Medical Foods and Diets Part 2: A Summary of the Impact on Cognition Dr. Lauren M. Young, Geriatric Fellow, Washington University at St. Louis and Dr. David Carr, Medical Director, Parc Provence

Over the last several years, a variety of dietary supplements, herbal products and medical foods have become popular as memory boosters or even tauted as products that slow the progression of Alzheimer's disease (AD). With approximately 5.4 million people living with Alzheimer's disease and few prescription medications available (of which have modest effectiveness of slowing the progression of Alzheimer's disease), the interest and use of medical foods and natural products are on the rise. Many of these can be found in household foods in your pantry or refrigerator.

Observational studies have shown diets such as the Mediterranean diet, which is rich in omega-3 polyunsaturated fatty acids (PUFA) as well as other antioxidants, may protect people from cognitive decline and dementia. The main omega-3 fatty acid used in the brain is docosahexaneoic acid (DHA). Fatty acids may be protective of dementia and cognitive decline by decreasing the cerebrovascular effects of inflammation, thrombosis and plaque formation through its effects on brain development and membrane function or may have a direct effect on the accumulation of beta-amyloid, a hallmark of Alzheimer's disease. In a 2012 Cochrane database system review of randomized controlled trials in patients 60 years and older free of dementia over a period of six to forty months, no benefit was seen with PUFA supplementation in cognitively healthy adults. Longer studies may be required to identify benefits associated with omega-3 supplementation. Omega-3 fatty acids can be found as an over-the-counter supplement, in enriched foods such as margarines or peanut butter, and in whole foods like salmon, herring, or white tuna, walnuts, flaxseed, and olive oil.

Coenzyme Q10 (CoQ10), also called ubiquinone when in its fully oxidized state, is a naturally occurring antioxidant in the body. It inhibits the initiation and the propagation of oxidation and can regenerate other antioxidants such as vitamin E. Oxidative stress can lead to cell death in the brain. Idebenone, a synthetic form of CoQ10, improved memory in rat studies but failed to slow cognitive decline in Alzheimer's disease in human studies as seen in a 2003 double blind, randomized, placebo controlled study of synthetic CoQ10. Dietary sources of CoQ10 include fish, meat, particularly in beef, pork, chicken heart, and chicken liver and to lesser extent dairy products. Other good sources of CoQ10 are vegetable oil and avocado. Most fruits are poor sources of CoQ10.

Antioxidants, such as vitamin E (alpha-tocopherol), vitamin C, and alpha-lipoic acid supplements were tested in a July 2012 double blind placebo controlled study published in the Archives of Neurology and were associated with accelerated decline in Mini-Mental status exam scores over a sixteen-week period. The antioxidants, including CoQ10, did not lower the levels of biomarkers in the cerebral spinal fluid (CSF) associated with Alzheimer's disease. These results are very concerning and highlight the difficulty of mimicking nature with the use of supplements.

There are many different forms of vitamin E. The second most common form of vitamin E is alphatocopherol, the most biologically active form, and is found in most supplements. The gamma type is the most common in the North American diet. Vitamin E has antioxidant properties that neutralize free radicals, which are potentially damaging to brain cells. Common foods rich in vitamin E are sunflower seeds, paprika, red chili powder, nuts, apricots, green olives, spinach and taro root. Although safe when consumed as a part of a regular diet (the daily recommended amount is 22 IU daily), multiple studies have shown that high-dose supplementation (400 IU or more) of vitamin E have been associated with increased risk of prostate cancer, cardiovascular death and an overall higher risk of dying. Most studies have not shown vitamin E to benefit cognition.

Polyphenols are chemicals produced by plants, which are protective against the sun's radiation. There are many different types of polyphenols, of which flavonoids are among the most resilient. Recent studies have shown polyphenols to have neuroprotective properties, potentially through anti-

inflammatory and anti-amyloid mechanisms. In addition to having protective properties associated with polyphenols, it is an antioxidant. Flavonoid-rich foods include berries, tree fruits, beans, particularly black and kidney beans and leafy greens. Other good sources include Brussels sprouts and asparagus. Resveratrol is a polyphenol found in grapes, peanuts and berries. It has been shown to reduce beta-amyloid in mice but has yet to show similar results among humans. More studies about its bioavailability, biotransformation and dietary synergy, along with a compilation of potential negative effects are needed.

A Spanish study using non-alcoholic red wine showed an increase of antioxidant enzymes, thought to be due to the polyphenolic composition of the wine. Moreover, a French study found that drinking 4-ounces of wine a day decreased the risk of Alzheimer's disease by 75%. However, any amount of alcohol can cause impaired cognition and should be avoided in individuals already suffering from cognitive impairment. Additionally, chronic overuse or abuse of alcohol may lead to multiple nutritional deficiencies, namely thiamine, which can cause a condition called Wernicke's encephalopathy.