Folic acid and neural tube defects in New Zealand: a cautionary tale?

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…Rarely has there been a case where the science has been so unequivocal, uncontroversial, and universally accepted, yet the development and implementation of appropriate policy continues to be problematic…

Improving Folate Intake in New Zealand: Policy implications
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History

The impact of diet on human fetal malformation was first systematically documented in Europe after the Second World War. Many countries experienced considerable deprivation both during and immediately after the conflict and there was a concurrent increase in observed “birth defects”.1

By the 1960s there were already suggestions that folic acid (a B group vitamin) might be involved in a particular group of “birth defects”—neural tube defects (NTDs). However, it was not until 1980–1981 that the first intervention studies were published demonstrating that vitamin supplementation, around the time of conception, in women who had a previous child affected by a NTD, led to a reduction in the risk of recurrence of NTD in subsequent pregnancies.2–4

In 1983, the MRC Vitamin Study Research Group launched a randomised double-blind prevention trial (in 33 centres in 7 countries) to determine whether folic acid taken around the time of conception could prevent NTDs in women at high risk because of a previous affected pregnancy.6

In 1984, another study was started in Hungary8 which also sought to establish the efficacy of periconceptional multivitamins in reducing the first occurrence of NTD.

Both of these studies, published in 1991 and 1992 respectively, concluded that there was evidence of benefit (the reduction in incidence of NTD both as a first occurrence and as a recurrence). The MRC trial showed a 72% reduction in NTD incidence amongst the infants of women who took the supplement when compared to the offspring of those who did not.

These developments were discussed in a review article in the *Journal of Paediatrics and Child Health* in 1992.7 The authors noted that despite the limitations in the studies, the evidence was in favour of some aspects of diet, and of folate in particular, being important in the aetiology of NTDs. They suggested that the challenges would be to find ways of improving the folic acid intake of all women of child-bearing age, and to evaluate the effect of any intervention.

The consensus was that folic acid supplementation in the range 360 mcg–4000 mcg per day, taken periconceptionally, would prevent up to 70% of NTDs. The
intervention appeared safe, cheap, and effective as a method of primary prevention of neural tube defects.

So what then happened in the intervening years?

Observation and recording of birth defects like spina bifida became an international collaboration in 1974 with the establishing of the International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS).

These initiatives facilitated the exchange of data on birth defects worldwide, and encouraged further collaborative research. The ICHBDMS now has more than 40 member programmes across five continents (and includes Australia and New Zealand).

There was an observed steady decline in NTD incidence, not all accounted for by the increasing termination of affected pregnancies in the 1990s. General improvements in nutrition and diet are thought likely to have also contributed.

Around the World

United States (US)—In 1991, the US Government recommendation to women who had a previous pregnancy with NTD was to take 4000 mcg folic acid daily for at least 1 month prior to conception.

In 1992, the recommendation was for all women of child-bearing age to consume 400 mcg folic acid per day, periconceptually, to reduce the risk of NTD occurrence.

In 1998, the US Government introduced mandatory fortification of all cereal grain products with 140 mcg of folic acid per 100 g of flour. In addition, they also recommended periconceptual supplementation with 400 mcg folic acid for all women except those with a history of a prior affected pregnancy (where the recommended supplementation was still 4000 mcg).

After these initiatives, median folate levels in non-pregnant women of reproductive age more than doubled, and the US reported a drop of 30% in cases of neural tube defects.

United Kingdom (UK)—In 1991, the UK Government recommended women with a previous NTD pregnancy take 5000 mcg folic acid periconceptually.

In 1992, this advisory was extended to all women and the dosage was reduced when the tablet availability had been arranged.

In 1995–1996, there was a national media campaign to improve folic acid intake by fortification (consumption of foods fortified with folic acid), supplementation, and dietary change.

In 2000, the COMA report recommended flour fortification (240 mcg folic acid per 100 g of flour), periconceptual supplementation (4000 mcg for the high risk group and 400 mcg for all other women), and dietary consumption of folate-rich foods.

In 2004, the Health Ministry decided not to proceed with the COMA recommendations (due to outstanding concerns about B12 deficiency in older people).

Australia—The number of cases of neural tube defects in Australia has been reduced by voluntary fortification of some foods, but this benefit has not been distributed across all of Australian society. The largest reduction of cases of disability from
neural tube defects has occurred because of antenatal detection (and consequent pregnant termination), to the extent where (in 2005) NTDs were the leading cause for late-stage termination of pregnancy in Australia.  

**New Zealand (NZ)**—NZ has contributed annual figures to the ICBDMS for about 25 years. These figures are collected by the Ministry of Health and include livebirths and stillbirths with a range of congenital abnormalities, including NTDs. However, because NZ has not collect the same data from terminations of pregnancy, the statistics are inevitably incomplete when it comes to the incidence of congenital abnormalities.

For NTDs, this lack of data from terminations is critical, as there is good evidence from many countries that the majority of affected cases are identified on antenatal ultrasound and terminated in the second trimester.

**Public health initiatives in NZ**

In 1993, in the NZ Sunday Times, there appeared an article noting:

> The Department of Health recommends women eat plenty of green leafy vegetables to reduce the risk of their baby being handicapped

In the same article, they quoted the Principal Medical Officer as saying:

> …the abundance of vegetables in NZ meant that there was no need to recommend ‘pills and potions’ to pregnant women. Instead they should simply ensure they ate plenty of green vegetables, lightly steamed, and salads

In the same year (1993), a letter to the *New Zealand Medical Journal* drew attention to the results and recommendations of the UK-MRC Trial. The then Public Health Commission issued a “letter to health professionals” and a public statement:

> All women planning a pregnancy should take a daily supplement of folic acid, 5000 mcg, for 4 weeks prior to conception and for the first trimester of pregnancy

In 1995, when smaller 800 mcg tablets became available, the Ministry of Health amended its advisory to include the lower dosage for women planning a pregnancy who had no history of NTDs, and the higher dose (5000 mcg) for women with a prior history. The revised advisory noted that diet alone was not sufficient to provide the levels of folic acid needed to reduce NTD risk. A target was set to “reduce spina bifida live birth incidence to one-third of the 1993 level by 1997”.

In 1999, another publication from the Ministry of Health, *Folate, Folic Acid, and Health* again noted that “the proportion of infant deaths due to birth defects remained at 24%”. The document further explored the levels of folate in women in the reproductive age group in NZ (low), and the scientific evidence supporting the health benefits of fortifying breads with folic acid.

In 2001, the Ministry of Health reprinted its brochure *Folic Acid and Spina bifida*, with advice on periconceptional supplementation.

In 2003, the Ministry released its Public Health Intelligence Occasional Bulletin Number 18: *Improving Folate Intake in New Zealand: Policy implications*. This document reviewed the (then) recommendations, and noted that NZ women did not have a sufficient daily intake of folic acid to reduce the risk of NTDs.
The options reviewed included the “status quo” (improving dietary folate, periconceptional supplementation and voluntary fortification) and mandatory fortification.

In July 2004, Food Standards Australia New Zealand (FSANZ) issued a consultation document, Proposal P295—Consideration of Mandatory Fortification with Folic Acid.15

This consultation sought to review the background science, literature, and research as well as the future options for reducing NTDs in NZ. The options included the “status quo” (diet, supplements, and voluntary fortification) or mandatory fortification of a food product (bread-making flour or bread) with folic acid. In conclusion, this document noted that improving folate intake in NZ would involve:

- A comprehensive, ongoing national campaign to increase awareness of and consumption of folate through diet, supplements, and fortification in women planning a pregnancy.
- Consideration of mandatory fortification of either bread or flour with folic acid.
- Continuing the policy of recommending daily folic acid supplements to women planning a pregnancy, either in combination with voluntary fortification (status quo) or with mandatory fortification.
- Continuing to monitor NTDs in NZ.
- Improving the reporting of NTDs in terminations of pregnancy.
- Monitoring folic acid intake and folate status of the NZ population.

After the public consultation there was a 2-year wait (until September 2006) before FSANZ issued their response to the submissions received in the consultation. This response noted that “the Proposal for mandatory folic acid fortification of bread had been approved by the Board of FSANZ”. It was also noted that this represented a “refinement” of the original proposal (which had been for the mandatory fortification of bread-making flour) following “targeted consultations with key stakeholder groups”.

In October 2006, the 9th Meeting of the Australia and New Zealand Food Regulation Ministerial Council met. The proposal for mandatory fortification of bread was considered. FSANZ were requested to review the proposal with respect of compliance (at each individual bakery?) and monitoring and to report back to the Council in 6 months.

Personal commentary

So why, despite the science and the public health initiatives, have we not made more progress?

The use of folic acid supplements in NZ is still low.13 Many women appear unaware that folic acid supplements will reduce the occurrence and recurrence of NTDs—if consumed prior to conception and for the first trimester (the critical time for the formation of the spinal column).
To compound the problem, about 50% of pregnancies appear to be unplanned. Anecdotally, some women start their folic acid supplements once they have a positive pregnancy test (usually 6–8 weeks after the last menstrual period [LMP]). This is too late to impact on spinal column formation which is complete by 56 days (8 weeks) gestation. What about diet? Most evidence suggests that less than half of pregnant women change their diet when pregnant.

It is clear that 10 years of public health advice regarding diet, supplements, and voluntary fortification have had limited impact on the true incidence of NTDs in NZ. Indeed, the greatest reduction in livebirths has probably been as a result of terminations of affected pregnancies, as seen in Australia. This experience has mirrored that in Europe.

Equally clear is the science which has demonstrated unequivocally that fortification of flour results in a significant reduction in the incidence of NTDs in the population. Whilst mandatory fortification alone may achieve only some of the estimated 70% reduction seen in the original research trials, the combination of mandatory fortification, periconceptional supplementation, and healthy diets will achieve a very significant reduction in a preventable disability and reduce the number of terminations for major fetal anomalies.

The proposed strategy from FSANZ (October 2006) steps outside the established science (where all the benefit has been demonstrated when folic acid is added to flour at source rather than to bread in the bakery); introduces the further complication of developing standards and monitoring for hundreds of individual bakeries rather than to four flour mills in NZ; and risks a significant impact on the overall effectiveness of the fortification initiative.

Currently approximately 25 children are liveborn or stillborn with an NTD each year in NZ. An equal or greater number are terminated each year for the same anomalies. Conservatively, over the last 15 years (since 1991), there have been 750 children affected by this preventable disability. At least half of these children were not born but were terminated in the second trimester. The survivors (10–15 per year) face a lifetime of medical intervention and significant physical disability.

Spina bifida is a preventable disability. We are talking here about the primary prevention of “birth defects”. Any reasonable person might ask why this seemingly straightforward public health initiative has floundered for so long. A lack of will perhaps? Or, a lack of care?

**Recommendations**

New Zealand should proceed with a **coordinated program** to reduce the incidence of NTDs in our children. The program should include:

- A comprehensive, ongoing **national campaign** to increase awareness of and consumption of folate through diet, supplements and fortified food in women planning a pregnancy.
- **Mandatory fortification of flour** to a level of 240 mcg of folic acid per 100 g of flour.
• A policy of recommending **daily folic acid supplements** to women planning a pregnancy, at a level of 800 mcg of folic acid per day for the general population and 5000 mcg per day for those women with an increased risk, for at least 8 weeks prior to conception and for the first 12 weeks of the pregnancy.

• The **mandatory monitoring** of all NTD livebirths, stillbirths, and terminations by the Ministry of Health—to evaluate the effectiveness of this public health intervention.

• Continued 5-yearly monitoring of the folic acid intake and folate status of the NZ population.

**Conclusion**

In 2000, the death of one child playing with a Pokemon toy received international media coverage and led to the recall of 70,000 toys.

In the same year, in Canada, 250 children were liveborn with NTDs and a further 250 were aborted. There was no public outcry, no media attention, and no response from politicians.

> What we need is to feel a sense of responsibility and failure every time a fetus is aborted because of an NTD, or a child is born with this preventable disability

Dr AGW Hunter, Canada, 2000.^{18}

It is our tragedy that the above words still apply in 2007.

**Competing interests:** None.

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**References:**


