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DMS DIGEST

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New Students Receive Medicine Cloaks

Dartmouth Medical School welcomed 75 first-year students into the medical profession with white coats, a hallmark of becoming a physician, September 15, in Kellogg Auditorium.

DMS Dean John Baldwin, MD, called the transition to medical school significant and different from previous educational experience. You are not quite a student, not quite a



Jeffrey Barrett dons his new coat, helped by Sue Ann Hennessy, assistant dean for student affairs.

doctor. It is "sometimes daunting and discouraging. It is highly experiential and depends on being there," he said.

Future physicians must demonstrate the ability to listen, discern, understand — not judge, not offer advice in areas unknown.

"Sometimes the best and the only salient role as a doctor is just to be there, to listen, to suffer sometimes. This is

just as important as using the technological knowledge you have gained. . . . We as physicians are fortunate to have as much to do with people as we do, to glean profound information about their basic selves, to invade their bodies, to share, to make a difference. Patients have given us this opportunity, this reason to be, this chance to be helpful." He urged, "Be grateful to your patients."

Associate Dean David Nierenberg, MD, followed on the meaning of a white coat: "It identifies one as a



DMS dean John Baldwin congratulates Trevor Braden, who is about to receive his white coat.

member of a profession. It identifies medical students and staff to patients. It symbolizes cleanliness. It implies the struggle to attain a certain level of skill and proficiency. "Wearing the white coat", he continued, "one should focus on

six concepts, the fundamentals of good medicine: altruism, accountability, confidentiality, sense of duty, honor and integrity, and respect for others." He concluded, "I want each of you to decide what your coat means to you, where and when to wear it. I hope it will represent a commitment to yourself, your classmates, your school, the medical community and your patients."

Each coat bore a pin from the Arnold P. Gold Foundation, representing humanism in medicine.

Dartmouth Named for Health Readiness

Dartmouth has been designated a national Center for Public Health Preparedness, one of five to play key roles in a comprehensive network to strengthen the country's front line against health threats, including epidemics and terrorist attacks. The new centers, established through the Centers of Disease Control and Prevention, are major components of an integrated national system to assure public health readiness. Two, including Dartmouth, are "specialty" centers, recognized for a particular expertise.

Dartmouth Medical School's pioneering Interactive Media Laboratory (IML) will be the leader for applied communications technology. It will provide specialized knowledge, research, educational and production support in computers and Internet applications for public health education and training.

"It is an honor and a tribute to the excellence of our information technology resources that Dartmouth has been selected to contribute to this mission that benefits public health and medicine," said DMS Dean John Baldwin, MD.

The IML, headed by Joseph V. Henderson, MD, associate professor of community and family medicine, has a record of cutting-edge interactive education and a long-time focus on E-learning (or distance learning). Dartmouth's new center will continue to research and develop E-learning models for the public health workforce that keep pace with the rapid technological evolution of computers and the Internet. "Professional education in public health will be increasingly facilitated by computers capable of displaying combinations of text, graphics, video and sound; broadband networks capable of delivering these multiple media to the home or office; and new methods for using these technologies for education and training," Henderson said. The laboratory is developing a prototype E-learning system for public health professional education that will be accessible on demand from any location worldwide.

Henderson calls the new center a "Collaboratory for Applied Communication Technology." It will provide a "virtual" forum to share E-learning ideas, information and experiences that help foster a community of developers, and house an interdisciplinary, core faculty at Dartmouth who will offer workshops at different locations and on the Internet. It will also produce exemplar E-learning programs for public health professionals and students, enabling learners to gain practical experience while creating useful programs.

Work Offers Insight into Childhood Brain Disease

Research at DMS has paved the way for exploring connections between cholesterol metabolism, brain function and possibly other neurodegenerative diseases. Scientists have found a link between the abnormal cholesterol metabolism observed in Niemann-Pick Type C (NP-C) disease and the degenerative changes that occur in the brain during this fatal hereditary disorder. Their work shows for the first time how a defect in cholesterol metabolism affects the response of live nerve cells to specific growth factors.

They detailed studies in mice that have a naturally occurring genetic mutation in the same gene associated with NP-C disease in humans in a June *Journal of Biological Chemistry*. These mice undergo many of the same pathological changes as human patients, including loss of motor coordination, seizures and premature death. Authors Robert Maue, PhD, and Leslie Henderson, PhD, associate professors of physiology and of biochemistry, who have a long standing interest in neuronal development, teamed up with TY Chang, PhD, professor and chair of biochemistry, an expert in cholesterol trafficking. Other authors were Anita Prasad, PhD (postdoctoral fellow), Colleen Paul (graduate student), and Li Lin (technician).

Their results, demonstrating that the functional deficits are already evident in the embryonic nervous system, emphasize the need for early identification and preventive treatment. In related work, Henderson and Maue have detailed the pattern of NP-C gene expression in the mouse brain (published in the September *Journal of Neurochemistry*), which could help pinpoint locations to target for treatment.

NP-C disease is a relatively rare disorder that affects an estimated 1 in 150,000 children who inherit a defective gene from both parents. While signs of nervous system dysfunction begin gradually and often are undetected until early childhood, the deterioration is relentless and most patients don't survive past their teens. The symptoms can be variable, making the diagnosis difficult. Even with the recent cloning of the gene (which encodes for a protein of unknown function), genetic screening for the condition is complicated and still in early development.

"In these young patients, the brain is slowly falling apart," Maue said. "We knew there was cholesterol accumulation in peripheral organs like the liver and spleen, and it was generally believed that this was a problem in the delivery system that moves cholesterol around in cells; so it was believed that in the brain it would be similar to a lipid storage disease. Still, no one saw cholesterol buildup in the brain and it was puzzling. It's like coming upon a car wreck; you see ten cars piled up, but don't know how it got started. We were looking for what triggered the wreck."

After determining that nerve cells from mice with the mutant gene did exhibit abnormal cholesterol metabolism, the researchers zeroed in on neuronal growth factors, which keep cells alive. "Without these factors, nerve cells in the brain essentially wither away and die," said Maue. Embryonic neurons from NP-C mice, they discovered, do not respond normally to brain-derived neurotrophic factor (BDNF), a factor important in nervous system development and maintenance. Specifically, they found that the receptor for BDNF was not being activated; somehow the abnormal cholesterol distribution interfered with the ability of the receptor to generate signals when the growth factor bound to it.

The researchers suggest that the problem may lie with microdomains, or lipid rafts, afloat in the cell membrane. These rafts appear to have elevated cholesterol levels and are thought to contain clusters of membrane proteins. One theory, Maue said, is that growth factor receptors also rest among these raft proteins, making it easier for them to interact with each other and generate signals. It is possible that the cholesterol abnormalities in NP-C mice nerve cells alter the lipid rafts in their cell membranes and interfere with the signals the receptors for BDNF generate.

Henderson and Maue are also using the NP-C mouse model to explore the potential for viral-mediated gene therapy in NP-C disease and pediatric brain disease. They have received support from the Ara Parseghian Medical Research Foundation and National Niemann-Pick Disease Foundation.

Emergency Response System Put In Place

DMS has installed a portable heart defibrillator on the third floor of Remsen for medical emergencies. It has also updated medical emergency response procedures and broadened education of faculty, students and staff in cardiopulmonary resuscitation (CPR). The automated external defibrillator (AED), with other rescue equipment, was recommended by a team set up last year to revamp and upgrade medical emergency readiness in the Remsen-Vail-Strasburgh, Dana Library and Gilman complex.

The goal is to maximize the ability to respond successfully, said Lee Witters, MD, professor of medicine and of biochemistry, who convened and led the committee. "We are a medical school and we should be prepared." He said it is important to heighten awareness of protocols and capabilities to respond among faculty, students and staff.

An October *New England Journal* reported that non medical personnel trained to use automated defibrillators can help save the lives of people who have sudden cardiac arrest, a major cause of death. Two studies, one at casinos, the other on airplanes, found increased survival rates when patients who suffered cardiac arrest were defibrillated almost immediately with the portable devices. A journal editorial called for making the defibrillators, which are simple to



Lee Witters (left) and Ryan Sahr display the portable defibrillator.

learn to operate, more available in public locations.

A laboratory environment requires an optimum level of safety and security. Moreover, the biomedical library and the increasing number of community programs or activities in the area bring a high volume of public traffic, including senior citizens. "We need to provide a reasonable rapid response for any visitor at this site," said Ryan Sahr, who heads the medical school's health education and rescue training community service (HEART).

"Defibrillators can be a lifesaving bridge during the first few critical minutes of a medical emergency until advanced life support providers arrive," Sahr explained. "They are becoming standard equipment in public venues so trained personnel can deliver defibrillation in the early crucial moments of a cardiac episode.

It makes sense because the technology is there and it is easy to use."

The defibrillator is centrally located in an alarmed first aid cabinet outside student affairs on Remsen 3. DMS personnel properly trained to use the device for sudden cardiac arrest may be called to respond, according to guidelines. The defibrillator station includes a users guide, appropriate first aid packs and a stocked trauma bag. DMS funded the \$3,500 ForeRunner defibrillator and will support training for graduate students in basic life support techniques with CPR and AED. Medical students and faculty physicians are already certified in CPR and many also for defibrillators.

The equipment and training were among recommendations the committee made to bring the DMS medical emergency program in line with the regional emergency response network, the latest technology and a college plan. Other suggestions call for increased awareness and wider training for all DMS personnel, better visibility and promotion of medical emergency response procedures and notification numbers.

For further information on training, e-mail Ryan Sahr at DMS.Heart@Dartmouth.edu. Sahr, AED coordinator, helps oversee guidelines for care of the first aid station and equipment with Alan Cook, DMS director of operations.

Photo by: Robert C. Nair

Medication Assists Elders with Mild Depression

For older people with mild depression, antidepressant medication improves symptoms faster than counseling or placebo, concluded the authors of an article published in a September *Journal of the American Medical Association*.

However, patients' overall improvement was modest after an 11-week course of medication, leading the authors to recommend a cautious approach to treating mild depression in elders. Primary authors include James Barrett, MD, and Thomas Oxman, MD, both of DMS.

Barrett was responsible for the overall direction and supervision of the \$2.5 million study, funded by the John A. Hartford Foundation of New York and the John D. and Catherine T. MacArthur Foundation of Chicago. Researchers studied 415 ethnically diverse patients over 60 with minor depression and dysthymia (mild, but long-term depression) in four cities: Lebanon, San Antonio, Seattle and Pittsburgh.

The study compared paroxetine (Paxil-SK Beecham) with problem-solving treatment-primary care (PST-PC). Mark Hegel, PhD, a DMS psychologist responsible for the PST-PC training in the study, said, "PST has the potential to be widely used because nurses and other primary care clinicians can learn the techniques and principles." It aims to help patients develop problem-solving skills.

New Tuberculosis Vaccine to be Tested

Infectious disease researchers from Dartmouth Medical School will begin a five-year study of tuberculosis (TB) and HIV infection in Africa early next year, with a \$2.4 million grant from the National Institutes of Health. They will explore why many AIDS patients in Africa develop a severe TB that spreads through the bloodstream and attempt to prevent it with a new booster vaccine. This complication, disseminated tuberculosis, has been found in 15 to 20% of persons dying with AIDS in developing countries.

In the early 1990s, Dartmouth investigators and colleagues in London and Kenya studying hospitalized AIDS patients in Africa, were surprised to find that 23% of patients dying with AIDS also had tuberculosis in the bloodstream, said principal investigator Ford von Reyn, MD, professor of medicine and chief of infectious disease. Subsequently, Dartmouth and other researchers documented similar complication rates in other developing countries.

Dartmouth investigators in Zambia showed that 12% of hospitalized AIDS patients had disseminated TB, said Richard Waddell, DSc, research assistant professor of medicine, who directed the study. Because symptoms were similar to advanced AIDS, TB was not recognized and many patients died before discharge.

The study in Dar es Salaam, Tanzania, with collaborators from Muhimbili Hospital Medical Center,

will test over 2,000 early HIV-infected patients for TB immunity, then follow them to determine risk factors for disseminated TB. "A principal objective is to determine why this complication develops in some patients, but not others, and to see if it can be prevented," said von Reyn.

Another objective is to determine if a new booster vaccine can prevent disseminated tuberculosis in AIDS patients. Dartmouth has pilot tested the vaccine — Mycobacterium vaccae, developed at SR Pharma plc in London — in the US, Finland and Zambia. It appeared to act as a booster vaccine in Zambian adults who had received the standard BCG vaccine against TB in childhood. BCG, a live vaccine, could not be safely re-administered to enhance TB immunity in adults with known HIV infection, explained von Reyn. However, M. vaccae is a killed vaccine, similar to vaccines used effectively to prevent tuberculosis before BCG was developed. Dartmouth researchers hope that multiple doses of the inactivated M. vaccae will boost immunity against TB in those with HIV. Patients will receive either five doses of the new vaccine or five doses of placebo over 12-months and be followed every three months to detect and treat TB and to determine if the vaccine reduces TB risk.

Dartmouth co-investigators are Waddell and Bernard Cole, PhD, assistant professor of community and family medicine.

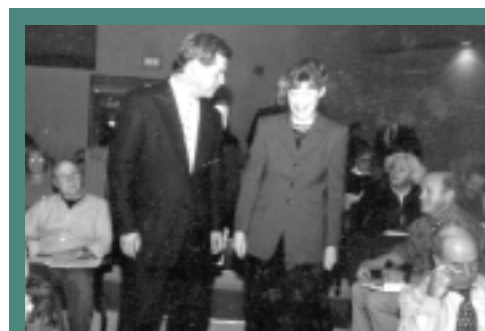
AHEC Support Renewed

The New Hampshire Area Health Education Center (AHEC) program was awarded \$3.9 million for continued support by the Health Resources and Services Administration for three years, effective October. A statewide consortium of academic and community programs headquartered at Dartmouth Medical School, the AHEC was established in 1997 to help increase health care access by enhancing distribution, quality and diversity of the health care work force.

"Dartmouth is gratified to serve the people of New Hampshire as a health care resource, and especially pleased to continue our productive collaboration in health education with partners throughout the state," said John C. Baldwin, MD, DMS dean. "We are honored to be deeply involved in the provision of health care, in the discovery of better health care practices and in the education of the citizens, patients, students and physicians of New Hampshire."

New Hampshire Senator Judd Gregg said, "This grant renewal brings us closer to meeting the health care needs of the people of New Hampshire. Providing information and educational materials about health care will help improve the delivery of health care services in our state."

Two centers — the Southern New Hampshire AHEC in Raymond and the Northern New Hampshire AHEC in Littleton — provide continuing education, library services, practice improvement, health careers recruitment and training. "This support will allow the AHEC to make a significant investment in development of the health care work force in New Hampshire over the next three years and to be an active partner in meeting the objectives of Healthy New Hampshire 2010," said Rosemary Orgren, PhD, who heads the AHEC program office.



Dartmouth Community Medical School on the Road — DMS Dean John C. Baldwin, MD, welcomed New Hampshire Governor Jeanne Shaheen, who opened the DCMS fall series in Manchester. She discussed state efforts to improve services for drug and alcohol addiction in the session, "Addiction: Gaining New Insights, Fighting Old Biases." Almost 200 enrolled in the course, "Medicine 2000 — New Options, Hard Choices."

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