



Dartmouth transplant surgeon David Axelrod, M.D., analyzed the cost of transplanting “marginal” versus “ideal” donated livers. On average, marginal organs cost \$84,000 more.

## Long-term study puts folate to the acid test

**F**olic acid, a B vitamin credited with building strong spines in infants, may have a dark side for colorectal health in adults. A decade-long study by the Polyp Prevention Study Group (PPSG), a consortium of researchers at Dartmouth and several other medical centers, found that people who took supplemental folic acid had at least as many adenomas—precursors of most colorectal cancers—as those who took a placebo.

**Tumors:** Epidemiological and animal studies have suggested that folic acid may inhibit the formation of tumors in the large intestine. Testing that hypothesis, the investigators discovered instead that giving folic acid to people with a history of adenomas had no more preventive effect than a placebo—and maybe less. The *Journal of the American Medical Association (JAMA)* published the study in its June 6 issue and also made it the subject of a JAMA Reports video news release.

Of 1,021 men and women aged 21 to 80 who enrolled in the study in 1994, almost 97% had a colonoscopy within three years. At least one adenoma was found in 44.1% of those taking 1 mg a day of folic acid, and in 42.4% of those taking the placebo. The incidence of an advanced lesion was 11.4% on folic acid and 8.6% on placebo. A few years later, the gaps between the two groups had widened.

DMS epidemiologist John Baron, M.D., the study’s lead investigator, calls the double-blind trial “very strong” in showing that folic acid does not decrease the risk of adenomas in people with previous tumors. But he said the results did not unequivocally show that folic acid increases adenoma risk. The paper, whose lead author was DMS’s Bernard Cole, Ph.D., said “evidence for an increased risk of adenomas . . . requires further research.”

The interest in further study stems from a 1996 U.S. law that mandated folic

acid fortification of enriched flour and uncooked cereal grains by 1998. Canada passed similar legislation in 1998. There has been strong evidence that the laws’ goal—reducing neural tube defects, spina bifida, and anencephaly in newborns—is being met. Some scientists had posited that fortification might also help reduce colorectal and other cancers.

However, an observational study in the July issue of *Cancer Epidemiology, Biomarkers & Prevention* offers compelling support of the PPSG conclusion. This study overlaid the timelines of folic acid fortification and of colorectal cancer incidence in the U.S. and Canada. It found that a steady decline in such cancers before fortification turned to an increase after that point. The finding didn’t surprise Baron. “Folate is a food for cancer,” he says. “Some of the earliest chemotherapeutic regimens [were designed to] block folate utilization.”

**Range:** So how much folate is too much? Baron chooses not to be an alarmist. “For most people, I’m guessing that fortification won’t be harmful,” he says. “But suppose you get a guy who eats breakfast cereal, likes bread, and takes multivitamins [with folic acid]? Now you’re getting to a range . . . [with] relatively little margin for safety.”

JAMES DICLERICO



Folic acid doesn’t foster colon health, found Baron.

### Breast stroke

Pre-menopausal women with very dense breasts are twice as likely to develop ductal carcinoma in situ (DCIS), an early form of breast cancer, as pre-menopausal women with scattered-density breasts. That’s according to a DMS-led study of data in the New Hampshire and Vermont mammography registries. “Our study,” wrote the investigators in *Cancer Causes and Control*, “is the first prospective assessment of breast density in relation to risk of DCIS, and the only study to separately examine the influence of density in premenopausal and postmenopausal women.”



### Chemobrain question

A study in rats has shed light on “chemobrain”—the mild cognitive impairment that many cancer patients feel after chemotherapy treatment. Working with DMS faculty, Dartmouth College grad student Jill MacLeod examined the effects of a standard breast cancer chemo regimen on learning and memory in rats. She found that rats treated with cyclophosphamide and doxorubicin had difficulty remembering some types of information. Her results, published in *Behavioural Brain Research*, suggest the drugs “may have toxic effects on the hippocampus” and cause “specific learning deficits shortly after treatment has ended.”

