Upper limit for intake of folate is invalid—government urged to fortify flour with folic acid

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There is no need for an upper limit of folate intake, according to a study by Queen Mary University of London and the School of Advanced Study, University of London.

The study shows that the maximum suggested intake of folate (1 mg/day) is based on a 'flawed' analysis. The findings support recent calls1 for the Department of Health to approve the fortification of flour with folic acid, in order to protect babies from having neural tube defects.

Anencephaly and spina bifida (collectively referred to as neural tube defects) are serious and relatively common birth defects, affecting 1 in every 500-1,000 pregnancies. In 1991, a Medical Research Council randomised trial showed that increasing folic acid intake immediately before and early in pregnancy prevented most cases of neural tube defects.

As a result, 81 countries, including the USA since 1998, have introduced mandatory folic acid fortification of cereals, which has been found to reduce the prevalence of neural tube defects, without any evidence of harm. In countries that have introduced fortification, the number of neural tube defects has decreased by up to a half.

Despite successive recommendations, the UK has not introduced

mandatory fortification. One reason given is that this might lead to more people having a folate intake above an 'upper limit' suggested by the US Institute of Medicine2 (IOM). However the new research, published in *Public Health Reviews*, says that the IOM analysis was 'flawed' and there is no need for an upper limit.

The IOM analysed the results of studies, mainly conducted half a century ago, on individuals with B12 deficiency who had been wrongly treated with folic acid, and claimed that neurological damage tended to occur more frequently in patients treated with higher doses of folic acid. The IOM concluded that treating individuals with vitamin B12 deficiency with higher doses of folic acid might lead to an increased risk of neurological damage.

The new re-analysis of the data finds no relationship between dose of folic acid and the development of neurological damage. The neurological damage was not caused by folic acid - it arose by not treating B12 deficiency with vitamin B12. As a result there is no need for a folate upper limit (just as there is no upper limit for other B vitamins such as B1, B2, B5 or B12).

Lead author Professor Sir Nicholas Wald from the Wolfson Institute of Preventive Medicine at Queen Mary, who also led the original 1991 randomised trial, said: "With the upper limit removed there is no scientific or medical reason for delaying the introduction of mandatory folic acid fortification in the UK and other countries that have not yet adopted this proven public health intervention.

"Failing to fortify flour with folic acid to prevent neural tube defects is like having a polio vaccine and not using it. Every day in the UK, on average two women have a termination of pregnancy because of a neural tube defect and every week two women give birth to an affected child."

Women who could become pregnant are advised to start taking a daily folic acid supplement, but most do not do so, emphasising the need for fortification. Even with fortification, women should still be advised to take folic acid supplements to achieve a greater level of protection than that afforded by fortification alone. The importance of fortification is that it provides a protective population safety net.

In the UK, white flour is already fortified with iron, calcium and other B vitamins (niacin and thiamin).

Co-author Professor Joan Morris from the Wolfson Institute of Preventive Medicine at Queen Mary said: "From 1998, when the United States introduced mandatory folic acid fortification, to 2017, an estimated 3,000 neural tube defects could have been prevented if the UK had adopted the same level of fortification as in the US. It's a completely avoidable tragedy."

Co-author Colin Blakemore, former head of the Medical Research Council, said "Spina bifida is one of the most common disabling birth defects, but British research has shown that this tragic condition is a vitamin deficiency that can easily be prevented. Eight-one other countries have benefited from this research, which was funded by the British taxpayer. It's time for the British public to reap the full benefits of that research."

More information: Nicholas J. Wald et al, Public health failure in the prevention of neural tube defects: time to abandon the tolerable upper intake level of folate, *Public Health Reviews* (2018). DOI: 10.1186/s40985-018-0079-6

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