CASE-BASED REVIEW



Failure to fortify staple foods with folic acid—still public health malpractice

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"One of the most exciting medical findings of the last part of the twentieth century is that folic acid, a simple, widely available, water-soluble vitamin, can prevent spina bifida and anencephaly (SBA). Not since the rubella vaccine became available 30 years ago have we had a comparable opportunity for primary prevention of such common and serious birth defects" [1].

"The opportunity to implement a sustainable, inexpensive passive population intervention to prevent major human diseases comes rarely. Folic acid fortification of centrally processed grains is one of those rare opportunities. Governments that have not moved to assure that centrally processed grains are almost all fortified with sufficient folic acid are acting irresponsibly. They are committing public health malpractice" [2].

Inever dreamed, in 1991, when I learned that folic acid would prevent spina bifida and anencephaly, that 31 years later we would be preventing only about 25% of global, preventable cases of spina bifida F and anencephaly F annually (F refers to Folic acid-preventable cases, the predominant cause of the two birth defects in countries that do not require fortification of food with folic acid) [3]. Part of my rationale in the 1980s for seeking funding for a randomized controlled trial was that if folic acid prevented spina bifida, folic acid could be added to staple foods eaten by the majority of the population, thus preventing spina bifida. This concept is similar to how large-scale population-based interventions with iodine and vitamin D prevented cretinism, goiter, and rickets.

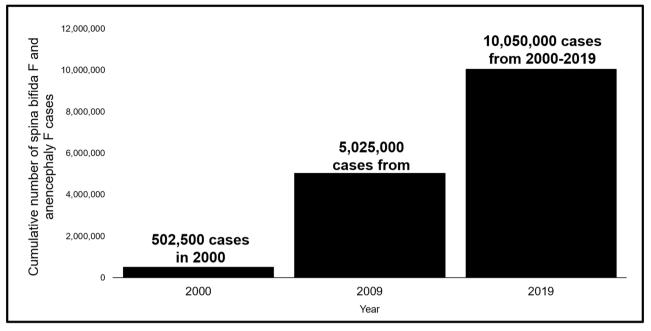
I marvel at the enormous success of philanthropy and government funding to reduce child mortality based upon old and new research demonstrating effective vaccines. Spina bifida F and an encephaly F are well-known causes of stillbirths, neonatal, perinatal, infant, and child mortality. It is proven that mandatory folic acid fortification of widely consumed foods is the most sustainable and cost-effective way to prevent these causes of mortality. Folic acid fortification has been successfully implemented in the USA, Costa Rica, Canada, and Oman since the late 1990s. Yet, philanthropy and government have failed to give sufficient priority to folic acid fortification programs on a global scale. The failure to support this proven way to help low- and middleincome countries achieve their child mortality reduction targets within the 2030 Sustainable Development Goals is especially difficult to understand [4].

The burden of the disease caused by countries' failures to fortify food with folic acid is very large. I estimate 10 million cases of spina bifida F and anencephaly F occurred globally in the first two decades of this century that were completely preventable through folic acid fortification of staple foods (Fig. 1). My estimate considers the global prevention of spina bifida F and an encephaly F at 25% in each of those years based on our recent published work, and this prevention proportion is likely an overestimate [5]. I assumed an average spina bifida and an encephaly rate of 50 per 10,000 pregnancies. This rate is higher than we assumed for our previously reported global estimate of the rate of prevention of spina bifida and anencephaly pregnancies in countries without folic acid fortification [5]. In those estimates, we used 25 per 10,000 as was reported in the March of Dimes Global Report on Birth Defects [6]. We continue to use the March of Dimes prevalence estimate, developed by Dr. Bernadette Modell, to assist with the interpretation of the global rate of prevention of spina

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Cumulative number of preventable cases of spina bifida F and anencephaly F that occurred globally between vears 2000 and 2019 due to a lack of folic acid fortification in over 100 countries:

= (134,000,000 births / year) × (50 cases of spina bifida F and anencephaly F / 10,000 births without folic acid fortification of staple foods) × (75% cases not being currently prevented through folic acid fortification of staple foods) × # years

Fig. 1 Number of cases of spina bifida F and anencephaly F that could have been prevented globally through folic acid fortification of staple foods between years 2000 and 2019. F folic acid-preventable cases of spina bifida and anencephaly

bifida and anencephaly, however, we stress that these are modeled estimates and likely underestimates of the actual global burden of the birth defects. A more recent estimate by Blencowe et al. [7], building on the Modell methodology, reported a global prevalence of 18 per 10,000 for neural tube defects, largely composed of spina bifida and anencephaly. In their paper, Blencowe et al. [7] state that their total NTD prevalence estimate is an underestimate of the actual burden, especially in low- and middle-income countries, with challenges in tracking pregnancy outcomes for NTD-associated early fetal losses, miscarriages, elective terminations, and stillbirths.

My estimation of the number of cases of spina bifida F and anencephaly F occurred globally between 2000 and 2019 was rather based on historic data from studies published before countries implemented fortification. MacMahon and Yen describe the Great American Epidemic of spina bifida and anencephaly that peaked in the 1930s at a combined prevalence of 45 per 10,000 births, falling gradually to 18 per 10,000 births in 1960 [8]. Elwood and Nevin conducted a population-based prevalence study of spina bifida and anencephaly in Belfast from 1964 to 1968, reporting a combined prevalence of spina bifida and anencephaly of 87 per 10,000 births [9]. Then the China-USA study from 1993 to 1995 found 48 per 10,000 births in the Northern region and 10 per 10,000 births in the Southern region of China [10]. More recently, Atlaw et al. [11] reported a prevalence of 50 per 10,000 births in Ethiopia, a country with a high prevalence of folate deficiency among women of reproductive age Ethiopian Public Health [12].

There is good news. Led by Drs. Jeffery Blount and Gail Rousseau, neurosurgeons have combined their talents to work toward global prevention of spina bifida F and anencephaly F as fast as possible. They formed the Global Alliance for Prevention of Spina Bifida F (GAPSBiF) to prevent spina bifida F (and an encephaly F). GAPSBiF is actively promoting a World Health Assembly resolution seeking all countries to require and enforce food fortification to prevent spina bifida F and an encephaly F [13]. These efforts are built upon a 2010 World Health Assembly resolution promoting birth defects prevention and a resolution issued by the International Society of Pediatrics Neurosurgeons (ISPN) Caceres et al. [14]. The resolution by the ISPN is an additional effort by neurosurgeons to accelerate the pace of spina bifida F and anencephaly F prevention through food fortification with folic acid in countries worldwide. Martinez et al. and Kancherla et al. reviewed scientific and policy data and provided a rationale for immediate implementation of required and enforced folic acid fortification of appropriate foods and for the urgent need for a WHA resolution for folic acid fortification [15, 16].

In the book *House on Fire: The Fight to Eradicate Small*pox, author and public health leader Dr. William Foege outlines landmarks necessary to build a successful global effort to prevent diseases [17]. Dr. Foege points to two necessary requirements for action: "social will" and "political will." I am encouraged by the neurosurgeons who are building social and political will by championing primary prevention of spina bifida F and anencephaly F. I am encouraged by the recent exploration of folic acid-fortified iodized salt because of its potential to help multiple countries improve their chances of preventing spina bifida F and anencephaly F and meeting their 2030 Sustainable Development Goals [18]. I am also encouraged by Rotarians who are interested in programs to prevent spina bifida F and anencephaly F.

In closing, I encourage philanthropy and governments to provide sufficient resources to maximize the number of countries that require, enforce, and monitor folic acid fortification. Let us end the current public health malpractice in time to help all countries achieve their 2030 Sustainable Development Goal targets by fortifying staple foods with folic acid.

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Declarations

Conflict of interest There are no competing interests to declare.

References

- Oakley GP Jr (1993) Folic acid-preventable spina bifida and anencephaly. JAMA 269(10):1292–1293
- Oakley GP Jr (2002) Inertia on folic acid fortification: public health malpractice. Teratology 66(1):44–54
- Medical Research Council (1991) Prevention of neural tube defects results of the Medical Research Council Vitamin Study. MRC Vitamin Study Research Group Lancet 338(8760):131–137
- 4. Kancherla V, Redpath B, Oakley GP Jr (2019) Reductions in child mortality by preventing spina bifida and anencephaly: implications in achieving Target 3.2 of the Sustainable Development Goals in developing countries. Birth Defects Res 111(14):958–966
- Kancherla V, Wagh K, Pachón H, Oakley GP Jr (2021) A 2019 global update on folic acid-preventable spina bifida and anencephaly. Birth Defects Res 113(1):77–89
- 6. Christianson A, Howson CP, Modell B (2006) March of Dimes global report on birth defects: the hidden toll of dying and disabled children. White Plains, NY: March of Dimes

- Blencowe H, Kancherla V, Moorthie S, Darlison MW, Modell B (2018) Estimates of global and regional prevalence of neural tube defects for 2015: a systematic analysis. Ann N Y Acad Sci 1414(1):31–46
- MacMahon B, Yen S (1971) Unrecognised epidemic of anencephaly and spina bifida. Lancet 1(7688):31–33
- Elwood JH, Nevin NC (1973) Anencephalus and spina bifida in Belfast (1964–1968). Ulster Med J 42(2):213–222
- Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Mulinare J, Zhao P, Wong LY, Gindler J, Hong SX, Correa A (1999) Prevention of neural-tube defects with folic acid in China. China-U.S. Collaborative Project for Neural Tube Defect Prevention. N Engl J Med 341(20):1485–90
- Atlaw D, Tekalegn Y, Sahiledengle B, Seyoum K, Solomon D, Gezahegn H, Tariku Z, Tekle Y, Chattu VK (2021) Magnitude and determinants of neural tube defect in Africa: a systematic review and meta-analysis. BMC Pregnancy Childbirth 21(1):426
- Ethiopian Public Health Institute (2016) Ethiopian National Micronutrient Survey Report, September 2016. Available at: https:// www.ephi.gov.et/images/pictures/download2009/National_MNS_ report.pdf. (Accessed 13 Oct 2022)
- Shlobin NA, Jordan T. Roach JT, Kancherla V, Caceres A, Ocal E, Ghotme K, Lam S, Park KB, Rosseau G Blount JP, Boop FA (2022) The role of neurosurgeons in global public health: the case of folic acid fortification of staple foods to prevent spina bifida. J Neurosurg: Pediatrics. (2022). In Press
- Caceres A, Blount JP, Messing-Jünger M, Chatterjee S, Fieggen G, Salomao JF (2021) The International Society for Pediatric Neurosurgery resolution on mandatory folic acid fortification of staple foods for prevention of spina bifida and anencephaly and associated disability and child mortality. Childs Nerv Syst 37(6):1809–1812
- 15. Kancherla V, Botto LD, Rowe LA, Shlobin NA, Caceres A, Arynchyna-Smith A, Zimmerman K, Blount J, Kibruyisfaw Z, Ghotme KA, Karmarkar S, Fieggen G, Roozen S, Oakley GP Jr, Rosseau G, Berry RJ (2022) Preventing birth defects, saving lives, and promoting health equity: an urgent call to action for universal mandatory food fortification with folic acid. Lancet Glob Health 10(7):e1053–e1057
- Martinez H, Pachón H, Kancherla V, Oakley GP (2021) Food fortification with folic acid for prevention of spina bifida and anencephaly: the need for a paradigm shift in evidence evaluation for policy-making. Am J Epidemiol 190(10):1972–1976
- 17. Foege W (2011) House on fire: the fight to eradicate smallpox. University of California Press, Berkeley and Los Angeles, California
- Kancherla V, Tsang B, Wagh K, Dixon M, Oakley GP Jr (2020) Modeling shows high potential of folic acid-fortified salt to accelerate global prevention of major neural tube defects. Birth Defects Res 112(18):1461–1474

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