers can avoid that risk by feeding their babies formula.

But in developing countries, formula may be unaffordable or unsafe. “Mothers either have no access to formula,” explains DMS researcher Ruth Connor, Ph.D., “or if they do have access it’s often a problem of getting clean water or a heat source to sterilize the formula.”

Fed: But surprisingly, the risk of a baby contracting HIV from its mother is not proportional to the amount of breast milk the baby receives. Several studies have found that babies who are mixed-fed—that is, who receive formula or other foods in addition to breast milk—are much more likely to contract HIV than those who are exclusively breast-fed.

“But the question is why? What is the mechanism behind this?” wonders DMS postdoctoral fellow Stephanie Dorosko, D.V.M., Ph.D. Scientists have speculated that other foods may cause a mild inflam-

mation in the intestine and make it more permeable, so it’s easier for the virus to enter the baby’s bloodstream. Dorosko and Connor set out to determine if that’s actually the case. Their hope is that a better understanding of the mechanism will lead to better advice for HIV-positive mothers in developing countries.

They decided to examine calprotectin, a marker of inflammation in the gut that’s used to screen for diseases such as irritable bowel syndrome and colon cancer. Calprotectin can easily be measured in feces and is stable at room temperature. The latter property is important, since they plan to eventually bring their study to African communities where refrigeration may not be readily available. But first, they decided to measure calprotectin in healthy infants—comparing levels in breast-only babies to those in mixed-fed babies.

Fecal: To do so, they teamed up with Suzanne Greeley, R.N., who facilitates a DHMC support group for new mothers. The moms filled out a questionnaire about their infants’ feeding habits and saved the babies’ diapers so their fecal calprotectin could be measured.

The results, published in the journal *Breastfeeding Medicine*, were unexpected. The researchers had assumed they’d see more inflammation in the mixed-fed babies, but calprotectin levels were higher in the breast-only babies. Dorosko suspects calprotectin may actually be protective in young infants. Connor wonders if infants in Africa will have higher calprotectin levels because they’re exposed to more contaminants in their food.

“It’s amazing how little is understood about how HIV is transmitted in breast milk,” says Connor. But she and Dorosko plan to continue to chip away at that information deficit. **KRISTEN GARNER**

“It’s amazing how little is understood” about HIV and breast milk.



ST. AVON/IR. JASTRZEBSKI

A mother’s HIV status is a factor in breast-feeding.

Watch and learn

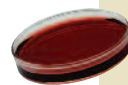
If you want something done right, goes the conventional wisdom, do it yourself. But according to Dartmouth research led by Emily Cross, Ph.D., if you just want to *learn* how to do something right, you can sit back and watch someone else do it. “The ability to improve by observation alone, without concurrent practice,” she wrote in *Cerebral Cortex*, “is a powerful capacity of humans.” Cross measured the brain activity of participants as they tried to learn dance sequences and found that studying the sequences passively activated the same neural regions as did actively practicing them.



Got calcium?

“Several national organizations recommend a high calcium intake to achieve optimum bone health,” wrote members of the DMS Departments of Medicine and of Community and Family Medicine in a recent article. But some research has called that recommendation into question. To help settle the dispute, the DMS team conducted a long-term study on the effects of calcium supplementation. In a recent issue of the *American Journal of Clinical Nutrition*, the researchers wrote that taking a daily supplement reduced the risk of bone fracture by 72%—but that the benefits disappeared once participants stopped taking the supplements.





Short-term mortality is the same for drug-resistant as for non-resistant staph infections. But, found a DMS study, mortality a year later is higher in resistant staph—51% vs. 32%.

Does the new beat out the tried and true?

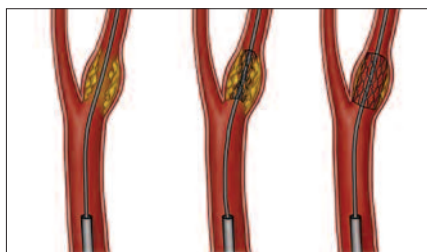
Few of the body's blood vessels are unimportant. But the carotid arteries rank right up there in significance, running through the neck and delivering blood to the brain. If plaque accumulates in a carotid artery, it can lead to a stroke.

There used to be just one way to treat a plaque buildup serious enough to require treatment—an operation called carotid endarterectomy (CEA). Then a procedure called carotid artery stenting (CAS) came along. But, says DMS vascular surgeon Philip Goodney, M.D., it's not clear which treatment is better.

For nearly 20 years, CEA has been considered the gold standard for treating plaque buildup in a carotid artery. Its disadvantage is that it's an invasive procedure; a vascular surgeon makes an incision in the neck and surgically removes plaque from the lining of the artery.

Mesh: In CAS, a catheter is inserted into a vessel in the patient's arm or groin and guided into the carotid artery. A device shaped like an umbrella is passed through the catheter and opened. Then a stent, or mesh cylinder, is placed at the narrowed point in the artery and expanded with a balloon, flattening the plaque against the artery wall. Any loose plaque is caught by the umbrella, which is closed and pulled out with the balloon and the catheter—leaving the stent in place.

CAS has been around since the late



In CAS, a catheter is inserted in the artery (left), then a stent is placed (center) and expanded (right).

1990s. "People were very familiar with balloons [and] stents" from their use in coronary surgery, says Goodney, so the concept caught on quickly. But CAS has not been studied as carefully as CEA. "We knew there was a lot of stenting going on. We didn't know how much. We didn't know where. We didn't know what it was doing to the overall rate of the open operation." There have been randomized trials comparing CEA and CAS, says Goodney, "but they've been kind of controversial because the findings haven't always shown that stenting is as good as endarterectomy. A lot of it depends on patient characteristics."

So he and several Dartmouth colleagues studied 134,194 Medicare and Medicaid claims for carotid revascularization—124,808 for CEA and 9,386 for CAS—between 1998 and 2004. They found that the overall number of procedures each year dropped slightly over the six-year period. But the prevalence of CAS increased by 149%—from 14.6 to 36.4 procedures per 100,000 Medicare beneficiaries—while the prevalence of CEA dropped 17%.

Trend: The results were published in the *Archives of Surgery*. But it's not yet clear, says Goodney, if the trend is a short-term anomaly or if stenting is replacing endarterectomy. "It could be that the poorest candidates for CEA now undergo CAS," the authors wrote.

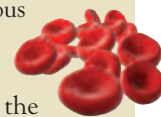
The next step is to look for patterns in where and by whom CAS is being done, says Goodney. "Is it vascular surgeons, cardiologists, radiologists, neurointerventionalists?" he asks. "Who is having the best results? And what patient selection and physician characteristics produce the best outcomes? I think stenting has a place, but we don't know exactly what the place is just yet." MATTHEW C. WIENCKE

A look at iron and age

In the world of superheroes, being Iron Man chalks up as a huge plus. But for mere mortals (female as well as male), having too much iron can be problematic. That's because as people age, they accumulate iron in their blood—and elevated iron levels have been linked to cancer. DMS's Leo Zacharski, M.D., reported in the *Journal of the National Cancer Institute* just how strong that link is. The findings are preliminary, he cautions, but "analysis showed a 37% reduction in overall cancer incidence with iron reduction" from periodic blood-letting.

Calculating clot risk

To investigate safety concerns about drug-eluting stents—tiny mesh tubes that prop open blood vessels—DMS researchers compared outcomes in about 67,000 Medicare patients, roughly half in the era before drug-eluting stents (DESs) and half afterward. Although other studies have suggested "some incremental risk" of a dangerous blood clot with DESs, "we can detect no adverse consequences to the health of the population," wrote DHMC cardiologist David Malenka, M.D., and his coauthors in the *Journal of the American Medical Association*. "Whatever the increased risk, . . . it is more than offset by a decrease in risk" of a renarrowing of the blood vessel.





DMS infectious disease expert Peter Wright, M.D., was invited by the *New England Journal of Medicine* to assess a new way of growing avian flu vaccines; he hailed it as promising.

“You are what you eat” applies to lab animals

As researchers toil away in their labs, they carefully control all aspects of an experiment to prevent unexpected variables from tainting their findings. But what if something that never crossed their minds distorts their data?

Diet: A team of DMS researchers—led by graduate student Courtney Kozul and Joshua Hamilton, Ph.D.—discovered just such a factor: the degree to which a lab animal’s diet can obscure the results of genetic studies. They set out to explore the effects of two amounts of arsenic—100 parts per billion (ppb) and 10 ppb—on gene expression in mice. But when they learned that a serving of non-purified lab chow contains as much as 390 ppb of arsenic, they decided to take a close look at lab animals’ diets.

Nonpurified chow consists of cereal and assorted sources of protein, including fishmeal, which often contains arsenic and other contaminants. Many animal facilities use such chow because it’s cheaper than a purified diet. Researchers may not even know what kind of food their lab animals get, and seldom is the information reported in scientific papers.

Poster: At a national meeting where the research was first presented, “hundreds of people came to my poster almost panicking,” says Kozul. They didn’t realize lab diets might be skewing their results. The findings have since been published in *Chemico-Biological Interactions*.

The study, funded by the National Institutes of Health, was conducted with male mice over a period of five weeks. The mice were divided into two groups; one ate regular chow and the other a purified diet with only 20 ppb of arsenic.

The experimental dose of arsenic was administered in the animals’ drinking water; some mice in each group got water with 100 ppb of arsenic and some got 10

ppb. Then, using a technique called microarray analysis, Kozul analyzed all 20,000 mouse genes. In the purified diet group, it was clear the 100-ppb dose altered the expression of many genes in the animals’ lungs and livers.

But in the regular-chow group, the contaminants “profoundly affect[ed] gene expression,” says Hamilton, making it possible to see the effects of the experimental doses. Of particular concern was the fact that the affected genes are involved in drug metabolism.

In previous studies, Hamilton’s team—which has always used a purified diet—has shown that arsenic in drinking water disrupts important hormones and contributes to cancer, cardiovascular disease, and diabetes. In 2006, their work led to a lowering of the federal limit for arsenic in drinking water—from 50 ppb to 10 ppb.

The study showed that “diet has profound effects on how our body responds,” says Hamilton. He has since left Dartmouth to be chief academic and scientific officer at the Marine Biological Laboratory in Woods Hole, Mass., but Kozul is continuing her research at DMS. Her latest finding was that arsenic affects genes that control the immune response of lung cells. **LAURA STEPHENSON CARTER**

The study showed that “diet has profound effects” on the body.



Kozul shows off regular chow, left, and purified.

ION GILBERT FOX

A BP of 120 over ecstatic

It’s hard to quantify happiness. Studies have shown that some nationalities, such as the Dutch, consistently report higher levels of contentment than, say, Germans, but cultural differences call those results into question. Dartmouth economist David Blanchflower, Ph.D., took a medical approach, arguing in the *Journal of Health Economics* for blood pressure (BP) as an indicator of well-being. He found in a survey of 15,000 people in 16 European nations that “happy countries seem to have fewer blood pressure problems.” So if you’re happy and you know it, your BP will surely show it.



Problematic polymorphisms

Scientists know smallpox vaccination can have side effects, but they don’t know why. To find out, researchers at DMS and several other institutions examined polymorphisms—slight genetic differences—at 1,442 locations on the human genome during a vaccination trial. They identified 36 sites that seemed to be linked to adverse reactions; in a second trial, three of those polymorphisms again correlated with side effects. “The fact that the results of our first study were independently replicated in the second study,” wrote the team in the *Journal of Infectious Diseases*, “strengthens the plausibility of these genetic associations.” ■

