A PHYSICIAN’S GUIDE TO THE ROLE OF NUTRITION AND DIET IN SUCCESSFUL COGNITIVE AGING

1. Introduction
Primary care physicians are often queried by older patients about the wisdom of vitamin supplementation and proper nutrition in maintaining normal intellectual function. The precise role of midlife or later-life nutrition in aging and dementia remains unclear, although individuals with reduced levels of natural antioxidants appear to experience increased age-related morbidity. The role of vitamins, minerals, dietary supplements, and herbal remedies also remains unclear (1). Physicians are often queried about the role of nutritional choices in intellectual function and aging. This segment outlines common nutritional issues where sufficient peer-reviewed data exists to make specific recommendations.

A three-step process can be used to determine a recommendation by a primary care clinician: 1) is the nutritional supplement safe at standard doses, 2) is there credible scientific evidence to suggest possible efficacy and, 3) is the supplement reasonably priced. Since nutritional supplements are not regulated by the FDA, patients cannot be sure of the product’s content, safety or efficacy.

2. Vitamin Supplementation As A Neuro-Protectant
Homocysteine is a thiol-containing amino acid produced by demethylation of methionine (2). In older persons, elevated serum levels of homocysteine are related to accelerated atherosclerosis, as well as increased risk for heart disease and stroke. The major cause of death in younger individuals with homocysteinuria produced by cystathionine β synthethase deficiency is atherosclerotic vascular disease. Elevation of serum homocysteine above 15 to 20 μmd/l predicts adverse cardiovascular outcomes and increased risk for cognitive decline with aging (3), (4), as well as increased plasma levels of β amyloid (5). Elevated homocysteine can be related to deficiencies of folic acid and B-complex vitamins. Folic acid deficiency and B-complex vitamin deficiencies are common in older individuals, including those without evidence of pernicious anemia. Low folate status as measured by red blood cell folate may be related to risk for dementia in all ethnic groups including Latinos (7). Chronic, low levels of folic acid, Vitamin B12 or B6 can produce symptoms of dementia (8), (9). Most diets that include some green, leafy vegetables, meats, and other “fortified” food staples contain sufficient folic acid and B-complex vitamins to achieve minimum daily requirement. A standard “daily” vitamin supplement for older individuals typically contains adequate folic acid and B-complex vitamins to achieve adequate
supplementation. Measurement of serum B12 and folate may be predictive of homocysteine levels. Neither evaluation will predict the onset of dementia; however, elevated homocysteine is associated with increased risk for cognitive loss in elders, cerebrovascular disease and dementia in older persons. Elevated homocysteine in a diabetic patient increases the risk for cognitive decline beyond the risk produced by diabetes (13).

Homocysteine levels (tHcy) may be linked to risk for dementia via vascular disease or other mechanisms. Supplementation of folic acid in the 0.5mgm to 5mgm range reduces tHcy by 25% and the concurrent use of vitamin B12 in the 0.5mgm range reduced tHcy by an additional 7% (10), (11). Typical, clinical supplementation includes both Folic acid and B12 to prevent unrecognized B12 deficiency (12). Supplementation of dietary niacin may also provide some protection against AD (6).

Clinicians are encouraged to discuss routine “senior” vitamin supplementation with midlife or older patients to reduce the potential risk factor associated with elevated homocysteine. Randomized controlled prospective studies have not been performed to confirm the “protective” effect of vitamin supplementation and available data does not show clear protective benefit (11), (12). A single study suggests that individuals who have suffered an acute myocardial infarction may have slightly worse outcome with post infarction supplementation of folic acid and B12. The risk-benefit and cost/potential benefit ratios would support vitamin usage in middle aged and older patients (14), (15). (Click here for additional information about homocysteine and dementia – 2513.411).

3. Antioxidants As Neuro-Protectants
Antioxidant supplementation as a cognitive protectant remains a controversial issue. Several longitudinal studies fail to confirm a relationship between antioxidant consumption and dementia risk (1), (16), (17), (18). Others studies have linked levels of natural antioxidants, such as Vitamin E, C, and beta carotene to risk reduction and reduction of inflammatory markers such as C-reactive protein (19). A wide range of food stuffs, including red wines, contain natural antioxidants which may reduce organ damage produced by excessive production of free radicals. Vitamin E is a potent antioxidant that may slow progression of Alzheimer’s disease. Rodent models of Alzheimer’s disease demonstrate reduced amyloid load with chronic antioxidant therapy (15). The therapeutic value of Vitamin E supplementation is unclear; however, this vitamin can produce toxicity when taken in large continuous doses. A standard supplementation of 300 units per day is included in many vitamins; however, some clinicians will prescribe 1,000 units of Vitamin E per day in persons at risk for Alzheimer’s disease. The beneficial effect of long-term, high-dose Vitamin E supplementation in humans remains controversial. Individuals receiving coumadin
should exercise great care and patients are recommended to discuss any Vitamin E supplement with their pharmacist to exclude drug-drug interactions. The use of other potential antioxidants, such as Gingko Biloba, is equally controversial. Insufficient data exists to recommend antioxidant therapy as a dementia prevention measure (32).

4. **Weight Control to Reduce Risk Factors for Dementia**

   Mid-life obesity and Type II diabetes are linked to dementia in later life (**CLICK HERE FOR MORE INFORMATION-2513.91**). The precise mechanism by which obesity and diabetes contribute to cognitive decline in later life remains unclear; however, obesity appears linked to the metabolic syndrome (20), (21). “Weight reduction” diets do not appear to impact risk of dementia; in fact, individuals who consume large amounts of tofu may have greater risk of cognitive decline (19), (22). Long-term dietary control with maintenance of normal body mass is probably beneficial to later life cognitive function. Prospective randomized studies comparing obese to normal individuals will not be performed and clinicians must advise middle-aged patients based on best available data. Many middle-aged caregivers of persons with dementia can be encouraged to maintain normal weight as a possible protective intervention against metabolic syndrome and increased risk of cognitive decline in their later life.

5. **The Role of Metals and Trace Elements in Dementia**

   A variety of trace elements or heavy metals have been linked to dementia or cognitive decline. Certain metals, such as lead, are neurotoxic and toxic levels in humans can produce cognitive loss. Aluminum is the metal that has received the greatest attention over time. Aluminum is found within neurofibrillary tangles and human aluminum toxicity can produce fibrillary masses within neurons. Dialysis dementia was produced by excessive amounts of aluminum in the dialysate.

   There is no conclusive evidence that links aluminum toxicity to Alzheimer’s disease. Acute or chronic exposure to many toxic substances, such as lead, can produce intellectual deficits and many metals can be found within neurofibrillary tangles. Amyloid has high affinity for certain metals, such as Fe (Iron), Al (aluminum), and Zn (zinc), which may promote the generation of reactive oxygen species (23). Aluminum is readily absorbed through the gastrointestinal tract; however, there is no evidence that individuals receiving aluminum-based antacids have suffered greater rates of intellectual decline. Anecdotal reports of improved cognitive function with chelation are not corroborated by randomized controlled studies and this potentially dangerous procedure is not recommended for individuals unless specific defined toxic levels of metals are identified. Available evidence does not support cognitive enhancement by
nutritional supplementation with vitamins and minerals beyond those routinely included in “senior vitamins”.

6. **Nutritional Programs or Dietary Supplementation to Protect Cognition**

Long-term consumption of typical “Mediterranean” diet that is rich in mono-saturated fatty acids may be protective against cognitive decline. A diet with low animal fat, but high fish and cereal consumption may be protective (33), (46). Features of the Mediterranean diet may reduce complications from the metabolic syndrome including reduction of markers of vascular inflammation such as creactive protein (CRP) (29). Trans-fatty acids are produced by the partial hydrogenation of vegetables oils that helps solidify the fat. These fats account for 2% to 3% of calories consumed in American diets, especially in “fast foods”. These artificial food substances increase vascular risk factors (34). Paradoxically, high tofu intake may be associated with increased risk for cognitive decline (22), (Table 1). Long-term consumption of diets that are high in fish content may diminish the risk for dementia (30), (31). High intake of unsaturated fatty acids in mid-life may reduce the long-term risk for Alzheimer’s disease in later life (49).

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<th>Study</th>
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<td>Omega 3 Fatty Acid</td>
<td>Inadequate Data</td>
<td>24</td>
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<tr>
<td>Meta n=12</td>
<td>Lecithin</td>
<td>Demonstrated no benefit</td>
<td>25</td>
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<tr>
<td>Meta n=11</td>
<td>AcetylL Carnitine</td>
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There is incomplete scientific evidence to prove a preventive or therapeutic effect of nutritional supplementation for older persons. Prospective randomized controlled studies have not been performed to examine the protective effect of these dietary supplements over decades. Many other herbal substances and nutritional supplements have been touted as possessing anti-aging, antioxidant or anti-Alzheimer benefits; however, these claims are not substantiated by randomized controlled studies.
Clinicians must distinguish a genuine preventive benefit from a placebo effect. Many psychotropic medication trials produce significant placebo effects in persons not receiving the active molecule. Many patients provide personal attestations that a specific combination of vitamins and dietary measures will substantially improve their intellectual vitality or sense of cognitive ability. Nationally advertised “memory enhancing supplements” are not shown to improve cognition or reverse cognitive loss through large scaled, randomized controlled studies. The active constituents for these products are often available in cheap, generic forms.

As long as the dietary programs do not produce other health problems and the supplements are not excessively expensive, the clinician can encourage the patient to continue those interventions which are perceived as beneficial. The secondary benefits to the patients beyond a possible placebo effect may include enhanced awareness of health maintenance and stress reduction produced by a sense of control and self-mastery.

7. Consumption of Alcohol as a Risk Factor for Dementia
A consumption of alcohol as an antioxidant or cognitive protectant is controversial and contradictory. Frenchmen who consume wine in moderation may have diminished risk of cognitive decline; however, these individuals may have other lifestyle features that are not captured by available research (48). Individuals with excessive alcohol consumption may sustain a wide range of health problems; however, moderate drinking is associated with slightly diminished risk for cognitive decline (CLICK HERE FOR MORE INFORMATION – 2513.2). Clinicians are not advised to encourage patients to commence drinking in later life as a health intervention. Heavy drinkers in all age groups should be encouraged to abstain or reduce alcohol consumption. Social drinkers can be advised that moderate drinking is acceptable within certain limits. Wine is probably the preferable beverage for these individuals. For more information on alcohol consumption in the elderly, please see DETA 2513.21.

Conclusion and Recommendation
Primary care doctors should examine three issues in crafting dietary recommendations for older patients: 1) safety, 2) evidence for efficacy, and 3) financial tolerability. A balanced diet with one or two servings of fish per week and basic vitamin supplementation is probably beneficial to all middle-aged and older individuals (32), (33), (34), (46), (47), (50). Normal weight in middle age should be maintained by proper diet and regular exercise. Folic acid and B-complex vitamin supplementation may be helpful to reduce risk factors associated with elevated homocysteine levels (28) although caution may be required in persons who have suffered an acute myocardial infarction (35). Moderate
alcohol consumption is acceptable (48). Patient handouts on weight, alcohol, and diet are available (Click here for handouts – 2513.25, 2513.45, 2513.45-1).

**Recommendations to Primary Care Clinicians**

1. Educate patients that nutritional behaviors in midlife may impact cognitive function in later life.
2. Encourage heart healthy diets with additional servings of fish and less red meat.
3. Advise patients to take a standard, daily vitamin with B-complex and folic acid.
4. Monitor patient’s weight, avoid central obesity, and provide nutritional advice.
5. Advise patients who drink alcohol to consume in moderation. Red wine is probably the best form of alcohol.
6. Advise patients to avoid extreme diets and maintain an active life with exercise.
References