

Abstract

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A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis.

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BACKGROUND: Nationwide fortification of enriched uncooked cereal grains with folic acid began in the United States and Canada in 1996 and 1997, respectively, and became mandatory in 1998. The rationale was to reduce the number of births complicated by neural tube defects. Concurrently, the United States and Canada experienced abrupt reversals of the downward trend in colorectal cancer (CRC) incidence that the two countries had enjoyed in the preceding decade: absolute rates of CRC began to increase in 1996 (United States) and 1998 (Canada), peaked in 1998 (United States) and 2000 (Canada), and have continued to exceed the pre-1996/1997 trends by 4 to 6 additional cases per 100,000 individuals.

DISCUSSION: In each country, the increase in CRC incidence from the prefortification trend falls significantly outside of the downward linear fit based on nonparametric 95% confidence intervals. The statistically significant increase in rates is also evident when the data for each country are analyzed separately for men and women. Changes in the rate of colorectal endoscopic procedures do not seem to account for this increase in CRC incidence. These observations alone do not prove causality but are consistent with the known effects of folate on existing neoplasms, as shown in both preclinical and clinical studies.

CONCLUSION: We therefore hypothesize that the institution of folic acid fortification may have been wholly or partly responsible for the observed increase in CRC rates in the mid-1990s. Further work is needed to definitively establish the nature of this relationship. In the meantime, deliberations about the institution or enhancement of fortification programs should be undertaken with these considerations in mind.

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