

[IMAGE]

## Fight Colorectal Cancer With Folic Acid

By James P. Meschino, DC, MS

Colorectal cancer (CRC) is the second most common cause of cancer mortality in the U.S. and Canada. Although genetic susceptibility plays a role in the etiology of CRC, dietary factors, including certain vitamins, have also been shown to influence the development of the disease in various studies.

A ground-breaking study published in the *World Journal of Gastroenterology* in 2008 demonstrated that a daily dosage of 5 mg of the B vitamin folic acid resulted in a significant reduction in the recurrence of colorectal adenoma. Among the 94 subjects who completed the study (49 in the folic acid group and 45 in the placebo group), there was a threefold increase in polyp recurrences in the placebo group compared to the group receiving folic acid supplementation. The mean number of recurrent polyps (called *adenomas*) at three years was 0.36 (SD, 0.69) for the folic-acid-treated group compared to 0.82 (SD, 1.17) for the placebo-treated group. Of note, patients under 70 years of age and those with left-sided colonic adenomas, or advanced adenomas, responded the best to folic acid supplementation.

### Origin of Colorectal Adenoma and Colorectal Cancer

Colorectal tumors arise from unregulated cell proliferation of intestinal epithelial cells through a multistep process, with the first step usually being the formation of premalignant adenomas. As such, colorectal adenomas are classified as benign tumors, which comprise epithelial cells of glandular structures or have glandular characteristics, or both.

folic acid - Copyright © Stock Photo / Register Mark The colon has numerous glands within its tissues, which tend to be simple and tubular in appearance. These small glands are classified as glands because they secrete mucus into the lumen of the colon. The purpose of these glands is to absorb water from the feces back into the blood and to secrete mucus into the lumen of the colon to lubricate the dehydrated feces. Failure to lubricate the feces can result in colonic damage by the feces as it passes toward the rectum.

Although adenomas are benign, over time they can transform into malignant tumors, at which point they are called adenocarcinomas. Adenocarcinoma accounts for 98 percent of all colorectal cancers. Adenomas of the colon, also called adenomatous polyps, are quite prevalent, especially after age 60. They are found

commonly at colonoscopy, upon which they are removed because of their tendency to become malignant.

The different types of colorectal adenomas include:

- Tubular adenoma
- Tubulovillous adenoma
- Villous adenoma
- Sessile serrated adenoma

### **How Folic Acid Prevents Adenoma Recurrence**

Studies have provided various clues as to how folic acid may prevent CRC and prevent recurrence of colorectal adenoma. In the 2008 study, it was suggested that the increased responsiveness of these subjects may have been due to greater tissue accumulation of folic acid. This is based on previous studies showing that mucosal folate levels may be a determining factor in the development of adenomas. Researchers have demonstrated that the levels of folate in adenoma, carcinoma, as well as normal-appearing adjacent mucosa, are lower than in corresponding polyp-free control subjects.

### **Are You at Risk for Deficiency?**

A low serum folic acid level (<4 ng/ml of serum) is where chromosome breaks have been seen.<sup>11</sup> The normal range for serum folate is 7-40 nmol/L, and the normal red blood cell folate reference range is 360-1,400 nmol/L, which is a direct measure of tissue folate stores.

Individuals at high risk for folic acid deficiency or marginal deficiency include women of childbearing age and non-Hispanic black women. Even when intake of folic acid from dietary supplements is included, 19 percent of female adolescents ages 14-18 years and 17 percent of women ages 19-30 years do not meet the Estimated Average Requirement (EAR) for folic acid intake. Additionally, 23 percent of non-Hispanic black women have inadequate total intake, compared with 13 percent of non-Hispanic white women.

Research has also shown that certain drugs, such as methotrexate, levopoda, niacin, phenytoin (Dilantin), carbamazepine, and theophylline, can markedly reduce folate levels in the body. Other well-documented factors that deplete folic acid include alcohol intake (even moderate amounts) and cigarette smoking.

### **Key Points to Discuss With Your Doctor**

Researchers leading the 2008 study concluded, "Our data, for the first time, show that the daily consumption of a high dose of folic acid over a period of 3 years prevents the recurrence of colorectal adenomas," adding that "none of the patients in the folate treatment group [was] found to have histologically aggressive adenomas or carcinoma at final endoscopy." They further indicated that the marked reduction in adenoma recurrence seen in this study could not be attributed to differences in other dietary or lifestyle factors, as all patients completed a detailed lifestyle questionnaire and nutritional assessment, with both study groups demonstrating statistically similar caloric, fiber, fat and protein intake, as well as similar baseline BMI, folate, B12 and calcium status. Additionally, the groups were similar with regard to aspirin use, and the number and type of adenoma at baseline.

Since colorectal cancer is an age-related disease typically diagnosed after the age of 50, any delay in the onset and subsequent progression of this disease through the use of dietary agents, such as folic acid, is likely to have significant health benefits.

In patients who have had previous colorectal adenoma, the groundbreaking 2008 study suggests supplementation with 5 mg per day of folic acid can help prevent colorectal adenoma recurrence by threefold compared to placebo. This research should be brought to the attention of all patients with a history of colorectal adenoma (those who have had colon polyps removed), as well as their attending physician / oncologist.

Finally, it is worth noting that prior to the folic acid food fortification program that commenced in January 1998, 15 percent of the U.S. adult population ingested less than the EAR for folic acid on a daily basis. The folate food fortification program has improved folate status significantly in recent years, but various groups remain at risk for suboptimal folate status, which may affect their risk of colorectal cancer.

It is also worth mentioning that a 19 percent reduction in neural-tube-defect birth prevalence occurred following folic acid fortification of the U.S. food supply. While some researchers have noted that factors other than fortification may have contributed to this decline, folic acid fortification is likely a main factor.

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**James Meschino, DC, MS**, practices in Toronto, Ontario, Canada and is the author of four nutrition books, including *The Meschino Optimal Living Program* and *Break the Weight Loss Barrier*.

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