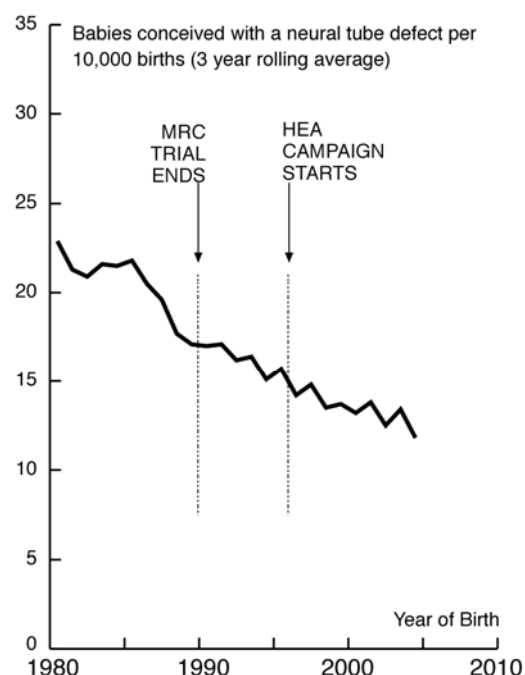


## FOLIC ACID (Commentary)

### Consequences of periconceptional folic acid use

**Advantages:** The potential benefits associated with folic acid supplementation are well established (and seem to be dose related), and several countries, including the US and Canada, have boosted the folate content of flour in the years that have now elapsed since the outcome of the MRC trial was first published in 1981. Other countries, including the UK, initially decided to concentrate on a campaign to alert women to the importance of an adequate folate intake, in order to minimise the risk of the fetus developing a neural tube defect (NTD) such as spina bifida or anencephaly. Unfortunately there is very little evidence that this policy has been successful in any of the countries where it has been tried. The graph shows the incidence of this condition (excluding babies with a chromosome anomaly and babies aborting spontaneously before 20 weeks gestation) in the north of England in the last 25 years. The number of conceptions had been as high as 45 per ten thousand births in the late 1950s, and had been declining steadily in the years before the Health Education Authority (HEA) launched their campaign in the UK in 1996. There is no good evidence that this campaign has speeded that decline.



Over £2 million was spent on the initial phase of that campaign. Even before it started the British public were purchasing a million bottles of 400 or 500 microgram-strength folate tablets over the counter every year, and it still remains cheaper for women to get folate without an NHS prescription than with one. It could be argued that further increasing the public's blind faith in the potency of commercial vitamin pills is probably not the most appropriate way to use public money. Neither does encouraging people to take more responsibility for their own health absolve public health authorities from all need to act. John Snow stopped cholera by taking the handle off the Broad Street pump – he did not just put a notice in the local paper. Folic acid is very cheap, and a 30 gram bottle can be bought by mail order for £8. The actual cost of fortifying the country's food supply would, therefore, only be a few pence per head per year, and fortification a more cost effective option than the strategy adopted to date, which merely lines the pockets of the multi-national pharmaceutical companies – companies that were fined a record £534 million by the European Commission in 2001 for abusing their monopoly status (Watson, 2001).

Anyone wanting to understand the challenge faced by children with spina bifida as they grow into adult life should read the reports by Hunt published in 1995 and 2003. The paper by Cherian *et al.*, 2005 reminds us that this is a scourge that also affects other less developed areas of the world too, and the US Surgeon General has estimated that neural tube effects may affect a quarter of a million of the world's newborn babies each year. It is worth remembering, however that serious disability is only common, in the absence of hydrocephalus, when the spinal lesion extends higher than the third lumbar vertebra (Verhoef *et al.*, 2006).

**Disadvantages:** There has been some debate as to whether routine folate supplementation might increase the risk of twin pregnancy, because twin pregnancy is known to increase the risk of preterm birth and the hazards that go with preterm birth (Lumley *et al.*, 2001). What was slightly unexpected about Lumley's analysis was the finding that the increased risk of twin pregnancy associated with routine supplementation seemed to be the same for low dose supplementation as for high dose supplementation. Concern has also been expressed that routine supplementation might increase the risk of early miscarriage. The population-based public health campaign in China, using a low dose supplement (400µg a day), found no evidence of increased miscarriage. There was no evidence of an increase in the risk of multiple birth either (Li *et al.*, 2003), but the same might not be true in a Caucasian population where the natural prevalence of twin birth is much higher.

**Balancing the risks:** A dietary supplement might, in theory, disturb the drug control of epilepsy, or mask anaemia from vitamin B<sub>12</sub> deficiency long enough for permanent spinal cord damage to occur (Wharton and Booth, 2001), but there is no good evidence that this happens and any formal trial would be impossibly complex to mount (Oakley, 2002). Indeed the policy of adding folate to flour has already

reaped dividends in Canada (Ray *et al.*, 2002; De Wals *et al.*, 2007) and the United States (Williams *et al.*, 2005; Rader and Schneeman, 2006) and there are no reports that any of the adverse effects that people feared such a policy might have on the health of older people have yet been detected. The only country to have taken what looks like a politically influenced decision to reject this approach seems to be the UK – the country that funded most of the definitive studies that showed that increased dietary folate could more than halve the incidence of this deeply crippling congenital disability. It is certainly to be hoped that the new draft report issued by the Food Standards Agency in the UK in December 2005 will eventually lead to a reappraisal. We should not overlook Hungarian evidence (Czeizel *et al.*, 2004, 2006) that the use of a periconceptional multivitamin capsule delivering 800 micrograms rather than 400 micrograms of folic acid a day, seems to also deliver a reduction in the number of other birth defects including cardiovascular and urinary tract abnormalities, and Danish evidence that the periconceptional intake of 400 micrograms of folic acid a day causes a 40% reduction in the incidence of cleft lip and/or palate (Wilcox *et al.*, 2007). Fear that supplementary fortification may increase the risk of colorectal seems to be one of the few concerns still causing UK regulatory authorities to postpone any decision on routine fortification (Bayston *et al.* 2007)

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