

## Measuring medication response

**T**reating depression in children and adolescents is a delicate business. It can involve counseling, cognitive behavioral therapy, the administration of antidepressant medications, or a combination of those therapies. If one type of medication doesn't work, the clinician may switch to another. But it may be weeks before an antidepressant shows any effect.

**Disorder:** Recently, Dartmouth child psychiatrist Craig Donnelly, M.D., led the first study to explore certain differences in how an antidepressant affects children versus adolescents with major depressive disorder. He reported, in the October 2006 issue of the *Journal of the American Academy of Child and Adolescent Psychiatry*, that preteens respond more quickly to sertraline (Zoloft) than adolescents do.

"I think the value of this study was to show that preteens were perhaps more sensitive to the effect of medicine," says Donnelly. He was not surprised by the results, however. "I think that child clinicians have for years assumed that younger children and children with other kinds of neurological issues—like mental retardation or autistic spectrum disorders or neurological syndromes—have more sensitive brains, more sensitive central nervous systems."

The 10-week, randomized, double-blind, placebo-controlled study included 177 children aged 6 to 11 and 199 adolescents aged 12 to 17. The children had an initial response to sertraline after about two weeks and a persistent response after four weeks; the adolescents had an initial response after about three weeks and a persistent response after 4.5 weeks. The findings will be useful for clinicians, parents, and patients, Donnelly feels. "If you're three or four weeks in with a pre-teen using this medicine and you're not seeing any beneficial effect, then it may be time to think about switching out or to adding in cognitive behavioral therapy or altering your treatment plan."

Some 7 million to 12 million children in the United States suffer from mental health disorders, according to the U.S. Department of Health and Human Services. As many as one in 33 children—and one in eight adolescents—may have clinical depression.

**Risk:** Yet many people fear using antidepressants in this population because they are associated with a risk of suicide. "But not treating major depression has huge risks," says Donnelly. Twenty percent of people with untreated major depression die by their own hand, he points out, and the increased use of antidepressants has resulted in a drop in the number of suicides. "What I tell parents is that the mortality and morbidity risk of major depression in childhood and adolescents far outweighs the risk the medication induces."

Donnelly also studied another antidepressant, in what he says is the largest federally funded, multisite autism treatment trial ever conducted in the U.S. He expects the results to be published within the next year. Funding for the sertraline trials was provided by Pfizer, Inc., the manufacturer of Zoloft.

Laura Stephenson Carter



Avoiding too much sun exposure remains the best way to prevent skin cancer.

## No new light regarding skin cancer

**M**ight aspirin, with its growing record of benefit to heart and colon health, also protect against common skin cancers? Not to any great extent was the conclusion of a recent study by researchers in DMS's Department of Community and Family Medicine.

Maria Grau, M.D., M.P.H., was the first author on the paper, which was published in the *International Journal of Cancer*. "Our results indicated only a weak and inconsistent preventive effect of aspirin and other nonsteroidal anti-inflammatory drugs [NSAIDs] against non-melanoma skin cancers," she explains. The study focused on basal cell cancer and squamous cell cancer (BCC/SCC), two common forms of skin cancer. Earlier experimental studies had consistently shown NSAIDs as having a protective effect against BCC/SCC, but this new epidemiological study provided little indication of an impact.

**Data:** Working with Grau on the study were John Baron, M.D., and Margaret Karagas, Ph.D. The team gleaned data on NSAID use from 1,805 subjects enrolled in a skin cancer trial that ran from 1983 to 1989. Its original purpose was to look at the effect on BCC/SCC of beta-carotene; subjects all had had a BCC and/or SCC in the previous three years and were randomized to receive either beta-carotene or a placebo. Data on their use of other medications, including NSAIDs, was collected quarterly; 1,256 of the subjects (about 70% of the total) reported NSAID use at least once. So the team decided to look at the data again to see if NSAIDs conferred any protection against a recurrence of BCC/SCC. But after controlling for assorted variables, there was only a "modest, insignificant reduction" in BCC/SCC among the subjects who reported taking NSAIDs.

The strength of the new analysis, say the authors, despite its equivocal finding, is that it was "the first to address the association between the use of aspirin and other NSAIDs and the risk of non-melanoma skin cancer in a closely monitored cohort of high-risk patients."

Unfortunately, the original aim of the study—to see if beta-carotene was effective at preventing skin cancer—did not prove out either. That means that "avoiding excessive exposure to the sun remains the most effective way to prevent skin cancer," concludes Baron. The conundrum, he adds wryly, is that sunlight delivers vitamin D, which is a known cancer preventative.

James DiClerico