What has happened with neural tube defects and womens' understanding of folate in Victoria since 1998?

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ABSTRACT

Objective: To describe the prevalence of neural tube defects (NTDs) in Victoria, and to evaluate women's knowledge and awareness of the importance of folate after the introduction of voluntary food fortification.

Design and setting: Descriptive study, set in Victoria, Australia, based on routinely collected data from the Victorian Birth Defects Register (VBDR) for 1998–2006, and responses by women aged 18–50 years to five questions relating to folate on the 2005 and 2006 Victorian Population Health Surveys (2314 and 2488 women, respectively).

Main outcome measures: Prevalence of NTDs, and extent of women's knowledge of the importance of folate in NTD prevention, comparing the period before and since voluntary food fortification and a folate awareness campaign.

Results: The total prevalence of pregnancies affected by NTDs declined from approximately 17 to 14 per 10 000 births from 1997 to 1999 (coinciding with the period when voluntary food fortification was introduced, and a 1-year folate awareness campaign was held). It has since remained static. Over the 9-year study period, the termination of pregnancy rate was 79%, resulting in three NTD-affected babies per 10 000 livebirths. Compared with women aged 30–34 years (the reference group), those aged 20–24 years had the greatest likelihood of having a baby with an NTD (adjusted odds ratio, 1.70; 95% CI, 1.33–2.18; $P < 0.001$). Women aged 18–24 years had the lowest rate of folate supplement use (15.9% in 2006), while women aged 30–34 years had the highest rate (30.3% in 2006).

Conclusions: There has been no further reduction in prevalence of NTDs in Victoria since 1999, and this prevalence remains well above that achievable through adequate folate intake. Accurate knowledge of folate consumption, population-based NTD prevalence data and folate awareness data are essential in monitoring the effectiveness of the mandatory fortification program to be implemented in Australia in the next 2 years.

MJA 2008; 189: 570–574

See also page 566

Neural tube defects (NTDs) are an important group of potentially preventable birth defects. Primary prevention interventions at population level have included efforts to increase awareness of the protective effect of adequate folate levels in the periconceptional period, as well as the introduction of folic acid supplements and fortification of basic foods with folic acid. The definitive evidence on the effectiveness of folate in NTD prevention is summarised in a Cochrane review.[1] Since 1993, the National Health and Medical Research Council (NHMRC) has recommended that all women of childbearing age should be offered advice about a folate-rich diet and offered folic acid supplementation with 0.5 mg per day in standard-risk pregnancies and 5 mg per day in higher-risk pregnancies (ie, for women with a family history of NTDs).[2] In this article, "folate" refers to the naturally occurring dietary form, but also to both folate and the synthetic equivalent, folic acid (used in supplements and to fortify food), when referring to awareness of the role of folate in pregnancy.

The issues around fortification of foods as a strategy to improve periconceptional folate levels have been widely reviewed by Food Standards Australia New Zealand.[3] Folate fortification of foods in Australia was implemented in 1997, and remains voluntary pending implementation of new recommendations. Subsequent modest rises in serum or red-cell folate levels in women of child bearing age were reported in women in Victoria (19% increment from pre-1996 to 2000 levels)[4] and Perth (increment of 38% from pre-fortification to 2001).[5] The recent decision to introduce mandatory fortification of bread flour in Australia and New Zealand aims to approximately double the current mean folic acid dietary intake, with a fortified diet supplying an estimated 200 μg of folic acid per day.[3]

Given that the protective effect of folic acid supplementation is dose-dependent,[6-8] such a modest increase in folate intake will potentially reduce the prevalence of NTD-affected pregnancies and related terminations by 15%.[9] Further supplementation will be required to achieve the lower prevalences of NTDs seen in other countries.[1] Therefore, public awareness of the role of folate in reducing the likelihood of NTDs remains extremely important. Since voluntary fortification was introduced in 1997, a folate awareness campaign was launched in Victoria in 1999. A trial to assess the level of folate awareness in the target population before this campaign reported a baseline level of awareness of 12%.[10] No further folate awareness strategies have been implemented in Victoria since this time.

Our aims in this study were to determine the prevalence of NTDs reported to the Victorian Birth Defects Register (VBDR) and to examine risk factors for the period 1998–2006, and then to compare these results with those for the same population for the period 1983–1997,[11] before any public health interventions (voluntary food fortification and a 1-year statewide awareness campaign) had been implemented. We also present NTD prevalence data in the context of the latest folate awareness data from the Victorian Population Health Survey (VPHS), as this will provide information relevant to monitoring and evaluating the recently approved mandatory flour fortification program in Australia and New Zealand.

METHODS

Prevalence data

Data on NTDs have been collected since 1983 by the VBDR in the Victorian Government Department of Human Services (http//:www.health.vic.gov.au/perinatal/). Data are routinely collected by midwives on the mandatory birth notification form (for births at 20 weeks' gestation and later), as well as being obtained from hospitals, obstetricians, maternal and child health nurses, paediatricians,

autopsy reports and cytogenetic laboratories. Data on terminations for birth defects before 20 weeks' gestation are obtained through a separate notification process. Coding uses the British Paediatric Association Classification of Disease.[12] NTDs included spina bifida (International classification of diseases, ninth revision [ICD-9] codes 741.00–741.99), anencephaly (740.00–740.99) and encephalocoele (742.00–742.99).

NTDs have been extremely well reported, with validation studies showing 100% reporting of structural defects visible at birth.[13,14] About 85% of terminations for birth defects before 20 weeks' gestation are reported to the VBDR.[15]

Awareness data

Questions on knowledge about and consumption of folate were introduced to the VPHS in 2005. Details of the survey methods are at <http://www.health.vic.gov.au/healthstatus/vphs>.

Statistical analysis

We performed univariable and multivariable analyses in SPSS, Version 12 (SPSS Inc, Chicago, Ill, USA); $P < 0.05$ was considered statistically significant. Variables previously identified as important risk factors (maternal age, epilepsy, plurality, urban or rural residence) were included in a multivariable analysis of 1997–2005 data. Maternal country of birth and parity were excluded from the multivariable analysis because of incompleteness of termination data.

RESULTS

Prevalence of NTDs

The total prevalence of NTDs (all affected pregnancies, including terminations) from 1998 to 2006 was 13 per 10 000 births (Box 1). Box 2 includes these data plus a 3-year moving average for 1990–2006, with data for 1990–1997 taken from a previous VBDR study.[11] Prevalence declined from 17 to 14 per 10 000 births between 1996 and 1999; this represents an 18% reduction, but there was no further decline after 1999.

Box 3 shows that only 15% of NTD-affected pregnancies resulted in survival of a baby beyond the neonatal period. Overall 79% of NTD-affected pregnancies were terminated, including 91% of those with a fetus with anencephaly, 70% of those with spina bifida and 61% of those with encephalocoele.

Box 4 shows the prevalence of babies born alive with an NTD. The 3-year moving average shows a 50% decline from 6 per 10 000 births in 1997 to 3 per 10 000 births over the study period.

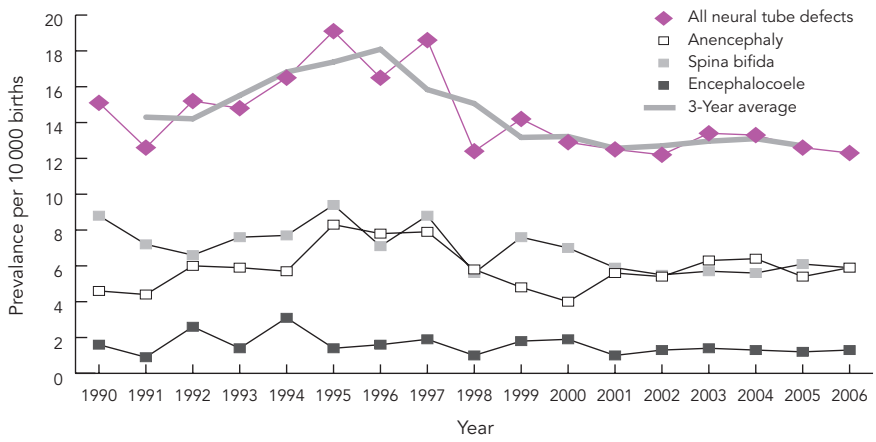
Box 5 shows that, having taken into account maternal age, epilepsy and multiple pregnancy, the factors that were significant in the univariable analysis remained so after adjustment in the multivariable analysis. Maternal age of less than 30 years, and particularly of less than 25 years, remained statistically significant. The risk conferred by maternal epilepsy increased after adjust-

1 Number and prevalence per 10 000 births of different types of neural tube defects (NTDs) reported to the Victorian Birth Defects Register, 1998–2006

Year	Total pregnancies*	No. (prevalence) of NTD-affected pregnancies*			
		All NTDs	Anencephaly	Spina bifida	Encephalocoele
1998	62 139	77 (12.4)	36 (5.8)	35 (5.6)	6 (1.0)
1999	62 747	89 (14.2)	30 (4.8)	48 (7.6)	11 (1.8)
2000	62 612	81 (12.9)	25 (4.0)	44 (7.0)	12 (1.9)
2001	62 193	78 (12.5)	35 (5.6)	37 (5.9)	6 (1.0)
2002	63 181	77 (12.2)	34 (5.4)	35 (5.5)	8 (1.3)
2003	63 601	85 (13.4)	40 (6.3)	36 (5.7)	9 (1.4)
2004	63 749	85 (13.3)	41 (6.4)	36 (5.6)	8 (1.3)
2005	66 700	84 (12.6)	35 (5.2)	41 (6.1)	8 (1.2)
2006	68 547	91 (12.3)	41 (5.9)	41 (5.9)	9 (1.3)
Total	575 469	747 (13.0)	317 (5.5)	353 (6.1)	77 (1.3)

* Including terminations for NTDs. ◆

2 Prevalence of neural tube defects by birth year, 1990–2006

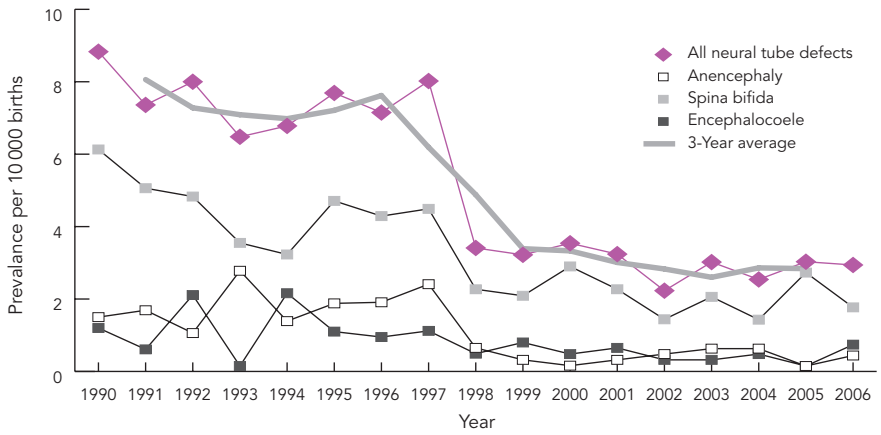


3 Outcome of all pregnancies affected by neural tube defects reported to the Victorian Birth Defects Register, 1998–2006

Neural tube defect	Total	Stillbirth	Livebirth		Termination	
			Survived > 28 days	Died ⩽ 28 days	Early (< 20 weeks)	Late (⩾ 20 weeks)
Anencephaly	317	8 (3%)	0	19 (6%)	252 (79%)	38 (12%)
Spina bifida	351*	5 (1%)	85 (24%)	15 (4%)	151 (43%)	95 (27%)
Encephalocoele	77	2 (3%)	27 (35%)	1 (1%)	33 (43%)	14 (18%)
All	745	15 (2%)	112 (15%)	35 (5%)	436 (59%)	147 (20%)

* Discrepancy in total number of spina bifida cases and therefore total neural tube defects between Box 1 and these data is because there were two pregnancies in 2006 for which the outcome was unknown. ◆

4 Prevalence of babies born alive with a neural tube defect by birth year, 1990–2006



ment, but did not reach statistical significance. The likelihood of an NTD in a multiple birth was lower than in singleton births, and there was no significant increased risk associated with rural residence. The likelihood of an NTD was significantly higher for mothers who had had three or more previous pregnancies, compared with primigravida mothers (univariable analysis only, data not shown). There were no reported NTD-affected births to Aboriginal mothers or to mothers with diabetes during the study period.

Awareness data

Box 6 shows that 17.7% of women surveyed in 2005 and 23.0% in 2006 were taking a daily folic acid supplement. The 18–24-years age group reported the lowest intake of folic acid. Overall, in 2006, 42.3% of women knew why women might be advised to take a folic acid supplement (indicated by correct answers to both parts of Question 2), an increase from 35.3% in 2005. The main source of information was general practitioners or doctors (about 29% in both years).

DISCUSSION

This study used high-quality data from a well established population-based register, which included termination data, allowing a much closer estimate of the real prevalence of NTD-affected pregnancies than can be made in countries where termination data are not available.

The most striking finding is the decrease in the prevalence of NTD-affected pregnancies from about 17 to 14 per 10 000 births from 1997 to 1999, coinciding with the introduction of voluntary folate fortification of foods and an awareness campaign. The 3-year moving average was used as a conservative estimate of the effect, taking into account annual fluctuations due to small numbers. Also, it is likely that the impact of voluntary fortification and the campaign would gradually have filtered through to the population over several years, rather than having a sudden effect. The total prevalence of pregnancies affected by NTDs has not decreased further since 1999; rather, the prevalence fluctuates around 13 per 10 000 births. The lack of further decline probably reflects the continuing passive, non-increasing uptake of fortified foods in the absence of a sustained folate-awareness strategy. The apparent increase in NTD prevalence in the 1990s is likely to be the specifically result of increased prenatal detection and notification

5 Univariable and multivariable analyses of potential maternal predictors of pregnancies affected by neural tube defects (NTDs), Victoria, 1998–2005

Potential predictor	Total	NTD	Rate per 10 000 births	Univariable analysis		Multivariable analysis	
				Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Maternal age							
< 20 years	15 636	22	14.07	1.37 (0.88–2.13)	0.16	1.19 (0.73–1.94)	0.48
20–24 years	61 455	104	16.92	1.65 (1.30–2.10)	< 0.001	1.70 (1.33–2.18)	< 0.001
25–29 years	144 208	199	13.80	1.35 (1.10–1.64)	0.001	1.39 (1.13–1.7)	0.002
30–34 years	182 235	187	10.26	1.0		1.0	
35–39 years	87 277	118	13.52	1.32 (1.05–1.66)	0.02	1.32 (1.04–1.69)	0.02
40 + years	16 071	20	12.44	1.21 (0.76–1.92)	0.41	1.13 (0.69–1.86)	0.63
Epilepsy							
No	504 081	650	12.89	1.0		1.0	
Yes	2 841	6	21.12	1.50 (0.62–3.61)	0.37	1.73 (0.77–3.86)	0.18
Singleton/multiple births							
Singleton	48 9520	639	13.05	1.0		1.0	
Multiple	17 402	17	9.77	0.75 (0.46–1.21)	0.24	0.84 (0.52–1.35)	0.47
Residence							
Urban	367 101	424	11.55	1.0		1.0	
Rural	139 724	183	13.10	1.11 (0.93–1.32)	0.25	1.11 (0.93–1.32)	0.26

6 Summary of affirmative responses by women aged 18–50 years to questions on folate use, by age group, in the 2005 and 2006 Victorian Population Health Surveys (2314 and 2488 women, respectively)

	Women's affirmative responses				
	Age group (years)				
Question and survey year	18–24	25–29	30–34	35–50	Total
1. Currently taking a folic acid supplement or multivitamin containing folic acid daily					
2005	12.3%	18.2%	24.2%	17.5%	17.7%
2006	15.9%	24.9%	30.3%	22.8%	23.0%
2. The main reason that women in age group might be advised to take folic acid is:					
To help to prevent birth defects					
2005	7.2%	8.6%	11.3%	8.3%	8.6%
2006	6.7%	9.9%	12.8%	7.3%	8.4%
A pregnancy-related issue					
2005	15.5%	38.9%	43.3%	22.2%	26.7%
2006	27.4%	42.0%	55.4%	27.0%	33.9%
3. For those taking folate, the main reason is:					
For general health or part of a multivitamin					
2005	77.6%	44.9%	19.5%	66.8%	57.1%
2006	61.1%	25.6%	42.7%	65.0%	58.1%
Because I could/am trying to become pregnant or am pregnant					
2005	9.3%	31.7%	51.4%	14.4%	24.5%
2006	6.6%	35.3%	38.1%	16.0%	21.5%
4. For those NOT taking folic acid, the main reason is:					
No reason/don't know anything about folate					
2005	73.2%	47.8%	50.2%	51.0%	55.2%
2006	72.3%	49.2%	40.7%	47.5%	51.9%
Because not planning to become pregnant					
2005	7.6%	16.8%	17.4%	12.9%	13.0%
2006	8.1%	9.1%	29.8%	13.5%	14.3%
5. Main source of information about folate:					
General practitioner or doctor					
2005	5.5%	31.2%	42.0%	30.2%	29.4%
2006	15.1%	35.1%	39.1%	27.5%	29.1%
Other health professional					
2005	7.0%	8.2%	12.8%	10.4%	10.1%
2006	13.7%	6.0%	11.4%	12.0%	11.3%
Don't know					
2005	25.3%	17.4%	6.9%	11.8%	13.5%
2006	14.2%	12.4%	9.1%	15.1%	13.4%

of anencephalic pregnancies, given that the prevalence of spina bifida or encephalocoele remained fairly constant in the same period (Box 2). The rate of termination for pregnancies affected by NTDs has increased, and there were almost 500 pregnancies terminated because of an NTD during our 9-year study period.

The 18% reduction in both total and birth prevalence of NTDs is far less than the postulated reduction achievable if periconceptional folate intake was optimised.[1] The prevalence of NTDs in Victoria (13 per 10 000 births) remains at least double that achieved in countries where mandatory fortification has been in place for a number of years (eg, 6.8 per 10 000 births in Alberta, Canada and 5.6 per 10 000 births in mainland United States).[16,17] Part of the approach to achieving further reductions would clearly be to improve individual women's knowledge of the importance of folate and their adherence to supplementation. The other part of the approach, aimed at the population level, is food fortification. After years of intense debate, a program for introducing mandatory fortification has now been approved for Australia[3] and is likely to be supported by the community.[18]

The VBDR data have shown the relatively increased vulnerability of younger women (younger than 30 years and certainly younger than 25 years) to having a baby with an NTD, with the risk being even higher than in our previous study.[11] In the 1983–1997 study, the 20–24-years age group had an odds ratio (OR) of 1.17 ($P=0.09$), while the same age group in our study had an OR of 1.70 ($P<0.001$). The VPHS data help explain this finding by showing considerable variation in use of and knowledge about folate between age groups, with younger women being less aware and less likely to be taking a supplement. The slight improvement in younger women's understanding that folate is needed for a pregnancy-related issue, and the fact that more women in this age group are now receiving information from health professionals is encouraging (Box 6).

Maternal epilepsy, another recognised risk factor for NTDs, conferred an increased OR of 1.73 in our study, but this is lower than the OR of 3.70 reported in the previous Victorian study.[11] This suggests that awareness of the importance of folate in this high-risk population has improved, probably among women themselves as well as among their health professionals.

The recent VPHS data show an increase in the proportion women taking a daily folate supplement, but overall use remains low at less than 30%. This is similar to 2005 South Australian findings indicating that 30% comply with supplementation in terms of both dose and timing.[19] Corresponding figures for Western Australia show a rate of folate supplement use of 29%–45%,[20] and the estimated rate among all Australian women of childbearing age is 36%.[9]

Most women who have any knowledge of folate see it as important for general health, rather than being specifically related to pregnancy. There has been no change in women's knowledge about the relationship between folate and birth defects, nor in reasons for not taking a supplement.

Conclusions

NTD prevalence is not declining and the results of the 2005 and 2006 VPHS clearly show that the women's knowledge of the importance of folate in primary prevention of NTDs has only improved marginally. Multivariable analysis of maternal risk factors clearly identify younger women as being at highest risk, with women aged between 20 and 24 years being the most vulnerable group. This is also the group with the lowest awareness of the importance of folate and lowest adherence to folic acid supplementation. These are important findings in preparing education and awareness campaigns to accompany the mandatory fortification program.

It is to be hoped that a combination of food fortification and education will result in an increased intake of folate and, therefore, a rise in serum folate levels of the population as a whole. Accurate knowledge of folate consumption patterns, correlated with blood levels, and population-based NTD prevalence and folate awareness data are essential in monitoring the effectiveness of the mandatory fortification program to be implemented in Australia in the next 2 years.

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COMPETING INTERESTS

None identified.

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