Perspectives in Practice

Choline- and Betaine-Defined Diets for Use in Clinical Research and for the Management of Trimethylaminuria

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ABSTRACT

This article describes the development of a series of choline- and betaine-controlled diets that were served to research subjects as part of an ongoing study of diet requirements in humans. These diets were developed based on the analysis of choline and betaine in individual foods. The calculated diets were compared with analyses of all foods combined into a single sample for each day. The laboratory analyses of choline and betaine in the whole-diet aliquots matched the estimated amounts in the diets that were calculated from the analyses of individual foods. These diets were adjusted for several levels of choline and betaine and were well accepted by research subjects who consumed them for a time period of up to 2 months. This article describes applications of this diet for use in clinical research on methyl-group requirements in humans and for use in clinical practice for counseling the client who requires a choline-controlled diet.
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A series of choline- and betaine-controlled diets have been developed and served to research subjects as part of an ongoing study of diet requirements in humans. The purpose of this article is to describe applications of these diets for use in clinical research on methyl-group requirements in humans and for use in clinical practice for counseling the client who requires a choline-controlled diet.

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Choline, or its metabolites, is needed for the structural integrity and signaling functions of cell membranes; it is a major source of methyl groups in the diet and it directly affects cholinergic neurotransmission, transmembrane signaling, and lipid transport/metabolism (1). The Institute of Medicine (IOM) of the National Academy of Sciences set an adequate intake (AI) level for choline of 550 mg/day for men and 425 mg/day for women (2).

Betaine is used by the kidney in the reabsorption of free water (3) and is the metabolite of choline that acts as a methyl-group donor in the remethylation of homocysteine. Methyltetrahydrofolate is the alternative dietary methyl-group donor and is metabolically interrelated with betaine (1). Both regulate the formation of S-adenosylmethionine and thereby influence methylation reactions. Diminished folate availability increases demand for choline as a methyl-group donor (4), and decreased choline-betaine availability increases demand for folate methyl groups (5). For this reason, both methyl-group donors must be considered in any attempts to understand how methyl status could be mechanistically related to disease processes. Researchers should be using experimental diets that are choline- and betaine-defined, as well as folate- and methionine-defined in investigations of human requirements.

Some humans with a defect in the flavin-containing monooxygenase-3 gene (FMO3) develop fishy body odor because they accumulate trimethylamine, a breakdown product formed from choline by bacteria in the gut (6-9). A choline-restricted diet is useful in these patients because it diminishes body odor (10); betaine does not need to be restricted because it is not a substrate for these bacteria. Diets for trimethylaminuric patients have heretofore been constructed without much information, and clinical care could be enhanced if the choline content of diets were better defined. Although the true incidence of this disorder is unknown, the proceedings from a 1999 National Institutes of Health–sponsored workshop on trimethylaminuria suggested that as much as 1% of the US population may have this autosomal recessive genetic defect (11). Studies show that there are individuals with different single nucleotide polymorphisms (SNPs) of the FMO3 genes resulting in differences in the way compounds metabolized by these genes are processed, and heterozygous individuals may present with milder forms of trimethylaminuria. A human FMO3 mutation database has been established (12,13) to catalog the various FMO3 gene SNPs.

Table 1. Research diet menu including actual amounts of food provided for a 2,500-kcal diet containing varying amounts of choline

Food item	Choline-deficient diet	Repletion Diets[a]			
		25%	50%	75%	100%
	← weight (g) →				
Breakfast					
Raw egg white, fresh	100	50	50	50	25
Wheat starch/lecithin bread[b]	20	20	40	65	85
Margarine	10	10	10	10	10
Soy protein beverage (recipe II)	300	240	200	0	0
Coffee, decaf instant	2	2	2	2	2
Cream substitute powder	2	2	2	2	2
Coca-Cola Classic,[c] caffeine-free	237	350	350	300	300
Morning snack					
Coca-Cola Classic[c]	237	350	350	300	300
Lunch					
Cheese	20	20	20	20	20
Wheat starch/lecithin bread[b]	25	25	40	60	85
Margarine	15	15	15	15	10
Applesauce, unsweetened	100	100	100	100	100
Soy protein beverage (recipe II)	300	240	200	250	200
Coca-Cola Classic, caffeine-free	474	350	350	300	300
Afternoon snack					
Coca-Cola Classic	237	350	350	300	300
Dinner					
Roasted turkey breast, no skin	20	20	20	20	20
French fries, from frozen	30	30	30	30	30
Wheat starch/lecithin bread[b]	0	20	35	60	85
Margarine	10	0	10	15	15
Soy protein beverage (recipe II)	300	240	200	200	200
Coca-Cola Classic	237	350	350	300	300
Bedtime snack					
Tortilla chips, plain	12	12	12	12	12
Coca-Cola Classic, caffeine-free	237	350	350	300	250

[a]Percentages show the approximate amount of choline based on the adequate intake.
[b]Wheat starch bread on depletion diet, lecithin bread on repletion diets.
[c]The Coca-Cola Co, Atlanta, GA.

METHODS

Description of Diet Composition

Choline is present in foods in several forms: choline, phosphatidylcholine, phosphocholine, and glycerophosphocholine (14). Betaine is also present in many foods (14). We created a research diet that delivers 550 mg total choline and 50 mg betaine per day per 70 kg body weight (approximately matching the AI for choline set by the IOM (2). Other research diets were prepared to deliver varying levels of choline: less than 50 mg (choline deficient) and 25%, 50%, 75%, and 100% of the AI as shown in Table 1. These diets were designed to be as nearly alike as possible with regard to the foods that were used. The adjustment for choline content was achieved with the use of two different breads that were specially prepared in the University of North Carolina General Clinical Research Center metabolic kitchen: lecithin bread and wheat starch bread, containing high and low levels of total choline, respectively.

Diets were adjusted to maintain body weight at energy levels ranging from 35 to 45 kcal/kg body weight, based on individual requirements. Each diet provided 0.8 g/kg high–biological value protein, 30% of energy from fat, and the remainder of energy from carbohydrates. Protein quality for each day of the diet was evaluated based on the amino acid profile of the total protein in all foods for that day (15). Cooked non–folate-fortified liquid egg whites and choline-free soy protein beverages were used to provide adequate amounts of high-quality protein during the choline-deficient and repletion phases. Cola or sugar-sweetened Kool-Aid (Kraft Foods, Northfield, IL), wheat starch bread, and canned fruits were used to add very–low-choline carbohydrate kilocalories. Fiber was added to the diet in the form of psyllium (Metamucil, Procter & Gamble Co, Cincinnati, OH) added to the soy-protein beverage. The soy-protein concentrate used in the beverage as the protein source was a special spray-dried soy-protein concentrate obtained from defatted soybean flakes by sequential extraction with aqueous ethanol, then with hydrochloric acid, pH 4.5 (The Solae Co [formerly Central Soya], St Louis, MO). Cold-pressed safflower oil (Loriva Brand, *n*Spired Natural Foods, San Leandro, CA) was used as the fat source, sucrose as the carbohydrate source, and the beverage was flavored with

Ingredient name	Recipe I[a] weight (g)	Recipe II[a] weight (g)
Soy protein concentrate[b]	95.8	95.8
Sugar, granulated	169.9	169.9
Salt, table	1.9	1.9
Vanilla extract, imitation	26.5	26.5
Safflower oil	55.5	88.0
Metamucil[c]	10.0	10.0
Distilled water	952.5	952.5
Total weight	1,312.1	1,338.6
Mix all ingredients and blend thoroughly. Chill before serving. Flavorings were added in measured amounts after beverages were portioned into individual servings.		

Figure 1. Recipe for soy beverage used in study. [a]Recipe I and Recipe II are identical with the exception of the amount of safflower oil. The two different recipes were used so that diets could be adjusted to meet individual protein requirements and maintain a constant level of 30% of kilocalories from fat. [b]Soy protein concentrate spray-dried from defatted soybean flakes and extracted with aqueous ethanol and then with hydrochloric acid pH 4.5 (The Solae Co [formerly Central Soya], St Louis, MO). [c]Metamucil, Proctor & Gamble Co, Cincinnati, OH.

Ingredient name	Weight (g)
Hodgkins Mill Bread Flour	1,000
Vital wheat gluten	40
Sugar	30
Yeast	20
Centrolex FP 30 Lecithin[a]	88
Salt	20
Water	635
Total of ingredients	1,833
Cooked weight (average of three preparations)	1,713
Mix flour and vital gluten. Cut lecithin into flour mixture. Mix yeast, warm water, and sugar and allow to bubble. Mix 12 minutes on medium speed. Allow to rise at 96°F and 70% relative humidity. Punch dough down after 52 and 77 minutes from start of mixing. Let rest 10 minutes. Place dough in pan lightly sprayed with vegetable oil. Let rise to ½ inch above edge of pan. Bake at 410°F for 20 minutes. Yield: 3 loaves.	

Figure 2. Recipe for lecithin bread used in study. [a]Lecithin containing 30% phosphatidylcholine (The Solae Co [formerly Central Soya], St Louis, MO).

either chocolate or strawberry syrup (Hershey's Brand, Hershey Foods Corp, Hershey, PA). The recipes for the soy-protein beverage are shown in Figure 1.

To provide adequate protein and maintain 30% of energy from fat at all kilocalorie levels, two recipes with different amounts of safflower oil were used. Diets were adjusted from less than 50 mg total choline to approximately 25%, 50%, 75%, and 100% of the AI for choline with a high–lecithin-content bread that was made using a lecithin ingredient containing 30% phosphatidylcholine (The Solae Co). The recipe for this bread was developed at The Solae Co, and the analysis for choline and betaine was done by our laboratory. The lecithin bread was prepared in the General Clinical Research Center metabolic kitchen to precise specifications for ingredient measurement, mixing, baking time, and temperature. A consistent product was produced throughout the study. The recipe is shown in Figure 2. The choline content of this bread was 200 mg choline per 100 g of bread.

These diets were compared with the 1997 Dietary Reference Intakes (DRIs) for men ages 25 to 50 as shown in Table 2. The US Department of Agriculture database (Number 14) was used to analyze these diets with Food Processor Software (ESHA Research, Inc, Salem, OR, Version 7.8, December 2001). Based on this analysis, multivitamin supplements were given to meet 100% of the daily requirements for all nutrients except choline. Supplements included vitamins A, D, thiamin, riboflavin, niacin, B-6, B-12, C, and chromium (Centrum Liquid, Wyeth Consumer Healthcare, Madison, NJ); folic acid (Solgar, Wyeth Consumer Healthcare); iron and selenium (GNC, Pittsburgh, PA); and zinc, calcium, magnesium, and manganese (Caltrate Plus, Wyeth Consumer Healthcare). Each diet had approximately 100 μg folate per day before supplementation.

Analysis of the Diet for Choline and Betaine

Individual foods for the diet were analyzed for choline by the Zeisel Laboratory (University of North Carolina, Chapel Hill) (14,16). In addition, aliquots were prepared [as described by Dennis and colleagues (17)] of whole-diet homogenates for each day of each diet: choline-deficient and 25%, 50%, 75%, and 100% of the AI for choline. The correlation between the analyses of the whole diet and the individual foods was excellent (Figure 3).

Recommendations for Controlled Choline Diets for Use in the Research Setting

We developed several research diets with defined choline and betaine content. These diets were well accepted by human volunteers and compliance was excellent. The 550-mg choline diet should deliver the recommended adequate intake of choline for humans. The choline-deficient diet described should deplete humans of choline and choline-related compounds in tissues. Because of the potential risk of physiological imbalance, these very–low-choline diets should be used in a clinical research setting for the investigation of questions related to methyl-group metabolism and not as therapeutic diets.

When many species of animals, including the baboon, are fed a choline-deficient diet, they deplete choline stores and develop liver dysfunction (18-22). Animals fed a choline-deficient diet may also develop growth retardation, renal dysfunction and hemorrhage, or bone abnormalities (21,23,24). Healthy male humans with normal folate and vitamin B-12 status fed a choline-deficient diet have diminished plasma choline and phosphatidylcholine concentrations and develop liver damage (increased plasma alanine aminotransferase) (25). Some humans (male and female) fed with total parenteral nutrition solutions devoid of choline, but adequate for methionine and folate, develop fatty liver and liver damage that resolves when a source of dietary choline is provided (26-32). Studies of

Table 2. Comparison of the nutrient analysis of the choline-deficient diet with the 1997 DRI[a] for males ages 25 to 50 years calculated using ESHA Food Processor Software[b]

Nutrient	Choline-deficient diet[c]	1997 DRI for males 25-50 y	% DRI provided by the diet
Vitamin A (RE[d])	286.5	1,000.0	29
Vitamin D (μg)	0.3	10.0	3
Vitamin E (mg)	21.2	10.0	212
Vitamin K (μg)	4.05	80.0	5
Vitamin B-1 (thiamine) (mg)	0.2	1.5	13
Vitamin B-2 (riboflavin) (mg)	0.8	1.7	44
Vitamin B-3 (niacin) (mg)	2.7	19.0	14
Vitamin B-6 (mg)	0.6	2.0	30
Vitamin B-12 (μg)	1.3	2.0	65
Vitamin C (mg)	13.2	60.0	22
Folate (μg)	110.0	200.0	55
Iron (mg)	16.9	10.0	169
Zinc (mg)	6.0	15.0	40
Iodine (μg)	33.4	150.0	22
Selenium (μg)	28.6	70.0	41
Calcium (mg)	580.6	1,000.0	58
Phosphorus (mg)	1,324.0	700.0	189
Magnesium (mg)	359.5	420.0	86

[a]DRI=Dietary Reference Intake.
[b]Version 7.8, December 2001, ESHA Research, Inc, Salem, OR.
[c]Average nutrient content of the 2-day menu of the choline-deficient diet.
[d]RE=retinol equivalents.

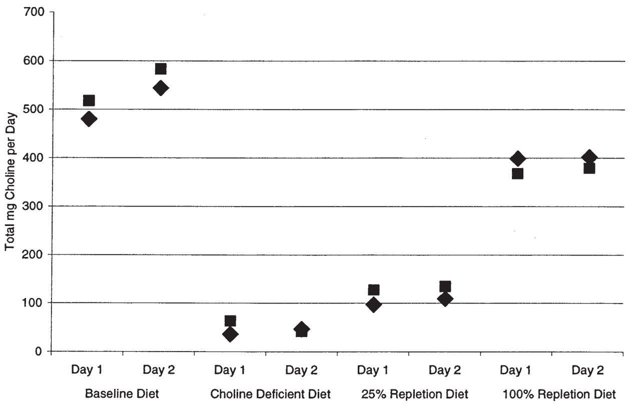

Figure 3. The sum of the individual food analyses was compared to the whole diet analysis. Individual foods (diamonds) for each day of the diet were analyzed for choline (as described in the methods section of the article) and the values summed. In addition, aliquots of whole diet homogenates (squares) for each day of each diet were prepared and analyzed.

the interrelationship of folate and choline demonstrate that choline is required as a methyl donor when folate intake is low (33). Fatty liver occurs because choline is required to make the phosphatidylcholine portion of the very–low-density lipoprotein particle (34,35). Thus, we recommend that the diet for individuals with trimethylaminuria be adjusted individually by the clinician with amounts of choline that minimize the fishy body odor without inducing liver dysfunction and other side effects. These patients should be supplemented with adequate folate to assure that there are adequate methyl groups available for the methylation of homocysteine to methionine. The more restricted diets should be used only in a research setting with full safety measures in place.

Recommendations for Controlled Choline Diets for the Treatment of Trimethylaminuria

A full discussion of the treatment of trimethylaminuria has been published elsewhere (36). These treatments include restriction of choline intake, vitamin supplementation with riboflavin and folate, restriction of dietary indoles and glucosinolates, drug treatment with oral antibiotics, and the use of laxatives. The latter two treatments are not feasible for long-term therapy. It is likely that the FMO3 gene is polymorphic, and individuals with different SNPs and heterozygous individuals may present with milder forms of trimethylaminuria. Therefore, different dietary levels of choline may be appropriate, and our discussion of the treatment of trimethylaminuria will be limited to choline-restricted diets (36).

A low-choline diet that contains high-quality protein and adequate amounts of breads, fruits, and vegetables can be provided to individuals with trimethylaminuria. Acceptable/palatable meal plans can be developed containing levels of choline as low as 100 mg per day. Meal plans should be developed according to individual preferences using the Dietary Guidelines (37) for inclusion of a variety of foods. Based on the analyses of individual foods previously published (14), foods were grouped according to three levels of choline for use in developing individualized diets (Table 3). Values for betaine are also provided.

It is apparent that foods that are very high in choline, including whole eggs, organ meats, cruciferous vegetables,

Table 3. Table of foods by food group and level of choline and betaine content

	USDA[a] Nutrient Data Bank No.[b]	Standard serving size	Weight (g)	Amount of choline per serving (mg)	Amount of betaine per serving (mg)
Foods Low in Choline (0–10 mg choline/serving)					
Milk, dairy, and cheese					
Creamer	01069	1 teaspoon	2	0.046	0.002
Sour cream	01056	1 tablespoon	12	2.440	0.090
Half & half	01050	1 tablespoon	15	2.523	0.102
Cheese	01009	1 oz	28	4.620	0.185
Cream cheese	01017	1 oz	28	7.619	0.204
Cottage cheese	01012	1/4 cup	55	10.131	0.407
Fruits and juices					
Pears, canned	09257	1/2 cup	133	2.580	0.346
Apple juice	09016	6 oz	180	3.312	0.414
Grapes	09132	1/2 cup	75	4.223	0.098
Peaches, canned, heavy syrup	09241	1/2 cup	131	4.454	0.354
Apples, raw	09003	1 medium	138	4.747	0.138
Raisins, seedless	09298	1 1/2 oz box	43	4.790	0.129
Peaches, raw	09236	1 medium	98	5.978	0.265
Watermelon, raw	09326	1 cup, diced	152	6.186	0.426
Strawberries, raw	09316	1 cup, whole	144	8.136	0.216
Prunes, canned	09288	5 each	86	8.308	0.378
Pears, raw	09252	1 medium	166	8.483	0.249
Blueberries, raw	09050	1 cup	145	8.758	0.261
Grapefruit, raw	09111	1/2 medium	128	9.638	0.192
Oranges	09200	1 medium	120	10.056	0.144
Vegetables					
Catsup	11935	1 tablespoon	15	1.580	0.026
Celery, raw	11143	1 stalk, medium	40	2.456	0.040
Cucumber, with peel, raw	11205	1/2 cup, sliced	52	3.094	0.036
Spinach, raw	11457	1/2 cup, chopped	15	3.312	101.178
Iceberg lettuce	11252	1 cup, shredded	55	3.685	0.044
Beets, raw	11080	1/2 cup, sliced	68	4.087	87.468
Peppers	11333	1/2 cup, chopped	75	4.155	0.060
Alfalfa seeds, sprouted, raw	11001	1 cup	33	4.752	0.129
Onion, raw	11282	1/2 cup, chopped	80	4.880	0.064
Beets, canned	11084	1/2 cup, sliced	85	5.185	283.637
Carrots, raw	11124	1/2 cup, sliced	60	5.274	0.234
Romaine lettuce	11251	1 cup	56	5.555	0.050
Mushrooms, raw	11260	1/2 cup, pieces	35	5.901	3.745
Carrots, cooked	11125	1/2 cup, sliced	78	6.841	0.101
Beets, cooked	11081	1/2 cup, sliced	85	7.557	150.408
Tomatoes, raw	11529	1 medium	123	8.290	0.086
Zucchini, cooked	11478	1/2 cup	90	8.424	0.234
Beans, snap, green	11061	1/2 cup	68	9.153	0.061
Meats, legumes, eggs					
Egg whites[c]	01124	1/4 cup	60	1.410	0.250
Pork sausage	07065	1 link	13	9.499	0.313
Cereals, breads, grains, starchy vegetables					
Rice, cooked	20045	1/2 cup	79	1.643	0.237
Saltine crackers	18228	5 each	15	2.939	8.288
White bread	18069	1 slice	25	3.043	26.203
Graham cracker, plain	18173	1 large rectangle	14	3.118	27.173
Tortillas	18363	1 medium, 6-inch diameter	24	3.185	0.091
Wheat cracker	18232	6 crackers	12	3.816	26.815

(continued)

Table 3. Table of foods by food group and level of choline and betaine content (continued)	USDA[a] Nutrient Data Bank No.[b]	Standard serving size	Weight (g)	Amount of choline per serving (mg)	Amount of betaine per serving (mg)
Cream of wheat, cooked	08105	1/2 cup	120	4.140	8.220
Biscuit, plain	18009	1 medium	51	4.534	21.925
Spaghetti noodles, cooked	20121	1/2 cup	70	4.662	70.735
Wheat bread	18064	1 slice	25	6.633	56.625
Danish pastry	18246	1 small	35	7.644	4.991
Cereal, oatmeal, cooked	08121	1/2 cup	117	8.681	3.569
Sweet potatoes, cooked	11602	1/2 cup	68	8.915	23.521
Brown rice, cooked	20037	1/2 cup	98	9.036	0.480
French fries, frozen, baked	11403	10 pieces	50	10.085	0.160
English muffins	18258	1 each	57	10.232	61.167
Fats and oils					
Canola oil[c]	04582	1 tablespoon	14	0.000	0.000
Olive oil	04053	1 tablespoon	14	0.041	0.014
Margarine[c]	04067	1 teaspoon	5	0.300	0.000
Italian dressing, reduced fat	04021	1 tablespoon	15	0.596	0.242
Butter, salted	01001	1 teaspoon	5	0.939	0.012
Italian dressing, regular	04114	1 tablespoon	15	1.860	0.002
Mayonnaise, imitation	04027	1 tablespoon	15	2.189	0.047
Mayonnaise, regular	04025	1 tablespoon	14	6.443	0.000
Spices and herbs					
Mustard seed, yellow	02024	1 teaspoon	3	3.680	0.056
Soups, sauces, and gravies					
Salsa	06164	1 tablespoon	16	1.872	0.040
Soy sauce	16123	1 tablespoon	16	5.285	6.334
Beverages					
Diet Coca-Cola[d]	14416	12 oz	355	0.000	0.249
Brewed tea	14355	1 cup	240	0.888	2.160
Decaffeinated coffee powder	14218	1 teaspoon	1.8	1.834	0.013
Cranberry juice cocktail	14242	6 oz	180	2.034	0.144
Orange crush	14150	12 oz	372	2.158	0.186
Coca-Cola[d]	14400	12 oz	370	2.479	0.333
White wine	14106	4 oz	120	6.180	0.180
Coffee	14209	1 cup	240	6.288	0.192
Snacks and sweets					
Chocolate chip cookie	18159	1 medium, $2\frac{1}{4}$-inch diameter	10	1.705	4.276
Strawberry preserve	19297	1 tablespoon	20	2.042	0.020
Corn chips	19003	1 oz	28	3.380	0.031
Potato chips	19411	1 oz	28	3.380	0.048
Popcorn, oil popped	19035	3 cups	33	4.613	0.122
Apple pie	18301	1/6 of 8-inch diameter	117	8.412	19.165
Foods Moderate in Choline (11–35 mg choline/serving)					
Milk, dairy, and cheese					
Yogurt, fruit	01121	6 oz	170	23.868	1.411
Yogurt, plain	01117	6 oz	170	25.840	1.445
Whole milk	01077	1 cup	240	34.296	1.464
Fruits and juices					
Bananas, raw	09040	1 medium	118	11.517	0.094
Melons, cantaloupe, raw	09181	1 cup, pieces	160	12.128	0.128
Orange juice, from frozen	09215	6 oz	180	19.890	0.450
Avocadoes, raw	09037	1 cup, sliced	146	20.703	0.964

(continued)

Table 3. Table of foods by food group and level of choline and betaine content (continued)					
	USDA[a] Nutrient Data Bank No.[b]	**Standard serving size**	**Weight (g)**	**Amount of choline per serving (mg)**	**Amount of betaine per serving (mg)**
Vegetables					
Yellow squash, cooked	11644	1/2 cup	100	10.570	0.210
Cabbage, cooked	11110	1/2 cup	75	11.588	0.255
Sauerkraut, canned	11439	1/2 cup	118	12.260	0.578
Yellow corn, cooked	11179	1/2 cup	62	13.609	0.093
Broccoli, cooked	11091	1/2 cup	40	16.024	0.052
Cauliflower	11136	1/2 cup	50	19.550	0.085
Peas, cooked	11313	1/2 cup	80	22.008	0.120
Spinach, cooked	11458	1/2 cup	90	22.302	652.869
Kale, cooked	11234	1 cup	130	23.777	0.000
Marinara, ready-to-serve, tomato pasta sauce	06931	1/2 cup	125	25.088	0.525
Brussels sprouts, cooked	11101	1/2 cup	75	30.458	0.113
Meats, legumes, eggs					
Peanuts, roasted	16089	1 oz	28	14.692	0.176
Pork sausage	07065	1 patty	27	19.729	0.651
Peanut butter	16098	2 tablespoons	32	20.166	0.250
Chicken hot dogs	07024	1 each	45	23.112	2.295
Beans, navy	16039	1/2 cup	90	24.237	0.063
Fish sticks	15027	3 oz	90	25.488	29.673
Bacon, cooked	10124	3 slices	24	29.974	0.850
Tofu, soft	16127	1/2 cup	120	32.844	0.480
Cereals, breads, grains, starchy vegetables					
Buckwheat groats, cooked	20010	1/2 cup	84	11.315	35.204
Mashed potatoes, home-prepared	11657	1/2 cup	105	15.078	0.452
Danish pastry	18246	$4\frac{1}{4}$-inch diameter	71	15.506	10.125
Plain muffins	18273	1 each	40	17.360	36.940
Oat bran, raw	20033	1/3 cup	31	18.157	11.061
Wheat bran	20077	1/2 cup	29	21.564	436.624
Danish pastry	18246	1 large rectangle	142	31.013	20.249
Soups, sauces, and gravies					
Chicken noodle soup	06419	1 cup	241	27.040	28.607
Beverages					
Beer, light	14006	12 oz	360	25.416	25.092
Beer, regular	14003	12 oz	360	34.956	34.992
Snacks and sweets					
Pretzel, hard, plain, salted	19047	1 oz	28	10.752	74.452
Sherbet, orange	19097	1/2 cup	74	11.537	0.437
Yogurt, frozen, soft-serve	19293	1/2 cup	72	16.567	0.626
Ice cream	19095	1/2 cup	72	18.749	0.756
Milk chocolate	19120	1 1/2 oz bar	46	21.211	1.205
Snickers[e] candy bar	19155	2-oz bar	57	23.210	0.627
Frosted cake	18140	1 slice	64	23.283	11.936
Cheese nachos	21078	6-8 nachos	113	29.776	0.780
Fast food					
Cheese pizza	21049	3 slices from 12-inch diameter	189	26.422	48.913
Hot dog and bun	21118	1 sandwich	98	29.459	43.404
Fast-food french fries	21138	1 medium	134	29.560	0.992
Fast-food hamburger, regular, single patty, plain	21107	1 sandwich	90	30.807	29.970

(continued)

Table 3. Table of foods by food group and level of choline and betaine content (continued)

	USDA[a] Nutrient Data Bank No.[b]	Standard serving size	Weight (g)	Amount of choline per serving (mg)	Amount of betaine per serving (mg)
Foods High in Choline (>35 mg choline/serving)					
Milk, dairy, and cheese					
Fat-free milk	01085	1 cup	240	37.512	4.584
2% milk	01079	1 cup	240	39.360	2.256
Meats, legumes, eggs					
Salmon	15086	3 oz	85	55.633	1.785
Chicken roasted (with skin)	05009	3 oz	85	55.956	4.735
Shrimp, canned	15152	3 oz	85	60.010	209.092
Beef, trim-cut, cooked	13004	3 oz	85	66.428	9.682
Chicken roasted (without skin)	05013	3 oz	85	66.929	4.871
Ground beef, 85% lean, broiled	23578	3 oz	85	67.422	8.118
Ground beef, 75% lean, broiled	23568	3 oz	85	69.998	7.208
Finfish, Atlantic cod	15016	3 oz	85	71.086	8.194
Pork loin, cooked	10046	3 oz	85	87.346	1.335
Soybeans, mature seeds, raw	16108	1/2 cup	93	107.759	1.934
Eggs	01123	1 each	50	125.500	0.295
Chicken liver	05028	3 oz	90	261.027	11.574
Beef liver, pan fried	13327	3 oz	85	355.487	5.389
Cereals, breads, grains, starchy vegetables					
Pancakes, plain	18290	3 each, 6-inch diameter	231	44.375	60.083
Wheat germ cereal, ready-to-eat, toasted	08084	1 cup	113	171.850	1576.330
Beverages					
Vanilla shake	14347	12 oz	360	65.556	4.212
Fast food					
Lasagna	22570	215 g (approximately 1 cup)	215	36.507	13.094
Cheeseburger, regular, plain	21089	1 sandwich	102	40.055	30.090
Chicken nuggets	21037	6 pieces	106	44.382	17.956
Tacos/burritos	21082	1 large	263	70.694	34.769

[a]USDA=US Department of Agriculture.
[b]Five-digit Nutrient Data Bank number that uniquely identifies a food item in the USDA National Nutrient Database for Standard Reference (http://www.nal.usda.gov/fnic/foodcomp/Data/SR16/sr16 doc.pdf).
[c]Data not previously published.
[d]The Coca-Cola Co, Atlanta, GA.
[e]Mars, Inc, McLean, VA.

legumes and legume products, fast foods, and some dairy products, would need to be limited. For diets that are at the lowest choline levels, one would include a variety of fruits and vegetables. To meet adequate energy requirements, a moderate amount of fats and oils and sweetened soft drinks would be required.

Diets at the lowest choline levels would require inclusion of a soy beverage and/or adequate amounts of egg white, as was used for this research, to provide adequate amounts of high-biological value protein. A multivitamin and mineral supplement would be required. For example, a very–low-choline diet might include the soy protein beverage; five servings of fruits and vegetables; five servings of breads, cereals, and other grains; adequate amounts of low-choline fats and oils; and one dessert food each day. It would be difficult to include either dairy products or meats at this level of choline restriction. However, some variety in high-quality protein in the diet can be achieved by consulting Table 3 and decreasing the number of servings from fruits, vegetables, and grains while adding different protein sources such as legumes, nuts, and cottage cheese. This type of planning should be done by the dietitian/clinician to assure that the level of choline remains at approximately 100 mg per day and the diet contains the required high-quality protein as well as an adequate variety of other nutrients.

A more moderate level of restriction, such as 200 to 300 mg choline per day, would provide much more variety in the diet and would include foods from all food groups. For example, a diet at the moderate level of choline may include 4 to 5 oz of meat, four to five servings of fruits and vegetables, five to six servings of bread, one to two servings of dairy foods, adequate amounts of low-choline fats and oils, and one dessert food each day.

CONCLUSIONS

We demonstrated the application of the analysis of individual foods for the development, calculation, and administration of choline-controlled diets in the research setting. We have grouped these foods according to choline levels and in a manner consistent with food groups that are already used by dietetics professionals to meet recommendations for healthful diets. Thus, the adaptation of these food analyses into groups can be used to develop diets that have known levels of choline and betaine and may be used in both research and clinical settings. This presentation allows the clinician to develop meal plans that will be palatable and well accepted by the individuals who must consume these diets, and can be adjusted with the use of multivitamin and mineral supplements to meet requirements for adequate intakes of all nutrients.

Our research recommendations:

- Calculate diets using choline and betaine analysis data and recipes provided in this article.
- Provide adequate energy and high-quality protein.
- Balance macronutrient amounts to provide a healthful diet.
- Compare diets to current DRIs and add vitamin and mineral supplements as needed.
- Monitor laboratory values for liver function.
- Monitor daily dietary intake and subject compliance.

Practice recommendations:

- Plan diets in accordance with the Dietary Guidelines and individual preferences to provide adequate protein, carbohydrates, and fat and to include a variety of foods using the low-choline foods in Table 3.
- Note that adjusting menu items to a smaller serving size, such as pork sausage and Danish pastry, allow more variety in the diet while still maintaining the appropriate level of choline and betaine.
- Recommend a multivitamin that contains 100% of the DRI for vitamins and minerals, particularly folate and riboflavin.
- Use software such as ESHA Food Processor to check protein quality of the diet.
- Add the soy beverage as needed to provide an adequate amount of quality protein in the diet.
- Monitor patient compliance, satisfaction, and therapeutic progress.

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