

Choline

Fact Sheet for Health Professionals

Introduction

Choline is an essential nutrient that is naturally present in some foods and available as a dietary supplement. Choline is a source of methyl groups needed for many steps in metabolism. The body needs choline to synthesize phosphatidylcholine and sphingomyelin, two major phospholipids vital for cell membranes. Therefore, all plant and animal cells need choline to preserve their structural integrity [1,2]. In addition, choline is needed to produce acetylcholine, an important neurotransmitter for memory, mood, muscle control, and other brain and nervous system functions [1-3]. Choline also plays important roles in modulating gene expression, cell membrane signaling, lipid transport and metabolism, and early brain development [1,2].

Humans can produce choline endogenously in the liver, mostly as phosphatidylcholine, but the amount that the body naturally synthesizes is not sufficient to meet human needs [4]. As a result, humans must obtain some choline from the diet. Premenopausal women might need less choline from the diet than children or other adults because estrogen induces the gene that catalyzes the biosynthesis of choline [4]. When a diet is deficient in folate, a B-vitamin that is also a methyl donor, the need for dietary choline rises because choline becomes the primary methyl donor [1].

The most common sources of choline in foods are the fat-soluble phospholipids phosphatidylcholine and sphingomyelin as well as the water-soluble compounds phosphocholine, glycerolphosphocholine, and free choline [1]. When these choline-containing compounds are ingested, pancreatic and mucosal enzymes liberate free choline from about half of the fat-soluble forms and some water-soluble forms [5]. Free choline, phosphocholine, and glycerophosphocholine are absorbed in the small intestine, enter the portal circulation, and are stored in the liver, where they are subsequently phosphorylated and distributed throughout the body to make cell membranes [1-3]. The remaining fat-soluble phospholipids (phosphatidylcholine and sphingomyelin) are absorbed intact, incorporated into chylomicrons, and secreted into the lymphatic circulation, where they are distributed to tissues and other organs, including the brain and placenta [1,6].

Choline status is not routinely measured in healthy people. In healthy adults, the concentration of choline in plasma ranges from 7 to 20 $\mu\text{mol/L}$ [2]. According to one study, the range is 7–9.3 $\mu\text{mol/L}$ in fasting adults [7]. Plasma choline levels do not decline below 50% of normal, even in individuals who have not eaten for more than a week [3]. This may be due to the hydrolysis of membrane phospholipids, a source of choline, to maintain plasma choline concentrations above this minimal level, or to endogenous synthesis [2].

the body sacrifices some structures to provide choline, also needed during stress and repair.

Recommended Intakes

Intake recommendations for choline and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) of the Institute of Medicine (IOM) [2]. DRIs is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. These values, which vary by age and sex, include:

many nutritional requirements have not been updated for over 10 or more years

- Recommended Dietary Allowance (RDA): Average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals; often used to plan nutritionally adequate diets for individuals.
- Adequate Intake (AI): Intake at this level is assumed to ensure nutritional adequacy; established when evidence is insufficient to develop an RDA.
- Estimated Average Requirement (EAR): Average daily level of intake estimated to meet the requirements of 50% of healthy individuals; usually used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them; can also be used to assess the nutrient intakes of individuals.
- Tolerable Upper Intake Level (UL): Maximum daily intake unlikely to cause adverse health effects.

Insufficient data were available to establish an EAR for choline, so the FNB established AIs for all ages that are based on the prevention of liver damage as measured by serum alanine aminotransferase levels [2]. The amount of choline that individuals need is influenced by the amount of methionine, betaine, and folate in the diet; gender; pregnancy; lactation; stage of development; ability to produce choline endogenously; and genetic mutations that affect choline needs [1,2,4,5]. Table 1 lists the current AIs for choline [2].

Table 1: Adequate Intakes (AIs) for Choline [2]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	125 mg/day	125 mg/day		
7–12 months	150 mg/day	150 mg/day		
1–3 years	200 mg/day	200 mg/day		
4–8 years	250 mg/day	250 mg/day		
9–13 years	375 mg/day	375 mg/day		
14–18 years	550 mg/day	400 mg/day	450 mg/day	550 mg/day
19+ years	550 mg/day	425 mg/day	450 mg/day	550 mg/day

Sources of Choline

Food

Many foods contain choline [4]. The main dietary sources of choline in the United States consist primarily of animal-based products that are particularly rich in choline—meat, poultry, fish, dairy products, and eggs [4,5,8-10]. Cruciferous vegetables and certain beans are also rich in choline, and other dietary sources of choline include nuts, seeds, and whole grains.

About half the dietary choline consumed in the United States is in the form of phosphatidylcholine [8,9]. Many foods also contain lecithin, a substance rich in phosphatidylcholine that is prepared during commercial purification of phospholipids; lecithin is a common food additive used as an emulsifying agent in processed foods, such as gravies, salad dressings, and margarine [1,3]. Choline is also present in breast milk and is added to most commercial infant formulas [3,4]. Precise estimates of the percentage absorption of the different forms of dietary choline in humans are not available [2,3].

Several food sources of choline are listed in Table 2.

Table 2: Choline Content of Selected Foods [11]

Food	Milligrams (mg) per serving	Percent DV*
Beef liver, pan fried, 3 ounces	356	65
Egg, hard boiled, 1 large egg	147	27
Beef top round, separable lean only, braised, 3 ounces	117	21
Soybeans, roasted, ½ cup	107	19
Chicken breast, roasted, 3 ounces	72	13
Beef, ground, 93% lean meat, broiled, 3 ounces	72	13
Fish, cod, Atlantic, cooked, dry heat, 3 ounces	71	13
Potatoes, red, baked, flesh and skin, 1 large potato	57	10
Wheat germ, toasted, 1 ounce	51	9
Beans, kidney, canned, ½ cup	45	8
Quinoa, cooked, 1 cup	43	8
Milk, 1% fat, 1 cup	43	8
Yogurt, vanilla, nonfat, 1 cup	38	7
Brussels sprouts, boiled, ½ cup	32	6
Broccoli, chopped, boiled, drained, ½ cup	31	6
Mushrooms, shiitake, cooked, ½ cup pieces	27	5
Cottage cheese, nonfat, 1 cup	26	5
Fish, tuna, white, canned in water, drained in solids, 3 ounces	25	5
Peanuts, dry roasted, ¼ cup	24	4
Cauliflower, 1" pieces, boiled, drained, ½ cup	24	4
Peas, green, boiled, ½ cup	24	4
Sunflower seeds, oil roasted, ¼ cup	19	3
Rice, brown, long-grain, cooked, 1 cup	19	3
Bread, pita, whole wheat, 1 large (6½ inch diameter)	17	3
Cabbage, boiled, ½ cup	15	3
Tangerine (mandarin orange), sections, ½ cup	10	2
Beans, snap, raw, ½ cup	8	1

male average
requirement 550
mg/day (see above)

Food	Milligrams (mg) per serving	Percent DV*
Kiwifruit, raw, ½ cup sliced	7	1
Carrots, raw, chopped, ½ cup	6	1
Apples, raw, with skin, quartered or chopped, ½ cup	2	0

*DV = Daily Value. The U.S. Food and Drug Administration (FDA) developed DVs to help consumers compare the nutrient contents of foods and dietary supplements within the context of a total diet. The DV for choline is 550 mg for adults and children age 4 years and older [12]. FDA does not require food labels to list choline content unless choline has been added to the food. Foods providing 20% or more of the DV are considered to be high sources of a nutrient, but foods providing lower percentages of the DV also contribute to a healthful diet.

The U.S. Department of Agriculture's (USDA's) FoodData Central (<https://fdc.nal.usda.gov/>) [11] lists the nutrient content of many foods and provides a comprehensive list of foods containing choline arranged by nutrient content (<https://www.nal.usda.gov/sites/www.nal.usda.gov/files/choline.pdf>).

Dietary supplements

Choline is available in dietary supplements containing choline only, in combination with B-complex vitamins, and in some multivitamin/multimineral products [13]. Typical amounts of choline in dietary supplements range from 10 mg to 250 mg. The forms of choline in dietary supplements include choline bitartrate, phosphatidylcholine, and lecithin. No studies have compared the relative bioavailability of choline from these different forms.

Choline Intakes and Status

Most people in the United States consume less than the AI for choline. An analysis of data from the 2013–2014 National Health and Nutrition Examination Survey (NHANES) found that the average daily choline intake from foods and beverages among children and teens is 256 mg for ages 2–19 [14]. In adults, the average daily choline intake from foods and beverages is 402 mg in men and 278 mg in women. Intakes from supplements contribute a very small amount to total choline intakes.

According to an analysis of 2007–2008 NHANES data, black males of all ages had lower mean choline intakes than their white and Hispanic counterparts, but choline intakes did not differ substantially among females of different races/ethnicities [10].

Choline Deficiency

Choline deficiency can cause muscle damage, liver damage, and nonalcoholic fatty liver disease (NAFLD or hepatosteatorosis) [1,2,4,15]. Although most people in the United States consume less than the AI of choline, frank choline deficiency in healthy, nonpregnant individuals is very rare, possibly because of the contribution of choline that the body synthesizes endogenously [1,5].

Groups at Risk of Choline Inadequacy

The following groups are among those most likely to have inadequate choline status.

Pregnant women

Approximately 90%–95% of pregnant women consume less choline than the AI [16]. Prenatal dietary supplements typically contain little if any choline [17]. The risk of inadequate choline status might be greater in pregnant and lactating women who do not take folic acid supplements, those with low vitamin B12 status, and those with a common variant in methylenetetrahydrofolate dehydrogenase (an enzyme that can affect folate status), all of which reduce the body's pool of methyl groups needed for metabolism [17-20].

Some evidence indicates that lower plasma or serum choline levels (e.g., serum concentration of 2.77 mmol/L in midpregnancy) are associated with an increased risk of neural tube defects [21,22]. However, other research found no relationship between plasma choline concentrations during pregnancy and neural tube defects in offspring [23].

People with certain genetic alterations

Genes involved in the metabolism of choline, folate, and methionine play a role in the pathways for choline production and use [24,25]. Humans have variations in the DNA sequences for these genes (single nucleotide polymorphisms [SNPs]), and these SNPs can have a strong influence on demands for dietary choline. For example, one common SNP in the *PEMT* gene reduces endogenous synthesis of choline in women induced by estrogen [26]. The prevalence of SNPs that alter requirements for dietary choline vary by race. In a study of 100 African, Asian, Caucasian, and Mexican Americans, individuals of European ancestry had a higher prevalence of four SNPs that increased the risk of organ dysfunction when these individuals consumed a low-choline diet [27].

Patients requiring total parenteral nutrition

At present, choline is not routinely added to commercial parenteral solutions for infants and adults [28,29]. As a result, adults and infants receiving total parenteral nutrition (TPN) over the long term have low plasma choline concentrations (approximately 5 nmol/ml in adults and 5.7 nmol/ml in infants), which can result in hepatic abnormalities, including NAFLD [30-32]. The American Society for Parenteral and Enteral Nutrition recommends the routine addition of choline to adult and pediatric parenteral nutrition formulations, and calls for the development of a commercially available parenteral product that contains choline [28].

Choline and Health

This section focuses on three conditions in which choline might play a role: cardiovascular and peripheral artery disease, neurological disorders, and NAFLD. Choline is involved in functions that overlap with those of folate and other B vitamins. Many studies do not assess the status of all B vitamins, which can confound results and obscure the true relationship between choline and the observed outcome.

Cardiovascular and peripheral artery disease

Some researchers have suggested that choline might protect cardiovascular health by reducing blood

pressure, altering lipid profiles, and reducing levels of plasma homocysteine [3]. Other research suggests that higher dietary choline might increase cardiovascular disease risk because some choline and other dietary ingredients, such as carnitine, are converted to trimethylamine (TMA) by intestinal bacteria. The TMA is then absorbed and converted by the liver into trimethylamine-N-oxide (TMAO), a substance that has been linked to a higher risk of cardiovascular disease [33,34].

Despite the hypothesis that choline might affect heart health, several large observational studies have found no significant associations between choline intakes and cardiovascular or peripheral artery disease risk. An analysis of 72,348 women in the Nurses' Health Study and 44,504 men in the Health Professionals Follow-up Study showed no association between choline intake and risk of peripheral artery disease in men or women [35]. Similarly, a prospective study in 14,430 middle-aged adults in the Atherosclerosis Risk in Communities Study found that over 14 years, risk of coronary heart disease was not significantly different in the highest choline intake quartile compared to the lowest quartile [36]. Choline intakes also had no association with cardiovascular disease risk in a study of 16,165 women participating in the European Prospective Investigation into Cancer and Nutrition [37].

However, a more recent analysis of data on 80,978 women from the Nurses' Health Study and 39,434 men from the Health Professionals Follow-Up Study found an increased risk of mortality in those consuming higher levels of choline [33]. The authors suggest that the higher risk might be due to increased production of TMAO, although they did not directly measure TMAO.

Additional research is needed to determine the relationship between choline intakes and cardiovascular and peripheral artery disease as well as the potential risks and benefits of choline supplementation to reduce the risk of these diseases.

Neurological disorders

People with Alzheimer's disease have lower levels of the enzyme that converts choline into acetylcholine in the brain [38]. In addition, because phosphatidylcholine can serve as a phospholipid precursor, it might help support the structural integrity of neurons and thus might promote cognitive function in elderly adults [8]. Some experts have therefore theorized that consuming higher levels of phosphatidylcholine could reduce the progression of dementia in people with Alzheimer's disease [38]. However, little research conducted to date supports this hypothesis, as described below.

A few observational studies have shown a link between cognitive performance in adults and both higher choline intakes and plasma concentrations. In one observational study in 2,195 adults aged 70–74 years in Norway, participants with plasma free choline concentrations lower than 8.4 $\mu\text{mol/L}$ (20th percentile of concentrations in the study population) had poorer sensorimotor speed, perceptual speed, executive function, and global cognition than those with choline concentrations higher than 8.4 $\mu\text{mol/L}$ [39]. A second study in 1,391 adults aged 36–83 years from the Framingham Offspring study who completed food frequency questionnaires from 1991 to 1995 and again from 1998 to 2001 found that those with higher choline intakes had better verbal memory and visual memory [40]. Furthermore, higher choline intakes during the earlier period were associated with smaller white matter hyperintensity volume (a high volume is a sign of small-vessel disease in the brain).

Some small randomized intervention trials have shown that choline supplements improve cognitive performance in adults [30,41]. However, a 2015 systematic review of 13 studies on the relationship

between choline levels and neurological outcomes in adults found that choline supplements did not result in clear improvements in cognition in healthy adults [8]. Similarly, a 2003 Cochrane review of 12 randomized trials in 265 patients with Alzheimer's disease, 21 with Parkinsonian dementia, and 90 with self-identified memory problems found no clear clinical benefits of lecithin supplementation for treating Alzheimer's disease or Parkinsonian dementia [38].

Future studies are needed to clarify the relationship between choline intakes and cognitive function and determine whether choline supplements might benefit patients with Alzheimer's disease or other forms of dementia.

Nonalcoholic fatty liver disease

NAFLD involves the accumulation of lipids in the livers of people who consume less than 20 g/day ethanol and who have no other known causes of steatosis [42,43]. (A single drink [e.g., 12 oz beer, 5 oz wine, or 1.5 oz hard liquor] contains about 12–14 g alcohol.) It is the most common chronic liver disorder, present in up to 65% of individuals who are overweight and 90% of those with obesity [1]. Although it is often benign, NAFLD can lead to steatohepatitis, fibrosis, cirrhosis, liver failure, and liver cancer [15]. Choline, especially phosphatidylcholine, is essential for transporting lipids from the liver [1]. Therefore, in choline deficiency, fat accumulates in the liver, which can result in NAFLD [44,45]. Although most women of childbearing age are resistant to NAFLD because of their high estrogen levels, at least 40% have a polymorphism that makes them insensitive to activation of the gene by estrogen; adequate consumption of dietary choline is particularly important for this population [46].

Data from a single large observational study support a link between choline deficiency and risk of NAFLD. Specifically, a cross-sectional study of 56,195 Chinese adults aged 40–75 years found an inverse relationship between dietary choline intakes and risk of NAFLD based on 24-hour dietary recall [47]. The risk of NAFLD was 32% lower in women in the highest quintile of choline intake (412 mg/day) compared to the lowest (179 mg/day) and 25% lower in men in the highest (452 mg/day) quintile compared to those in the lowest quintile (199 mg/day). However, choline intake was associated with NAFLD in normal-weight women only and not in those with overweight or obesity. This difference by weight status was not observed in men.

In a cross-sectional study of 664 adults and children from the Nonalcoholic Steatohepatitis Clinical Research Network, postmenopausal women who had nonalcoholic steatohepatitis (an extreme form of NAFLD involving liver inflammation and fibrosis) and a choline intake less than 50% of the AI had more severe fibrosis, but the results showed no relationship between choline intake and degree of liver steatosis [48].

Only limited data are available on the use of choline to treat NAFLD. For example, in a study of 57 adults who consumed a diet that included less than 50 mg choline per 70 kg body weight per day (<10% of the AI) for up to 42 days, 37 of the participants developed liver dysfunction [45]. Liver function returned to normal in 29 participants in this study after they were fed a diet containing 25%–75% of the choline AI and in 8 who consumed an ad libitum diet. A pilot study in 15 adults on TPN found that NAFLD resolved completely in all patients who received their usual TPN regimen with an additional 2 g choline and in none of the patients who received their usual TPN regimen only [49].

Adequate choline intake is needed for proper liver function and to prevent NAFLD, but more research is needed to further clarify the role of choline in preventing or treating NAFLD [50].

Health Risks from Excessive Choline

High intakes of choline are associated with a fishy body odor, vomiting, excessive sweating and salivation, hypotension, and liver toxicity [1,2]. Choline consumption has been shown to increase production of TMAO, a substance that has been linked to a higher risk of cardiovascular disease, in a dose-dependent manner in adults.

The FNB has established ULs for choline from food and supplements based on the amounts of choline that are associated with hypotension and fishy body odor (see Table 3) [2]. The ULs apply to healthy children and adults, but not to those taking high doses of choline under medical supervision. The FNB was unable to establish ULs for infants due to the lack of data on adverse effects in this age group.

Table 3: Tolerable Upper Intake Levels (ULs) for Choline [2]

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*				
7–12 months*				
1–3 years	1,000 mg	1,000 mg		
4–8 years	1,000 mg	1,000 mg		
9–13 years	2,000 mg	2,000 mg		
14–18 years	3,000 mg	3,000 mg	3,000 mg	3,000 mg
19+ years	3,500 mg	3,500 mg	3,500 mg	3,500 mg

*Not possible to establish; breast milk, formula, and food should be the only sources of choline for infants.

Interactions with Medications

Choline is not known to have any clinically relevant interactions with medications.

Choline and Healthful Diets

The federal government’s 2020-2025 *Dietary Guidelines for Americans* notes that “Because foods provide an array of nutrients and other components that have benefits for health, nutritional needs should be met primarily through foods. ... In some cases, fortified foods and dietary supplements are useful when it is not possible otherwise to meet needs for one or more nutrients (e.g., during specific life stages such as pregnancy).”

For more information about building a healthy dietary pattern, refer to the *Dietary Guidelines for Americans* (<https://www.dietaryguidelines.gov>) and the U.S. Department of Agriculture’s *MyPlate*. (<https://www.choosemyplate.gov/>).

The *Dietary Guidelines for Americans* describes a healthy dietary pattern as one that:

- Includes a variety of vegetables; fruits; grains (at least half whole grains); fat-free and low-fat milk, yogurt, and cheese; and oils.

Many vegetables, fruits, whole grains, and dairy products contain choline.

- Includes a variety of protein foods such as lean meats; poultry; eggs; seafood; beans, peas, and lentils; nuts and seeds; and soy products.

Fish, beef, poultry, eggs, and some beans and nuts are rich sources of choline.

- Limits foods and beverages higher in added sugars, saturated fat, and sodium.
- Limits alcoholic beverages.
- Stays within your daily calorie needs.

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