Letters to the Editor

The basis of recommendations for docosahexaenoic and arachidonic acids in infant formula: absolute or relative standards?

Dear Sir:

Brenna et al (1) conducted a meta-analysis of human milk docosahexaenoic acid (DHA) and arachidonic acid (AA) contents worldwide. Their study consisted of 65 reports on 2474 women with mostly Western dietary habits. In agreement with at least 2 previous studies (2, 3), they concluded that milk DHA is more variable than is milk AA and that the ratio of DHA to AA varies widely. The calculated mean (±SD) values for DHA (0.32 ± 0.22% by wt) and AA (0.47 ± 0.13% by wt) were suggested to serve as a guide for infant feeding.

Although Brenna et al’s conclusion on variation is consistent with one of our previous reports (2), we currently feel that the low variation in AA might in reality derive from a sampling bias. We found much higher milk AA (median: 0.70 mol%) and high DHA (0.75 mol%) contents in lactating women in Doromoni (Tanzania) (4). Their milk showed a clear correlation between DHA and AA. Both of these long-chain polyunsaturated (LCP) fatty acids could be traced to life-long consumption of DHA- and AA-rich fish from nearby freshwater, Lake Kitangiri. It seems that milk AA is notably dependent on long-term AA intake, because supplementation of lactating women in Jerusalem with 300 mg AA for 1 wk did not increase milk AA (5). The sizeable short- and long-term dietary influences on human milk fatty acid composition raise the question of whether the resulting variance should be taken as testimony of the wide variety of foods that are tolerated by humans and their offspring or whether it indicates a lack of evolutionary pressure because of a rather constant dietary composition in the past. We recommend that worldwide human milk fatty acid composition should not be used as guide for infant formula. Just as Western serum cholesterol concentrations and vitamin D status should not serve as targets for recommendations, it seems inappropriate to use calculated mean milk DHA and AA concentrations of mostly Western women as a basis for infant formulas. At least 3 arguments favor higher intakes of both DHA and AA by our ancient ancestors, who consumed diets that were much closer to the environment on which our genome has adapted during the past 2–3 million years of evolution. First, the sites at which their fossil remains have been discovered support the notion that evolution to Homo sapiens took place on an LCP n–3-rich diet from African ecosystems that were located in places where the land meets with water (6, 7). Food from these ecosystems is rich in iodine, vitamins A and D, and n–3 fatty acids of both vegetable and animal origin. Contrary to popular belief, our ancient ancestors did not need fishing gear to benefit from the abundance of LCP n–3 fatty acids, and probably of LCP n–6 fatty acids, in such ecosystems, where it is relatively easy to hunt and gather anything ranging from spawning catfish, shellfish, and crustaceans (lobster, crab, shrimp, etc) to eggs, birds, and reptiles, which all ultimately receive their LCP n–3 fatty acids from plankton via the local food chain. The resulting diet with a high content of iodine, vitamins A and D, and LCP fatty acids seems to have been somewhat abandoned since the Out-of-Africa Diaspora, because deficiencies of these nutrients are among the most widely encountered in the current world population (6, 8). Second, epidemiologic data have shown a negative association of fish oil with coronary artery disease (CAD) and of fish consumption with (postpartum) depression. Landmark trials with α-linolenic acid (9), fish oil (10), and eicosapentaenoic acid (EPA) (11) in CAD and with EPA in depression and schizophrenia (12) support the causality of these relations. As acknowledged by Brenna et al (1), the intake of marine food in inland and developed countries is usually low. Many authoritative organizations have issued recommendations to the general public ranging from “choose fish as a food item more often” to “consume 3 servings of fish per week.” One may wonder what the milk DHA and resulting DHA status would be of children born to parents reaching the necessary DHA status to decrease their risks of CAD and psychiatric disease. If their parents would benefit from a higher than current Western DHA status, which cannot be achieved by the mere consumption of α-linolenic acid, it seems reasonable to assume that this DHA status is appropriate across the Homo sapiens life cycle and that our genes may have evolved on this high DHA status. Meanwhile, it has also become clear that LCP fatty acids are not only important structural components of membranes but together with their eicosanoid metabolites, are firmly implicated in gene expression, eg, as modulators of nuclear transcription factors such as peroxisome-proliferator activated receptors, sterol regulatory element-binding protein, and nuclear transcription factor xB. Finally, many randomized controlled trials that used formulas with and without LCP fatty acids, and measured outcome variables such as retinal function, visual acuity, behavior, and cognitive and motor developments, have shown beneficial effects of LCP, notably of LCP n–3 fatty acids, in both preterm and term infants. Preterm infants benefit most, but many of the effects are transient. The effects are especially the result of DHA, but AA might be important for preserving the balance between n–3 and n–6 fatty acids. The present consensus from human and animal studies is that LCP fatty acid supplements have no effect on growth, neonatal brain DHA is positively related to cognitive and behavioral performance, the differences are difficult to detect with currently available tools, and that the encountered differences may nevertheless be relevant (13). All of these studies have been performed with DHA and AA intakes in the current Western human milk range, which might explain the modest effects.

In conclusion, we agree that DHA seems to be the most variable fatty acid in human milk worldwide. The variance in AA, however, may be underestimated because of sampling bias. Higher AA concentrations occur in women who consume diets similar to our ancient diet, which is part of the environment on which our genes evolved. Current Western human milk DHA contents do not comply with the recommendations of authoritative organizations, which advise increases in fish intake, and should consequently not serve as a guide for infant feeding. It would be of interest to see whether infant feeding...
formulas with LCP fatty acid contents consistent with those of non-Western, traditionally eating populations would produce more pronounced effects using the many endpoints that have been studied with limited success until now.

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REFERENCES


Reply to FAJ Muskiet et al

Dear Sir:

We find ourselves in substantial agreement with the comments of Kuipers et al concerning our recent article on worldwide breast-milk docosahexaenoic acid (DHA) and arachidonic acid (AA) concentrations (1). However, contrary to the characterization in their opening paragraph, a careful review of our article shows that we did not suggest that the calculated mean values for breast-milk DHA and AA, in some sense, are the best values against which infant feeding should be based. We suggested that the distribution of these fatty acids will be a valuable guide for infant feeding and are pleased to have the chance to amplify this point.

The distribution of breast-milk DHA and AA includes information about minimum, maximum, distribution breadth, and ratios of DHA to AA. Our intent in using the word guide was to convey that this and other information is of value in making recommendations concerning infant feeding, including breastfeeding. Certainly the mean (or median or mode) worldwide breast-milk DHA or AA concentrations calculated by any procedure should not be the only criteria used for establishing targets for DHA and AA contents in infant formulas for some of the very reasons that Kuipers et al discuss. Indeed, we explicitly noted in the beginning of our article’s Discussion that there are multiple ways to calculate such figures-of-merit based on any particular data set. Although our calculations indicate that the means are robust to alternative calculation strategies, we did not suggest that these means are optimum for the average infant, let alone for any particular infant.

Studies of optimal DHA and AA for infant feeding beyond present mean values are indeed needed. Our long-standing interest in this matter is reflected, in part, in our recent publications reporting on studies of the influence of 1.0% DHA formula (with 0.67% AA) on tissue DHA and AA concentrations in animals (2). These concentrations support cerebral cortex DHA concentrations greater than for formulas with 0.33% and induce widespread alterations in gene expression (3). Notably, 0.33% DHA is the approximate level used in most, but not all, North American infant formulas. We argue, based on the worldwide distribution, that 1.0% DHA is within the high end of current breast-milk concentrations and, thus, is a nutritional and not a supranutritional level.

We are aware of ongoing studies into the origins of human diet and the implications for modern humans, as discussed in detail by others (4, 5). It is important to note that these ideas continue to be controversial. We believe that it is premature to draw definitive conclusions about contemporary infant feeding based solely on the dietary norms of hypothetical ancestors when contemporary physiology can be studied. However, the vigor with which such matters are argued reflects their proponent’s contention that they are of importance to contemporary humans as another guide to human nutrition. We agree.

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