Editorial

The prevention of neural tube defects in Ireland

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Neural tube defects (NTDs) are a group of serious congenital malformations, including anencephaly, encephalocele and spina bifida (SB) which are associated with failure of closure of the neural tube during early embryonic development. They affect approximately one in 1000 births globally, and constitute an important challenge in terms of mortality, morbidity, social and financial costs. Studies indicate that approximately two thirds, but not all, cases of NTDs are preventable\(^1\). The burden of disease associated with NTDs is higher in Ireland than in other countries. Ireland has the highest fertility rate in the European Union (EU), and more than twice as many babies with spina bifida are live-born in Ireland compared with the rest of the EU. It is estimated that there are about 500 patients with SB in Ireland. The prevention of NTDs should therefore be a higher healthcare priority in this country than in other well-resourced countries.

Early observational studies suggested that NTDs may be prevented by folic acid (FA) supplementation. In a randomised control trial (RCT) led by the UK Medical Research Council (MRC), the administration of 4.0mg FA daily from randomisation until 12 weeks of pregnancy prevented 72% (CI 29 – 88%) of recurrences of NTDs\(^2\). The following year a Hungarian RCT was published which examined the use of 0.8mg FA daily in 4,573 women planning a pregnancy. The women in the intervention arm took the FA for at least a month before conception and for >8 weeks of pregnancy. There were no NTDs in women taking FA compared with 7 in controls (p<0.03)\(^3\). After these landmark studies, recommendations advising women on periconceptional FA were published internationally, and in 1993, the Irish Department of Health advised “all women likely to become pregnant should take 400mcg folic acid prior to conception and during the first 12 weeks of pregnancy”.

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Three different strategies may improve maternal folate levels: increased dietary intake of natural folate, FA supplementation and FA food fortification. Efforts to improve women’s dietary habits so that they consume more folate-rich foods have had little success\(^4\). In almost all women, a healthy diet alone is insufficient to achieve the threshold of maternal RBC folate $>906$ nmol/l which is considered optimal for the prevention of NTDs\(^5\). Despite national recommendations on periconceptional FA supplementation, the prevalence of NTDs remained static in many countries. As half of pregnancies are unplanned, only a small minority of women start FA before closure of the neural tube\(^6\). As a result, many countries adopted a policy of mandatory FA food fortification, albeit at different levels. This new strategy has resulted in a decrease in NTDs particularly in North and South America.

In 2006, the Food Safety Authority in Ireland (FSAI) published a comprehensive report recommending mandatory FA food fortification. Two years later the FSAI published an implementation report which recommended deferral of mandatory fortification, in part, because of a reported decrease in the number of NTDs nationally. Subsequently, in 2011 a comprehensive national audit using multiple data sources with cross-checking confirmed an increase in the number of babies born with SB\(^7\). The audit found that the incidence over the three years 2009–11 was 1.04/1000 births and while rates had fallen dramatically before the publications of recommendations on supplementation in 1993, there had been no improvement in the intervening years. There was also evidence that FA supplementation rates had fallen, and that the level of voluntary FA food fortification had decreased\(^6\). Further reports from Eurocat also showed that across Europe there has been little or no improvement in NTD rates since the early 1990s\(^8\). In response, the FSAI published a new report recommending mandatory FA food fortification with continuation of voluntary supplementation as the preferred option to tackle the lack of success in reducing NTD rates in Ireland\(^9\).

In January 2017, The US Preventive Services Task Force published a systematic review of 24 studies to update its recommendations on FA supplementation among women of childbearing age to prevent NTDs\(^10\). It concluded that despite mandatory FA fortification in the US and an accompanied decline in NTD prevalence, dietary intake variations resulted in suboptimal serum folate levels in nearly 25\% of the target population, highlighting the ongoing importance of FA supplementation. It reaffirmed its 2009 recommendation that all women of childbearing age should supplement their diet with 0.4 or 0.8 mg FA daily\(^10\). Current supplementation and voluntary fortification strategies to prevent NTDs have had little impact in Ireland and the rest of the EU. All women should continue to follow the national Healthy Eating guidelines for folate, but they should be made aware that increasing their natural dietary folate is unlikely to prevent NTDs.
As half of pregnancies are unplanned worldwide, all women who may become pregnant, whether intentionally or not, should be advised to use FA supplementation. Women who plan to conceive also may have limited knowledge about the purpose of FA supplementation and the need to start FA before pregnancy. Therefore, the wording of current national guidelines needs to be revised and communicated in a consistent and sustained way using both traditional and modern communication channels. However, the evidence is that a supplementation strategy alone is unlikely to be successful, particularly for women who are most disadvantaged socially and economically.

The current national policy of voluntary FA food fortification has not worked, and mandatory fortification needs to be implemented as recommended by the FSAI in 2006 and 2016. The legislative and regulatory challenges of mandatory fortification cannot be underestimated particularly as, increasingly, food and food ingredients cross borders. This is another issue for the growing list of issues post Brexit given the strong interdependencies between the food industries in Ireland and the U.K. Nonetheless, countries less well resourced than Ireland have successfully implemented mandatory FA food fortification.

Changes in supplementation and fortification strategies also need to be underpinned by ongoing surveillance not only of NTD rates nationally, but also of dietary intakes of natural and fortified folate and biomarkers of folate metabolism to ensure that the intended benefits of mandatory fortification do not have unintended consequences for vulnerable groups.

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