Unintentional Weight Loss in Long Term Care Residents with Alzheimer’s Disease and Weight Response with the Use of Docosahexaenoic Acid (DHA)/Eicosapentaenoic Acid (EPA) and Bioflavonoids: A Case Series

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INTRODUCTION
Cachexia/dehydration may be the immediate cause of death in the end stage of dementia in as many as 35% of nursing home residents. Cachexia is associated with suppressed appetite, food intake and body weight while proinflammatory cytokines are increased. Proinflammatory cytokines directly result in feeding suppression and lower intake of nutrients and cachexia is nearly always accompanied by anorexia. IL-1beta and tumor necrosis factor alpha (TNFα) act on the glucose-sensitive neurons in the satiety and hunger sites in the hypothalamus. An association between high levels of circulating TNFα and unexplained weight loss in AD has been shown. Serum TNFα has been shown to be lower in mild-moderate Alzheimer’s disease (AD) compared to severe AD. The levels of TNFα, IL-1beta, IL-6, and IL-10 were elevated in the sera of patients with dementia. A minority of studies have shown no significant differences between AD subjects and controls in the mean serum levels of TNFα and other cytokines. Brain synthesis of cytokines has been shown in peripheral models of cancer, peripheral inflammation, and during peripheral cytokine administration and strikingly increased CSF levels of TNFα have been demonstrated in AD.

RESULTS
Table 1 summarizes the intervention and patient characteristics. Each resident was given 570 mg DHA and 870 mg EPA plus 225 mg of bioflavonoid per day. A proprietary formulation of bioflavonoids, OPC-3® was used. OPC-3 consists of an isotonic formulation of well studied flavonoids derived from extracts of bilberries, citrus fruit, French maritime pine bark, and grape seeds. The usual interventions were continued. Weights were followed over the 6 month period following the intervention.

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METHODS
Two residents in one facility, cared for by the investigator, in a moderate stage of dementia with 10% or greater weight loss over the previous six months despite the usual interventions at the facility (the addition of fortified foods, 2 Cal Supplement® bid, offering snack tid, and 1 on 1 assistance with meals in a small dining room setting) were chosen. A TSH, CBC, complete metabolic profile, urinalysis, physical examination, medication review and Cornell Scale for Depression in Dementia (CDD) were performed during the 6 month period. Both residents were on an acetycholinesterase inhibitor (ACHE) and had a 10 day washout prior to intervention.

After informed consent was obtained from the family of each resident, 570 mg DHA and 870 mg EPA plus 225 mg of bioflavonoid per day were administered. A proprietary formulation of bioflavonoids, OPC-3® was used. OPC-3 consists of an isotonic formulation of well studied flavonoids derived from extracts of bilberries, citrus fruit, French maritime pine bark, red wine (resveratrol), and grape seeds. The usual interventions were continued. Weights were followed over the 6 month period following the intervention.

DISCUSSION/CONCLUSION
The importance of ingesting foods and supplements high in antioxidants is becoming more valued as oxidative stress from reactive oxygen species is being uncovered as a common pathologic mechanism to inflammatory states by the induction of proinflammatory cytokines.

In recent years, the constituents in fruits and vegetables predominantly responsible for their health benefits have been identified as bioflavonoids which are anti-inflammatory. Reductions of plasma oxidative stress status by 10.1% and plasma C-reactive protein by 52.1% have been demonstrated with OPC-3 use. Adequate dietary intake of omega-3 polyunsaturated fatty acids increases tissue concentrations of EPA and DHA that reduce proinflammatory cytokine production and downregulate inflammation.

Although this was an uncontrolled intervention, resident 1 showed clinically meaningful weight gain through the entire 6 month observation period and resident 2 showed stabilization of weight loss within 30 days of the intervention with continued weight maintenance throughout the 6 month observation period. Resident 1 also showed weight loss when the intervention was discontinued and clinically meaningful weight gain when restarted.

CONCLUSION
Given the evidence in the literature supporting a mechanism for these nutritional interventions with our observed improvement in weight and appetite, further study in a controlled setting is warranted.

REFERENCES
1. Dinarello CA. Interleukin 1 and interleukin 18 as mediators of inflammation and the aging process. Am J Clin Nutr 2006;83(2): 447S–455S.