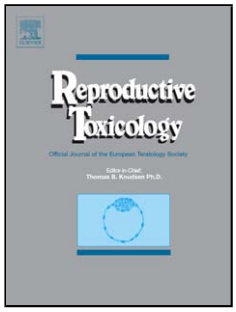

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Bio-monitoring the Elimination of Folic Acid-Preventable Spina Bifida and Anencephaly

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Since 1991, we have had unequivocal evidence that folate deficiency is the primary cause of spina bifida and anencephaly (SBA) in most of the world.(1, 2) Thus, if all women of reproductive age consume enough folic acid, we can eliminate Folic Acid-Preventable Spina Bifida and Anencephaly (FAP SBA) by primary prevention. It is seldom that we have such an opportunity to prevent severe and common birth defects. Unfortunately, we are far from accomplishing the elimination of these birth defects.(3)

A key feature of the successful polio eradication campaign has been timely monitoring of the progress or lack of it and the ability to determine when polio is eradicated in a country.(4) The efforts to eliminate folic acid-preventable spina bifida and anencephaly also need a reliable, timely indicator to determine when required folic acid fortification programs have been successfully implemented and when a state or a country has prevented all or almost all FAP SBA.

Pre- and post-fortification serum/plasma and/or red blood cell folates have been measured in a variety of research designs—from nationally representative surveys to convenience samples.(5-8) These data show that before folic acid fortification the mean serum/plasma folate concentration is about 4 ng/ml and rises almost immediately to 8 or more ng/ml after the successful implementation of required folic acid fortification programs. Red cell folate levels also rise after a period of several months.(9) Thus the simple measurement of plasma or red cell folate can provide the evidence needed to know if the fortification was successfully implemented.

The implementation of a folic acid fortification program may not provide enough folic acid to eliminate FAP SBA. If we knew the serum/plasma or RBC folate level that would assure the prevention of all FAP SBA, serum/plasma or RBC surveys could determine whether or FAP SBA had been eliminated. There has yet to be a generally agreed upon serum/plasma or RBC folate level that assures the elimination of FAP SBA.(10) In the absence of such a consensus, Bar-Oz and his colleagues in a paper in this issue assume that elimination or near elimination would occur when all women have a RBC folate of at least 900 nmol/L. Given the available evidence, their assumption is a reasonable one, albeit one that might go up or down with new data. They show that, before fortification, almost no women in Ontario had RBC folate levels above 900 nmol/L. After fortification, 40% remained below this cut point and were assumed to be at unnecessary risk. These and other data show that folic acid fortification of flour in Canada has been highly effective in raising RBC folate concentrations and there has been a sustantial prevention of FAP SBA.(7, 11, 12) It is likely that, were the concentration of folic acid in flour doubled in Canada, most women would have RBC folate concentrations above 900 nmol/L and most, if not all, FAP SBA would be prevented.

As important as their paper is in assessing current prevention in Ontario, it is more important that they have applied a biomarker approach to monitor the progress toward the elimination of FAP SBA. Their approach should be considered the current best way to determine the proportion of women at unnecessary risk for FAP SBA. It is likely that their method can be improved. We need to build consensus and perform studies that will validate the most appropriate epidemiological and laboratory methods to assess the

progress towards the elimination of FAP SBA in every country. A serum/plasma and/or RBC folate survey would likely be a more timely and less expensive approach to evaluate prevention than would surveys of pregnancies affected with SBA. Since blood folates rise after fortification, within a year of the implementation of fortification programs, one can estimate the proportion of women still at risk of having pregnancies with FAP SBA. It would take several years for enough babies to be born with spina bifida and anencephaly, for the data to be collected and analyzed, and for policy recommendations to be made about needed changes in the fortification program. A folate bio-monitoring program would be less expensive and could provide key data for policy within a year of fortification.

Currently no group is funded to design and implement a folate bio-monitoring program. For polio eradication, the CDC has had substantial and sustained funding to provide leadership and technical assistance to the polio eradication effort. Appropriations by Congress, currently about $200 million a year, have been essential to the success of this program. Given the success that CDC has had in prevention, it would seem reasonable for Congress also to provide CDC with sufficient, sustained resources to provide leadership and technical assistance to accelerate the elimination of FAP SBA around the world. Alternatively, foundations, other governments or industry could provide the support for such a center.

This global technical assistance center and network should provide any country the epidemiological and laboratory support to monitor the progress towards the elimination

of FAP SBA. There will be many activities and projects for this center. Initially the center should:

1. Help countries conduct surveys of serum/plasma or RBC folate to determine whether or not mandatory folic acid fortification programs have been successfully implemented

2. Establish a task force to prepare and distribute a manual on how to monitor progress towards the elimination of FAP SBA.

3. Advocate for and use new research that will improve our ability to determine progress toward elimination in an accurately and timely manner.

Work to achieve mandatory folic acid fortification should not wait for the establishment of this center or its products. The mandatory folic acid fortification programs in North America and in Chile have been highly successful in preventing birth defects, even though no country is known to have eliminated them. There remains an urgent need for countries that have yet to require fortification to implement such programs now. Failure to do so means that thousands of children will be born each year with preventable spina bifida and anencephaly and that millions of people will have unnecessary folate deficiency anemia. Readers of this journal are in a unique position to advocate for the urgent elimination of FAP SBA. We hope that as many as possible will work to provide the political will to prevent these birth defects.

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