

## **Harvard Clinical Nutrition Research Center**

**Start Date: 1994**

**Status: Ongoing**

**Funding Agency: NIDDK**

**Website: [www.hms.harvard.edu/nutrition](http://www.hms.harvard.edu/nutrition)**

### **Organization and Goals**

The Harvard Clinical Nutrition Research Center's (HCNRC) goals are to:

- Promote research in basic areas relevant to clinical nutritional science;
- Promote the study of clinical nutrition within the Harvard Medical School (HMS), Harvard School of Public Health (HSPH) and Massachusetts Institute of Technology (M.I.T.) communities;
- Promote interactions among scientists exploring diverse fields within clinical nutrition;
- Attract basic investigators to the study of nutrition; and
- Promote an environment and mechanism to develop new investigators focused on clinical nutrition research.

### **Core Laboratories**

**Administrative Core:** W. Allan Walker, M.D., Director and Steve Grinspoon, M.D., Associate Professor of Medicine, Director of the Nutrition Metabolism Unit at Massachusetts General Hospital and Walter Willett, M.D., Dr. P.H., Fredrick John Stare Professor of Epidemiology and Nutrition, Chairman of Nutrition, Department of Nutrition, Harvard School of Public Health are Associate Directors

#### *External Advisory Group Members*

Dennis Bier, M.D., Professor of Pediatrics, Director of the USDA, Children's Nutrition Research Center, Baylor School of Medicine, Houston, TX (Chairman)

Curberto Garza, M.D., Ph.D., Professor and Chairman (Emeritus), Graduate Division of Nutrition, Cornell University, Ithaca, New York

Irwin Rosenberg, M.D., Professor of Medicine and Nutrition (Emeritus), Former Director of USDA Human Nutrition Research Center on Aging, Tufts New England Medical Center, Boston, MA

Richard Rivlin, M.D., Professor of Medicine, Weill Medical College of Cornell University, Director, Anne Fisher Nutrition Center, Director of CNRU, NCI, New York, NY

Virginia Stallings, M.D., Professor of Pediatrics, University of Pennsylvania, Chief, Nutrition Section, Division GI and Nutrition Section, Division GI and Nutrition, Children's Hospital of Philadelphia, PA

Steven Zeisel, M.D., Ph.D., Kenan Distinguished University Professor, Chairman, Department of Nutrition, University of North Carolina School of Medicine and Public Health, Director, CNRU at UNC, Chapel Hill, NC

**Biostatistics:** David Schoenfeld, M.D., Director

**Genomic and Proteomics:** Frederick Ausubel, Ph.D., Director

**Morphology/Cell Biology/Tissue Culture:** David Newburg, Ph.D.

**Mass Spectrometry:** Tom Jaksic, M.D., Ph.D., Director

### **Pilot and Feasibility Studies**

**Prospective Studies of Diet and Eye Disease in Women.** William G. Christen, Ph.D., Associate Professor, Harvard Medical School, Associate Epidemiologist, Division of Preventative Medicine, Brigham and Women's Hospital. The major aim of this proposal is to conduct analyses of dietary predictors of age-related maculopathy (ARM) and cataract in women. ARM and cataract are two leading causes of visual impairment in older Americans. The analyses proposed will use detailed nutritional and behavioral data collected in the Women's Health Study (WHS), a randomized trial in the primary prevention of CVD and cancer among 39,876 apparently healthy female health professionals. A total of 39,345 women (98.7 percent) returned a 131-item validated semi quantitative food-frequency questionnaire at baseline in 1993. In this initial investigation of dietary determinants of ARM and cataract in our study populations, the intent is to take an alternative approach to the study of single nutrients or foods, considering more global aspects of diet. Analyses will be conducted to determine whether total glycemic load is associated with risks of cataract in women and whether dietary pattern, the evaluation of how foods and nutrients are consumed in combination, is associated with risks of ARM and cataract in women. The principal investigator qualifies for the Pilot and Feasibility Project as an established scientist not currently focused on nutrition per se who wishes to initiate studies of potentially modifiable nutritional determinants of ARM and cataract in women. This work will form the basis of future grant proposals.

**Fast Food Feeding in Youth.** Cara Ebbeling, Ph.D., Instructor in Pediatrics, Harvard Medical School, Research Associate, Department of Medicine, Division of Endocrinology, Children's Hospital. The adverse affects of a "toxic food environment" is likely contributing to the youth obesity epidemic. Over the last few decades, increased consumption and sales of unhealthful fast food has paralleled the rising prevalence of obesity. Enormous serving sizes and rapid meal delivery are among the variables that may contribute to excess energy intake from fast food. The primary aim of the proposed pilot study is to assess the affects of fast food meals, varying in serving size and rate of delivery, on energy intake in adolescents (N=24). Using a three-period crossover design, we will evaluate three acute feeding conditions. Under Condition A, the total amount of food in a large fast food meal will be delivered on a single tray at Time 0 (start of meal). Under Condition B, the same fast food meal will be equally divided among 4 separate trays, with all trays delivered at Time 0. Under Condition C, the meal again will be equally divided among 4 separate trays, but the trays will be delivered at 15-minute time intervals (Time 0, 15 minutes, 30 minutes, and 45 minutes). We hypothesize that energy intake will be higher under Condition A than C, and intermediate under Condition B. Secondary outcomes include eating rate (assessed by videotape) and energy intake during the day of the visit and the day following the visit (determined by dietary recall). We will compare primary and secondary outcomes across feeding conditions using analysis of variance (ANOVA) and controlling for covariates (i.e., body mass index, energy intake during the day prior to feeding, physical activity and energy expenditure, dietary restraint, hunger, and relative meal size). This line of scientific inquiry has far-reaching significance from clinical and public health perspectives given that millions of adolescents eat fast food on a weekly basis. Moreover, the proposed study will provide necessary pilot data for NIH grant applications. Future studies will be designed to elucidate the physiological and psychological mechanisms that interact with external variables

(e.g., serving size and rate of meal delivery) to mediate the effects of fast food on eating behaviors, energy intake, weight gain, and obesity in youth.

**Effects of Leptin Administration on Inflammatory Markers.** Steven Grinspoon, M.D., Associate Professor, HMS. School, Department of Medicine, Neuroendocrine Unit, MGH. Leptin, an adipocyte-derived cytokine, is a marker of nutritional status that has been recently implicated in the proinflammatory immune response. Previous studies have associated leptin with increased blood pressure, heart rate, and markers of inflammation such as C-reactive protein, independent of BMI, suggesting that increased leptin levels associated with obesity also contribute to increased cardiovascular risk in this population. The goal of the present study is to investigate the markers of inflammation in response to physiologic leptin administration in healthy young women over a four-day fast. We will examine the relationship between leptin and traditional markers of inflammation and cardiovascular risk, specifically CRP, TNF-alpha, IL-1, IL-2, IL-6, adiponectin, white blood cell and platelet counts, PAI-1, tPA, fibrinogen, angiotensin II, and a lipid panel (cholesterol, triglycerides, HDL, LDL). We hypothesize that physiologic leptin administration will prevent fasting-induced immuno-suppression and may increase markers of inflammation. Potential mechanisms include an effect of leptin to increase lipolysis or indirect effects on other adipocytokines, including IL-6, which may subsequently trigger the inflammatory cascade.

**Identification of and Characterization of Glycoconjugate Receptor of Probiotics.** Nanda Nanthakumar, Ph.D., Instructor in Pediatrics, Harvard Medical School, Assistant Biologist, Developmental Gastroenterology Laboratory, Pediatric Service, MGH. The intestinal epithelium provides a barrier that prevents the luminal gut microflora in the breaching of the host. In contrast, *Salmonella typhimurium* and *Listeria monocytogenes* are gram-negative and gram-positive enteric pathogen, respectively, evolved strategies to breach this epithelial barrier by invading the intestinal epithelium and initiating inflammatory response at the site leading to comprehensive mucosal immune response. The resident microflora of the GI tract plays an important role in inhibiting colonization of enteric pathogen. A few species of gram-positive *Lactobacilli* prevent infection of these enteric pathogens and are able to prevent initial inflammatory response of the intestinal epithelium, such as IL-8 induction. These commensal microflora are defined as probiotics because when they are consumed in sufficient quantities, they are able to prevent infection, an inflammatory response leading to diarrhea by undefined mechanism(s). Colonization of both commensal and pathogens requires initial adhesion to the gut lumen. The glycoproteins and glycolipids expressed on the apical surface of the epithelium provide docking sites for these bacteria. When specific glycoconjugates were masked by lectins specific for blood group B and H (O) antigen, *Salmonella* infection was prevented to the same extent as probiotics *Lactobacilli*. The data suggest that specific *Lactobacillus* compete for the same glycoconjugates receptors on the surface of the intestinal epithelium that are necessary for infection of enteric pathogen and prevent inflammatory response. Therefore, the aim of this study is to identify these glycoconjugate receptors expressed on the lumen of the gut that enables the probiotics *Lactobacilli* to colonize and prevent infection by enteric pathogens and attenuates epithelial inflammatory response. As part of this research application, I plan to characterize and identify the receptor and elucidate the signaling pathway by which probiotics *Lactobacilli* prevents *Salmonella* and *Listeria* infection and modulate the mucosal immune responses in the human intestinal epithelium.

### **Funding Derived from Previous Pilot and Feasibility Studies and Core Facilities**

**The Role of Protective Nutrients in Necrotizing Enterocolitis.** Nanthakumar, N. Funding: R-21 application (under review – submitted 10/01/05), R21 DK075710.

**Ontogeny of the Human Intestinal Barrier and NEC.** Walker, WA. Funding: RO1 DK70260-11, 05/05-04/10.

**Effects of Adrenal and Gonadal Hormone Replacement in Young Women with Anorexia Nervosa.** Gordon, CM. Funding: RO1 HD043869, 04/04 – 03/08.

**Androgen Effects on HIV-infected Women.** Grinspoon, S. Funding: RO1 DK54167, 09/03 – 03/08.

**Glucogan Biosynthesis and Metabolism.** Habener, J. Funding: RO1 DK30834, 04/05 – 03/10.

**Effects of Anorexia on Peak Bone Mass.** Klibanski, A. Funding: DK062249, 07/03 – 03/08.

**Photobiology of Vitamin D.** Holick, M. Funding: AR36963, 04/02 – 03/07.

**Lipids, Inflammation and Insulin Receptors.** Hotamisligi, H. Funding: DK064360, 06/04 – 05/08.

**Protein Metabolism in Critically Ill Surgical Neonates.** Jaksic, T. Funding: HD41531, 04/03 – 03/07.

**Community Expansion – Fantastic Kids.** Lenders, C. Funding: New Balance Award, Nutrition and Fitness for Life Program, 10/04 –09/07, \$1,000,000.

### **Scientific Advances/Accomplishments**

The HCNRC's productivity is understood by specific advances in nutrition-relevant studies made by HCNRC investigators and P/F recipients using NCRU resources. These advances have been accomplished by collaboration among HCNRC investigators with support of the HCNRC core laboratories.

**Multivitamin Supplements and HIV Disease Progression and Mortality.** (N Engl Med 2004; 351:23-32) Dr. Wafai Fawzi, an investigator in the HCNRC, has published his results using multivitamin supplements in newborn infants of HIV positive mothers to reduce morbidity and mortality. His results show that multivitamins delay the progression of HIV disease and represent a low cost means of delaying the use of antiretroviral therapy in HIV-infected women. In these studies, Dr. Fawzi used the Biostatistics Program of the HCNRC.

**Arginine, Citrulline, and Nitric Oxide Metabolism in End-State Renal Disease Patients.** (J Clin Invest 2000; 105:1219-1225) Dr. Leticia Castillo, an investigator in the HCNRC, has made a series of observations on amino acid metabolism and end-stage renal disease (ESRD). These studies on intensive care patients have helped to define the pathophysiologic basis for de novo arginine synthesis and for elevated NO synthesis and its pathophysiologic basis in ESRD. Dr. Castillo has extensively used the Mass Spectrometry Core, formerly under the direction of Dr.

Vernon Young at M.I.T. She has recently relocated to the USDA Clinical Nutrition Center at Baylor School of Medicine.

**Molecular Basis for Type II Diabetes.** (Science 2004; 306:457-461) Dr. Gokhan Hotamisligil, an original Investigator in the HCNRC, has recently published a series of observations which identify the molecular basis of Type II diabetes as it related to obesity. He and his team have shown that obesity causes endoplasmic reticulum (ER) stress in adipocytes from these patients. These findings demonstrate that ER stress is critical to peripheral insulin resistance in Type II diabetes at the molecular, cellular, and organ levels. These observations may lead to important new therapies for Type II diabetes associated with overweight and obesity. Dr. Hotamisligil and his team extensively used the Cell Biology Core of the HCNRC.

**Inflammatory Markers and Risk of Developing Type II Diabetes in Women.** (Diabetes 2004; 53:693-700) Dr. Joann Manson, as the newly established Director of Women's Studies at the Brigham and Women's Hospital and a new Investigator in the HCNRC, has recently published important predictive markers for women developing Type II diabetes. Inflammatory markers (TNF- $\alpha$ , IL-6, CRP, etc.) are important predictors in overweight women going onto develop Type II diabetes. These data were obtained from the Nurses Health Study and may represent the basis for using dietary supplements to reduce inflammation, e.g., omega-3-fatty acids, etc. with this group of women. She used the Biostatistics Program of the HCNRC.

**Obesity as an Important Risk Factor in Cardiovascular Disease in Adolescence.** (Circulation 2005; 111:1970-1977) Dr. Elizabeth Goodman, a new Investigator in the HCNRC, has recently returned to Boston from the Children's Hospital in Cincinnati. She now studies health policy in adolescent patients with regard to obesity and its risk for developing cardiovascular disease in later adulthood. This recent observation underscores the importance of preventing obesity in pediatrics before adolescence to decrease the long term risk of chronic disease. Dr. Goodman uses the Biostatistics Program of the HCNRC.

### **Specific Accomplishments**

**Women's Health.** The Division of Preventative Medicine at Brigham and Women's Hospital is headed by Dr. Joann Manson. In 2002, Dr. Manson became the Co-Director of the Connors Center for Women's Health and Gender Biology at the Brigham and Women's Hospital. In 2003, she was the first recipient of the newly established Elizabeth F. Brigham Endowed Professorship in Women's Health at HMS. After participating in our annual symposium several years ago on "Nutrition and Women's Health", Dr. Manson joined the Center as an Investigator. As a result of this move, we have attracted additional Investigators (Drs. Gillman, Christen, and Buring) and Associate Investigators (Drs. Tavares and Oken) into the Center. Dr. Christen received a pilot feasibility award from the center last year. These additions to the Center have allowed us to establish a new program of investigators in biomedical base (Section D).

In 1995, Dr. Stanley Lewis (Chief, Clinical Cardiology) and Isil Yasar, Manager of Cardiology, asked Dr. Francine Welty to be the Director of the Women's Cardiovascular Health Program at Deaconess Hospital and to utilize her expertise in preventative cardiology in women, including the use of hormone replacement therapy and lipid lowering drugs. She has published on gender differences in coronary angioplasty using the very large Deaconess Hospital database. In addition, she has published invited reviews on gender differences in coronary heart disease and use of nutrition to treat hyperlipidemia. When Dr. Welty working with Dr. Walker successfully applied

for a Nutrition Academic Award from NIDDK (KO7 DK029474) as part of the Division of Nutrition (DON), she was introduced to the HCNRC. As a result of joining the Center as an Associate Investigator, she successfully competed for a P/F grant which has led to RO1 funding and Investigator status in the HCNRC renewal. When the Deaconess-Beth Israel merger occurred, Dr. Welty became the Director of Cardiovascular Care for Women at the West Campus. She also consults on patients in the Cardiovascular Health and Lipid Center at the Beth Israel-Deaconess Medical Center and focuses on nutrition management of hyperlipidemia. This important new addition to the HCNRC priority programs adds to our strong theme in lipid metabolism and prevention of cardiac disease in the Biomedical Research Base (Section D).

### **Obesity Programs.**

#### **Center for the Study of Nutrition and Medicine at Beth Israel-Deaconess Health**

**Center (BIDMC).** Now in its eighth year of operation, the Center for the Study of Nutrition and Medicine (CSNM) has continued to advance the interdisciplinary field of nutritional medicine. The Center has supported the Nutrition Screening Initiative, which focuses on nutritional screening in the elderly, as well as the Massachusetts Medical Society's Nutrition Committee and the U.S. Department of Health and Human Services' effort to establish healthy weights for adult Americans. The Center has also made major advances in the methodology needed to achieve these goals using sound principals of diet and health foods for special dietary purpose and exercise. The Center is conducting several clinical trials, four of which are ongoing from the previous year. Two of these continuing programs are long-term outcome studies funded by the NIH after the completion of highly successful feasibility studies. The "Women's Intervention with Nutrition Study" is a collaborative effort conducted at the American Health Foundation, Harbor-UCLA Medical Center, the University of Minnesota, and CSNM, as well as twenty other clinical sites across the country. Two thousand women with stage I or II node negative breast adenocarcinoma will be enrolled throughout the United States. These women will be randomized into one of two groups: one will reduce dietary fat intake to  $\leq 16$  percent of total calories and the other will maintain a regular dietary pattern with  $\geq 25$  percent total calories from dietary fat. The hypothesis is that decreased dietary fat will reduce cancer recurrence. CSNM is acting as both a clinical site and as a Regional Coordinating Center. The CSNM also supports the Boston Research Eating Disorders Group (BRED), a collaborative group established for research, education and clinical referrals. This collaborative effort with the Department of Psychiatry will extend to our Harvard Continuing Medical Education Program in the treatment of obesity and eating disorders. Nutritional medicine has dramatically improved existing assessment devices for diet readiness, food aptitude and binge behavior directed at getting the right treatment to the right patients, thus minimizing dropout and relapse. In keeping with the priority of technology transfer, the Center's efforts are communicated both in professional journals and lay publications, including NEJM Health News. As a result of the HCRNC enrichment programs, Drs. Blackburn and Kaplan (MGH) have combined forces to begin a large clinical trial on the role of calcium addition and reduction in sucrose in orange juice in the treatment of overweight patients. In addition, Dr. Jin Rong Zhou, a junior faculty member in the Center for the Study of Nutrition and Medicine, obtained a P/F award and has subsequently received RO1 funding in the same topic. Drs. George Blackburn and Bruce Bistrian from the Nutrition Programs at BIDMC provide an added commitment to the HCNRC application to further broaden the nutrition enrichment base. These established clinical nutrition investigators will add to our Biomedical Research Base and utilize the General Clinical Research Center (GCRC) at BIDMC and the Mass Spectrometry Core at the HCNRC.

**Obesity Center at MGH.** Dr. Kaplan is the Director of the newly-formed Massachusetts General Hospital Weight Center. The goal of this combined research and clinical Center is to identify means of stratifying obesity into distinct clinical syndromes. Clinical programs of the Center include comprehensive evaluation and multidisciplinary care for adults and children with obesity. Most patients seen in the Center participate in one or more components of the Center's clinical research activities. The main focus of clinical research during the initial establishment of the Center is the design and development of an Obesity Registry Database and a Tissue, DNA, Cell and Serum Repository. Once established, these clinical resources will be used to support epidemiological, genetic and clinical studies of obesity and its treatment. Drs. Kaplan and Hoppin have joined the HCNRC in the new application. Dr. Alison Hoppin, a pediatric nutritionist, has worked with Dr. Kaplan to determine nutritional factors *in utero* that predict childhood obesity. She has had a KO8 award (KO8 DK02754) and Center P/F funding to study this problem in animal models and plans to apply for an R-21 award to complete the observations. Drs. Kaplan and Hoppin have joined the Center as part of the new application. Dr. Kaplan has supervised Dr. Copeland in a previous P/F application. Dr. Kaplan has also been added to the Executive Committee to represent obesity programs within the Harvard Medical community.

**The OWL Program at CH.** The Optimal Weight for Life Program (OWL) at Children's Hospital, Boston is a multi-disciplinary care clinic dedicated to the evaluation of treatment of children who are overweight. Dr. David Ludwig leads the team composed of physicians, nurse practitioners, dietitians and a psychologist, specializing in endocrinology, gastroenterology and behavioral medicine. Their goal is to provide state-of-the-art care for overweight children, to develop innovative treatments for pediatric obesity through clinical research and to promote public awareness and prevention effects. Since its inception in June 1997, they have treated over 500 children from infancy through adolescence and have sponsored several major clinical research protocols. These protocols on the GCRC at CH will also utilize the Mass Spectrometry Core. Dr. Ebbeling, an Assistant Professor of Pediatrics at HMS is a P/F awardee and Associate Investigator in the HCNRC. She works closely with Dr. Ludwig. Dr. Ludwig joins the HCNRC renewal as a new Investigator.

**Inflammatory Bowel Disease.** Two major studies have been funded by the Harvard CNRC in the last two years which related to IBD. These include a P/F study by Haining Shi, DMV, Ph.D. on the influence of helminth infections on the chronic inflammation of IBD. Dr. Shi has evidence that helminth infection can modify the TH1, TH2 and TH3 response in the lamina propria of the intestine, thereby modifying chronic inflammatory response to pathogens (a predominant TH1 response) to a self-limited acute inflammation. In addition, Dr. Tor Savidge, the Director of the Morphology/Cell Culture/Immunology Core for the HCNRC has evidence that glial cells in the gut are involved in the inflammatory response of IBD. Both these projects have been recently funded by the Crohn's Colitis Foundation of America (January, 2001). In addition, the Harvard CNRU has collaborated for the last four years with the Center for the Study of Inflammatory Bowel Disease (CSIBD) funded as a gastrointestinal center by NIDDK to provide an introductory lecture and laboratory course in molecular biology to fellows and junior faculty in the Centers (see Education Activities/Accomplishments).

**AIDS.** The Harvard CNRC has begun to address the nutritional needs of patients with HIV as a major theme in its 2000–2001 goals. We have funded an important P/F study and glucose metabolism and insulin resistance as the basis for the lipodystrophy associated with this problem. This seminal study has led to RO1 support for the next five years. This study, in addition to

studies of nutritional needs of HIV infected infants of HIV positive mothers, have been major commitments by the Center. We also plan a postgraduate research symposium on this topic within the next two years. We have also expanded our nutrition based postgraduate training to educate M.D.s in clinical research in this area.

**Program on Early Determinants of Adult Health.** Dr. Matt Gillman, a medicine-pediatric nutritional epidemiologist, who is a member of the Preventative Medicine Division of the Brigham and Women's Hospital and an Investigator in the Department of Nutrition at the HSPH, has joined the Center as an Investigator. Dr. Gillman and his junior faculty study the role of intrauterine nutrition in programming newborns who may develop chronic nutrition related diseases (Type II diabetes, obesity, cardiovascular disease, etc.) in later adulthood. Dr. Gillman and his junior faculty (Drs. Oken and Tavaras) have joined the Center after participating in a symposium on pediatric obesity. They plan to apply for P/F funding and will use the Mass Spectrometry Core and Biostatistics Program. Several medical students interested in nutrition have taken summer fellowships sponsored by the DON with Dr. Gillman and his associates. Ms. Jenny Stillwagon, a junior HMS student, has been awarded a predoctoral fellowship to continue studies with Drs. Oken and Gillman.

**International AIDS Program at HSPH.** Dr. Wafai Fawzi is an Associate Professor of Nutrition at HSPH and an Investigator in a NIH supported study of protective nutrient effects in the prevention of AIDS in offspring of HIV positive mothers in Tanzania. Preliminary results of the study have recently been published in the New England Journal of Medicine. Dr. Fawzi was attracted to the Center after an interaction with Dr. Walker through a Fogarty International Training Grant application that they shared which funded medical doctors to train at Harvard from Tanzania and China. He works closely with Dr. Duggan at CH on this project.

**Division of Nutrition.** In 1996, the Faculty Council at HMS established a DON. The DON is charged with organizing the nutritional community at HMS and in its major teaching hospitals (MGH, Brigham & Women's, Beth Israel Deaconess, and Children's Hospital) to provide teaching and nutrition at the undergraduate medical school level and at the post graduate level. In addition, it has the responsibility for promoting basic nutrition and clinical research and postgraduate education. Dr. Walker is the Director of the DON and Dr. George Blackburn is its Associate Director. He has stepped down from the Division Chief of Pediatric GI and Nutrition to spend more time addressing nutrition issues. The DON works closely with the Harvard CNRU and the Department of Nutrition at HSPH. This association has helped broaden the research base of Harvard CNRC and generate many novel P/F applications. The DON is also committed to medical school and postgraduate education. It has recently received a Bristol Myers Unrestricted Research Grant to expand the PF Program and provide additional funds for postgraduate education.

**Division of Complementary and Alternative Medicine at HMS.** Dr. David Eisenberg, at the Beth Israel Deaconess Medical Center, is the new Director of this division. He works closely with the Harvard CNRC and DON in undergraduate teaching and clinical research projects. As a result of the investigators and core facilities in the Harvard CNRC, Dr. Eisenberg will apply for a Complementary and Alternative Medicine Center grant from NIH next year. Dr. Walker is on the new division's executive committee. Members of both divisions are eligible to apply for pilot feasibility funding. A joint project on alternative medicine/nutrition treatment of aged patients will be funded by a private foundation.



## **Educational Activities/Accomplishments**

**HMS Nutrition Curriculum Committee.** The DON and HCNRC have established a subcommittee of the HMS Curriculum Committee. This committee comprised of educators, nutritionists and representatives of all four years of Harvard Medical School have critiqued the four year curriculum and have begun to add nutrition lectures, cases and electives to help educate medical students. This year this subcommittee has reassessed the entire four year medical school curriculum to include practical nutrition in courses during all four years. Two pilot programs on clinical rotations have included the history of nutrition, as well as nutrition and physical exams, and these have been very popular with students. The DON has also funded a summer research program for first year students to have summer experiences in various aspects of nutrition. We have also expanded our website for students.

**Nutrition Academic Award (NAA).** The major thrust of the Clinical Nutrition Research Center at Harvard has been undergraduate medical education and postgraduate nutrition symposia and courses for M.D.s, dietitians, other healthcare providers and the public. Drs. Walker (PI) and Welty (Co-PI) have successfully competed for one of the twenty-one Nutrition Academic Awards (NAA) from NIH (K07 DK02974-01) to develop a curriculum in nutrition for Harvard medical students. This award allows for funds to expand the HMS website for access by medical students throughout the US. A generic website with a recommended four year nutrition curriculum has been posted. We have a New England NAA yearly retreat to share teaching programs in nutrition for medical students.

**Cardiovascular Health.** Recognizing the importance of nutrition in preventative medicine, the HMS Department of Preventive Medicine, since its establishment in 1991, has emphasized nutrition in its educational mission. Nutrition programs are presented primarily to medical students through an elective course offering, to the public through our evening nutrition course, and to scientists through a postdoctoral fellowship program in Preventive Medicine.

**Harvard Medical School Nutrition Course.** This is a one semester course given by the Department of Preventive Medicine that addresses the relationship of dietary habits to major diseases that afflict Western industrialized countries, i.e. cardiovascular diseases, primarily coronary heart disease, strokes, and hypertension, as well as cancer, diabetes, obesity, anorexia and bulimia. The course is taken by students in all four years, but because of the scheduling, primarily by first and second year students. The course is elective and enrollment has been 42 to 77 students per year over the past 7 years since the Department was created. In the academic year 1993–1994, the course became required for all medical students according to an action by the Curriculum Committee of HMS, and it has been taught in both the fall and spring semesters. Drs. Walker, Lo, Willett and Duggan are active teachers in that course. The DON at HMS is actively identifying preceptors in various hospitals for this course. Dr. Welty has also established a nutrition OSKI for senior students.

**Course in Nutrition and Health for the Public.** A class in heart healthy nutrition is given four times per year in the evenings for the public. Individuals and spouses are encouraged to enroll and emphasis is on diets which reduce blood lipids, cholesterol, and foster nutritionally prudent dietary habits. The course is taught by dietitians with participation of cardiologists (Drs. Welty and Lo) and internists (Drs. Grinspoon and Gulick) and includes a didactic session, answering questions of the attendees, and a cooking demonstration with a meal served and recipes provided. This class is given for two hours weekly for 6 weeks and has been growing in popularity. Two

programs lined to the HCNRC for this purpose are: 1) the NEMC Food Study Program and 2) the Harvard Business School Food Policy Committee.

**Nutrition Education of Patients.** The Harvard-MGH Cardiovascular Health Center under the direction of Dr. Richard Pasternack has a strong nutritional component with counseling and nutrition instruction for all individuals participating in this program which is the major clinical activity of the Department of Preventive Medicine, HMS. One activity of this Center is to approach patients at the MGH, who enter for heart attacks or suspected coronary artery disease, with information and counseling regarding dietary risk factors and ways to alter their eating habits accordingly. Nurses on the hospital floors are instructed in such Phase I cardiac rehabilitation dietary practices, and the physician staff, hopefully, will also recognize the benefits of dietary modification to avoid further coronary artery disease. This is a time when patients can be most readily motivated to improve their eating habits.

**A Weekly Lipid Clinic at the MGH and CH.** The Lipid Clinic sees patients with various serum lipid disorders or coronary heart disease and uses dietary modification of fat intake as the mainstay of its cholesterol and triglyceride reduction program as well as for weight control. Drs. Tod Gulick (MGH) and Ellis Neufeld (CH) participate in this program.

**Preventive Medicine Newsletter.** Because of the interest of the staff of the Cardiovascular Health Center in the potential of omega 3 fatty acids of marine origin to prevent atherosclerosis, we publish a quarterly 6 to 8 page newsletter, "Omega 3 News," for general public circulation to inform interested individuals in the current status of research on omega 3 fatty acids in nutrition. This responsibility has now been assumed by the Newsletter from the International Society for the Study of Fatty Acids and Lipids (ISSFAL). The food and fishing industries support and subscribe to this newsletter but so do many investigators in academic and industrial settings. Subscriptions in the fourth year of this quarterly publications number some 2500. The newsletter has a distinguished Editorial Board with members from the United States, Canada, and Europe representing both academia and fishing interests.

**Pediatric Nutrition Lay Education.** The Combined Program in Pediatric Gastroenterology and Nutrition at Harvard has a quarterly newsletter which it distributes to 70,000 plus readers which covers topics in nutrition for pediatric patients (food-borne illness, vitamins, obesity, etc.). In addition, Harvard Publications and McGraw Hill Publishers have asked Dr. Walker and the DON to provide two books for parents regarding nutrition. "Eat, Drink and Be Healthy for Kids" and "Nutrition and Pregnancy: Impact on Newborn and Childhood Health," written with help from a medical writer, will provide patients with insight into these nutritional issues.

**Lay Public Newsletter.** The Harvard Health Letter is distributed to 20,000 plus lay readers. Under the direction of Dr. Bruce Bistrian, an Investigator in our program, it provides timely articles on healthy diets and on inappropriate dietary habits.

**Website.** In 2002, the HCNRC revised a website ([www.hms.harvard.edu/nutrition](http://www.hms.harvard.edu/nutrition)). As part of this site, we have provided information on healthy diet for the public to access. We have also allowed access through this site to other sites specifically geared for public information, including an obesity information site and cancer and nutrition information websites at the NIH. We also plan to coordinate efforts with the DON at HMS and Department of Nutrition at HSPH to provide additional information for cancer patients, patients with post-myocardial infarction, and patients in weight reduction programs at MGH and CH. These include referral information

for nutrition preventative programs in the Boston area. These efforts have resulted in an additional link to a newly established website in the Department of Nutrition at the Harvard School of Public Health developed by Dr. Lillian Cheng for the lay public to update them on the latest information in dietary supplements and functional foods ([www.hsph.harvard.edu/prc/news.html](http://www.hsph.harvard.edu/prc/news.html)). In addition we have linked our education information on the Harvard CNRU website and the Harvard DON website to an education website for HMS students as an additional resource for their nutrition resource.

**Boston Nutrition Seminars.** The Harvard Clinical Nutrition Research Center and the Boston Obesity Clinical Nutrition Research Centers jointly sponsor a monthly seminar at the M.I.T. Faculty Club. Basic and clinical research scientists from the greater Boston area and throughout the United States and Europe are invited to present. If a Visiting Scientist from outside of Boston comes, he or she is encouraged to meet individually with members of the Center with a mutual research interest. These seminars and the discussions have led to collaborative projects within the Center. For example, Dr. Rudolph Leibel of Columbia reviewed the genetic basis for obesity. Dr. Jonathan Gitlin of Washington University of St. Louis reviewed intrauterine nutrition and cognitive function.

**Annual Nutrition Symposium at HMS.** Each year beginning in 1996, the HCNRC in conjunction with the DON at HMS and the Department of Nutrition at HSPH jointly sponsor a nutrition symposium. The funding for this program comes from industry, the American Digestive Health Foundation and conference grants from the NIH. Speakers from throughout the United States who are experts on the topic are asked to review their work. Academic nutritionists and scientists from industry attend and participate in extensive discussion. These symposia have catalyzed industry-sponsored research programs and collaborations among investigators. The symposium for last year was entitled “How Do We Deal With the Obesity Epidemic? Perspective from Industry Government and Academia” (2003) and “Pediatric Obesity: Prevention and Identification” (2004). These symposia will be published as supplements in AJCN or JN each year. This year’s symposium “Metabolic Syndrome and the Prevention of Cancer” will be published in September 2006 and will be on our website.

**Longwood Medical Area Nutrition Conference.** This group is comprised of the four Nutrition Support Services in the Longwood Medical area. It includes The Children's Hospital (coordinator of the conference), the Brigham and Women's Hospital, the New England Deaconess Hospital and the Beth Israel Hospital, now the BIDMC. Conferences are held bi-monthly. In 1997, the NSS at MGH was included. The conference focuses on case presentations; two cases are presented at each meeting. This forum provides an opportunity to exchange both clinical and research expertise as well as to teach fellows, students and inexperienced clinicians in the practical aspects of nutrition support.

**Combined Nutrition Conference—The Children's Hospital.** Seminars are held 2-4 times per month and involve the Clinical Nutrition Service staff and others interested in nutrition (oncology, intensive care, pulmonary, etc.). Speakers and topics are chosen by a representative of each service and include both research and applied nutrition subjects

**Didactic Nutrition Sessions.** The Clinical Nutrition Service at CH and MGH actively participates in the nutrition training of the medical, nursing and dietetic staff at our institution. Regularly scheduled training includes a housestaff core lecture series; lectures on the nursing in-service program; joint program in neonatology nutrition lectures; and grand rounds, morbidity

and mortality rounds and clinical pathology conferences. As well, the CNS takes an active role in the daily bedside teaching of the medical staff around the practical, applied aspects of nutrition as it relates to direct patient care. Comparable didactic sessions are held on the NSS at BIDMC and MGH for adult patients.

**Postgraduate Course for Dieticians and Nutritionists: Harvard Medical School Advances in Hyperalimentation.** This course, which is administered by Dr. George L. Blackburn, is held annually at the New England Deaconess Hospital under the auspices of the DON at HMS. Various members of The Children's Hospital Nutrition Support Service have participated in this three-day course. Involvement generally includes didactic lectures, case presentations and/or roundtable participation. In this application, Dr. Blackburn joins the HCNRC and anticipates core interaction with Dr. Blackburn and his group. Drs. Willett, Duggan, Walker and Lo are active participants in this course. This course is web cast on the DON website.

**Industry/NIH-supported Programs.** The DON at HMS has resubmitted a five year R-25 application to NCI to support a teaching program in Nutrition and Cancer for Harvard medical students, postgraduates and for public information access. The public information component will provide website access, brochures, and lectures to lay audiences for updated nutritional recommendations for prevention and to supplement treatment of cancer patients. The Dannon Foundation has supported a campaign to provide information to the public on healthy diets, and the Gerber's Food Foundation has supported a campaign on healthy diets for children. These efforts will continue in the next funding period and are published in an AJCN supplement.

**Postgraduate Education at HMS.** As DON and HCNRC have expanded their influence at HMS, more medical doctors are planning formal postgraduate education experiences in nutritional sciences or a postgraduate degree (MS or DSc) in nutrition at the Harvard School of Public Health. Accordingly, we now have two training grants for medical doctors to obtain clinical and basic research experience in nutrition. Dr. Steve Grinspoon has recently successfully competed for T-32 (T32 HD052961) through NICHD. As part of the DON, Dr. Walter Willett had ten years of T-32 (T32 DK07703) support for the Department of Nutrition at Harvard School of Public Health from NIDDK.

### **Benefits and Interactions Resulting from the Existence of the CNRU**

Beyond the scientific achievements embodied by the specific advances noted above and the publications of Center investigators, the Center has facilitated progress in the field more broadly on a national basis through a number of its activities. These include extending the scope of the Molecular Biology Lecture and Laboratory Course to include investigators in other NIH-supported centers (Center for the Study of Inflammatory Bowel Disease and Reproductive Biology Center at MGH), the Boston Obesity Nutrition Research Center (BONRC) and to other CNRU's throughout the United States. Since this expansion began in the second year of the Center's existence, 25 scientists outside the HCNRC have taken the course.

The Harvard CNRU has been a catalyst for the establishment of a DON at HMS. The DON now works closely with members of the Department of Nutrition at HSPH to provide medical school and graduate school teaching programs in nutrition and a postgraduate yearly national symposium for academics and industrial scientists. This interaction has also resulted in the addition of new programs, e.g., women's health initiatives, obesity, and foodborne infection, to the Center's educational progress.

In addition, all NIH supported centers in Boston (CNRU, ONRC, two Diabetes Centers, and two Digestive Disease Centers) have met to identify ways in which core facilities, educational programs and information services to the public can be shared or jointly expanded. This recent event will be a major benefit to all participating centers in the future. We have also worked closely with the five NIH-funded GCRC's in Boston to facilitate P/F funding for patient related research projects. We are now using the CRC at Children's Hospital to study children in clinical nutrition studies begun with adult patients at other facilities. This Clinical Nutrition Research Center at Children's has been invaluable in facilitating research projects which recognize the need to study pediatric patients along with adults. As a result of these collaborations two major grants have been funded this year.