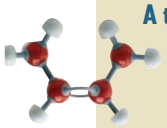


A team of toxic-metal researchers at DMS found that exposure to arsenic in drinking water even at low levels can disrupt the function of certain receptors and affect hormone activity.

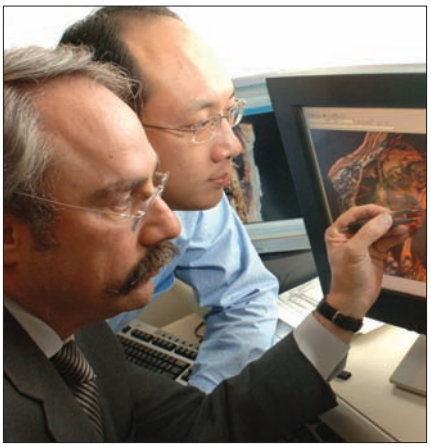
Heart model provides realistic feedback

Thub dub. Thub dub. A healthy heart uses a two-step motion—first relaxing, then contracting—to pump blood throughout the body. A failing heart, however, can't produce a strong, coordinated contraction—causing further damage to the organ and allowing blood to pool in other parts of the body.

Problem: A technique called cardiac resynchronization therapy (CRT) can help address this problem. But, so far, it has involved a lot of guesswork—guesswork that could be avoided, according to Justin Pearlman, M.D.

Pearlman, a Dartmouth cardiologist who's also trained as an engineer, and Heng Huang, a doctoral student in computer science, have created a computer-based model that represents "every little bump and cranny" of an individual's heart, Pearlman says. Consisting of high-resolution MRI images, the model can simulate each heart's unique motion and the stresses and strains that every square inch experiences as it pumps.

Why is this important? In CRT, pacemaker leads—tiny wires—are placed on areas of the heart that are not contracting well. By transmitting small electrical impulses, the leads help coordinate the contraction. For the patient, successful CRT can mean the difference "between being short of breath [while] lying in bed and being able to go shopping," Pearlman explains. But the key to optimizing the therapy lies in finding the best spots to place the leads.



JON GILBERT FOX

Pearlman, left, and Huang view their 3D model.

Currently, cardiologists use two-dimensional or static three-dimensional reconstructions of patients' hearts to find the best spots. But "measurements play a very small role" in that process, according to Pearlman. "With our model, we're measuring actual tissue properties, stresses and strains," wall thickening, ballistic motions, and many other factors. And Pearlman's model even allows physicians to try placing leads in various locations. So instead of "experimenting on patients," says Pearlman, "we can experiment on the computer copy of their heart."

System: Pearlman and Huang's model—which uses a new mathematical system that the two invented—is just one of several innovations by Pearlman. He's also developed ways to measure how much oxygen is getting to every part of the heart. "As a heart starts to fail," he explains, "tiny vessels can get plugged up and you can have microvascular disease. Clinically, we have no test for that." No test other than his, that is.

Word of Pearlman's inventions is spreading, and he is seeing more and more patients from Boston. He and Huang would like to continue testing and refining their heart model—as well as Pearlman's other creations—but they're worried that a gap in funding may halt their progress. "Frankly, we've been spending our energy on the model and the medicine," says Pearlman, "rather than on [a] sales pitch and traveling road show."

So they will now try to keep an eye on the flow of funding—as well as the flow of blood in ailing hearts. JENNIFER DURGIN

A fine balance

New research shows that Vioxx—the blockbuster painkiller pulled from the market in 2004 because it increased the risk of heart attacks—reduces the risk of precancerous tumors in the colon and rectum. The findings, soon to be published in *Gastroenterology*, "show once again the potential for nonsteroidal anti-inflammatory drugs, or NSAIDS, to interfere with the development of cancer in the colon and rectum," says DMS's John Baron, M.D., who led the study. But the "serious toxicity" of Vioxx and similar drugs must be weighed carefully against their chemopreventive powers, he and his coauthors caution.

No bowl of cherries

It's not surprising to learn that women newly diagnosed with breast cancer are often worried, nervous, fearful, and depressed. But little formal research has quantified those symptoms. A new Dartmouth-led study, published in *Cancer*, helps fill that gap in knowledge. Nearly half of newly diagnosed breast cancer patients showed high levels of emotional distress or met the criteria for psychiatric disorders, found DMS psychologist Mark Hegel, Ph.D., and his collaborators. "Future research should refine current screening procedures and develop interventions," they say.

DMS's Samuel Finlayson, M.D., was invited by the *Journal of the American Medical Association* to write an editorial on a study of where minorities and the uninsured get surgery.

Gender gap persists in physician income

Name a medical specialty in which female physicians generally make as much as males: Ob-gyn, you say? Pediatrics? Psychiatry, perhaps? Wrong on all counts, according to several recent DMS studies on how gender and race influence doctors' income.

"In every specialty we looked at, when compared to their white male counterparts, white females make about 15 to 20 percent less income after correcting for a variety of factors," says William Weeks, M.D., M.B.A. Race seemed to have a less dramatic effect, with black males tending to make less than white males but more than females of either race.

Disparity: Weeks's research partner (and wife), Amy Wallace, M.D., M.P.H., says the consistency of the income disparity surprised them. In ob-gyn, she says, "we anticipated no difference [between males and females], because patients prefer females and they probably account now for at least half of the field—so it is really surprising that they don't make more."

Weeks and Wallace, who have appointments in DMS's Department of Psychiatry and are members of the VA Outcomes Group, have now studied about a dozen specialties. Their three latest studies—on ob-gyn, general surgery, and diagnostic radiology—were published in 2006 issues of *Obstetrics & Gynecology*, the *Journal of the American College of Surgeons*, and *Academic Radiology*.

They draw their data from phone surveys conducted in the 1990s by the American Medical Association. In ob-gyn, for example, the weighted sample included 709 white males, 162 white females, 40 black males, and 26 black females—all in nonfederal, office-based practices.

Adjusted: The researchers then adjust for such factors as years in practice, hours worked, type of patients, board certification, and practice ownership. This is important because females tend to work fewer hours, are more likely to be nonowners, and are less likely to be board-certified than white males. Black males, though, typically report working more hours than white males and disproportionately serving the medically indigent.

Weeks and Wallace were surprised not only by the consistency of the gender gap, but also by the relatively low disparity between black males and white males. In their paper on general surgeons, for example, they noted that black males had lower incomes, "but not substantially so." Says Wallace, "We expected that race would make more of a difference than it did, but it turns out that gender's really most important."

The strength of these studies, the researchers say, is that they looked nationally at a range of specialties. "We took a chance cutting [the data] into so many slices, because every time you lose numbers you lose the opportunity for statistical significance," Wallace concedes. But the consistency of their findings allays that concern. They hope this work will inspire further probing into the "whys" of the income disparities. "It is disconcerting," Weeks says, "that women go through the same long training period, work the same long hours, but seem to be getting short shrift on income." James DiClerico

For every $1,000 in adjusted income that the average white male ob-gyn earns, a white woman makes $837 and a black woman makes $850.

Mighty mouse

DMS scientists have created a mouse that can exercise three times as long as a normal mouse, without any particular training. The key to the mouse's might is a genetic mutation that appears to increase glycogen content in skeletal muscle. Published in the *American Journal of Physiology: Endocrinology and Metabolism*, the research has implications for anyone with a muscle disease—and especially the elderly, who often have deteriorating muscles, Lee Witters, M.D., recently explained in a Dartmouth press release. "We now wonder if it's possible to achieve . . . muscular fitness without having to exercise," he added.

Cellular call

It's well known that embryos generate stem cells, but the precursor tissues of the placenta and umbilical cord may, too—at least in mice—according to new research from DMS. Stem cells that can differentiate into a wide variety of blood cells seem to originate in the tissues that form the placenta and umbilical cord, rather than migrating from the embryo, found the researchers, led by biochemist Nancy Speck, Ph.D. In their paper, published in *Development*, they do not comment on how their findings may affect the national stem-cell debate but call for more research into the area.

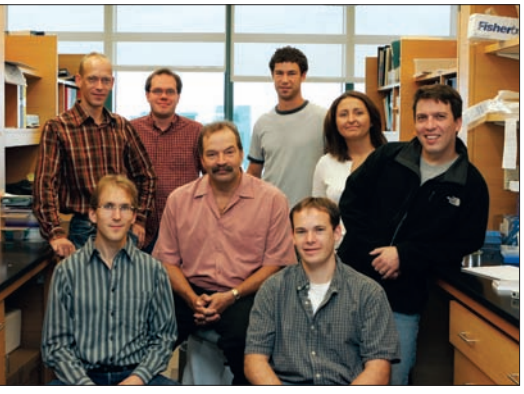
After adjusting for physical activity, DMS researchers found that children with a TV in their bedroom are more apt to be overweight; they studied 2,343 children aged 9 to 12.

A new role is discovered for mast cells

Mast cells usually get a bad rap, as the culprits behind allergies and asthma symptoms. But their reputation got a boost recently, when DMS researchers discovered that they play a crucial role in transplantation tolerance.

Blue: Mast cells, it turns out, are a bit like Jekyll and Hyde. In some situations, like during an allergic reaction, they promote inflammation and immune responses; in other situations, however, they do just the opposite. This finding is "so out of the blue!" says Dartmouth immunologist Randolph Noelle, Ph.D., who heads the lab that made the discovery.

For many years, Noelle's lab has been studying how the body rejects or accepts a transplanted organ or skin graft, and they've found a way to induce transplant tolerance in mice. "We can do a skin graft on a mouse and have it stay forever," says Noelle, without the mouse's immune system attacking the foreign skin and without the long-term use of immunosuppressive drugs. Prolonged tolerance, they noticed, was associated with two types of immune cells—regulatory T-cells and mast cells. But what were mast cells—known for promoting strong immune responses—doing in a place that was protected from immune system attacks, they wondered?



JOSEPH MEHLING

Randy Noelle—center, surrounded by members of his lab—had a paper on mast cells in *Nature*.

The researchers hypothesized that the mast cells were actually suppressing inflammation and protecting the graft. To test this theory, they tried inducing prolonged graft tolerance in mice that were deficient in mast cells. The grafts didn't take. The team then tested whether injecting such mice with lab-grown mast cells—prior to the graft transplant and the immunosuppressive treatment—made a difference. It did. These mice were able to maintain their grafts twice as long. Although other factors may be involved, "these results strongly suggest an indispensable role for mast cells" in skin transplant tolerance, Noelle and his team wrote recently in *Nature*.

The results may also explain "why mast cells are located in very specific sites within tissues (for example, nerves, vessels, hair follicles, or epithelia)," wrote a University of Oxford immunologist in an accompanying editorial. "Also, is it possible that the mast cells found within tumours contribute some immune privilege?"

Heal: High concentrations of mast cells in certain tumors often indicate a bad prognosis, Noelle explains. And other research has suggested that mast cells promote blood vessel growth and tissue remodeling—both of which help tumors grow. "What [the mast cells] are trying to do is wound heal," says Noelle. In the case of a transplant, dampening inflammation, facilitating blood vessel growth, and assisting in tissue remodeling are helpful. In cancer, those actions are anything but.

Noelle's team is now searching for molecular targets that could be used to shut down mast cell accumulation in tumors. They're also working with DHMC transplant surgeons to see if what they've found in mice correlates with what happens in humans. "We're not mast cell people," Noelle says, so "a number of us are completely retooling." JENNIFER DURGIN

Deliverables

Women who develop gestational diabetes mellitus (GDM) "are at increased risk of persistent glucose intolerance after delivery, and yet many are not retested" after giving birth, researchers at Dartmouth and Brown discovered recently. They found that less than half of women with GDM got postpartum glucose testing, but more than a third of those who did had abnormal glucose tolerance. "With the magnitude of the public health problem posed by the rising incidence of diabetes in the United States, further attention needs to be given to these high-risk women," the authors conclude in the journal *Obstetrics and Gynecology*.

Pumping iron

Since "iron deficiency is a major human nutritional problem wherever plant-based diets are common"—as Dartmouth researcher Mary Lou Guerinot, Ph.D., and her colleagues noted in the journal *Science*—learning how and where plants store iron may one day help scientists engineer more nutritious food sources. And Guerinot and her team have made such a discovery. "We have uncovered a fundamental aspect of seed biology that will ultimately aid the development of nutrient-rich seed," they wrote, to the benefit of "both human health and agricultural productivity." ■