



Swings and Roundabouts of Folic Acid

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When I first read the early reports that folic acid and vitamins might prevent neural tube defects like spina bifida in babies, I started wondering about the health of the mothers. Did they not have enough folic acid in their diet, or could they not absorb it? What happened to the long term health of those women, and why was no-one interested in following them up? They might have healthier babies if they took supplements in early pregnancy, but what about the rest of their lives? What if the folate deficient women did not survive long enough to rear the children?

It seemed as if preventative medicine was concentrating solely on reducing the burden of handicap - which is very important - but was uninterested in the long term health of the mothers. If they did not like folate-rich foods, could not obtain them, or could not afford them, what sort of diet were they going to give the children? And if the mothers had a genetic absorption problem, wouldn't the children have it too? Babies with neural tube defects might simply be the extreme indicator of a much wider problem affecting general health of mothers and families.

Women with only moderate levels of folic acid have a fivefold greater risk of precancerous lesions in the cervix than women with high levels.⁽¹⁾ Folic acid reduces precancerous cells in the lungs of smokers.⁽²⁾ It may also help to prevent heart disease and colorectal cancer.⁽³⁾ No-one seems keen on telling women that oral contraceptives lower folic acid levels, and after they stop taking the Pill it may be four months before folic acid in their tissues is back to normal - but what about the women in whom it is genetically abnormal in the first place?

Anyway, folic acid deficiency alone does not explain why neural tube defects are more common in some countries than others (2.8 per 1000 births in Hungary and 0.6 in the USA). Within the British Isles, they are commoner in Wales and the west coast of Scotland, and in Ireland. We do not know how folic acid works. This may seem like an academic question - so long as it does work, why should we care? But as I shall show, the answer may matter a great deal.

It has now been proved in randomized trials, that if mothers start taking folic acid before they become pregnant, and continue to do so in early pregnancy, neural tube defects can be reduced. Medication is both cheap and effective, and that is an enormous benefit. Mothers who have already had an affected pregnancy are known to be at increased risk in future. The Medical Research Council trial of 1800 such high-risk mothers proved that it was the folic acid that dramatically reduced the risk - by 72%. Giving

women other vitamins without the folic acid did not work.⁽⁴⁾ Long term follow up of the babies was promised, but so far no reports have appeared 6 years later. That is a pity because this group had the highest dose. However, there were small numbers in each group, so possible differences might not show up as significant.

A larger study in Hungary of 7,500 ordinary women with no previous affected babies (most were wanting to conceive their first child) took a smaller dose of folic acid (0.8 mg) plus other vitamins, or a low dose supplement of minerals. This is a particularly important study, because it shows what is more likely to happen with a mass public programme of prevention. None of the 2,000 mothers who had the folic acid and other vitamins produced a baby with a neural tube defect, but six of the control mothers did.⁽⁵⁾ What is more, other defects like limb abnormalities were also less common in the multivitamin group.⁽³⁾

Folic acid seems remarkably safe - but is it totally safe for the fetus? The Health Education Authority confidently assures women it is: "Folic acid cannot harm you or your baby"⁽⁶⁾ and recommends that women take a supplement of 0.4 mg. Doctors from the National Institute of Child Health in the USA are more cautious, and point out that little is known about the possible toxicity of high dose folate to the fetus or the mother. And although low doses seem safe, we cannot be absolutely sure.⁽⁷⁾

So far, only the Hungarians have published a follow up study, of the babies between 8-13 months⁽⁸⁾ There was little difference between the two groups except for one thing - the babies who had vitamins in the womb had more asthma, bronchitis and allergic skin problems, and the difference was significant. This does not prove that folic acid or other vitamins caused the problem, but it was a large, randomised study and that is certainly a possibility. With large numbers of our young children already taking their inhalers to school, it's a problem worth thinking about.

There were other differences. The vitaminised mothers had the advantage of conceiving more quickly. The authors even wondered if it was because the vitamins had perked up their sex life, but found that was not so.⁽⁹⁾ Earlier conception could be an advantage to women trying to get pregnant. However, more of the folic acid mothers had multiple births, particularly identical twins, and this needs further exploration.⁽¹⁰⁾ If this is a greater risk, it is not one all women would choose, particularly as twins are more likely to be premature, and to be handicapped or die at birth. And of course two babies are more expensive to rear than one. Even a small national increase in the rate of twinning would be costly to the NHS, since twins are more likely to need beds in expensive special care baby units.

Unfortunately the MRC trial gave no information as to whether there were more multiple births in their trial.

Now a new question has arisen. The authors of the Hungarian study have revealed that the vitamin group had a 16 % higher miscarriage rate than the placebo, group [\(11\)](#) Among the 2,700 supplemented pregnancies there were 27 fewer malformations, but there were 51 more spontaneous abortions - almost twice as many as the number of birth defects avoided. For every 1,000 women who got pregnant on folic acid and vitamins, there would be 10 fewer malformed births but 18 more miscarriages.

Hungary has an above-average risk of babies with neural tube defects. Would the benefits be less in a low risk country, but the losses be just as great? The authors suggest that folic acid might be a weak abortifacient, and that it may actually prevent neural tube defects by helping the body to reject the malformed baby more effectively - but also encourage rejection of other babies too.

When women have a baby with a neural tube defect it could be because Nature's mechanism of spontaneously aborting handicapped babies does not work as well for them as other women. For example, Japan has very few babies with neural tube defects, but when aborted fetuses were studied, many more were found. The defects happen in Japanese babies too, but they are miscarried.

Many, perhaps most, women would choose to take an effective, cheap vitamin supplement rather than undergo the tiniest risk of having a child with a severe handicap, or having to go through an abortion. But if there is one thing we learn from the AIMS helpline it is how complex and individual are the choices that women have to make for themselves and their families, and how their priorities differ.

Suppose you are longing for a baby, and have already had one or more miscarriages of apparently normal babies. You are affluent and middle class, have a good diet, and therefore at low risk of having a baby with a neural tube defect. (The incidence of neural tube defects is actually declining). You live in a low risk area, and do not have Celtic blood. The choice of abortion is always open to you if you have a severely handicapped fetus. Do you choose folic acid with a possible slightly increased risk of losing a healthy fetus or not? Suppose you are a woman, again in a low risk area, who has a strong family history of asthma and eczema. Perhaps you had a sibling or child who actually died of asthma. Would you choose folic acid before your next conception if there was a small increased risk of your baby developing those problems?

So the folic acid miracle - though it is a tremendous advance - is not as simple as it may appear.

NOTE: It is very important that women taking medicine for epilepsy should NOT take folic acid without first getting medical advice.

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