Folic acid and the prevention of neural tube defects

Power of the state in attitudes to health has already expanded too much

EDITOR,—Nicholas J Wald and Carol Bower advocate the compulsory addition of folic acid to flour to prevent 1000 of the 1500 pregnancies in which the fetus has spina bifida that occur annually.¹ Few cases of children with spina bifida being born would be prevented. Most cases are already discovered in utero and terminations occur in most cases, so the main financial saving would be that of fewer terminations being performed. Ultrasound screening of pregnancies would undoubtedly continue, so there would be no savings there. Any savings made must be set against the cost of fortification.

When health policies entailing compulsion are proposed the transitory nature of medical "truths" must be borne in mind. Which general practitioner has not smiled wryly on going through an old patient's notes? Such records are a catalogue of misguided and unsafe medical ideas, though each was firmly held at the time. To make a treatment compulsory—fortification is a form of mass treatment of the population—is to imply that the medical belief on which it is based has achieved the status of permanent truth. If later the treatment is found to be either ineffective or dangerous for reasons not apparent when it was introduced the standing of medicine will suffer accordingly, and rightly so.

An extension of the fortification of flour or bread would bring with it detrimental social effects. There has already been too great an expansion of the power and influence of the state in attitudes to health. People are encouraged to see themselves as unhealthy, and the worried well are a growing group in general practitioners' surgeries. An extension of compulsory policies of the type advocated would serve to enhance the belief that the people of Britain need to have their dietary habits dictated. Where next? The compulsory skimming of milk?

Groups such as overweight people, those who are exercise shy, and parents opposed to vaccination of their children are increasingly seen as worthy of criticism. Those women of childbearing age who choose for whatever reason to avoid fortified flour would be at considerable risk of being seen as reckless, selfish, and undeserving of sympathy should they have the misfortune of giving birth to a child with spina bifida.

The weed that has been called "health fascism" and "coercive healthism"² is already well established. A policy of compulsory fortification of flour

with folic acid would be a fertiliser we can well do without.

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1 Wald NJ, Bower C. Folic acid and the prevention of neural tube defects. *BMJ* 1995;310:1019-20. (22 April.)

2 Skrabanek P. *The death of humane medicine*. London: Social Affairs Unit, 1994.

Chapati flour should be fortified as well

EDITOR,—All those who have a serious interest in improving the nation's health should endorse the recommendations made by Nicholas J Wald and Carol Bower to support the fortification of flour to prevent neural tube defects.¹ It is heartening to see a true population-wide strategy for a population-wide problem. Other solutions—such as pre-conceptional encouragement of an increased intake of folic acid—are not only naive but, like other pre-conceptional approaches, likely to be ineffective.

If the whole population at risk is to be reached effectively by this policy one caveat must be added to the proposals. Fortification of wheat flour and bread alone is not enough: the proposed policy will have no impact on those Asian communities who do not eat bread. To learn from the lessons of previous programmes against rickets and to prevent inequalities from creeping into the out-comes to be expected we should also aim to fortify chapati flour with folic acid.

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Most pregnant women do not take folic acid

EDITOR,—Preliminary results from a postal survey carried out by general practitioners along the Eden Valley in Cumbria support the assertions made by Nicholas J Wald and Carol Bower.¹ Three hundred and twenty one women who had delivered in the past year were asked anonymously whether they had taken folic acid during or before that pregnancy. Altogether 254 (79%) women replied, of whom 68 had taken folic acid before conception and 111 had started taking it only after finding that they were pregnant. The most common reported source of information about folic acid was the patient's general practitioner (131) followed by the media (67).

We are looking at ways of increasing awareness by means of leaflets given out with contraceptive advice, posters, and local media. We hope to show

an increase in women taking folic acid before conception as many now probably start taking it after closure of the neural tube. Should we fail to show an increase then presumably fortification of food should be considered.

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Preconceptional supplementation is impractical

EDITOR,—We agree with Nicholas J Wald and Carol Bower that the only way of ensuring an adequate intake of folic acid by pregnant women to prevent neural tube defects is by means of fortification of food as opposed to supplementation.¹ Supplements need to be started within 30 days of conception, and women would therefore need educating before conception.² There seems to be little demand for preconception clinics in primary care, and women of lower socioeconomic background (who are at higher risk of neural tube defects) are poor users of such preventive services.

It has been suggested that advice on folate supplementation could be given by general practitioners opportunistically at consultations about contraception. To see if this is a realistic way of targeting information at those likely to benefit we undertook a study in our inner city group practice. The available case notes of women who delivered in 1993 were examined. All consultations made by these 143 women (who represented 6.5% of the practice's population of 16-44 year old women) in the 12 months preceding conception were noted: 86% attended for general medical consultations and 46% for advice on contraception.

As one cannot predict who will conceive in the near future (and only two out of three pregnancies are planned), counselling on the use of folate supplements would need to be given to all women of childbearing age who consult. This would still capture only part of the population. Our calculations (table) show that advice would have to be given in 78 general medical consultations or 25 consultations about contraception to reach one woman who will deliver in the next year.

With the incidence of neural tube defects at one in 1000 and folate supplements being assumed to have a 70% protective effect, general practitioners would have to give advice during 35 714 consultations about contraception or 111 428 general medical consultations to prevent one neural tube defect.³ This is assuming that women plan their pregnancies, attend for consultations, remember and wish to comply with advice given, and can afford folate supplementation.

Number of consultations in practice of 9178 patients (of whom 2186 were aged 16-44) required to target one woman delivering in next year

	Consultations about contraception	General medical consultations (including for contraception)
Observed consulting rate among women/year	0.78	4.4
Total No of consultations/year	0.78 × 2186 = 1705	4.4 × 2186 = 9618
No of women delivering in 1993 who attended in 12 months before conception	69	123
No of consultations required to reach one woman delivering in next year	1705/69 = 25	9618/123 = 78

Advice to authors

We prefer short letters that relate to a recently published article and we are unlikely to publish letters longer than 400 words and containing over five references. Letters may be shortened. Your letters should be typed with double spacing and include a word count. All authors need to sign the letter and provide one current appointment and address. We encourage you to declare any conflict of interest. Please enclose a stamped addressed envelope if you require an acknowledgment.

If we are to succeed in reducing the number of pregnancies in which the fetus has a neural tube defect we must adopt a policy of fortification of food. This approach is both simple and cheap and most likely to serve those at risk.

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Folate has potential to cause harm

EDITOR,—Nicholas J Wald and Carol Bower favour a population strategy rather than a selective strategy to prevent 1000 neural tube defects annually in the United Kingdom, with compulsory fortification of flour with folic acid.¹ They could perhaps have strengthened their case by referring to other potential benefits of their proposal—for example, in mental health, especially in psychiatric and geriatric populations.² Instead, however, they rather undermine their case by inaccurately minimising the disadvantages of their policy.

Their statement that "even in large doses folic acid has not been shown to cause harm" should not pass unchallenged. Although they acknowledge that folic acid may mask the anaemia of pernicious anaemia, they fail to emphasise that it may precipitate neurological complications in this context, as colleagues and I have shown.³ This can occur in the absence of anaemia, macrocytosis, or even a low serum vitamin B-12 concentration. The authors suggest that the problem of masking pernicious anaemia could be resolved by education, but apparently they do not favour a selective educational approach to prevent neural tube defects.

The risk that seizures may increase in patients with epilepsy⁴ is rather casually dismissed by the suggestion that higher doses of antiepileptic drugs might be needed, as if this in itself did not carry any risk.

A wider and more detailed consideration of all the advantages and disadvantages of the authors' proposals would be appropriate.

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Evidence based medicine

Example was flawed

EDITOR,—While I admire the intended efforts of evidence based medicine to reinforce clinical practice with up to date research, the article by William Rosenberg and Anna Donald highlights the flaws in this system.¹ The example that the

authors cite—of an elderly woman with non-rheumatic atrial fibrillation—is interesting. The risk-benefit analysis outlined makes no mention of therapeutic reference ranges, which are inextricably linked to any analysis of outcome measures associated with management with oral anti-coagulants. Thus, after it has been established that the patient would be more likely to benefit from treatment with warfarin, the clinical decision to have a target international normalised ratio of 1.5-2.0 is apparently picked out of thin air. This therapeutic range is too narrow to be of practical use and does not agree with the British Society of Haematology's current guidelines.² If strong advocates of evidence based medicine make such experientially based decisions, what chance do the rest of us have?

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Megatrials are subordinate to medical science

EDITOR,—Evidence based medicine started life as a flawed but marvellously refreshing approach to clinical practice and continuing education.¹ Unfortunately, it has recently been taken up by politicians and managers and is currently being packaged and promoted as a panacea, at the expense of medical science.

The main defining feature of evidence based medicine is its assertion that randomised controlled trials, especially "megatrials," should serve as the basis for clinical practice. For instance, William Rosenberg and Anna Donald deplore "the gaps between research evidence and clinical practice,"² as if megatrials told clinicians what to do and the job of clinicians was simply to do it.

But this whole notion of a gap between research and practice is misconceived. The results of megatrials—even in the rare circumstances that they are available and have been replicated—offer knowledge only at the population level.³ To apply this to the care of individual patients would be a classic example of the ecological fallacy: group averages tell us nothing about causal processes in the individuals who compose that group.

Furthermore, the population sampling achieved by a megatrial is non-random and subject to large selection bias. Megatrials are typically performed in specialised research settings. Despite this, some trials have included fewer than 10% of eligible patients.⁴ Even after admission, drop outs and crossovers between the comparison groups inevitably occur.⁵

The result of a megatrial cannot be extrapolated to a target population without substantial adjustments being made, and these adjustments will need to be based on contextual scientific knowledge. The epidemiological emphasis of evidence based medicine is mistaken. Science provides the innovations, the causal hypotheses, and the framework within which megatrials have their function.

Megatrials have an important role, but it is subordinate to medical science and consists mostly of checking predictions and refining protocols. If we needed to make a choice between medical science and megatrials as the basis of clinical practice then we would have to choose science.⁶

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Must be applied critically

EDITOR,—William Rosenberg and Anna Donald make a clear case for evidence based medicine.¹ Logically one would assume that there could be no case against such an approach. They describe a relatively tedious method of gathering evidence to answer a clinical question. Their method entails performing appropriate searches from scratch. Developments in systematic reviews—particularly in maternity care—have led to the gathering of evidence being simplified. In short, someone else's meta-analysis has already answered your question. Problems can arise when results of meta-analysis are not viewed critically and in an informed manner. I am aware that one purchaser refused to fund ultrasound scanning for anomalies in the second trimester because meta-analysis had shown that it detected only largely lethal anomalies.

In the development of a policy for induction of labour in our unit I suggested routine "cervical stretch and sweep" for pregnancies proceeding beyond term. I was challenged because a recently published book, summarising several meta-analyses, states that "there is too little evidence to assess the effectiveness of this technique."² This statement is supported by reference to a meta-analysis in the *Cochrane Database of Systematic Reviews*.³ This review was performed in 1989 and last amended more than three years ago. Since then a well conducted randomised controlled trial has been published,⁴ accompanied by a favourable review article.⁵ The compilers of the Cochrane database have not yet updated their meta-analysis to take account of these publications, and the book² has not been updated either, leading to a false interpretation of the value of a useful clinical intervention.

Purchasers and other decision makers should avoid adopting the findings of incomplete or out of date meta-analysis uncritically. Is there scope for a trial of evidence based medicine, assessing all outcomes and with full economic data?

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Many questions cannot be answered by evidence based medicine

EDITOR,—We envisage that databases for evidence based medicine would answer the question "What is best practice?" and that hospital based audit would check that best practice is being achieved. Our audit programme has examined pain relief for tonsillectomy. In the 58 children audited, nine tonsillar blocks were performed; additional oral