

Methionine- Restricted Diet...

Who needs it?

Methionine is an essential amino acid – one of the building blocks of protein that cannot be produced by the human body so must come from our food. It is one of two sulfur-containing amino acids (the other is cysteine). Methionine is an intermediary in the synthesis of cysteine, carnitine, taurine, and other compounds. It protects liver cells, and helps to prevent lipid peroxidation, and possibly atherosclerosis and elevated cholesterol. Although methionine is essential to human life, some people benefit by limiting, but not eliminating methionine in their diets. For such individuals a methionine-restricted diet may be advised.

Should I be on a methionine-restricted diet?

Some individuals need to restrict methionine due to inherited disorders that affect methionine metabolism. There is growing interest in methionine restricted diets for those who are unaffected by these genetic metabolic disorders. Evidence suggests that such diets could enhance longevity and help to prevent or treat certain chronic health conditions. The most common indications for a methionine-restricted diet are:

i) MTHFR variants. MTHFR gene mutations can lead to elevated homocysteine. Methionine restriction is commonly recommended to help reduce homocysteine accumulation.

ii) Cancer. While human studies are sparse, there is some

evidence that cancer cells grow less robustly, and sometimes undergo apoptosis (cell death) when deprived of methionine.

iii) Depression. High methionine intakes can elevate homocysteine levels and risk of depression.

iv) Lifespan extension. Low methionine diets increase metabolic flexibility and overall insulin sensitivity and improve lipid metabolism while decreasing systemic inflammation.

v) Insulin resistance. Methionine restriction has been shown to reduce adiposity and improve insulin sensitivity.

vi) Homocystinuria. This inherited disorder of metabolism often requires a low methionine diet.

If methionine-restriction may help kill cancer cells and increase longevity, shouldn't everyone be on a methionine-restricted diet?

We don't know for sure, but it is an option for those who are interested in employing a novel dietary strategy for disease risk reduction. While severe methionine restriction is rarely advised, a moderate methionine restriction may be beneficial. The most concentrated methionine sources are animal products such as meat, poultry and fish. You will see from the table below that the eating pattern that is lowest in methionine is a purely plant-based diet or vegan diet. Other vegetarian or near-vegetarian diets are lower in methionine than omnivores

diets, but not as low as vegan diets. For most people, simply eating a plant-based diet is likely sufficient for reducing methionine intake. Those with metabolic disorders or other conditions that may warrant methionine restriction can further restrict methionine by limiting high methionine plant-based foods.

If a methionine restricted diet is indicated for me, how much methionine should I be eating each day?

The RDA (recommended dietary allowance) for methionine + cysteine (adults 19 yrs+) is 19 mg/kg/day, while the EAR (estimated average requirement) is 15 mg/kg/day. People should not dip too much below these levels as they represent the lower end of what is needed for human health. Methionine-restricted diets allow 800-1200 mg methionine per day for most adults. For methionine alone, 15 mg/kg is thought to be a reasonable lower limit. So, if a therapeutic, methionine-restricted diet is indicated for you, multiply your healthy body weight by 15 to find a level of methionine intake that is appropriate. Let's say your healthy body weight is 60 kg, you would need 900 mg methionine per day.

Are there any downsides to severely restricting methionine?

Absolutely. There is some evidence that a lack of methionine could reduce levels of S-Adenosylmethionine or SAM-e increasing risk of depression. A lack of methionine has also been linked to senile graying of hair. When you restrict methionine you are naturally restricting protein, at least to some degree. Ensuring sufficient protein is essential to health. Protein is necessary for building, strengthening and repairing body tissues, for making antibodies, hormones, enzymes and other compounds that are critical to every body process. A lack of protein can result in muscle loss,

increased risk of bone fractures and undesirable changes in hair and skin. Seniors tend to absorb protein less efficiently, so they may need to consume 15-25% more protein than other adults in order to absorb the same amount. So while methionine restriction can be beneficial, it is important that we meet our needs for methionine, and for protein.

METHIONINE IN COMMON FOODS

(SOURCE: THE USDA NUTRIENT DATABASE RELEASE 28)

Methionine (mg/serving)
0-50 mg
51-100 mg
101-150 mg
151-200 mg
201-250 mg
251-300 mg
301+ mg

Vegetables	Weight	Measure	Methionine (mg)
Asparagus, cooked	180 g	1 cup	50
Green beans, cooked	125 g	1 cup	29

Yellow beans, cooked	135 g	1 cup	24
Beets, cooked, sliced	170 g	1 cup	32
Broccoli rab, raw, chopped	40 g	1 cup	19
Broccoli, raw, chopped	91 g	1 cup	35
Burdock root, raw	118 g	1 cup	11
Cabbage, chinese, cooked, shredded	179 g	1 cup	15
Cabbage, cooked	150 g	1 cup	9
Carrots, raw, chopped	128 g	1 cup	26
Cauliflower, raw, chopped	107 g	1 cup	21
Celery, raw, chopped	101 g	1 cup	5
Chard, swiss, raw	36 g	1 cup	7
Chard, swiss, cooked	175 g	1 cup	35
Collards, raw	36 g	1 cup	12
Collards, cooked	170 g	1 cup	68
Cucumber, raw	104 g	1 cup	6
Eggplant, cooked	99 g	1 cup	9
Endive, raw	50 g	1 cup	8
Kale, raw, chopped	67 g	1 cup	18
Kale, cooked	130 g	1 cup	23
Kohlrabi, raw	135 g	1 cup	18
Leeks, cooked	124 g	1 leek	12
Lettuce, raw, shredded	36-47 g	1 cup	6-7
Mountain yam, cooked	145 g	1 cup	33
Mushrooms, cooked	156 g	1 cup	34
Mustard greens, cooked	150 g	1 cup	32
Okra, cooked	160 g	1 cup	32
Onions, cooked	210 g	1 cup	23
Parsley, fresh, chopped	60 g	1 cup	25

Pepper, sweet, raw, chopped	149 g	1 cup	9
Pumpkin, cooked, mashed	245 g	1 cup	20
Radicchio, raw	40 g	1 cup	3
Radishes, raw	116 g	1 cup	12
Seaweed, laver, raw	26 g	10 sheets	38
Spinach, raw	30 g	1 cup	16
Squash, summer, cooked	180 g	1 cup	23
Squash, winter, cooked	205 g	1 cup	23
Taro, cooked, sliced	132 g	1 cup	9
Tomatoes, fresh	149 g	1 cup	9
Tomato sauce	245 g	1 cup	17
Turnip greens, cooked	144 g	1 cup	37
Turnips, cooked, cubes	156 g	1 cup	14
Watercress, raw	34 g	1 cup	7
Yam, cooked	136 g	1 cup	27
Yardlong bean, cooked	104 g	1 cup	37
Zucchini, raw, chopped	124 g	1 cup	22
Brussels sprouts, cooked	155 g	1 cup	54
Hearts of palm, canned	146 g	1 cup	61
Potatoes, white + skin	148 g	1 med	56
Spinach, cooked	180 g	1 cup	99
Sweet potato, cooked	200 g	1 cup	74
Corn, sweet, cooked	165	1 cup	112
Peas, cooked	160 g	1 cup	130
Peas, raw	145 g	1 cup	119
Fruits			
Apples, raw, sliced	125 g	1 cup	1
Apricots, dried	65 g	0.5 cup	10

Apricots, raw	155 g	1 cup	9
Bananas, raw, mashed	225 g	1 cup	18
Blueberries, raw	148 g	1 cup	18
Cherimoya, raw	160 g	1 cup	34
Cranberries, raw, chopped	110 g	1 cup	3
Dates	147 g	1 cup	32
Figs, raw	64 g	1 large (2.5")	4
Gogi berries, dried	28 g	5 Tbsp	24
Grapefruit sections	230 g	1 cup	12-18
Grapes, fresh	92 g	1 cup	19
Guava, fresh	165 g	1 cup	26
Kiwi, raw, sliced	180 g	1 cup	43
Limes, raw	67 g	1 fruit	1
Mango, raw	165 g	1 cup	13
Melon, cantaloupe, raw	177 g	1 cup	21
Melon, honeydew, raw	170 g	1 cup	8
Nectarines, raw, sliced	143 g	1 cup	8
Olives, ripe, jumbo	15 g	1	2
Orange, raw, sections	180 g	1 cup	36
Papaya, raw	145 g	1 cup	3
Peach, raw	154 g	1 cup	15
Pear, Asian, raw	122 g	1 fruit	7
Pear, raw, slices	140 g	1 cup	3
Persimmons, raw	25 g	1 fruit	2
Pineapple, raw, chunks	165 g	1 cup	20
Plantains, raw, sliced	148 g	1 cup	25
Plums, raw, sliced	165 g	1 cup	13
Plums, dried	174 g	1 cup	28

Raisins, seedless	165 g	1 cup	35
Strawberries, raw	152 g	1 cup	3
Tangerines, raw, sections	195 g	1 cup	4
Watermelon, raw, balls	154 g	1 cup	9
Avocado, raw, cubes	150 g	1 cup	57
Figs, dried	149 g	1 cup	51
Jackfruit, raw	165 g	1 cup	56
Legumes			
Black-eyed peas, cooked	165 g	1 cup	74
Hummus, homemade	60 g	1/4 cup	48
Miso	17 g	1 Tbsp	22
Okara	122 g	1 cup	50
Soy sauce (tamari)	18 g	1 Tbsp	30
Soy sauce (wheat and soy shoyu, low Na)	14 g	1 Tbsp	13
Soy milk, fortified	243 g	1 cup	39
Fava beans, cooked	170 g	1 cup	105
Lentils, sprouted, raw	77 g	1 cup	81
Lima beans, cooked	170 g	1 cup	116
Pigeon peas, red gram	168 g	1 cup	128
Soybeans, sprouted, cooked	94 g	1 cup	84
Tofu, soft	120 g	2.5 x 2.75 x 1"	101
Tofu, regular (medium firm)	124 g	0.5 cup	134
Tofu, firm (with calcium sulfate and nigari)	126 g	0.5 cup	139
Veggie sausages	50 g	2 links	126
Adzuki beans, cooked	230 g	1 cup	182
Chickpeas, cooked	164 g	1 cup	190

Cowpeas, cooked	171 g	1 cup	188
Kidney beans, cooked	177	1 cup	200
Lentils, cooked	198	1 cup	152
Lupins, cooked	166 g	1 cup	183
Mung beans, cooked	202 g	1 cup	170
Refried beans, canned reduced sodium	238 g	1 cup	155
Split peas, cooked	196 g	1 cup	167
Black turtle beans, cooked	185 g	1 cup	228
Black beans, cooked	172 g	1 cup	229
Cranberry beans, cooked	177 g	1 cup	248
Edamame, cooked	155 g	1 cup	215
Great Northern beans, cooked	177 g	1 cup	221
Navy beans, cooked	182 g	1 cup	201
Pink beans, cooked	169 g	1 cup	230
Small white beans, cooked	179 g	1 cup	242
Veggie burgers or soyburgers	70 g	1 patty	204
Tempeh	166 g	1 cup	290
Tofu, firm (prepared with calcium sulfate)	126 g	0.5 cup	266
White beans, cooked	179 g	1 cup	261
Soybeans, mature, cooked	172 g		385
Soy nuts, dry roasted	93 g	1 cup	497
Grains			
Hominy, yellow	160 g	1 cup	50
Tapioca, uncooked	38 g	0.25 cup	1
Noodles, japanese, soba, cooked	114 g	1 cup	82

Barley. cooked	157	1 cup	68
Buckwheat groats, cooked	168 g	1 cup	74
Cornmeal	39 g	0.25 cup	64
Pasta, wheat, cooked	124 g	1 cup	79
Pasta, gluten-free, cooked, corn and quinoa	166 g	1 cup	98
Pasta, gluten-free, cooked, corn	140 g	1 cup	77
Sorghum grain, uncooked	48 g	0.25 cup	81
Triticale, uncooked	48 g	0.25 cup	98
Rice, white, long grain	158 g	1 cup	100
Amaranth, uncooked	48 g	0.25 cup	109
Millet, cooked	174 g	1 cup	122
Oats, uncooked	39 g	0.25 cup	122
Oat bran, cooked	219 g	1 cup	109
Pasta, gluten-free, cooked, brown rice	169 g	1 cup	134
Pasta, gluten-free, cooked, corn and rice	141 g	1 cup	102
Rice, brown, long grain	202 g	1 cup	117
Spelt, uncooked	44 g	0.25 cup	112
Wheat bran	58 g	1 cup	136
Wheat, hard, uncooked	48 g	0.25 cup	111
Wheat, sprouted	108 g	1 cup	125
Quinoa, cooked	185 g	1 cup	178
Kamut, cooked	172 g	1 cup	167
Wild rice, cooked	164 g	1 cup	195
Teff, uncooked	48 g	0.25 cup	207
Teff, cooked	252 g	1 cup	315
Nuts			

Acorns, dried	28.35 g	1 ounce	39
Almonds	28.35 g	1 ounce	44
Almond butter	16 g	1 Tbsp	20
Cashew butter	16 g	1 Tbsp	50
Chestnuts, dried, European	28.35 g	1 ounce	33
Coconut, fresh, shredded	80 g	1 cup	50
Coconut, dried, shredded	28.35 g	1 ounce	37
Coconut water	240 g	1 cup	31
Macadamia nuts	28.35 g	1 ounce	7
Coconut milk, canned	240 g	1 cup	86
Hazelnuts	28.35 g	1 ounce	63
Pecans	28.35	1 ounce	54
Pine nuts	28.35 g	1 ounce	59
Peanuts, dry roasted	28.35 g	1 ounce	82
Walnuts, English	28.35 g	1 ounce	67
Cashews	28.35 g	1 ounce	103
Pistachio nuts	28.35 g	1 ounce	102
Brazil nuts	28.35 g	1 ounce	319
Seeds			
Tahini (sesame seed butter), raw	15 g	1 Tbsp	88
Flaxseeds	28.35	1 ounce	105
Sunflower seeds	28.35 g	1 ounce	119
Chia seeds	28.35 g	1 ounce	167
Pumpkin seeds	28.35 g	1 ounce	171
Sesame seeds	28.35 g	1 ounce	159
Hempseeds (about 3 Tbsp)	28.35 g	1 ounce	264
Animal products			
Eggs	33 g	1 large	132

Cheese, brie	28.35	1 ounce	168
Cheese, gouda	28.35	1 ounce	204
Milk, 1%	245 g	1 cup	215
Milk, 3.25%	244 g	1 cup	203
Yogurt, low fat, fruit	170	6 ounces	219
Cheese, parmesan, hard	28.35	1 ounce	272
Yogurt, plain, skim milk	170	6 ounces	287
Beef, lean, cooked	85 g	3 ounces	648
Chicken breast, cooked	85 g	3 ounces	675
Crab, cooked	134 g	1 leg	730
Fish, cod	85 g	3 ounces	448
Fish, salmon	85 g	3 ounces	640
Fish, tuna, canned	85 g	3 ounces	733
Ham, cooked	85 g	3 ounces	435
Lobster, cooked	145 g	1 cup	689
Pork, cooked	85 g	3 ounces	609
Shrimp, cooked	85 g	3 ounces	565
Turkey, roasted	85 g	3 ounces	670

NOTES:

1. These figures in this table were sourced from the USDA National Nutrient Database for Standard Reference Release 28. <http://ndb.nal.usda.gov/ndb/nutrients/index>
2. The chart is set up using food groups (e.g. vegetables, fruits, legumes, etc.). Within each group, you will notice a variety of colors which represent different categories of methionine concentration (see key that precedes the chart). Within each color category, foods

appear in alphabetical order.

Selected References

Cavuoto P, Fenech MF. A review of methionine dependency and the role of methionine restriction in cancer growth control and life-span extension. *Cancer Treat Rev.* 2012 Oct;38(6):726-36.

Durando X, Thivat E, Gimbergues P, Cellarier E, Abrial C, Dib M, Tacca O, Chollet P. [Methionine dependency of cancer cells: a new therapeutic approach?]. *Bull Cancer.* 2008 Jan;95(1):69-76.

Hasek BE, Stewart LK, Henagan TM, Boudreau A, Lenard NR, Black C, Shin J, Huypens P, Malloy VL, Plaisance EP, Krajcik RA, Orentreich N, Gettys TW. Dietary methionine restriction enhances metabolic flexibility and increases uncoupled respiration in both fed and fasted states. *Am J Physiol Regul Integr Comp Physiol.* 2010 Sep;299(3):R728-39.

Orgeron ML, Stone KP, Wanders D, Cortez CC, Van NT, Gettys TW. The impact of dietary methionine restriction on biomarkers of metabolic health. *Prog Mol Biol Transl Sci.* 2014;121:351-76.

Patil YN, Dille KN, Burk DH, Cortez CC, Gettys TW. Cellular and molecular remodeling of inguinal adipose tissue mitochondria by dietary methionine restriction. *J Nutr Biochem.* 2015 Nov;26(11):1235-47.

Plaisance EP, Greenway FL, Boudreau A, Hill KL, Johnson WD, Krajcik RA, Perrone CE, Orentreich N, Cefalu WT, Gettys TW. Dietary methionine restriction increases fat oxidation in obese adults with metabolic syndrome. *J Clin Endocrinol Metab.* 2011 May;96(5):E836-40.

Tapia-Rojas C, Lindsay CB, Montecinos-Oliva C, Arrazola MS, Retamales RM, Bunout D, Hirsch S, Inestrosa NC. Is L-

methionine a trigger factor for Alzheimer's-like neurodegeneration?: Changes in A β oligomers, tau phosphorylation, synaptic proteins, Wnt signaling and behavioral impairment in wild-type mice. *Mol Neurodegener.* 2015 Nov 21;10(1):62.

Trimmer EE. Methylene tetrahydrofolate reductase: biochemical characterization and medical significance. *Curr Pharm Des.* 2013;19(14):2574-93.

Wanders D, Burk DH, Cortez CC, Van NT, Stone KP, Baker M, Mendoza T, Mynatt RL, Gettys TW. UCP1 is an essential mediator of the effects of methionine restriction on energy balance but not insulin sensitivity. *FASEB J.* 2015 Jun;29(6):2603-15.