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ADVANCES IN PEDIATRICS

Docosahexaenoic Acid and Arachidonic Acid Nutrition in Early Development

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• Docosahexaenoic acid (DHA) • Growth
• Long-chain polyunsaturated fatty acids (LCPUFA) • Programming

Key points

- Docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid, and arachidonic acid (ARA), an omega-6 polyunsaturated fatty acid, are nutrients that were first added to formulas in the United States in 2002.
- DHA intake is low in the US population and this has implications for development.
- Early studies found more mature cortical visual function in infants fed formulas containing DHA and ARA and this led to a claim for improved visual acuity after these fatty acids were added to infant formula.
- Recent studies found positive effects of feeding DHA and ARA in infancy on cognition, brain connectivity, and allergy in early childhood, which provides evidence that these fatty acids program cognitive and immune development.
- The optimal balance of DHA and ARA intake during infancy is still not known, but current best practice suggests that the amount of DHA in infant formula should not exceed the amount of ARA.

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- The effect of DHA and ARA status and supplementation in infancy has been largely evaluated through global developmental assessments focused on attainment of normative milestones, although more granular measures of specific cognitive function may be more sensitive markers of these effects.

INTRODUCTION

Docosahexaenoic acid (DHA; 22:6ω3) is an omega-3 fatty acid with 22 carbons and 6 double bonds (22:6n-3). Arachidonic acid (ARA; 20:4ω6) is an omega-6 fatty acid with 20 carbons and 4 double bonds. These two fatty acids are the predominant long-chain (20 and 22 carbons) polyunsaturated fatty acids (LCPUFAs) in human brain [1,2]. Brain DHA begins to accumulate around 22 weeks' gestation and the absolute amount per gram of brain as well as the weight percent of total fatty acids increases progressively from 22 weeks until at least 2 years of age [3–6]. The absolute amount of ARA per gram of brain also increases in brain but decreases in weight percent of total fatty acids after birth [1].

All human milk contains ARA and DHA to support DHA and ARA requirements for the growing and developing brain as well as other organs and tissue after birth. In human milk, the amount of ARA typically exceeds that of DHA. Milk ARA content is also less varied than DHA and, unlike DHA, does not seem to be linked to maternal intake. Because worldwide DHA intake is variable, milk DHA content is variable across cultures. Reports of milk DHA concentration range from 0.05% of total fatty acids in vegan vegetarians [7] to 2.8% in the marine region of China, where a diet high in seafood is consumed [8]; the median value of DHA in human milk worldwide is ~0.3% [9]. Women in the United States have low milk DHA levels (levels around 0.1% DHA are typical [10]) unless they regularly consume DHA or a supplement during and/or after their pregnancy. Jensen and colleagues [11] found that a supplement of 200 mg of DHA per day in US women could increase milk DHA to ~0.3% of total fatty acids, which is the amount that the European Food Safety Authority (EFSA) requires in infant formula in order to make a claim for support of infant visual development [12].

Red blood cell DHA and ARA levels are lower in infants fed formula without DHA and ARA, compared with infants fed human milk [10,13,14]; this is evidence of lower status. However, autopsy studies find lower brain DHA levels and higher omega-6 LCPUFA levels in infants fed formula without LCPUFA [14–16]. In term infants, frontal cortex DHA level is about 20% [14] lower if fed formulas without DHA and ARA. In preterm infants, who do not have the same opportunity to accumulate DHA from placental transfer, the amount of DHA that accumulates is ~50% less if formula is lacking in DHA and ARA [15].

DHA, ARA, and docosatetraenoic acid (DTA; 22:4ω6) are the major LCPUFAs in brain phosphoglycerides [6,14,15,17]; however, the amount of