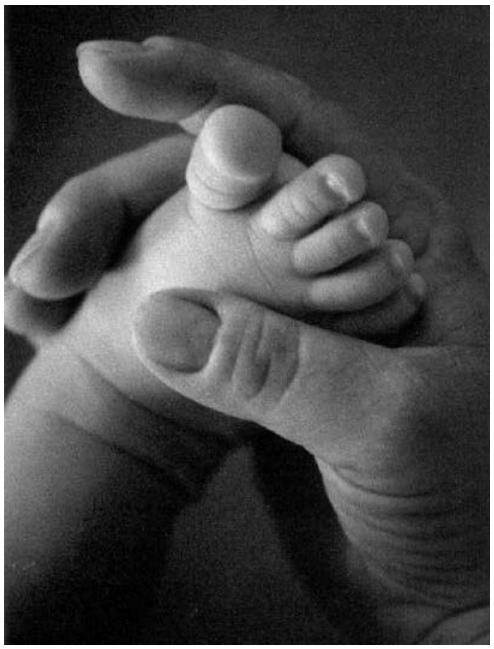
NUTRITION closeUP

Special Report



CHOLINE:
The "New" Essential Nutrient

Discovered **in 1948, choline remained virtually unrecognized as an essential nutrient until 1998, when recommended daily intake amounts were finally issued by the National Academy of Sciences. Much has been proven—and much more has been suggested— in recent research about choline's vital contributions to human health. Among other benefits, choline has been found to play a role in memory function, in fetal brain development, and in the prevention of heart disease, fatty liver, and neural tube defects.**

Location

- Choline is found as phosphatidylcholine (or lecithin) in the phospholipid bilayer of cell membranes and in sphingomyelin, a critical component of the myelin sheath that surrounds nerve fibers.
- Acetylcholine, an important neurotransmitter, is comprised partly of choline.
- Choline is also found in the liver, where it plays a role in methionine and lipoprotein formation.

Function

- Choline contributes to the proper structure and function of cell membranes.
- As part of the sphingomyelin that makes up the myelin sheath, choline insulates nerve fibers and aids in the rapid conduction of electrical impulses.
- Choline is a precursor of betaine, an osmolyte used by the kidney to control water balance.
- Choline functions in the liver as a source of methyl groups required for lipoprotein formation and for the synthesis of methionine from homocysteine.
- Choline is also necessary for the synthesis of acetylcholine, an important neurotransmitter involved in memory storage and muscle control.
- Choline is an active component of surfactant in the lung. Neonate surfactant deficiency leads to respiratory distress syndrome in premature infants.

"**Pregnancy** and **lactation** are periods when maternal reserves of choline are **depleted**. At the same time, the **availability of choline** for normal development of the brain is **critical**."

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Key Research

Consequences of Choline Deficiency

- Studies show evidence of an interrelationship between choline, methionine, and methylfolate. Rats fed a choline-free diet decreased their hepatic folate content by 31-40% after two weeks. After five weeks on a choline-free diet, rats decreased hepatic folate by 50% relative to controls. Hepatic folate levels returned to normal with choline feeding.

  Niculescu MD, Zeisel SH. Diet, methyl donors, and DNA methylation: interactions between dietary folate, methionine and choline. *Am Soc for Nutr Sci* 2002:2333S-2335S.

- Acute symptoms of choline deficiency in animals include: fatty liver, liver cell death, and liver cell cancer. Long term deficiency of choline in rats results in hepatocellular carcinoma.

  da Costa KA, Garner SC, Chang J, Zeisel SH. Effects of prolonged (1 year) choline deficiency and subsequent re-feeding of choline on 1,2- sn-diradylglycerol, fatty acids and protein kinase C in rat liver. *Carcinogenesis* 1995;16:327-334.

- Prenatal choline deficiency in rats causes increased cell death, decreased cell growth and differentiation, and alterations in the development of nervous tissue located in the fetal brain septum and hippocampal regions of the brain associated with learning and memory.

  Fisher M, Zeisel SH, Mar MH, Sadler TW. Inhibitors of choline uptake and metabolism cause developmental abnormalities in neurulating mouse embryos. Teratology 2001;64:114-122.

- Human studies show choline deficiency results in liver damage as well. Fatty liver is associated with insufficient phosphotidylcholine (lecithin) needed for synthesis of very low density lipoproteins (VLDL) to remove triacylglycerol (triglycerides) from the liver. Patients maintained on total parenteral nutrition (TPN) for four weeks without a choline source exhibited fatty liver and higher levels of serum alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase, confirming the requirement of choline for long term home TPN patients.

  Buchman AL, Ament ME, Sohel M, Dubin M, Jenden DJ, Roch M, Pownall H, Farley W, Awal M, Ahn C. Choline deficiency causes reversible hepatic abnormalities in patients receiving parenteral nutrition: proof of a human choline requirement: a placebo-controlled study. *J Parenter Enteral Nutr* 2001 25;5:260-8.

- In studies with humans, both verbal and visual memory is impaired in patients receiving long term TPN, but shows improvement with choline intake.

  Buchman AL, Sohel M, Brown M, Jenden DJ,, Ahn C, Roch M, Brawley TL. Verbal and visual memory improve after choline supplementation in long-term total parenteral nutrition: a pilot study. J Parenter Enteral Nutr 200125;1:30-35.

Role of Choline in the Body

- Choline functions as a methyl donor in the synthesis of methionine from homocysteine. Choline's role as a methyl donor is especially important when folate intake is low. In fact, it has been shown that methionine and folic acid together might prevent neural tube defects such as spina bifida and exencephaly by supporting methyl group metabolism or by decreasing homocysteine levels.

  Fisher M, Zeisel SH, Mar MH, Sadler TW. Perturbations in choline metabolism cause neural tube defects in mouse embryos in vitro. FASEB Journal 2002 16:619-621.

- Choline also plays an important role in preventing heart disease. By participating in the synthesis of methionine from the amino acid homocysteine, a known risk factor for cardiovascular disease, buildup of homocysteine can be prevented. In addition, lecithin (phosphatidylcholine) has been used as a treatment to lower cholesterol concentrations because lecithin-cholesterol acyltransferase assists in removing cholesterol from body tissues.

  Food and Nutrition Board of the Institute of Medicine. Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. National Academy Press, Washington, DC, 1998.

- Required for normal development of brain tissue in the developing fetus. Rat pups that received choline in utero and during important periods of brain formation were found to have enhanced memory and enhanced brain function throughout life, extending into old age.

  Zeisel SH. Choline needed for normal development of memory. J Am Coll Nutr 2000 19;5S:528S-531S.

- Results of studies with rats indicate that differences in the intake of choline during specific periods of development lead to changes in the electrophysiology of regions of the brain that last well into adulthood. These changes in the threshold for nerve impulse stimulation may underlie the enhancement of visual-spatial memory, seen after prenatal choline supplementation. Findings such as these indicate the importance of choline intake during pregnancy for development of brain and memory function.

  Albright CD, Friedrich CB, Brown EC, Mar MH, Zeisel SH. Maternal dietary choline availability alters mitosis, apoptosis and the localization of TOAD-64 protein in the developing fetal rat septum. Brain Res Dev Brain Res 1999 115;2:123-129.
  Jones JP, Mech WH, Williams CL, Wilson WA, Swartzwelder HS. Choline availability to the developing rat fetus alters adult hippocampal long-term potentiation. Brain Res Dev Brain Res 1999 118;1-2:159-167.

History of Choline

1862 Discovery of choline

1866 Choline was first chemically synthesized
Choline was determined necessary to prevent fatty liver and death in dogs without pancreas

1946 Choline deficient diet led to liver cancer in rats

1975 Choline was found to cause accelerated synthesis and release of acetylcholine by neurons

1998 Choline was identified as an essential nutrient for humans
Recommended daily intake amounts issued by the National Academy of Sciences

Recommended Intake

Life Stage	Adequate Intake*
Infants	
0-6 mo	125
7-12 mo	150
Children	
1-3 y	200
4-8 y	250
Males	
9-13 y	375
>13 y	550
Females	
9-13 y	375
14-18 y	400
>19 y	425
Pregnant	450
Lactating	550

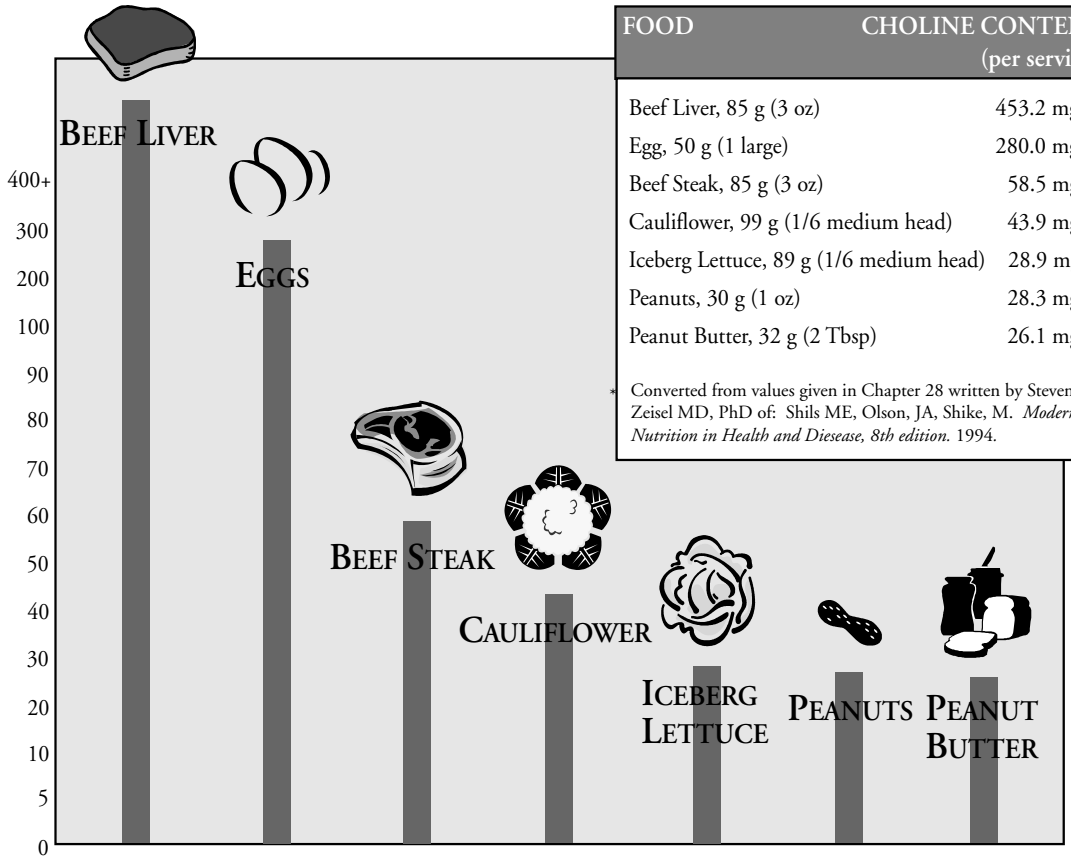
*Amounts expressed in mg/day

Although the liver can make some of its own choline, this production is inadequate to meet the body's needs. Males may have a higher choline requirement than females. For women, choline production within the body may decrease after menopause.

Of special interest is the need for choline during pregnancy and lactation when serum choline levels are diminished. Demand for choline by a developing fetus could put the mother and fetus at risk for choline deficiency. For this reason, pregnant women are advised to consume 450 mg/day. Because choline is also necessary for milk production, the recommended daily intake for lactating women is also elevated to 550 mg/day).

The critical adverse effects of excessive choline intake are hypotension, with side effects indicating cholinergic basis such as sweating, diarrhea, and fishy body odor. The Tolerable Upper Intake Level (UL) for adults is 3.5 g/day.

Choline Sources



FOOD	CHOLINE CONTENT (per serving)
Beef Liver, 85 g (3 oz)	453.2 mg
Egg, 50 g (1 large)	280.0 mg
Beef Steak, 85 g (3 oz)	58.5 mg
Cauliflower, 99 g (1/6 medium head)	43.9 mg
Iceberg Lettuce, 89 g (1/6 medium head)	28.9 mg
Peanuts, 30 g (1 oz)	28.3 mg
Peanut Butter, 32 g (2 Tbsp)	26.1 mg

Converted from values given in Chapter 28 written by Steven H. Zeisel MD, PhD of: Shils ME, Olson, JA, Shike, M. *Modern Nutrition in Health and Diesease, 8th edition.* 1994.

In 2001, the Food and Drug Administration (FDA) allowed a nutrient content claim on labels of foods that meet the following criteria to be termed "good" or "excellent" sources of choline:

Excellent
source of choline

Must contain at least 110 mg of choline per serving,
(20% of the Daily Value for choline based on 550 mg reference)

Good
source of choline

Must contain at least 55 mg of choline per serving,
(10% of the Daily Value for choline based on 550 mg reference)