

## Invited commentary

### Increasing evidence in favour of mandatory fortification with folic acid

Folic acid fortification of grain foods on a mandatory basis has been in place in the USA since 1998. Because of the safety concerns surrounding this issue, the Food and Drug Administration in the USA, responsible for implementing the new fortification legislation, opted for the relatively low folic acid concentration of 1400 µg/kg product, (United States Department of Health and Human Services, Food and Drug Administration, 1996). This level of folic acid was projected to result in a mean additional intake of 100 µg/d in the US population and was considered low enough to almost certainly carry no risk, but some argued that it would turn out to be ineffective in preventing neural tube defects (NTD). However, evidence just published indicates that the incidence of NTD in the USA has declined by almost 20% as a result of the new folic acid fortification policy (Honein *et al.* 2001). These results will undoubtedly renew pressure on the UK government to implement a similar policy.

Mandatory folic acid fortification for the UK was in fact proposed last year by the Government's Committee on Medical Aspects of Food and Nutrition Policy (COMA; Department of Health, 2000). Since its publication, the COMA report has been undergoing consultation, being undertaken jointly by the four UK Health Departments and the Foods Standards Agency. The main conclusion of the report was that: 'universal folic acid fortification of flour at 240 µg/100 g in food products as consumed would have a significant effect in preventing NTD-affected conceptions and births without resulting in unacceptably high intakes in any group of the population'. The recommended fortification level of 240 µg/100 g flour (2400 µg/kg flour) has been estimated to increase mean folic acid intakes by 200 µg/d which, in turn, is predicted to reduce the incidence of NTD-affected pregnancies by 41%. The report puts this reduction into context (based on 1997/1998 NTD data), as being equivalent to the prevention of thirty-eight of the ninety-three NTD-affected births in England and Wales, thirty of the seventy-four in Scotland, and six of the fourteen in Northern Ireland. Although the report focused primarily on the proven role of folic acid in the prevention of NTD, the potential benefit of folic acid in reducing the risk of cardiovascular disease via homocysteine-lowering (Boushey *et al.* 1995) was also acknowledged.

The conclusions of the recent COMA report (Department of Health, 2000) were based on a detailed risk–benefit assessment. Such an assessment, which estimates the likely benefits of folic acid fortification in terms of NTD reduction, as well as the risk of overexposure in those with high intakes, requires the manipulation of a representative dietary survey database, sometimes referred to as dietary modelling. In the COMA report, estimates of the exposure of different groups in the population to additional folic acid

were made by modelling dietary intake data from four National Diet and Nutrition Surveys for each age group, at five possible levels of fortification of flour as consumed in finished products: 1400 µg/kg; 2000 µg/kg; 2400 µg/kg; 2800 µg/kg; 4800 µg/kg. At each of these fortification levels, an estimation was provided as to the number of NTD-affected births per year which would be prevented, as well as the percentage of people over 50 years who would be exposed to a folic acid intake greater than 1 mg/d (equivalent to the upper tolerable intake level). The concern here primarily relates to the potential masking of the anaemia (and therefore the possibility of delaying the diagnosis) of vitamin B<sub>12</sub> deficiency amongst older people exposed to high folic acid intakes.

The other key strength of the risk–benefit assessment performed by COMA (Department of Health, 2000) was the availability of good data by which the additional folic acid intake at the various fortification levels could be related to NTD risk. For this purpose the placebo-controlled trial of Daly *et al.* (1997) was used. This study predicted the effects on NTD risk of folic acid intervention at 100, 200 or 400 µg/d administered over a 6-month period, on the basis of the responses of red cell folate concentration, which had previously been established to relate to NTD risk in a continuous dose–response inverse relationship (Daly *et al.* 1995). The reliability of this approach as a basis for predicting NTD risk has now been confirmed by the recent US evidence. Daly *et al.* (1997) predicted a 22% reduced risk of NTD arising from the US fortification programme delivering an additional 100 µg/d folic acid. This compares very closely with the actual US experience reported by Honein *et al.* (2001) in which NTD reported on birth certificates fell from 37.8 per 100 000 live births before fortification to 30.5 per 100 000 live births after fortification, representing a 19% decline in NTD. The incidence of spina bifida fell by 23%. Thus, there can be a good degree of confidence in COMA's predicted 41% reduction in the incidence of NTD-affected pregnancies arising from the recommended fortification level of 2400 µg/kg flour; projected to deliver an additional 200 µg/d folic acid in the UK (Department of Health, 2000).

The paper by Moynihan *et al.* (2001) in the present issue of the *British Journal of Nutrition* is timely and will contribute to the current folic acid fortification debate. The study employs dietary modelling of a 1990 dietary survey of 379 Northumberland schoolchildren aged 11–12 years to predict the consequences on the folic acid intake of adolescents if flour were fortified at the recommended level of 2400 µg/kg (Department of Health, 2000). Of concern, in the absence of mandatory fortification, a substantial proportion of these schoolchildren (7% girls, 10% boys) failed to achieve even the lower reference nutrient intake for

folate of 100  $\mu\text{g}/\text{d}$ , a reference level considered sufficient for only 2.5% of a population (Department of Health, 1991) and likely to be revised upwards in the near future. If white flour were fortified with folic acid at the recommended level of 2400  $\mu\text{g}/\text{kg}$ , the results predict that all subjects would have total folate intakes above the lower reference nutrient intake, and mean intakes would increase to 343 and 365  $\mu\text{g}/\text{d}$  for girls and boys respectively. Of note is the similarity in the estimates of additional folic acid intake arising from fortification at 2400  $\mu\text{g}/\text{kg}$  amongst girls in the 11–12 year age group in the Moynihan *et al.* (2001) study (191  $\mu\text{g}/\text{d}$ ) compared with the recent COMA report (188  $\mu\text{g}/\text{d}$ ; Department of Health, 2000), despite the differences in the survey samples and in the dietary methodologies employed to collect the original data.

Food fortification in general remains an important issue for policy makers. Current fortification policy varies considerably across different European countries, with major implications for European Union food legislation and trade. In certain countries (e.g. Scandinavian countries), the fortification of food with any nutrient is forbidden, others (e.g. The Netherlands) specifically forbid fortification with folic acid, while others (like the UK and Ireland) currently permit the fortification of foods with a range of nutrients on a voluntary basis. The specific issue of mandatory folic acid fortification is somewhat of a separate, more urgent case, with many governments currently considering the introduction of new policy in this regard. The paper by Moynihan *et al.* (2001) in this issue of the *British Journal of Nutrition*, and other reports specifically dealing with folic acid fortification (Daly *et al.* 1997; Cuskelly *et al.* 1999), should help to inform the current debate. No decision has yet been made in the UK, but the recent US experience will surely place this issue high on the Government's agenda.

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