



ALPHA & OMEGA

BETTER BRAIN FOR LIFE

FOR HEALTHY DEVELOPMENT
THAT LASTS A LIFETIME





Choline and **DHA** are under-consumed in the diet, but vital for brain development and brain aging. The support this supplement provides helps secure **healthy development that lasts a lifetime.**

Individualize Your Recommendation for a Healthy Pregnancy

Pregnancy is a time of hope and excitement. As a new life buds and grows, the foundation is laid for future health and wellness. It's a time of great opportunity.

But it can also be a time of great challenge.

- American women are having children at an older age, and at a time when managing a healthy weight is a greater challenge.
- American women are also pursuing diet patterns that aren't sufficient in nutrients required for a healthy pregnancy; for mother or baby.

Choline and the omega-3 fatty acid **DHA** are two nutritional supplements that may be beneficial to women, from pre-conception and while breast feeding.



Treating the Individual and her Unique Needs

Pregnancy today is not a one-size-fits-all situation. Diet patterns can vary from a standard western diet to a vegan diet, with the nutritional concerns about choline and DHA that come with each. Women may not know they're pregnant and may unknowingly expose their fetus to alcohol in the early stages of development, meaning their fetus may have greater need for nutritional supplementation to offset damage.

Athletes may begin pregnancy with depleted nutrient status. Some genetic alterations may increase a person's need for these nutrients. And older, heavier moms may need these supplemental nutrients to offset the effects of chronic inflammation and normal aging.

By recommending Alpha and Omega Prenatal supplement with choline and DHA to meet the needs of each patient, health professionals are supporting healthy development that lasts a lifetime.

Missing Pieces: Choline and DHA

Choline is required for the body's normal function and DHA is conditionally essential, as well. These nutrients support normal functions of the liver, neurons, metabolism, inflammatory response systems and nervous system in mothers. In a growing fetus, these nutrients support healthy growth and organ development, specifically in the brain.

Independently, both choline and DHA have been studied for their importance on early neural development. Early life is particularly sensitive to nutritional status.

- Nutritional insufficiencies can be challenging as the brain establishes pathways for learning and other higher order functions.
- The development of brain structures and the visual system depends on having sufficient building blocks for growth.
- Choline is a building block for neurotransmitters, the covering of nerve cells, and membranes that surround cells.
- DHA supports brain development as well as retinal development – photoreceptors in the retina are enriched with DHA – and can moderate inflammation which is especially important for those who may have chronic inflammation due to obesity or other chronic illness.

DHA and choline work together in the brain.

DHA and choline ensure that cells have functional membranes. DHA specifically is important as an unsaturated fat. It allows cell membranes to be flexible, fluid and keep the proteins moving in and out, especially in regard to the normal flow of neurotransmitters between synapses. In states of DHA deficiency, cell membranes may be less flexible, requiring more neurotransmitters to achieve an effect---learning a new fact for example---and possibly leading to dysfunction in the system.

DHA is typically bound to a type of choline called GPL (glycerophospholipid), and at 32 weeks gestation, this combination appears in a greater ratio within the brain, suggesting a key role in development. DHA concentrations continue to increase as the brain grows, until around age eight.

After pregnancy, supplemental DHA can support a woman's mood, and restore her levels of DHA during lactation, ensuring both mom and baby get adequate amounts daily. Prenatal vitamins, the universally recommended solution to address dietary gaps, may not be enough even if a woman takes them as directed. Citing the importance of choline for mom and baby, delegates at a recent American Medical Association meeting recommended promoting evidence-based amounts of choline in prenatal supplements. In the case of DHA, the amount may not be enough for both mother and baby especially since many diets fail to meet the suggested DHA intake.

Supplementation with Alpha and Omega prenatal vitamin ensures sufficient amounts of these vital nutrients for every woman and her baby.



Choline Bio Basics (Linus Pauling: Choline; accessed Feb. 2018)

Essential nutrient (required by the body for normal function but not made in enough abundance by the liver)

- Although choline is clearly essential to life, there is only one published study examining the effects of inadequate dietary intake in healthy men. (DRI for... Choline, 1998)

Choline is typically found bound to a glycerol backbone along with fatty acid and phosphoric acid (phospholipid).

Choline is the beginning compound for a number of vital derivatives (metabolites):

- Acetylcholine: neurotransmitter necessary for neuron activity related to memory, muscle control, and the body's internal clock; also found throughout the cells of the body affecting numerous body systems, such as the skin, cardiovascular, digestive, reproductive and immune systems. (Beckmann and Lips, 2013)
- Betaine: used in pathways that support cardiovascular health through the conversion of homocysteine to methionine.
- Sphingomyelin: essential for healthy cell membranes and the covering of nerve fibers; precursor for cell signaling molecules
- Phosphatidylcholine: essential for healthy cell membranes; accounts for most of the choline in the body's tissues; precursor for cell signaling molecules, and necessary for removing fat and cholesterol from the liver. Choline can be broken out of this molecule by pancreatic enzymes. (DRI for... Choline, 1998)
- Glycerophosphorylcholine (also called glycerophosphocholine): choline with the glycerol backbone and phosphoric acid, but no fatty acids. Water-soluble, absorbed by the liver. (DRI for... Choline, 1998)

Choline is transported across the blood-brain barrier, "...at a rate that is proportional to the serum choline concentration [meaning if choline is low, less is available for brain function]. In the neonate this choline transporter has an especially high capacity". (DRI for... Choline, 1998)

Studies in rodents suggest that dietary intake of choline early in life can diminish the severity of memory deficits in aged animals. (DRI for... Choline, 1998)

In mice, one study found that adaptations in choline metabolism occur as a result of mild changes in folate metabolism, which the authors presume is to preserve methyl group homeostasis. (Chew et al.; J Nutr 2011)

Known to be necessary for:

- Metabolism of amino acids and nucleic acids, compounds used in the growth and development of tissues including the brain, normal fat removal from the liver, which supports the lipid balance throughout the body, healthy metabolism, healthy DNA maintenance, normal fetal brain development.
- Special Populations:
 - Postmenopausal women have a greater need for choline in the diet due to the decrease in biosynthesis of choline induced by estrogen. (Fischer et al.; Am J Clin Nutr, 2010)
 - Women with a polymorphism of the PEMT gene have a greater need for choline in the diet. (Fischer et al.; Am J Clin Nutr, 2010). In one small study, the majority of the women (78 percent) with a particular change in the PEMT gene developed organ disruption on a low choline diet. (da Costa et al.; FASEB J 2006)
 - Half of all pregnancies are unplanned so many pregnant women may unknowingly expose their fetus to alcohol during early development. Alcohol exposure damages neurons and development of brain structures, both which require choline. In one rat study and in one unpublished human study (Bell, 2017; Nat Acad Sci, p.193), choline supported the healthy development of fetuses exposed to alcohol. Choline as a supplement for infants, especially those who are not breastfed, may also support neurological development. (Bell, 2017; Nat Acad Sci, p.193) Additionally, the placenta delivers maternal stores of choline to the fetus during pregnancy. (DRI for... Choline, 1998)
 - Lactating women secrete "a substantial amount of choline" in human milk. (DRI for... Choline, 1998)
 - Athletes, specifically marathon runners and triathletes, have decreased plasma choline concentrations according to some studies and may benefit from supplementation. (DRI for... Choline, 1998)
 - Delegates at the American Medical Association voted to support evidence based amounts of choline in prenatal vitamins. (AMA)

Dietary intake in America

- Recommended intake of 550 mg/day for men and 425 mg/day for women (DRI for... Choline, 1998)
- Milk, liver, eggs, and peanuts are rich in choline. (DRI for... Choline, 1998)
- Choline consumption varies among the population. Only about 10 percent of the American population exceeds the adequate intake for choline based on the 2009 – 2012 national nutritional study. (Wallace and Fulgoni; J Am Coll Nutr 2016)
- Gut microbiome may respond to choline imbalance and contribute to dysfunction. (Spencer et al. Gastroenterology, 2011)
- Choline consumed preconception may support healthy brain development
- Upper tolerable intake is between 1 and 3.5 grams depending on age group. (DRI for... Choline, 1998)
- Choline is inextricably tied to B vitamin metabolism; for example in one rat study, liver folate levels decreased after choline-deficiency; diets deficient in both choline and methionine also reported low liver folate concentrations; and in rats deprived of choline, homocysteine levels in plasma doubled. (DRI for... Choline, 1998)
- Choline need is influenced by amount of folate and methionine in diet, gender, age, pregnancy, lactation state.

Brain health

Rodent studies suggest choline in early life may support normal memory retrieval function at an advanced age. (DRI for... Choline, 1998)

Cardiovascular health

Studies in animals and humans have found interesting results when choline is examined for supporting normal cardiovascular function. (DRI for... Choline, 1998)

Normal cell proliferation

Animal studies have found that choline is associated with normal cell growth in liver cells. (DRI for... Choline, 1998)

Alpha-glycerophosphocholine, or A-GPC

In a double-blind, placebo-controlled crossover trial that included 13 healthy college-age males, six days of supplementation with 600 mg of A-GPC per day may support strength enhancement in the lower body. The authors suggest that a potential mechanism of action could be through augmented acetylcholine synthesis in neurons. (Bellar et al. J Int Soc Sports Nutr, 2015)

In a rat study, pretreatment and post-treatment with A-GPC supported healthy inflammation in the small intestine. (Tőkös et al. Eur J Nutr, 2015)

In a rat study, brain areas exposed to radiation were supported by A-GPC when given both before and after the challenge. (Plangár et al. J Neurooncol, 2014) Similar findings were reported in a zebrafish embryo model (Szabó et al., Zebrafish, 2016)

In a rat study, mitochondria were supported by administration of A-GPC, through management of normal oxidative stress. (Striffler et al. PLoS One, 2016)

In a rat study, A-GPC supported microvascular blood flow and tissue health in a liver challenge. (Hartmann et al. J Surg Res, 2014) Microvascular support was also observed in regard to the blood brain barrier in another rat study. (Tayebati et al., CNS Neurol Disord Drug Targets, 2015)

In a rat study, the effect of A-GPC on brain dopamine, serotonin, and specific transporters were evaluated and determined to merit further investigation in clinical application. (Tayebati et al. CNS Neurol Disord Drug Targets, 2013)

In a mouse study, the normal effects of aging were managed by inclusion of A-GPC in food as measured by senescent cell grading, protein deposition and knee joint health. (Matsubara et al., Biosci Biotechnol Biochem, 2017)

Omega-3 Fatty acids: DHA

Omega-3 fatty acids are essential nutrients. (Linus Pauling: Essential Fatty Acids, accessed February 2018)

Omega-3 fatty acids constitute about 15 to 20 percent of total brain fatty acids; lipids in general make up about 50 percent of the brain's dry weight. (Youdim et al.; Int J Dev Neurosci 2000; Luchtman and Song; Neuropharmacology 2013)

DHA is the most abundant fatty acid in the brain's most abundant type of lipid called phospholipids. (Youdim et al.; Int J Dev Neurosci 2000) (Luchtman and Song; Neuropharmacology 2013)

DHA and the omega-6 fatty acid arachidonic acid are particularly enriched in cell membranes, especially in neural tissue. (3,4,5). As part of phospholipids, omega-3 fatty acids affect the cell's, "...fluidity, flexibility, permeability, and the activity of membrane-bound enzymes. (Linus Pauling: Essential Fatty Acids, accessed February 2018)

The fatty acid composition of synaptic membranes from adult rats changes during development: DHA increased 34 percent during development and continues to increase until about age 8. (Hitzemann and Johnson; Neurochem Res 1983 (Niebylski and Salem; Biophys 1994) (Slater et al.; J Biol Chem 1994) (Zeruga et al; Biochim Biophys Acta, 1995)

DHA is particularly important for retinal health. Photoreceptors in the eye are enriched with DHA (10). Research suggests that DHA is required for normal development and function of the retina, and that permanent abnormalities can occur in the case of inadequate DHA. (Linus Pauling: Essential Fatty Acids, accessed February 2018)

DHA is also a precursor for anti-inflammatory molecules (hydroxyl fatty acids), inflammation modulating molecules, and isoprostanes. DHA provides the building blocks for molecules that actively mediate inflammatory response and resolves that normal function. (Linus Pauling: Essential Fatty Acids, accessed February 2018)

DHA, like other omega-6 and omega-3 fatty acids can modulate gene expression. (Linus Pauling: Essential Fatty Acids, accessed February 2018)

Prenatal fish oil supplementation is associated with a lower risk of failing a problem-solving domain up to 3 years of age. (Vollet). Epidemiological investigations have linked consumption of fish and seafood during pregnancy with better outcomes for offspring. (Linus Pauling: Essential Fatty Acids, accessed February 2018)

Consumption of omega-3 fatty acid supplements during pregnancy may extend gestation and support healthy birthweight. (Linus Pauling: Essential Fatty Acids, accessed February 2018) Deprivation of brain DHA due to prematurity or dietary lack of omega-3 fatty acids may have lasting impact on cognitive function according to a mouse study. (Lozada et al.; J Nutr 2017)

Diets of vegetarian or vegan mothers have lower DHA in breast milk than omnivore mothers, perhaps showing that while metabolic pathways exist for conversion of DHA, preferred omega-3s are important as a dietary component. ((Burdge et al.; J Nutr Sci, 2017))

Levels of DHA in children drop once breast feeding ceases, showing that diet choices can have significant impact on nutrients available for continued development. (Rogers et al.; Pharmacol Res 2014)

GOED recommends 700 – 1000 mg of EPA+DHA daily for pregnant or lactating women. (GOED)

In a mouse study, malnutrition, including deficiency of polyunsaturated fatty acids, in the mother and post-natal deprivation of DHA and arachidonic acid increased the risk of schizophrenia-like behavior in offspring. (Maekawa et al.; Transl Psychiatry 2017)

In a national survey of households, results demonstrated that omega-3 fatty acid intake is a concern in pregnant women and women of childbearing age in the United States, and that socioeconomically disadvantaged populations are more susceptible to potential deficiencies. (Nordgren et al.; Nutrients 2017)