



Colon cancer and dietary fat, phosphorus, and calcium in Hawaiian-Japanese men

Dear Sir:

In a recent paper, Heilbrun et al (1) reported an attempt to test the hypothesis of Newmark et al relating colon-cancer risk to a high level of dietary fat coupled with a high-dietary intake of dietary phosphate and a low intake of calcium (2). The authors found little support for the hypothesis in a cohort of Japanese men in Hawaii, however, they quite properly recognized a series of limitations in their study and indicated that they do not regard this study as a definitive test of the hypothesis.

We wish to point out a few additional limitations of their study as it relates to the hypothesis.

a) The population studied consisted of Japanese males born between 1900 and 1919, examined in 1965 to 1968, and under continuous surveillance since then. It is not stated if these men were born in Japan or Hawaii or how many years they resided in Hawaii. These factors would weigh heavily on their diet and life-style during their lifetimes. This is hardly representative of a Western population on a Western diet and life-style noted for its high-fat and phosphate-rich meat intake, which was the subject of the Newmark hypothesis.

b) The mean daily fat intake in the two groups of subjects in the study was ~69 and ~77 g. The high-fat daily intake group was 98 g, claimed to be 36.3% of total calories representing a total daily intake of ~2450 kcal. This is at the lower end of the US Recommended Daily Allowance of calories (2900 to 2400 kcal) for adult men age 19–75 (3). The fat intake, however, is considerably lower than the estimate for the US of up to 150 g/day (4).

c) The daily phosphorus intake of this study group is estimated at 1105–1172 mg, compared with 1500–1600 mg for the US (3). This lower phosphorus intake, coupled with the

lowered fat intake, suggests a lower meat intake than the mean for the US since meat represents a significant proportion of fat and phosphate in the average US diet.

d) The median daily calcium intake for both case (445 mg) and control subjects (501 mg) was well below the current US RDA of 800 mg (3) and less than half of the proposed RDA of 1200 mg. From the data of Table 1, < 25% of the subjects, both case and control, had an adequate intake. The study thus basically includes a large majority on inadequate calcium intake, in both comparison groups, clearly not a proper test of the Newmark hypothesis (5). In the original hypothesis we chose the highest literature estimate of daily calcium intake available, 930 mg, to illustrate potential inadequacy even at this high level (2).

e) The estimates of diet were made on the basis of 24-h recall, and Heilbrun et al properly qualify the known limits of this type of measurement. However, even if accurate, this does not indicate the diet(s) during the many years prior that presumably were more influential, physiologically and biochemically, during the long carcinogenic developmental process. A more appropriate-type study would be a prospective study with diets evaluated over a prolonged period, as was done by Garland et al (6).

f) The calcium hypothesis is supported by two laboratory studies in mice (7, 8) and by a clinical intervention study using a dietary supplement of 1250 mg of calcium/day (9).

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Reply to letter by Newmark and Wargovich

Dear Sir:

We wish to thank Drs Newmark and Wargovich for showing such keen interest in our paper (1). The additional limitations of our study (comments *b-e*) were all discussed in the paper as published. It does not seem necessary to repeat them here.

Regarding comment *a*), please note that 88% of our Japanese male cohort were born in Hawaii. The remaining men moved to Hawaii at a mean age of 13. Thus, they all have substantial exposure to Western life-style. This seems further supported by the fact that the age-standardized colon cancer incidence rate for Hawaii Japanese males is now among the top 9% of such rates among 134 male populations from around the world (2).

One clarification regarding comment *e*) is that the Japan-Hawaii Cancer Study *already* is a prospective study, as noted in the first sentence of the abstract (1). Perhaps, the 28-day diet history method used by Garland et al (3) would be preferable to our 24-h diet recalls,

but both dietary methods have their limitations. We discussed the limitations of our method in the paper (1).

We are aware that the dietary intakes of these men are lower than the RDA and have discussed this in our paper. We wondered whether the hypothesis is relevant only for populations consuming the RDA of calories, calcium, and phosphorus.

The fundamental point is that the hypothesis was based upon literature estimates of intakes of three nutrients. It has apparently not been examined in human populations with respect to colon cancer per se. We simply tried to do that in an established prospective cohort study with baseline dietary data and documented colon-cancer incidence. We believe the limitations of our study were adequately discussed in our paper. Usually one single study neither proves nor disproves a hypothesis, but each relevant study published broadens the information base from which a given hypothesis may be re-evaluated.