A dose of good sense: Accounting for genetics

The FDA has only recently modified in June 2005 to indicate that patients who are homozygous for a specific allele of the gene that produces UGT1A1 (whose full name is UDP-glucuronosyl transferase 1A1) should receive a lower dose of the drug. This recommendation was based on the observation that UGT1A1, an enzyme involved in breaking down the active metabolite of Camptosar, shows reduced activity in about 10% of the population, those who have a specific form of the gene for UGT1A1.

When such patients receive a standard dose of Camptosar, the metabolite accumulates in their plasma, potentially exposing them to toxic levels of the drug. By doing a genetic test prior to treatment, physicians can identify patients at risk of drug toxicity and treat them with a lower dose of the drug.

**Assay:** The company that developed the UGT1A1 assay offered Dartmouth a chance to pioneer its use based on earlier successful collaborations, says Dr. Gregory Tsongalis, director of DHMC’s Molecular Pathology Laboratory. About 20 to 30 assays were performed in the first six weeks, and Tsongalis expects the numbers to grow. "Many inquiries are coming through the patients themselves," he notes.

The program fits in well with the overall development of pharmacogenetics in the Department of Pathology. Tsongalis says the department has several other genetic screening tests under development; he hopes that the

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**Not Asleep at the Wheel**

The nation faces a “Yawning gap in sleep care,” according to a wag of a headline writer at USA Today. Narrowing that gap — getting out the word that behavioral therapy can be more effective than heavily advertised sleeping pills—is no laughing matter to the nation’s 25 million chronic insomniacs, however. But thanks to Michael Sateia, M.D., chief of sleep disorders at DHMC and immediate past president of the American Academy of Sleep Medicine (AASM), there’s some progress.

Sleeping pills can be a reasonable solution for occasional insomnia, Sateia told USA Today, but behavioral modification is the best solution for long-term sleep problems. Sleep specialists don’t have the deep pockets of pharmaceutical companies to promote the concept, however. But one of the achievements of Sateia’s term in the AASM presidency was launching a program to improve awareness of and access to behavioral sleep therapy.

Other achievements of his term in office included gaining national approval for a specialty exam in sleep medicine; revising the international manual of sleep disorders; launching the Journal of Clinical Sleep Medicine; and initiating a public education program (see www.sleepeducation.com). But, from the sound of that list, perhaps not getting a lot of sleep. A.S.

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**Reinforcing Family Values**

Number of doctors in Kenya's first family medicine residency program: Nine. Population of Kenya: 34 million. Having a family medicine program based in Kenya that trains Kenyans: priceless—or at least that’s the conclusion that Kevin Shannon, an assistant professor of community and family medicine at DMS, has come to.

“There were already medicine, pediatrics, and surgery residents being trained” in Kenya, says Shannon, who is the coordinator of the new program, which began in 2005 and is a joint endeavor between Kenya’s Moi University and Kijabe Hospital. “But the needs of rural areas and city slums have not been met by those [specialties],” he continues. “Family medicine is the specialty with adequate breadth and quality to be able to make a difference in the life and health of Kenyans across the country,” Shannon plans to head the residency at Kijabe Hospital through 2007.

J.D.
UGT1A1 assay will be only the first of an array of screenings.

Meanwhile, the FDA is rethinking how variability in drug response should be factored into the approval process for new drugs. The FDA would like to see genetic screening used to define more precisely those who will receive maximal effect from, or be endangered by, a particular drug. Yet not all of the parties involved in the approval process are happy with this approach.

Detect: For example, Aczone, a new drug for acne, received FDA approval in July 2005. As a condition of its approval, the FDA stipulated that potential patients be screened to detect if they have a specific enzyme deficiency that could predispose them to developing hemolytic anemia while they’re taking the drug. But the manufacturers of Aczone view genetic testing requirements as an attempt to limit the population of patients who can be prescribed their product and challenged the FDA decision. They are arguing that the at-risk population is very small and that anemia was not seen during preapproval trials.

Yet Tsongalis and others feel that the benefit to patients outweighs such concerns. Furthermore, he suggests that genetic screening might even work to drug-makers’ benefit. “Right now certain patient populations that could benefit from a drug are excluded based on the population response,” he says. “Genetic testing could open up new markets for drugs that would not have been approved otherwise.”

Joseph Melton, Ph.D.

Guided imagery wins converts at DHMC

When a pillar of academic medicine—Dr. William Nugent, a distinguished cardiovascular surgeon—calls his discovery of guided imagery “an epiphany,” people sit up and take notice. A technique that used to be on the fringes of respectability, it is gaining converts daily.

Guided imagery incorporates the power of the mind to help the body heal, maintain health, or relax. Involving a combination of touch, smell, sight, and sound, it aims to forge a balance between mind, body, and spirit. Proponents say that tapping into the mind-body connection can strengthen the immune system, reduce anxiety, ease pain, and improve sleep.

Sheila Harvey Tanzer of Hanover, N.H., has used guided imagery as a patient. “In 1993,” she says, “Dr. Richard Barth removed 18 inches of my colon. The night I went home, my abdominal pain sent me right back to DHMC. Dr. Barth said adhesions had caused a small bowel obstruction. If it didn’t straighten out in a week, he would have to operate again.”

The next day Briane Pinkson, a DHMC nurse and massage therapist, showed up and introduced Tanzer to guided imagery. “Close your eyes,” Tanzer recalls her saying. “Breathe deeply. Imagine you are half an inch tall. With a lamp in your hand, enter your intestines and walk through the twists and turns step by step. Keep going until you come out into the light. Then repeat.”

Eight days later, Tanzer was wheeled in for another x-ray. Afterward, she recalls Barth reporting, “Your obstruction isn’t just better. It is gone.”

Improving: Nugent seems an unlikely proponent of guided imagery. The walls of his office are lined with diplomas and certificates from prestigious institutions. “About 10 years ago,” he says, “I was leading teams from dozens of hospitals in a forum devoted to improving patient health care and healing. . . . Someone handed me a guided imagery CD. I listened to it that night in my hotel room. For me, it was an epiphany.” The CD had been produced by Diane Tusek, B.S.N., former director of guided imagery at the Cleveland Clinic and the founder of Guided Imagery, Inc.

Today, Nugent, who is chief of cardiothoracic surgery, has Tusek’s CD given to all the section’s patients before surgery. Tusek recalls Nugent telling her about the day he walked into the prep area at DHMC and saw his patients wearing head-phones and the others without them. He said to himself, “All patients must have this help.” Tusek says Nugent was one of the first doctors to “step out of the box.”

A decade later, guided imagery is increasingly accepted in mainstream medicine. Two studies affirming its value have been conducted at Harvard teaching hospitals. And a Blue Shield of California study found that guided imagery increased patient satisfaction and cut costs by $2,000 per patient. But the data is still soft. A senior editor at the New England Journal of Medicine admitted recently that “guided imagery is a recognized form of relaxation and pain control,” though its value “is difficult to quantify in tests.”

Study: Nugent, asked if he had considered conducting a study himself, replies, “I should do it, but right now surgery absorbs all my time.”

Tanzer reflects on her experience with guided imagery. “I still wonder about it,” she says. “Something happened, I don’t know what. . . . I continue to use meditation and visualization, and this daily discipline has deepened my inner peace—a gift as invaluable in good health as it is in a time of sickness.”

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A decade