

PERICONCEPTIONAL FOLATE AND THE PREVENTION OF NEURAL TUBE DEFECTS POLICY

The Public Health Association of Australia notes:

1. Neural tube defects or NTDs (spina bifida, anencephaly, and encephalocele) result from incomplete closure of the neural tube early in pregnancy. This leads to damage to the brain or spinal cord during development.

2. Evidence from international randomised control trials shows that daily maternal use of supplements containing folate prior to and during early pregnancy can reduce both the recurrenceⁱ, as well as first occurrence of neural tube defectsⁱⁱ. A meta-analysis of the trials estimated that as much as a 70% reduction in neural tube defects is possible with peri-conceptional supplementation with folic acid. A summary of all related findings has been published in the Cochrane libraryⁱⁱⁱ.

3. Although the mechanism by which folate produces this effect is not known, it has been recommended that all women planning, or likely, to become pregnant should have an increased intake of folate daily for at least one month prior to pregnancy and during the first trimester.

4. The limitations of public education alone in reducing the rate of NTDs and the potential of public education campaigns to increase further inequalities in the rates of NTDs amongst disadvantaged populations and young women.

5. Increased folate levels can be achieved by:
-taking a daily supplement containing folic acid
-eating foods rich in folate, including foods fortified with folic acid.

6. The National Health and Medical Research Council (NHMRC) recommended
-for women with no family history of NTD, a supplement of 0.5mg folic acid daily
-for women with a family history of NTD, a supplement of 5mg folic acid daily^{iv}.

7. Fortification of food provides an extra source of folate to women periconceptionally. This is important because many pregnancies are unplanned (approx 40%)^v. Moreover, despite active health promotion campaigns in SA, Vic and WA, many women in these States are unaware of the importance of folate (up to 70%) and many women do not take folic acid supplements periconceptionally (up to 70%)^{vi, vii, viii}. There has been neither a co-ordinated nor sustained national approach to improving folate awareness.

8. Voluntary fortification of certain foods was allowed for the prevention of NTDs in Australia and New Zealand in 1995. Since then, over 100 foods (mainly breakfast cereals) have been fortified with folic acid^{ix}. However, there remain no conclusive data that this method will ensure an adequate folate supply to all women at risk.

9. A pilot permitting a health claim on Folate and Neural Tube Defects (NTDs) was approved by the Australia New Zealand Food Authority (now Food Standards Australia New Zealand - FSANZ) in November 1998.

10. Using data from Birth Defect Registries in SA, Vic and WA, the overall birth prevalence of NTDs (including terminations, still births and live births) has been estimated. In SA it has decreased from 1.9 per 1000 (1986-1996) to 1.5 per 1000 (1997-2001), and in WA from 1.9 per 1000 (1980-1995) to 1.4 per 1000 (1996-2002). In Victoria, the prevalence decreased from 1.8 per 1000 (1995-1997) to 1.3 per 1000 (2004-2006). These declines reflect the impact of periconceptional folic acid intake from voluntary food fortification and supplementation.

11. Mandatory fortification with folic acid in Australia was approved in 2007, to address the inequitable reach of health promotion and voluntary fortification and the need for adequate folate status very early in pregnancy. Wheat flour for bread making is to be fortified with 230-280µg folic acid per 100 gm flour, by September 2009. Flour designated as organic will be exempt. Approval for voluntary fortification of foods, with the exception of bread, will continue.

(<http://www.foodstandards.gov.au/newsroom/factsheets/factsheets2008/mandatoryfolicacidfo3931.cfm>). In a number of countries where it has been introduced, a decline in prevalence of NTDs has been reported^{x, xi}.

12. Mandatory fortification results in everyone in the population being exposed to increased levels of folate and NTDs are not very common. In considering mandatory fortification in Australia, the benefits for a few were balanced against the potential risk of harm for many. Potential risks raised were:

- i) that high doses of folic acid may mask the diagnosis of vitamin B12 deficiency^{xi}. However, there are now data from the US which demonstrate that rates of B12 deficiency, without anaemia, have not increased since fortification was mandated in 1998^{xiii}.
- ii) that high folate levels may impair anticonvulsant therapies^{iv)}. This must be taken into account in clinical management.
- iii) Twinning rates may be greater in women with increased folic acid intake, however, this has not been confirmed in two recent studies^{xiii) xiv)}.
- iv) potentiation of some cancers.

13. Efforts to reduce NTDs are carried out with the full understanding that not all NTDs will be prevented by folic acid and that there are many people with NTDs living in the community. Therefore appropriate services and support for those with NTDs and their families should be readily available.

14. Given that the majority of home-based care-giving to a person with a birth defect may be full time and preclude pursuit of personal further education, employment, social

and recreational activities, promoting an adequate intake of folate to prevent NTDs and so prevent care-givers' exclusion from full community participation is also important.

The Public Health Association of Australia endorses:

15. The NHMRC guidelines, which recommend that:

- All women planning a pregnancy or likely to become pregnant be offered appropriate advice about folate for the prevention of NTD, and offered genetic counselling where applicable.
- There is provision of health promotion programs targeted to both the public and health professionals.
- Further research is conducted and monitoring of NTDs is continued.

The Public Health Association of Australia resolves that:

16. The Board, Branches and Special Interest Groups will actively encourage relevant state and national bodies to appropriately fund sustainable health promotion and education programs for women of child bearing age and school-aged children and adolescents with specific recognition that different strategies are required for specific subgroups, especially high risk groups.

The Public Health Association of Australia recommends that:

17. Food fortification, health promotion and education policies and programs are evaluated to determine their effectiveness and public health impact, including the incidence, prevalence and presentation of unfavourable outcomes.

18. Policy in this area should be reviewed regularly to take into account changes in the understanding of all outcomes, as relevant, reliable data become available.

19. State and national governments identify ways in which folate supplementation can be funded so that women are not financially disadvantaged.

20. Information be made available in plain English and other commonly used languages at all primary care services, particularly general practice on: the NHMRC recommendations for folate intake in the format of tablets, the natural dietary sources of folate, and fortified food sources. Appropriate foodstuff preparation advice should also be available.

21. Information should be made available at all primary care services, particularly general practice, on the availability of and access to genetic counselling services.

ADOPTED 1996, REVISED AND RE-ENDORSED 1998, 2004, 2006 AND 2008

First adopted at the 1996 Annual General Meeting of the Public Health Association of Australia and amended at the AGM 1998. Revised and re-endorsed in 2004, 2006 and as part of the 2008 policy review process.

ⁱ Medical Research Council Vitamin Study Research Group (1991) 'Prevention of neural tube defects: results of the Medical Research Council Vitamin Study Research Group, *Lancet*, 338, 131-137.

ⁱⁱ Czeizel & Dudas (1992) 'Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation, *New England Journal of Medicine*, 327(26), 1832-1835.

ⁱⁱⁱ Lumley, J., Watson, L., Watson, M. & Bower, C. (2001) 'Periconceptional supplementation with folate and/or multivitamins for preventing neural tube defects. *Cochrane Database Systemic Review*, 3: CDOO1056.

^{iv} National Health and Medical Research Council (1993) NHMRC Revised statement on the relationship between dietary folic acid and neural tube defects such as spina bifida.

^v Marsack, C.R., Alsop, C.L. Kurinczuk, J.J. and Bower, C. (1995) 'Pre-pregnancy counselling for the primary prevention of birth defects: rubella vaccination and folate intake', *Medical Journal of Australia*, 162:403-406.

^{vi} Chan, A, Pickering, J., Haan, E.A., Netting, M., Burford, A., Johnson, A., et al. (2001) "'Folate before pregnancy": the impact on women and health professionals of a population-based health promotion campaign in South Australia', *Med J Aust*, 174, 631-636.

^{vii} Watson, M., Watson, L., Bell, R. and Halliday, J. (2001) 'The increasing knowledge of the role of periconceptional folate in Victorian women of child-bearing age: follow-up of a randomised community intervention trial, *Aust NZ J Public Health*, 25, 389-95.

^{viii} Bower, C., Blum, L., O'Daly, K., Higgins, C., Loutsky, F. and Kosky, C. (1998) 'Promotion of folate for the prevention of neural tube defects: knowledge and use of periconceptional folic acid supplements in Western Australia, 1992-1995', *Aust NZ J Public Health* 1997, 21, 716-721. Erratum: *Aust NZ J Public Health* 1998, 22, 72.

^{ix} Abraham, B. and Webb, K (2001) Interim evaluation of the voluntary folate fortification policy. Canberra: Australian Food and Nutrition Monitoring Unit.

^x Waller, D.K., Tita, A.T.N., and Annegers, J.F. (2003) 'Rates of twinning before and after fortification of foods in the US with folic acid, Texas, 1996 to 1998', *Paediatr Perinat Epidemiol*, 17, 378-383.

^{xi} Honein, M.A., Paulozzi, L.J., Mathews, T.J., Erickson, J.D. and Wong, L.Y. (2001), 'Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects, *JAMA*, 285, 2981-6.

^{xii} Folic acid safety and toxicity; a brief review (1989) *American Journal of Clinical Nutrition*, 50: 353-358.

^{xiii} Mills, J.L., Von Kohorn, I., Conley, M.R., Zeller, J.A., Cox, C., Williamson, R.E. and Defour, D.R. (2003) 'Low vitamin B-12 concentrations in patients without anaemia: the effect of folic acid fortification of grain' *Am J Clin Nutr*, 77, 1474-1477.

^{xiv} Li, Z., Ginder, J., Wang, H., Berry, R.J., Li, S., Correa, A., Zheng, J.C., Erickson, J.D., and Wang, Y. (2003) 'Folic acid supplements during early pregnancy and likelihood of multiple births: a population-based cohort study', *Lancet*, 361, 380-384.

Bower, C., S. Eades, et al. (2004). "Trends in neural tube defects in Western Australia in Indigenous and non-Indigenous populations." *Paediatric and Perinatal Epidemiology* **18**: 277-80.

Ray, J. G., G. Singh, et al. (2004). "Evidence for suboptimal use of periconceptional folic acid supplements globally." *BJOG: an International Journal of Obstetrics & Gynaecology* **111**: 399-408.

Bower, C., M. Miller, et al. (2004). "Folate promotion in Western Australia and the prevention of neural tube defects." *Australian and New Zealand Journal of Public Health* **28**: 458-464.

Health Claims:

Williams, P., J. McHenry, et al. (2001). "Impact evaluation of a folate education campaign with and without the use of a health claim." *Australian and New Zealand Journal of Public Health* **25**: 396-404.

Lawrence, M. (2006). "Evaluation of the implementation of the folate-neural tube defect health claim and its impact on the availability of folate-fortified food in Australia." *Australian and New Zealand Journal of Public Health* **30**: 363-368.

NTD trends in other countries with fortification

De Wals, P., F. Tairou, et al. (2007). "Reduction in neural-tube defects after folic acid fortification in Canada." *New England Journal of Medicine* **357**: 135-142.

Hertrampf E, Cortes F. Folic acid fortification of wheat flour: Chile. *Nutrition Reviews* 2004; 62:S44-48.

Cancer refs

Mason, J. B., A. Dickstein, et al. (2007). "A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis." *Cancer Epidemiology, Biomarkers and Prevention* **16**: 1325-9.

Kim, Y. I. (2006). "Folate: a magic bullet or a double edged sword for colorectal cancer prevention?" *Gut* **55**: 1387-1389.

Twinning ref

Muggli EE and Halliday, JL. Folic Acid and Risk of Twinning: A systematic review of the recent literature, July 1994-July 2006. *Med J Aus*, 186:243-248 (2007)

General reference on Victorian situation:

What has happened with Neural Tube Defects and women's' understanding of folate in Victoria since 1998? Louise du Plessis, Rod W Hunt, Ashley Fletcher, Merilyn Riley, Jane Halliday (accepted *Med J Aust*)