Selected Abstracts From the "Wellness For Persons With Dementia" Symposium

Organizer and Chair: Nancy B. Emerson Lombardo, Ph.D., Boston University, School of Medicine, Boston MA, USA

The Promise and Methodological Challenges of Nutritional Interventions Applied to Persons with Dementia **Akira Ueki, M.D., Ph.D. Jichi Medical School, Saitam, Japan**

Preliminary results from the Japanese diet trial, which builds on previous epidemiological and animal studies, suggest that nutritional interventions hold great promise for slowing progression or lowering risk of AD. Gene-environmental interactions affecting AD pertinent to nutrition will be outlined. However there are challenging methodological issues applying nutritional interventions to persons with dementia. Caregivers are absolutely necessary for dietary recording and assessment, cooking, and correcting abnormal eating behavior of the patients. Positive effects of a dietary intervention on cognitive function do not necessarily establish that the dietary factors are effective per se. Being part of the treatment group, effects of the diet on emotion, and unmeasured factors, can all affect clinical results.

Nutrition and Prevention of Alzheimer Disease **Bruno Vellas, M.D., Ph.D. Centre de Gariatrie, Toulouse, France**

Epidemiology studies, including both regional incidence and the analysis of specific risk factors for Alzheimer's disease, indicate that substantial prevention of the disease is a practical possibility. Epidemiology has identified a rich diversity of specific prevention strategies relating to nutrition, dietary supplements, lifestyle, food and environmental toxins, and in some cases medication, many of which have a capacity to reduce Alzheimer's risk significantly. Omega 3, fish, gingko, vitamins are some examples with some large long-term double blind randomized trials now in process. The interaction of these risk factors with brain biology is increasingly understood.

Nutrition and Alzheimer's Disease: What the Evidence Shows **Martha Clare Morris, Ph.D. Rush University Medical Center, Chicago, Illinois, USA** The field of diet and Alzheimer's disease is in its infancy. Even so, there is promising evidence that a number of dietary factors may be related to the development of Alzheimer's disease. Dr. Morris's talk summarizes the evidence thus far for several areas of study including: 1) antioxidants, fruits & vegetables, 2) fish and the omega-3 fatty acids, 3) the B-vitamins, and 4) fat composition and trace metals. For each set of dietary components, she presents evidence from laboratory and animal models that shed light on possible biologic mechanisms, as well as the available evidence from epidemiologic studies.

Differences in Dietary Intake and Cognitive Function and the Memory Preservation Diet **Nancy B. Emerson Lombardo, Ph.D. and Antonio Martin M.D. Ph.D. Boston University School of Medicine, Bedford, MA, USA**

Alzheimer's disease (AD) is an age-related and irreversible brain disorder that occurs gradually and results in memory loss, behavior and personality changes, and a decline in thinking abilities. These losses are related to the changes that occur ion the connections between nerve cells in the brain and the eventual death of many of these cells. Evidence suggests a convergence between nutrition-related protective/risk factors for AD

and those identified for chronic diseases such as stroke, diabetes and vascular diseases thought to elevate risk for AD. Martin's previous studies in identifying nutritional factors implicated in cognitive decline associated with aging demonstrated that vitamins E and C and omega 3 poly-unsaturated fatty acids (PUFAs) may be very important in the removal of amyloid, protecting brain cells and modulating inflammatory processes relevant to onset of AD and its progress. We have also shown that these nutrients are important in brain cell membrane repair and function, microgliosis, inflammation, impaired blood flow, and oxidative damage. The evidence-based Memory Preservation Diet^{TM} ©2006 (Emerson Lombardo, Martin, Volicer et al.) aims to improve the nutritional status of the elderly and preserve their cognitive functions.

Nutritional Status Predicts Progression to Dementia and Rapid Cognitive Decline; Consequences of Malnutrition in Persons with Alzheimer's Disease **Bruno Vellas, M.D., Ph.D. Centre de Gariatrie, Toulouse, France**

It is well known that nutritional problems are very often associated with dementia of the Alzheimer's type (DAT). Some studies have demonstrated that weight loss can precede the diagnosis by several years. One of several studies that will be discussed in this session demonstrated that nutritional status, as measured by the Mini Nutritional Assessment Instrument (MNA) of 157 persons with early stage probable Alzheimer's disease with CDR of 0.5, is strongly associated with patients' progress in a year's time to full blown dementia with a CDR of 1.0. In this study, multivariate analyses including other baseline measures such as MMSE, weight, BMI, ADL and IADL found that only the ADAS-cog was also associated with the progression of dementia. Dr. Vellas and colleagues developed the MNA to measure nutrition status. The MNA is used widely throughout Europe and elsewhere in studies of nutrition and aging; this instrument will be shared with session participants.

The Japanese diet trial for patients with Alzheimer's disease: Proper nutrition can slow progression of AD **Ueki A, Otsuka M, Sato T, Sauvaget C*. Jichi Medical School, Saitama, Japan *National Institute of Public Health, Wako, Japan**

Many epidemiological studies have shown that a high consumption of vegetables, fruits, and fish prevents Alzheimer's disease (AD), and that excess intakes of total calorie, total fat, saturated fat, and/or sweets are risk factors. However, the efficacy of a dietary approach for the treatment of clinically prominent dementia has not yet been elucidated. Therapies using single antioxidant vitamin or multiple vitamins cocktail for cognitive decline have proven unpromising. Recent studies have shown that a dietary pattern is more important than individual foods or nutrients for maintenance of human health. Traditional Japanese diet, consisting of vegetables, and fish, some fruit and very little sugar, is one of the ideal dietary patterns. We examined the efficacy of a dietary intervention on the course of cognitive decline in AD patients by recommending proper nutrition through a traditional Japanese diet. The intervention group consisted of 64 participants including 43 AD patients with MMSE 10–23, and 21 patients with mild cognitive impairment (MCI) with MMSE of 24–27 who received dietary recommendations to follow a traditional Japanese diet. Of these, 20 AD patients and 7 MCI patients had good adherence to the dietary recommendations; MCI patients had the worst adherence. The control group consisted of 69 AD patients and 22 MCI patients who did not receive any dietary recommendations. All AD patients in both groups took donepezil; none took lipid-lowering drugs. The basic nutritional intervention consisted of 4 major points: (1) taking green-yellow vegetables at least twice a day and fruits at least once a day, (2) at least one fish dish a day, (3) avoiding too much sweets, and (4) reducing total calorie intake. Adherence to the 4 major goals was monitored by 4-day nutritional records, and adherence to each dietary recommendation was scored 0 or 1 (maximum score: 4) by a dietitian at each visit to the clinic every 6 months. Serum triglyceride level, fasting glucose level, and insulin secretion were also used for estimating eating behavior. Cognitive function was assessed by Mini-Mental State Examination (MMSE), and the scores were compared between the intervention and control groups. The observation period was 30 months.

There was a significant effect on the time course of MMSE scores between AD patients in the intervention and control groups. The difference started from the 12th month and became more significant at the 30th month. The intervention group preserved or even showed 2 points higher scores of MMSE than the scores measured at baseline. In the "intent to treat" analysis, this effect was noted in all subgroups of research subjects in terms of baseline MMSE scores; i.e., MCI patients (MMSE 24–27), mild cases of AD (MMSE 20–23), and severe cases of AD (MMSE 10–19). However, subjects who were found not to have adhered to the

dietary recommendations, experienced average cognitive decline rates similar to those subjects in the control group. Conclusion: Though return to "normal" cognitive function could not be expected, a dietary intervention consisting of the traditional Japanese diet is useful for slowing or maintaining cognitive function of AD patients for at least 30 months. Adherence to the dietary recommendation was most important, and the percent calories from fat and consumption of vegetables most correlated with cognitive function at 30 months. Serum triglyceride level was a good marker for monitoring excessive intake of sugar and sweet foods. The nutritional approach will open up a new therapeutic tool, which may act synergistically with medical treatment and physical exercise to maintain quality of life of demented patients. Standardization of intervention methodology for different ethnicities and cross-ethnic studies with a larger scale are needed for confirmation of present results

Alzheimer's Disease: Working Now Towards Future Prevention **Bruno Vellas, M.D., Ph.D. Centre de Gariatrie, Toulouse, France**

In the next 20 years, we will probably be able to prevent neurodegenerative diseases like Alzheimer's disease, just as we have seen in the past 20 years knowledge developed about prevention of cardio-vascular disease. We have already identified many risk factors: obesity, high blood pressure, hypercholesterolemia, diabetes, and fat. Conversely, we also have identified protective measures that focus on nutrition, fish, vitamins, physical and intellectual activity. This session presents two 5-year studies and methodologies: the GuidAge Study, a randomized, placebo controlled trial of Gingko biloba EGB 761 in 2800 elderly persons with memory complaints, and the Omega 3 Study, a five-year double-blind randomized (omega3 vs. placebo) trial in 4000 elderly persons.

Eating Your Way to Healthy Brain Aging **James Joseph, Ph.D. Jean Mayer USDA Human Nutrition Center, Tufts University, Boston, MA, USA**

It is prudent to try to establish methods that may be utilized today to alter the course of aging. Research from our laboratory suggests that eating a variety of vegetables and fruits high in antioxidants, especially berries, which are very nutrient intense foods, can decrease the enhanced vulnerability to oxidative stress (OS) that occurs in aging. These reductions in OS are expressed as improvements in behavior. There appear to be additional multiple mechanisms, including en-

hancement of neuronal communication that involves increased signaling, neurogenesis, and anti-inflammatory action involved in the beneficial effects observed from these nutrient intense foods.

Eating Your Way to Healthy Brain Aging: Apples and nutriceuticals **Thomas E. Shea, Ph.D., Center for Cellular Neurobiology and Neurodegeneration Research, University of MassachusettsLowell, Lowell, Massachusetts, USA**

A growing body of evidence indicates that consumption of diets rich in fruits and vegetables can delay the onset and/or progression of neurodegeneration, including that which accompanies Alzheimer's disease. We discuss recent studies demonstrating that apple juice represents one excellent dietary source and how it works, an overlooked mechanism by which S-adenosyl methionine (SAMe) maximizes use of our endogenous antioxidants, and how combinatorial supplements provide maximal neuroprotection.

Curry Spice and Healthy Fats: an Ounce of Prevention from AD? **Greg M. Cole, Ph.D. Greater Los Angeles Veteran's Administration Medical Center, Sepulveda, California, USA**

Epidemiology suggests that non-steroidal anti-inflammatory drugs (Cox inhibitors like naproxen) and antioxidants like vitamin E may reduce risk for Alzheimer's and possibly other diseases, but clinical trials have raised serious questions about their safety and efficacy. Alternatives include the omega-3 fatty acid, DHA, and the curry spice component, curcumin, which has been used as an antioxidant food preservative and anti-inflammatory drug in India. We find curcumin not only effectively controls inflammation, oxidative damage and amyloid toxicity in transgenic mouse models, it also directly binds amyloid peptides limiting their aggregation *in vitro* and reduces amyloid accumulation *in vivo*. Curcumin also promotes microglial amyloid clearance, and fights cancer. The omega 3 fatty acid DHA also has a favorable epidemiology and reduces oxidative damage, neurodegeneration and amyloid in vitro and in animal models where it also reduces cognitive deficits. Because of its great safety profile (safe enough for infant formula) and proven efficacy with cardiovascular disease, DHA is an outstanding candidate for prevention trials. Curcumin and DHA have compelling safety profiles making them candidates for primary prevention and treatment trials, respectively. Join us as we share the positive lab results regarding curcumin and DHA efficacy.

What the Beagles Got: Healthy Brain Aging with an Antioxidant Diet and Behavioral Enrichment **Elizabeth Head, Ph.D. Alzheimer's Disease Research Center, Irvine, California, USA**

Aged canines (beagles), experience progressive cognitive decline and accumulate brain pathology. We provided aged beagles with: a diet of vitamins E, C, fruits, vegetables and two mitochondrial co-factors (lipoic acid and carnitine), and/or behavioral en- richment (social interaction, physical exercise and cognitive enrichment). Over time, both treatments improved aged beagles' memory and maintained their learning ability. The combination of both treatments was more efficacious than either treatment alone. The antioxidant diet reduced amyloid-β plaques in the brain. An antioxidant enriched diet and behavioral enrichments may improve and maintain cognition, as well as promote successful brain aging.