Healthful Living May Slow Alzheimer's Disease

BY BRUCE K. DIXON

Chicago Bureau

CHICAGO — A concerted effort to take better care of the brain with more healthful behaviors is likely to reduce the future incidence of Alzheimer's disease and may even slow disease progression in those who already have the disease, Dr. Nancy Emerson Lombardo said.

Cardiovascular health and glucose metabolism contribute to brain health, and the rise in obesity and other chronic illnesses has a direct impact on brain health, Dr. Lombardo said at a conference on dementia sponsored by the Alzheimer's Association.

Dr. Lombardo of the Boston University Medical Center has developed a lifestyle program trademarked as "Be Well," based on research into the effects of nutrition on brain health.

"Be Well" dovetails with the Alzheimer's Association's "Maintain Your Brain" campaign, as well as the Centers for Disease Control and Prevention's brain health planning effort that was recently funded by Congress (for more information, visit www.alz.org).

Dr. Lombardo explains that healthy brain tissue is better able to withstand the ravages of age, genetic vulnerabilities, environmental stresses, accidents, toxins, and disease. Healthy lifestyles "help us enhance and strengthen neurons, dendrites, and other body and brain cells."

In addition, said Dr. Lombardo, obesitv increases inflammation which, in turn, increases oxidative stress, possibly resulting in diabetes, heart disease, stroke, arthritis, osteoporosis, some cancers, and Alzheimer's disease (AD). "What harms the heart also harms the brain. Obesity, high blood pressure, diabetes, and heart problems all increase the risk for dementia. The future of all our obese young people is really scary," she remarked.

5 years, the prevalence of the disease would be halved, said Dr. Lombardo, who placed nutritional deficiency and excessive calories at the top of the list of societal factors threatening brain health in the Unit-

Dr. Lombardo's Memory Preservation Diet reflects a convergence of independent research findings that nutrition can protect

Other factors that adversely affect brain and body health include increases in stress, social disconnections, insufficient sleep, and environmental toxins.

against AD, as well as diabetes and vascular diseases, which themselves are thought to elevate risk for AD.

"The first human placebocontrolled rand o m i z e d clinical trial to be reported using marine-derived omega-3

fatty acids with persons with AD both confirmed the indications of the epidemiological and lab studies but also [suggested] the limitations of a single nutrient" for affecting the course of AD, she said (Arch. Neurol. 2006;63:1402-8).

In this Swedish trial of 174 AD patients, consumption of a daily intake of 1.7 grams of docosahexaenoic acid (DHA) and 0.6 grams of eicosapentaenoic acid (EPA) significantly slowed disease progression, but only in those with very mild dementia (Mini-Mental State Examination [MMSE] scores above 27).

The only AD diet study to date, carried out in Japan, reported that a daily regimen of fish along with additional fruits and vegetables and consumption of fewer sweets slowed progression of AD (J. Nutr. Health Aging 2004;8:432).

This controlled clinical trial with 56 subjects compared standard medical care with a daily diet of 80-90 g of fish, two servings of green vegetables, one serving of fruit, 1.3 L of water, and reduced sweets. All participants were on cholinesterase inhibitors.

Those in the diet treatment group had stable MMSE scores, sustained over a 30month period, but scores declined by 6 points during the same time in control participants.

When and how we eat is also important, said Dr. Lombardo, stressing that it's important to have breakfast and to eat sitting at a table, preferably with other people.

Other societal factors that adversely affect brain and body health include lack of exercise, increases in stress, insufficient sleep, social disconnections, and environmental toxins, Dr. Lombardo said.

BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information. Daytrana™ (methylphenidate transdermal system)

Daytrana** (methylophenidate transdermal system)

CII Rx Only

INDICATION AND USAGE

Attention Delicit Hyperactivity Disorder (ADHD): Daytrana** (methylophenidate transdermal system) is indicated for the treatment of Attention Delicit Hyperactivity Disorder (ADHD): Daytrana** (a waitable in 10, 15, 20, and 30 mg dosing strengths. The efficacy of Daytrana** was established in the controlled clinical trials in children with ADHD.

Special Diagnostic Considerations: Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosts requires the use not only of medical but of special psychological, educational, and social erosuces. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the child and not solely on the presence of the required number of DSM+VTR* characteristics.

Need for Comprehensive Treatment Program: Daytrana** is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome. Drug treatment may not be indicated for all children with this syndrome. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders; including psychosis, Appropriate educational placement is essential and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of theronicity and severity of the child's symptoms.

Long-Term Use: The effectiveness of Daytrana** for long-term use, i.e., for more than 7 weeks, has not been systematically evaluated in controlled trials. The physician who elects to use Daytrana** for extended periods should periodically re-evaluate the long-term usefulness of Daytrana** for long-term use, i.e., for more than 7 weeks, has not been systematically evaluated in controlled trials. The physician w

symptoms.

**Hypersensitivity to Methylphenidate: Daytrana™ is contraindicated in patients known to be hypersensitive to methylphenidate or other components of the product (polyester/ethylene vinyl acetate laminate film backing, acrylic adhesive, silicone adhesive, and fluorophymer-coated polyester).

Glaucoma: Daytrana™** is contraindicated in patients with glaucoma.**

Tiess: Daytrana™ is contraindicated in patients with motor tics or with a family history or diagnosis of Tourette's syndrome

Serious Cardiovascular Events Sudden Death and Pre-existing Structural Cardiac Abnormalities or Other Serious Heart Problems

dren and Adolescents
den death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with
ctural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an
eased risk of sudden death, stimulant products generally should not be used in children or adolescents with known
us structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac
elems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug.

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and eaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD.

bugh the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having

us structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, cornorary artery disease, or other

us cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs.

retension and Other Cardiovascular Conditions

ulant medications cause a modest increase in average blood pressure (about 2-4 mmHg) and average heart rate (about 3
my (see ADVERSE REACTIONS), and individuals may have larger increases. While the mean changes alone would not be

cled to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pres
Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in

d pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or

ricular arrhythmia.

diarrhea, or vomiting.

Patients who develop contact sensitization to Daytrana™ and require oral treatment with methylphenidate should be initiated on oral medication under close medical supervision. It is possible that some patients sensitized to methylphenidate should be placed and methylphenidate by exposure to Daytrana™ may not be able to take methylphenidate in any form. A study designed to provoke skin sensitization revealed a signal for Daytrana™ to be an irritant and also a contact sensitizer. This study involved an induction phase consisting of continuous exposure to the same skin site for 3 weeks, followed by a 2 week rest period, and then challenge/rechallenge. Under conditions of the study, Daytrana™ was more irritatina both the placebo patch control and the negative control (saline). Of 133 subjects who participated in the challenge phase of the sensitization study, at least 18 (13.5%) were confirmed to have been sensitization shaped based on the results of the challenge and/or rechallenge phases of the study.

Using Daytrana™ as prescribed, alternating application sites on the hip, no cases of contact sensitization were reported. However, since patients were not specifically assessed for sensitization in the clinical effectiveness studies, it is unknown what the true incidence of sensitization is when Daytrana™ is used as directed.

Psychiatric Adverse Events

Pre-Existing Psychosis

Administration of stimulants may exacerbate symptoms of hebavior distance in the contact sensitization of stimulants may exacerbate symptoms of hebavior distance.

nusis:
If stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a preic disorder.

existing psychotic disorder. Bipplant Inlines:
Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder, such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, such readment greater and the strength of the strength of the strength of the strength of the strength psychotic or manic Symptoms.
Emergence of New Psychotic or manic Symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate. In a pooled analysis of multiple short term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients with events out of 3.482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Augression

Swill revens our or proce exposed in children and adolescents with ADHD, and has been reported in clinical the postmarketing experience of some medications indicated for the treatment of ADHD. Although there is no systicence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be done to find the appearance of or worsening of aggressive behavior or hostility, and the appearance of or worsening of aggressive behavior or hostility, and the appearance of or worsening of aggressive behavior or hostility or hostility or appearance or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of their methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of the properties of th

Drug Dependence
Daytrana™ should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behavior. Frank psycholic episodes can occur, especially with parenteral abuse. Careful supervision is required during withdrawal from abusive use, since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that

iothing may rub it. Ina™ should be applied 2 hours before the desired effect. Daytrana™ should be removed approximately 9 hours after it is d. although the effects from the patch will last for several more hours.

Daytrana™ should be applied 2 nours before the eiserice elect. Daytrana™ should be included by the effects from the patch will last for several more hours.

The parent or caregiver should be encouraged to use the administration chart included with each carton of Daytrana™ to monitor application and removal time, and method of disposal.

If there is an unacceptable duration of appetite loss or insomnia in the evening, taking the patch off earlier may be attempted before decreasing the patch size.

Skin redness or itching is common with Daytrana™, and small bumps on the skin may also occur in some patients. If any swelling or blistering occurs the patch should not be worn and the patient should be seen by the prescriber.

Drug Interactions: Daytrana™ should not be used in patients being treated (currently or within the preceding two weeks) with monoamine oxidase inhibitors (see CORTRANIDICATIONS-Monoamine Oxidase inhibitors), Because of a possible effect on blood pressure, Daytrana™ should be used cautiously with pressor agents.

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If lifestyle can delay the onset of AD by

Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. Human pharmacologic studies have shown that methylphenidate may inhibit the metabolism of coumarin anticoagulan anticonvulsants (e.g., phenobarbital, phenytoin, primidone), and some tricyclic drugs (e.g., imipramine, clomipramir desipramine) and selective serotonin reuptake inhibitors. Downward dose adjustments of these drugs may be required wh given concomitantly with methylphenidate. It may be necessary to adjust the dosage and monitor plasma drug concentratio (or, in the case of coumarin, cagulation times), when initiating or discontinuing methylphenidate. Serious adverse events have been reported in concomitant use of methylphenidate with clonidine, although no causality for t combination has been established. The safety of using methylphenidate in combination with clonidine or other centrally acti-

Continuous Breeding study. The study was conducted at doses up to 160 mg/kg/day.

Pregnancy

Tregnancy

Category C: Animal reproduction studies with transdermal methylphenidate have not been performed. In a study in which oral methylphenidate was given to pregnant rabbits during the period of organogenesis at doses up to 200 mg/kg/day no teratogenic effects were seen, although an increase in the incidence of a variation, dilation of the lateral ventricles, was seen at 200 mg/kg/day, this dose also produced matemal bioxicily. A previously conducted study in rabbits showed teratogenic effects were seen although as light delay in the period of organogenesis at doses up to 100 mg/kg/day, no teratogenic effects were seen although a slight delay in fetal skeletal or of organogenesis at doses up to 100 mg/kg/day, no teratogenic effects were seen although a slight delay in fetal skeletal ossification was seen at doses of 60 mg/kg/day and above; these doses caused some maternal toxicity.

In a study in which oral methylphenidate was given to rats throughout pregnancy and lactation at doses up to 60 mg/kg/day, and above; these doses caused some maternal toxicity.

Adequate and well-controlled studies in pregnant women have not been conducted. Daytrana™ should be used during pregnancy only if the potential risk in pregnant women have not been conducted. Daytrana™ should be used during menancy and proven the pregnancy only if the potential risk administered to a nursing woman.

Pediatric Use: The safety and efficacy of Daytrana™ in children under 6 years old have not been established. Long-term effects of methylphenidate in children have not been well established (see MarkNINS).

In a study conducted in young rats, methylphenidate is excreted in human milk, eaution should be exercised if Daytrana™ is children under 6 years old have not been established. Long-term fetest of methylphenidate in children have not been well established (see MarkNINS).

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