Fatty acids in context
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Maternal depression and child development after prenatal DHA supplementation.

Dr Makrides and colleagues\textsuperscript{79} reported that supplementation with 800 mg per day of DHA and 100 mg per day of eicosapentaenoic acid in pregnant women neither lowered levels of postpartum depression nor improved mean cognitive and language development scores in their offspring, compared with a control group receiving vegetable oil capsules. In addition, girls exposed to DHA in utero had poorer mean adaptive behavior and language scores.

The absence of clear positive effects and the possible presence of negative effects in the children raise the question whether DHA supplementation is justifiable (not only during pregnancy, but in general). The answer depends on the interpretation of previously found low DHA in postpartum depression (and other pathophysiological states).\textsuperscript{117} Because association is not proof of causation, “low” levels may not necessarily mean “deficient” levels, but may represent adequate or even adaptive levels. Fatty acid status depends not only on dietary intake, but also on endogenous metabolism; e.g. oxidative stress is associated with lower DHA levels.\textsuperscript{118} Lower levels of DHA may represent an adaptive process because cell membranes with less unsaturated fatty acids (such as DHA) are more resistant to oxidation.\textsuperscript{118}

If so, supplementation is questionable and may have deleterious effects. DHA, with its many double bonds, is vulnerable to enzymatic and nonenzymatic peroxidation, and lipid peroxidation products may exert harmful effects (neurodegeneration, atherosclerosis).\textsuperscript{119} In a supplementation study using various DHA concentrations, at 800 mg per day (similar to the study by Makrides et al.), several lipid peroxidation product levels started to increase.\textsuperscript{120} Supplementation studies should routinely include measurements of lipid peroxidation products, as well as systematic analyses of lipid peroxidation products in the supplementation capsules (including placebos). Ex vivo, these oils are also subject to lipid peroxidation,\textsuperscript{119} possibly resulting in supplementation with potentially harmful lipid peroxidation products instead of DHA.

Some subpopulations might benefit from supplementation because of polymorphisms in DHA synthesizing enzymes leading to lower DHA levels.\textsuperscript{118} The finding in the study by Makrides et al. that supplementation resulted in fewer children with a delayed cognitive development, although the mean scores did not differ, could point to such a subpopulation.

**CONFLICT OF INTEREST DISCLOSURES**

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.