



DMS's Kent Hymel, M.D., led a study of head trauma in children under 3 years of age. The deeper the injury, his team found, the more likely it was to have been the result of abuse.

Tool quantifies pancreatic transplant risk

Pancreas transplantation can save the life of patients with type 1 diabetes, offering a possible cure for those whose pancreas does not produce enough insulin on its own. Unfortunately, the failure rate for donated pancreases is higher than for kidneys or livers. Furthermore, the number of pancreases available for donation is not only insufficient to meet the demand, but the supply is declining. The need is most pressing for patients awaiting a simultaneous kidney and pancreas transplant, as they are usually on dialysis and may die before suitable organs are available.

To try to make sure patients who need a pancreas can get the one best suited for them, David Axelrod, M.D., chief of transplantation surgery at DHMC, has developed a method to systematically assess pancreases available for donation. Working with collaborators at the University of Michigan and Northwestern, Axelrod identified risk factors suggesting when a donated pancreas won't last long in the patient receiving the transplant, which could help surgeons select appropriate organs and develop improved policies for allocating them.

Factors: Called the pancreatic donor risk index (PDRI), the tool includes 10 factors

that can affect the likelihood of a successful transplant. These include the donor's age, gender, race, body mass index, height, and cause of death. Another factor is whether the donor's death falls into the category of "cardiac death," meaning that the donor was declared dead because of a loss of heart function rather than brain function. The index also considers how much time passed between harvesting the organ and transplantation.

Index: The factors are entered into a formula, producing a number that allows for a simple comparison of different pancreases. The index uses 1.0 as the median risk. An organ with a PDRI above 1.0 would be at greater risk of failure within the first year after surgery, while one with a PDRI below 1.0 would be more likely to remain viable.

The factors that have the greatest influence are age, body mass index, and donation after cardiac death. For example, if a 28-year-old donor's pancreas has a PDRI of 1.0, keeping everything the same but increasing the donor's age to 45 raises the PDRI 56%, to 1.56.

The index can be used to determine which organs might be a good option for which patients. Pancreas transplants are performed in three circumstances: at the same time as a kidney transplant, following an earlier kidney transplant, or alone in a patient without kidney failure.

Simultaneous: Axelrod found that organs with a higher PDRI are more likely to survive a year in patients who have a simultaneous kidney transplant than in those who undergo a pancreas transplant alone or after a kidney transplant. Doctors can use this information to increase the pool of acceptable organs for patients having simultaneous transplants, possibly reducing the number of people awaiting the life-saving procedure. ROGER P. SMITH, PH.D.

The tool includes 10 factors that affect the likelihood of success.



MARK WASHBURN

Axelrod, right, is chief of transplantation surgery.

Backdrop

Back surgeries are getting increasingly complex, according to a team of researchers that included Dartmouth-Hitchcock orthopaedist Sohail Mirza, M.D. The overall rate of surgery for lumbar spinal stenosis—a narrowing of the spinal canal in the lower back—dropped between 2002 and 2007 among Medicare beneficiaries, but the rate of the most complex surgeries for this condition grew rapidly. As a result, Mirza and his coauthors noted, "although the overall procedure rate fell 1.4%, aggregate hospital charges increased 40%."



Knife point

After nine years of waiting, surgeons and cardiologists at Dartmouth-Hitchcock and around the country finally got the results of a much-anticipated clinical trial. DHMC was one of 117 institutions that took part in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST), which assessed whether endarterectomy (a surgical procedure) or stenting (a minimally invasive procedure) is more effective at preventing strokes and heart attacks in at-risk patients. The trial showed that, overall, the procedures are equally effective. But patients older than 70 did somewhat better with surgery, while those 69 and under did better with stenting.



For a **WEB EXTRA** link to a podcast interview with Douglas Staiger, see dartmed.dartmouth.edu/su10/we03.



More Medicare enrollees are getting new joints, reports the *Dartmouth Atlas of Health Care*; from 2000-01 to 2005-06, hip replacements rose 15%, knees 48%, and shoulders 67%.

Doctors' hours are dropping

After decades of working exceptionally long hours, U.S. physicians have steadily shortened their workweek in recent years. A study led by Dartmouth economist Douglas Staiger, Ph.D., found that doctors today are working an average of 51 hours a week, a substantial decline from the 55 hours a week they worked throughout the 1980s and 1990s.

Trends: The four-hour change is “very unusual for an occupation,” Staiger says. To analyze trends in physician hours, he and his colleagues used three decades of data from a monthly U.S. Census Bureau survey. They were “really surprised at how broad-based the decline was,” Staiger says. All groups of physicians—men, women, younger doctors, older doctors, residents, and nonresidents—saw a substantial decline in hours.

The average hours worked by nonresident doctors declined from 53 hours a week in 1997 to 50 hours a week in 2007. Residents' hours dropped even more, from 66 to 59 hours a week over the same period, due to limits placed on resident work-hours in 2003. Hours worked by nonresident physicians over the age of 45 showed

the smallest change, dropping from 51 to 49 hours a week from 1997 to 2007.

The researchers found a strong correlation between the number of hours worked and physician fees. Inflation-adjusted fees were constant during the early 1990s but dropped by 25% from 1995 to 2006. “When fees go down, that last hour of work is less rewarding,” financially and in other ways, Staiger explains. The decline in fees was associated with the rise of managed care in the mid-1990s and with

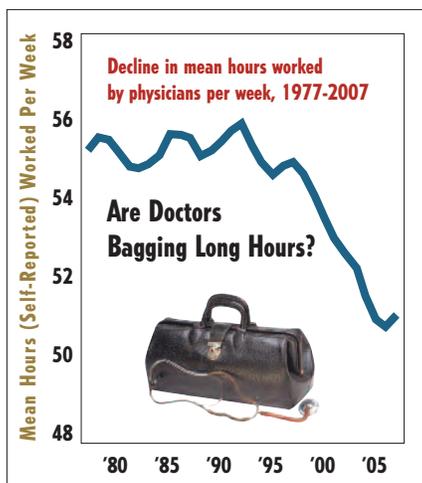
“When fees go down, that last hour of work is less rewarding.”

increased competition in the health-care arena. Staiger also says that changes such as increased scrutiny of doctors by insurance companies could be “having as large of an effect as the fees per se” on the number of hours worked, though he doesn't have data to prove that connection.

Forecasts: The supply of physicians is a hot topic in academic and policy circles. How many doctors will the country need, and how many will it have? The impact of the decline in hours isn't clear. Usually, Staiger says, physician supply forecasts “assume that physician hours will remain at their traditionally high levels.” But the three-hour drop for nonresidents is roughly equivalent to cutting 36,000 physicians from the workforce. So the study, which was published in the *Journal of the American Medical Association*, could be seen as evidence that a doctor shortage truly is just around the corner. (For more about the physician supply debate, see dartmed.dartmouth.edu/sp09/f03.)

But Staiger notes that the survey used for the study did not include information about doctors' specialties. The most important issue, he says, is not simply the raw number of physicians but “getting the right kinds of physicians to the right parts [of the country] to serve the right population.”

KATHERINE VONDERHAAR



This graph shows the drop for physicians overall.

Healthy communication

Dartmouth researchers reported that communication between mothers and daughters plays a large role in determining whether young women receive the HPV vaccination.

They surveyed almost 1,000 female undergraduates to determine their knowledge of HPV, their perceptions of HPV risk, and the openness of their communication with their mothers. Just under half (49%)



had received at least one shot in the three-shot vaccine series. “The mother's approval of HPV vaccination, mother-daughter communication about sex, and daughter's perceptions of vulnerability to HPV were positively associated with vaccination status,” the researchers wrote in *Pediatrics*.

Water proof

Tens of millions of people use drinking water containing levels of arsenic—a known carcinogen—above the maximum recommended by the World Health Organization.

Now, DMS researchers have reported that arsenic might trigger a cell signaling pathway called Hedgehog that is associated with several cancers. Patients exposed to arsenic had high levels of Hedgehog signaling. “Our study provides for the first time evidence that links activation of the Hedgehog pathway with arsenic exposure,” they wrote in the journal *Cancer Research*.





DMS's Laura Barre, M.D., studied 183 older adults and found they were at higher risk of frailty (such as weight loss, weakness, or low activity) if they had a serious mental illness.

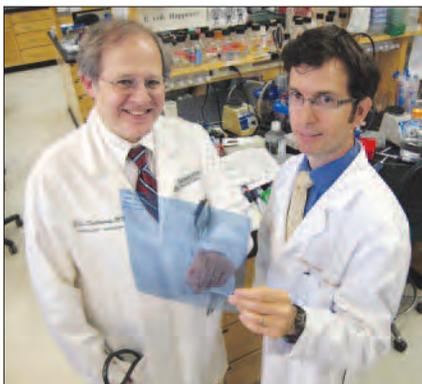
Rogue molecule is linked to lung cancer

A tiny snippet of RNA promotes lung cancer in mice and men, Dartmouth researchers have discovered. MicroRNAs (miRNAs) are small RNA molecules that regulate gene expression. "They were originally discovered as playing critical roles in development," says Ethan Dmitrovsky, M.D., DMS's Andrew G. Wallace Professor of Pharmacology and Toxicology.

The first miRNA was discovered in 1993. Since then, hundreds more have been described. They can degrade or impair messenger RNA, putting the brakes on protein production. In healthy cells, this plays a role in regulating the expression of genes. But when the process goes haywire, it can lead to disease, including lymphoma, leukemia, colon cancer, and breast cancer.

Dmitrovsky's team has identified one miRNA, miR-31, that causes lung cancer when it goes rogue. The finding appeared in the *Journal of Clinical Investigation*.

Lab: Xi Liu, Ph.D., now a postdoctoral fellow at the National Cancer Institute, headed up the study as a graduate student in Dmitrovsky's lab. First, the team engineered a mouse to overexpress a human protein in its lungs. The protein, cyclin E, is known to play a role in human lung cancer.



Dmitrovsky, left, and Lorenzo Sempere, a research associate in his lab, continue to study miR-31.

cer. As planned, the engineered mice went on to develop "many features of human lung cancer," Dmitrovsky says.

Tissue: The researchers then set out to look for miRNAs that were expressed more strongly in cancerous tissue from the engineered mice than in healthy mouse lung tissue. Ten molecules stood out. The team examined whether those 10 miRNAs were also overexpressed in samples of human lung cancer tissue. "Of the 10, we found three that were prominently overexpressed in both mouse and human lung cancer," Dmitrovsky explains. None of the three had previously been linked to lung cancer.

These results were promising, but the researchers were just getting warmed up. Next, they experimentally overexpressed and repressed levels of those three miRNAs to see what would happen. "We found only one, miR-31, that was cancer causing," Dmitrovsky says. When its expression was ramped up, tumors grew. When its expression was knocked back, cancer growth was significantly reduced in both mouse and human cell lines.

Pathway: Looking still deeper, the team identified genes involved in the cancer-causing pathway. They found that miR-31 inhibits two tumor-suppressor genes, allowing lung cancer to grow. "This would imply that targeting miR-31 represents a potential treatment for lung cancer," Dmitrovsky says.

That, not surprisingly, is where his research is headed next—to see if modified forms of miR-31 can be used to inhibit the growth of lung cancer. "This is a new and evolving field," Dmitrovsky says. The field may be green, but he and his colleagues are making significant strides in understanding how tiny pieces of RNA can wreak havoc on cells—and how to keep that from happening. **KIRSTEN WEIR**

None of the miRNAs had previously been linked to lung cancer.

Sensational study

A DMS-led team assessed if teenagers who exhibit sensation seeking—the "tendency to seek out novel and exciting stimuli"—are more likely to start drinking or smoking. They surveyed adolescents aged 10 to 14 and used a series of questions to rate their sensation-seeking tendencies. The team reported in *Addiction* that "sensation seeking was found to be a moderately strong predictor of binge drinking and a strong predictor of established smoking." The authors argue that interventions to prevent binge drinking and smoking among adolescents should primarily target sensation seekers.



A PSA about PSA screening

"There is growing concern that older adults are at risk for exposure to potentially harmful treatments for which the promised benefit is small, if not absent," wrote Julie Bynum, M.D., and her coauthors in the *Journal of the American Geriatrics Society*. They examined rates of prostate-specific antigen (PSA) screening in men 80 and older. PSA testing can signal a risk of prostate cancer but also involves potential harms and, in some populations, a low likelihood of benefit. Bynum found that rates of screening in this age group varied from 2% to 38% and that regions with higher rates had higher overall Medicare expenditures. ■

