I first wrote about folic acid in this column about eighteen months ago (Wickham 2007). At that time, I wanted to highlight the fact that supplementation may carry potential downsides as well as significantly reducing the risk of neural tube defects in babies (e.g. Mitchell et al 2004). Less advantageous consequences of supplementation include an increased likelihood of multiple births (Werler et al 1997, Martin and Park 1999), concerns about the role of folic acid in carcinogenesis (Eichholzer et al 2006) and the possibility that folic acid and vitamin B12 supplementation may methylate or otherwise affect genes in humans as well as mice (Ainsworth 2006).

While the recommendation that women planning a pregnancy should take folic acid supplements has been relatively standard throughout the industrialised world for a number of years, public health policymakers have taken a range of approaches to the question of mandatory mass supplementation through food. In some countries, governments mandate that folic acid should be added to commonly eaten foods such as bread and cereals during production. Others are avoiding this because they perceive that the risks of folic acid either to specific groups (e.g. elderly people, who are an "at risk" group for vitamin B12 deficiency, which can be masked by folic acid supplementation) or the population as a whole outweigh the perceived benefits of supplementing pregnant women.

A new risk debate

Since my previous article, this debate has deepened, primarily in response to the publication of a randomised controlled trial which explored the link between folic acid supplementation and the likelihood of developing adenomas (Cole et al 2007). Laboratory work had suggested that folic acid supplementation might confer a degree of protection against the development of colorectal adenomas, although the results of different studies were not wholly in agreement with each other. Cole et al (2007) studied 1021 men and women who had a recent history of colorectal adenoma but who had not experienced an invasive large intestine carcinoma. Contrary to what the research team may have expected, however, the results not only failed to support the hypothesis that folic acid offers a degree of protection in this area; they actually suggested that folic acid supplementation might increase the likelihood of colorectal neoplasia. This latter finding was not statistically significant, but it does raise concerns and the researchers recommended that further research be carried out.

On the other side of the fence, Bayston et al (2007) argue with a number of the finer points of the Cole et al (2007) study, suggesting that it is important to clearly differentiate between the nature of adenomas and carcinomas, and citing other reasons which may explain these unexpected findings. The original research team responded by further supporting their position with epidemiological data (Mason et al 2007) and the debate has continued in medical journals and online journal discussion forums ever since. The key issue for all involved is whether these concerns justify not supplementing the population as a whole until more studies have been carried out.

What about pregnant women?

But what about those women who remain unaware of this new evidence and continue to believe that supplementation is a wholly good thing? The last time I raised this issue in these pages, I suggested that maybe more information should be made available to women on the totality of this issue. Not one of the authors who I have encountered in this area has discussed the need to reconsider the situation for women who are pregnant or planning to become pregnant. Instead, they are busily debating whether or not to supplement the remainder of the population, while essentially leaving women to continue taking their supplements.

Barbara Hewson (2004) makes it very clear in her analysis of the legal issues around the concept of informed choice that there are no grounds on which it is reasonable to treat pregnant women as a class of people with fewer rights that the rest of the population, and she urges that such attitudes should be challenged. Surely the withholding of the details of this debate from pregnant and planning-to-be-pregnant women is a textbook example of a situation which should be challenged?

Maternity Drug Controversies

If all or any of this sounds familiar, perhaps that is because it bears some resemblance to the debate that raged a decade and a half ago around the question of whether neonatal vitamin K increases the risk of cancer. At the height of the vitamin K controversy, the media were reporting on a study whose results suggested that the risk of childhood cancer was increased by vitamin K supplementation (Golding et al 1992). Subsequent realisation that the study methodology wasn't as robust as it might have been caused some people to begin to assure parents that vitamin K did not carry a risk of cancer after all. In fact, it would have been more

accurate to say that the concern which led to the original study remained, and that, unfortunately, we did not have adequate evidence to be able to answer the question either way. We still don't.

In theory, there are a number of things we could learn from looking at these kinds of debates. I would like to highlight two aspects that I see as among the most important. The first of these is our tendency to rush prophylactic interventions into practice on the basis of efficacy but without looking deeply at the possible risks. It can be argued that some possible risks may not be known about until a whole population has been exposed to the prophylaxis for a length of time. But does this justify treating pregnant women and / or their babies as metaphorical guinea pigs, or would it be better to give women full facts rather than simple recommendations?

One possible solution would be to change our attitude towards the way we offer prophylaxis from a public health / herd-based approach whereby the goal is to get as many people as possible to take up the offer of prophylaxis to a more individualised sharing of information about the state of our knowledge around whatever we are offering, in order that women themselves can decide. Yes, it takes more time if this is carried out as part of a discussion, but a number of good sources of written information are available and there always seem to be enough resources around when it is deemed necessary to recommend public health interventions to the population as a whole.

Who should decide?

The second issue concerns the way that many of those who engage in these kinds of debates (including myself) feel passionately about the issues. There are, however, significant differences in the approach taken by those who feel passionately that we must use all the technologies available to us with the key goal being the health of the population, and those who feel passionately that we must respect the autonomy of the individual and enable people to make the choices that are right for them. Many of those who are researching and writing about this issue sit in the first 'camp'. They believe that it is up to them to debate the issues in academic and medical forums in order to decide what the public should be fed in terms of recommendations or, as in this case, actual substances.

Public health policymakers may well see this as being a question for them, and not pregnant women, to consider. I suspect, however, that pregnant women, consumer groups, midwives and journalists may not agree with such a stance, and it may only be a matter of time before this becomes newsworthy. Midwives have arguably fewer opportunities to talk to women about issues such as folic acid supplementation than about issues such as vitamin K because, like other aspects of pre-conception care, women have often made and implemented their decision weeks or months before they meet a midwife. But if nothing else, perhaps we can learn from this latest controversy-to-be and look for more ways of letting women know about the context in which these kinds of recommendations are born.

References

Ainsworth C (2006) Mother's diet can tinker with baby's genes. Can be accessed at: http://www.nature.com/news/2006/060529/full/060529-10.html

Bayston R, Russell A, Wald NJ and Hoffbrand AV (2007) Folic acid fortification and cancer risk (correspondence), *Lancet* **370**: 2004.

Eichholzer M, Tönz O and Zimmermann R (2006) Folic acid: a public-health challenge Lancet 367: 1352–61

Cole BF, Baron JA, Sandler RS *et al* (2007) Folic acid for the prevention of colorectal adenomas: a randomized clinical trial, *JAMA* 297: 2351–2359.

Golding J, Greenwood R, Birmingham K et al (1992) Childhood cancer, intramuscular vitamin K, and pethidine given during labour. BMJ 305(6849): 341-46.

Hewson B (2004) Informed Choice in Maternity Care. In Kirkham, M (2004) Informed Choice in Maternity Care. Basingstoke, Palgrave Macmillan.

Martin JA and Park MM (1999). Trends in twin and triplet births:1980–97. National Vital Statistics Reports 47: 1–16.

Mason JB, Cole BF, Baron JA, Kim Y-I and Smith AD (2008) Folic acid fortification and cancer risk (correspondence). Lancet 371(9621): 1335

Mitchell LE, Adzick NS, Melchionne J et al (2004) Spina bifida, Lancet **364**: 1885–1895.

Werler MM, Cragan JD, Wasserman CR et al (1997) Multivitamin supplementation and multiple births. American Journal of Medical Genetics 1997; 71: 93–96.

Wickham, S (2007) Folic acid: is there a problem? Practising Midwife, 10(4): 35