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**Issue:** Folic Acid and Vitamin B12 associated with increased  
risk of cancer and death in subjects with ischaemic  
heart disease in Norway

**Publication Date:** 18 November 2009

**Study conclusions:**

Analysis was conducted on the follow-up outcome from 2 randomised, placebo-controlled clinical trials. A total of 6,837 subjects with ischaemic heart disease were treated with B vitamins for a median of 39 months and 6,291 subjects completed 38 months of post-trial observational follow-up. Subjects were randomly assigned to receive one of the treatments:

1. Folic acid (0.8 mg/day), Vitamin B12 (cyanocobalamin; 0.4 mg/day) and Vitamin B6 (pyridoxine hydrochloride; 40 mg/day)
2. Folic acid (0.8 mg/day) plus Vitamin B12 (0.4 mg/day)
3. Vitamin B6 alone (40 mg/day)
4. Placebo

Treatment with folic acid plus vitamin B12 was associated with 21% increase in total cancer incidence, and 38% increase in cancer death and 18% increase in all-cause death.

**Response:**

1. The result derived from the post-study follow-up is not confirmatory. It should be noted that the 2 original studies were not designed to look into the association between folic acid and cancer. Further studies on intake of folic acid, Vitamin B12 and B6 in non-smoking population and in other geographical locations are necessary. The authors wrote in the Comment section that 'our findings need confirmation in other populations'. In conclusion, this study does not rule out the beneficial effect of folic acid as documented in the body of scientific literature.
2. From public health standpoint, the study provides another confirmation that smoking increases the risk of lung cancer. It is not clear as to why patients who were given high dose of folic acid were more likely to develop lung cancer than those in the control group.

It could be due to confounding factors in the folic acid supplemented group, such as lifestyle and occupational exposures that skewed the incidence of cancer to higher percentage. It is important to note that these results are inconsistent with the larger body of scientific literature. In fact, the authors themselves point out, 'Epidemiological studies have demonstrated no associations between intakes of folate or folic acid and lung cancer risk.' Other inconsistent findings include no effect of folic acid on either colorectal or prostate.

3. Taken in balance, considering the existing scientific data, consumers and health professionals should continue to feel confident in the safety and efficacy of consuming the recommended amounts of folic acid as part of healthy diet and lifestyle. IADSA concurs with the accompanying editorial in JAMA<sup>1</sup> which states that 'the findings do not nullify the potential long-term benefits that folic acid fortification may have on population health.'

18 November 2009

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#### Reference

1. Drake B, Colditz G. Assessing Cancer Prevention Studies—A Matter of Time. *Journal of the American Medical Association (JAMA)*. 2009; 302(19): 2152-2153.