Study to Focus on Improving Cardiovascular Health in African Americans

Dr. Mike Lefevre, Director of the Pennington Center’s lipoprotein laboratory, will soon begin studying the link between healthy diet, genetic factors, and biological mechanisms in African Americans to combat cardiovascular disease (CVD).

Reduction in CVD through dietary change offers considerable potential for a beneficial impact on public health, according to Lefevre, who is also Chief of the Pennington Center’s Division of Functional Foods Research and Professor in the Division of Nutrition of Chronic Disease.

Lefevre and several collaborators at the Pennington Center recently received a four-year, $9.5 million research grant to conduct the study. The grant was awarded by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

“It’s an ambitious study, but one we believe we’re well suited for,” said Lefevre, who noted that LSU’s Pennington Center is one of only five funding recipients selected nationwide. The others are Tulane University, the University of Minnesota, Johns Hopkins University, and the University of Maryland.

“We will try to identify factors—both genetic and non-genetic—that predict how well one responds to a heart-healthy diet,” Lefevre noted. “Diet is the first line of treatment for cardiovascular disease patients. A prudent diet can lower blood pressure to the same extent as many medications. You can effectively lower your cholesterol by 10% through diet.”

Dr. Lefevre said he and his team “will be recruiting for two and a half to three years to solicit participants for this study,” with a goal of bringing in 400 individuals, ages 18 to 45. The study will examine pairs of siblings, he explained, and will accept multiple persons in a family.

Lefevre said professional recruiters will work with the local African-American community to raise the level of awareness and generate enthusiasm about the study. In addition to receiving monetary compensation for being part of the study, each participant will receive personalized diet counseling, he said.

“There are few studies that have looked at genetic interactions in African Americans,” Dr. Lefevre stated. One of those that did so, he pointed out, was the HERITAGE Family Study conducted by Dr. Claude Bouchard, Executive Director of the Pennington Center. It sought to identify genes that determine the extent of improvements in physical fitness and CVD and diabetes risk factors following exercise training in both African Americans and Caucasians.

Lefevre said the choice of the Pennington Center as one of the five funding recipients is due to a team effort: “It goes back to the groundwork laid by Dr. Bouchard and his predecessor, Dr. (George) Bray, with the outstanding team they have assembled here.”

Volunteer information: www.pbrc.edu
We are all excited as plans are being made to move into the new 180,000 square feet Basic Science building later this fall. A portion of the office and laboratory space in this new building will be occupied by some of our current faculty. In addition, we are recruiting new scientists to begin filling the space available in this extraordinary new facility. Dr. David York and Bob McNees are responsible for this operation. We are taking advantage of this move to create a network of eight thematic laboratories, each grouping several faculty and occupying a quadrant in the research space of a floor. This strategy should facilitate the interactions among colleagues with common interests and the mentoring of junior faculty as a result of close contact with more senior scientists. We hope that this approach will create an environment conducive to more cutting-edge research and improve the overall productivity of Pennington Biomedical Research Center (PBRC) scientists.

On the other hand, we have had to postpone the planned construction of the new Clinical Research building. The poor performance of the stock market and the sluggish economic environment has resulted in the stagnation of the endowment administered by the Pennington Medical Foundation. The board of directors of the Foundation felt that we should not move forward with the construction until the economy has recovered and the endowment is clearly in a growing mode. We all hope that these conditions will soon prevail as we badly need additional clinical research space. Just to keep up with current demands, we have ordered four new trailers. They will be used to house clinical research staff in the interim period. It is likely that we will have to bring in more of these temporary facilities in the coming months.

The first six months of 2003 have been characterized by change at the Pennington Center. First, we have proceeded with the reorganization of the Division of Obesity Research. To facilitate the interactions among colleagues having research interests in common, we have established two divisions, instead of one. This has resulted in the creation of the Division of Clinical Obesity and Metabolic Syndrome, which Dr. George Bray has kindly accepted to serve as Chief. The basic science faculty is now grouped in a Division of Experimental Obesity, and Dr. Leslie Kozak has been appointed as Chief of this division.

The clinical faculty has now been grouped into four new clinical research units: Clinical Physiology and Metabolism, Clinical Trials, Health Behavior, and Epidemiology and Public Health. This breakdown will assist in better organizing the structure of clinical-based research and will facilitate our recruitment efforts.

Obesity is rampant in the United States and has been acknowledged as the second leading cause of death, behind smoking. Efforts to understand and manage this complex disease have met with limited success. The National Institutes of Health, in an attempt to step up research in obesity, have recently awarded the PBRC a $1.3 million, five-year institutional training grant entitled, “Obesity: From Genes to Man.” This grant award resulted from the collaboration of Phillip Brantley, PhD, Director of The Pennington Center’s Division of Educational Programs, and David York, PhD, Executive Director of Basic Research at the Pennington Center. The objective of this program is to recruit and train post-doctoral fellows to pursue obesity research that transcends traditional scientific boundaries, e.g., genetic, molecular, physiological and behavioral, and instead address research questions that involve multiple areas of obesity research. Two trainees will be recruited each year during the initial years of the project with the intent that each trainee will spend two to three years under the mentorship of at least two Pennington Center senior scientists. The ultimate goal is that trainees will acquire the knowledge and skills to become independent scientists with their own external funding and tackle complex questions in obesity research.

We continue to add to our research faculty. Dr. Christopher Morrison joined the faculty in July as an Assistant Professor. Dr. Morrison began his scientific training with a BS from LSU and then went on to earn a PhD from the University of Missouri. After receiving his degree, he moved to the University of Washington where he was a postdoctoral fellow. His research focused on the hypothalamic signaling molecules and neuronal circuits utilized by leptin and insulin to regulate energy homeostasis.

Jeffrey Gimble, MD, PhD joined the faculty in August. Dr. Gimble received his BA in Biology from Dartmouth College and his MA and PhD in cell biology from Yale University. His MD is also from Yale. Dr. Gimble was Vice President, Tissue Engineering, and co-founder of Artecel Sciences in Durham, NC and then Chief Scientific Officer of Artecel from 2001 until coming to PBRC. Prior to going into private industry, he was on the faculty at the University of Oklahoma Health Sciences Center. Dr. Gimble is planning on continuing his research in stem cell technologies with a view to applications in adipose tissue biology, nutrition and human health and disease issues.

Several major changes have also taken place in the administration and management of PBRC. Mark Alise has been appointed as Director of Fiscal Operations. Alise replaced John Farrell, who held the position for 13 years before his retirement on May 19. Prior to this appointment, Alise had seven years experience with LSU. He received his BS degree in accounting from LSU in 1980, a baccalaureate and a licentiate in sacred theology from the Pontifical Gregorian University in Rome in 1984 and 1986, respectively, and an MBA from LSU in 1997. He is currently enrolled in the LSU PhD program in Educational Leadership and Research.

Gena Doucet was appointed Director of Human Resource Management in June. Doucet came to the Pennington Center after more than four years with LSU Human Resource Management. Prior to that, she spent a year in banking and more than six years in the chemical industry in Louisiana. She holds a BS in business and an MBA from the University of Southwestern Louisiana, since renamed the University of Louisiana-Lafayette. Doucet replaces Evelyn Bennett, a 13-year employee of the Pennington Center who retired in June.

Anne Jarrett, who has been serving in the capacity...
The regain of weight after initial weight loss—a major factor contributing to the escalating epidemic of overweight and obesity—is the focus of a large clinical trial being conducted by principal investigator, Dr. Phillip J. Brantley, Director of the Pennington Center’s Division of Educational Programs and Chief of its Behavioral Medicine Laboratory.

Dr. Catherine Champagne and Dr. David Harsha are co-principal investigators for the project. Dr. Betty Kennedy is also an investigator on the study.

The purpose of the study is to determine the effects of two innovative behavioral interventions, each designed to maintain frequent contacts, compared to a usual-care control group. If the interventions are effective, they should complement ongoing efforts to stem the obesity epidemic and ultimately prevent obesity-related cardiovascular disease.

Control of overweight/obesity is increasingly recognized as a high national priority because of its contribution to cardiovascular disease (CVD) risk factors, and ultimately to CVD itself.

The short-term success of behavioral interventions for weight loss has been documented repeatedly. Unfortunately, because weight regain is extremely common, a disappointingly small proportion of individuals achieve long-term weight control.

Of the factors associated with sustained weight loss, one of the most important is continued intervention with frequent contacts.

"There have been a number of published studies on weight loss, but very few have examined weight loss maintenance, which may involve an emphasis on different skills and behaviors than those required for weight loss," Dr. Brantley said.

Under the Weight Loss Maintenance Trial being conducted by Brantley and his colleagues, overweight and obese individuals who are taking medication for hypertension and/or dyslipidemia enter a five-month weight-loss program. Those persons who lose at least nine pounds are then randomized into one of three groups:

(1) a personal-contact intervention that provides monthly personal contacts with a trained interventionist, primarily via telephone, and to a lesser extent by in-person visits
(2) an interactive-technology intervention that provides frequent contacts through a state-of-the-art, interactive, web-based program supplemented by other communication technologies, or
(3) a self-directed, usual-care control group.

The primary outcome is weight change from the end of the initial weight-loss program to the end of the 30-month weight-maintenance intervention period. Other outcomes include weight change in subgroups, control and prevalence of CVD risk factors, measures of behavior change, and cost of implementation.

Dr. Brantley has received a $1.9 million, four-year award from the National Heart, Lung, and Blood Institute for the Weight Loss Maintenance Trial. He is awaiting approval for a fifth year to complete the project, which would increase the funding to $2.3 million.

"So many people go from one weight-loss program to another, only to regain the weight," Brantley said. "We want to get people off the roller coaster of weight loss and weight regain and put them on a program they can stick with for life."

Dr. Brantley said he and his colleagues are "particularly interested in recruiting African-American participants" and will include training materials tailored to the African-American culture.

"This study will also allow participation by people who don’t usually qualify for studies at The Pennington Center because they are taking medication for high blood pressure or other medical conditions," he added.
Aging and Nutrition: Major Focus of Research

More than 40 international scientists gathered recently at LSU’s Lod Cook Conference Center in Baton Rouge to participate in a symposium focusing on the role of nutrition in healthy aging. It was the second in a series being conducted by the Pennington Center.

The Pennington Biomedical Research Foundation served as major sponsor for the symposium, co-chaired by Dr. Eric Ravussin, Chief of the Pennington Center’s Health and Performance Enhancement Division; Dr. Robert S. Schwartz, head of the Division of Geriatric Medicine at the University of Colorado Health Sciences Center; and Dr. Richard Weindruch, Professor of Medicine at the University of Wisconsin at Madison. Dr. Phillip J. Brantley and Lacie Michel of the Pennington Center’s Division of Educational Programs planned and coordinated the symposium. The first symposium in the series was held in December 2002, focusing on the potential benefits of plant-based compounds in preventing cardiovascular disease; the third one, which will address obesity, is being planned for December 2003.

Entitled “Mechanisms and Retardation of Aging,” the symposium in May brought together a select group of scientists who are conducting cutting-edge research in nutrition and aging. They shared their findings and developed conclusions and recommendations for future research.

Two sessions, each of which included the presentation of several scientific papers, focused on (1) aging in tissues and organs and (2) mechanisms of life extension. Accompanying each session were a keynote address and a roundtable discussion by participants.

Dr. Ravussin said the assembled scientists agreed that a few of the topics discussed hold particular interest for further study and possible publication in high-quality journals. Among those topics, he said, are:

• Age-related alterations in genomic imprinting that may increase the susceptibility for some forms of cancer.
• Evaluate new paradigms on the effect of calorie restriction on the immune system.
• Evaluate in a systematic manner the effect of genetic manipulations in rodents on life span.
• Need for identification of reliable “biomarkers” of aging.
• There’s a need now to focus on strategies for a healthier life,” Dr. Ravussin noted. “We have never faced such growth in a segment of the population as we will with the elderly. A large percentage will be people over 85, who must function physically and cognitively.”

The U.S. population over age 65 is projected to grow from 35 million in 2000 to 70 million in 2030. The largest increase in aging is occurring among those 85 years and older. By the year 2020, there will be close to 10 million Americans above the age of 85.

Aging is a complex process and is only just beginning to be understood. There are many factors involved in the aging process, including changes in cellular and tissue metabolism, environmental assault, and the relationship between nutrition and physical activity. •

Study Goal: Learning about the Long-term Benefits of a Reduction of Calories on Aging

Coming off an international symposium it hosted in May, the Pennington Center is currently moving forward with a major study on the possible benefits of a long-term reduction of calories on aging.

Dr. Eric Ravussin, Chief of the Pennington Center’s Health and Performance Enhancement Division and principal investigator for the study, co-chaired the symposium, which focused on the role of nutrition in healthy aging.

“Our environment now is very conducive to obesity,” said Ravussin. “The thinking is that caloric restriction may change how the body’s metabolism handles the food. These changes may play significant roles in the aging process, especially by decreasing some of the deleterious byproducts of food oxidation.”

“The study will examine whether a two-year calorie deficit reduces the risks of age-related chronic diseases—such as heart disease, hypertension, and type 2 diabetes—and leads to longer and more productive lives. The study is being funded by a seven-year, $12.4 million grant from the National Institutes of Health (NIH). The grant is the largest ever given by the NIH to the Pennington Center.

The theory that reduced calories lower the risks of age-related diseases in humans is based on animal studies showing that restricting calories from birth to early adulthood prolongs life. Animals that receive a quality, low-calorie diet live longer than those consuming more daily calories.

“It is important to understand that we are talking about restricted-calorie diets that are high-quality and nutrient-dense,” said Dr. Ravussin. "If the quality of the diet is poor and insufficient in some vitamins and essential nutrients, we wouldn’t see any benefits, but rather the same problems observed when poor nutrition is practiced.”

Volunteer participants in the study, who are healthy and slightly overweight, are engaged for a seven-month testing period.
The Pennington Biomedical Research Center is looking for healthy, slightly overweight volunteers to participate in a 7-month research study testing the effects of diet on healthy aging. Participants receive $4,700 for completing the study. Volunteers will eat breakfast and dinner meals at the Pennington Center, with lunches and weekend meals packed to go for a three-month period, followed by three months of following a prescribed diet at home. In addition, participants will receive dietary counseling and free medical evaluation. Participants will also be asked to do one of the following:

1. Follow a reduced calorie diet
2. Follow a reduced calorie diet using a liquid diet
3. Increase physical activity while on a reduced calorie diet
4. Follow a standard diet

There will be a five-day in-patient stay required on three separate occasions. Volunteers will go through various testing, including fat and muscle biopsies.

To qualify, volunteers must be:
- Slightly overweight, 25-30 BMI (calculate your BMI via the website of pbrc.edu)
- Non-smoker
- Non-diabetic
- On no medications (birthcontrol ok)
- Women: age 25-45 (must be pre-menopausal)
- Men: age 25-50

Please visit the CALERIE web site for more information or e-mail CALERIE@pbrc.edu
New Research Projects Underway

In 2003, researchers at Pennington Biomedical Research Center injected mice with human prostate cancer cells. The study, to promote healthy weight and fitness in U.S. Army personnel, was led by principal investigator Dr. Donald Williamson. Co-investigators for the four-year study are Drs. Donna Ryan, Pamela Davis Martin, Ray Allen, Tiffany Stewart and Corby Martin. The primary aims of this research project are (1) development of a computer-based data collection system for tracking body weight/body fat and fitness in career soldiers, (2) development of an internet-based intervention to promote healthy nutrition and physical fitness and (3) testing the efficacy of this internet-based intervention for the prevention of weight gain and promotion of physical fitness in career soldiers. The Weight Loss Maintenance Trial is being conducted by principal investigator Dr. Phillip J. Brantley, joined by Drs. David Harsha, Catherine Champagne and Betty Kennedy. The study, funded for four years, focuses on the regain of weight after initial weight loss. Its purpose is to determine the effects of two innovative behavioral interventions, each designed to maintain frequent contacts, compared to a usual-care control group.

The study of the agouti-related protein (AGRP) and its role in human obesity is headed by Dr. George Argyropoulos, working with Pennington Center collaborators Drs. Claude Bouchard, Steven Smith, Jacqueline Stephens and Eric Ravussin. The five-year study centers on control of food intake by the hypothalamus and other hormone-secreting organs. When AGRP is overexpressed in animals, they develop obesity. The scientists will try to find genetic mutations that can predispose humans to obesity.

The five-year study of agouti and melanocortins in relation to obesity and diabetes is led by Dr. Randall Mynatt. Collaborators are Drs. Jacqueline Stephens, Steven Smith, Thomas Gettys, Andrey Ptitsyn, Hans-Rudolf Berthoud and Leslie Kozak. The agouti gene was the first "obesity" gene cloned, and over the past 10 years the system it regulates has become recognized as a major regulator of body fat stores. To understand the potential function of agouti in human fat, Dr. Mynatt has engineered transgenic mice that produce high levels of agouti in their fat. These mice become obese and develop type 2 diabetes.

The three-year study to develop a treatment for prostate cancer is headed by Dr. Carola Leuschner, with Dr. William Hansel serving as a consultant. Laboratory mice will be inoculated with human prostate cancer cells so that treatment regimens, treatment efficacies on killing metastases and potential side effects of drugs can be observed. Membrane-disrupting peptides, which are connected with hormone ligands, destroy cell membranes only from cells that carry the receptors for those ligands. This construct ensures highest specificity to the target cells. These peptides, created in a laboratory, are similar to peptides found in bee venom.

of Director of Sponsored Projects since joining in the Pennington Center in 1999, has recently been named Director of the newly-established department of Intellectual Property, Legal, and Regulatory Affairs. We have experienced a considerable increase in the volume of activities in these areas over the last two years and anticipate even more growth over the last two years and anticipate even more growth over in the coming years. Ms. Jarrett is highly qualified to become the Director of this new office, as she has already dealt with such issues almost on a daily basis since her arrival at the Center. In her new position, Ms. Jarrett will also serve as Chair of the soon-to-be-established PBRC Technology Transfer Committee.

The symposium series continues to be a success. The first in a series of Scientific Symposia sponsored by the Pennington Biomedical Research Foundation was held in December, 2002 at the Lod Cook Conference Center. Michael Lefevre, PhD of the Pennington Center chaired the symposium on “The Role for Polyphenols in Cardiovascular Disease.” In May 2003, our second Scientific Symposium allowed an international panel of scientists to address “Mechanisms and Retardation of Aging.” Eric Ravussin, PhD served as the chairperson of the symposium. The co-chairs of this symposium were Robert Schwartz, MD from the University of Colorado Health Sciences Center and Richard Weindrich, PhD of the University of Wisconsin at Madison. The third symposium in this series will be held in early December, 2003. It is titled “Physical Activity: The Thermogenic Regulator of Obesity?” and will be chaired by Leslie Kozak, PhD of the Pennington Center and Marc Reitman from Merck Research Laboratories. Dr. Phil Brantley, Director of Education Programs and his assistant, Lacie Michel, have been instrumental in planning and organizing the varied logistics of these events.

Finally, it is with sadness that we will bid farewell to two of our clinical faculty members. Drs. Jennifer Lovejoy and Michael Hamilton will be leaving the Center at the end of August. Dr. Lovejoy joined the Pennington faculty in 1991 and was awarded the Douglas L. Manship Endowed Professorship in 1997. During her tenure at the Pennington Center, she has played an important role as the leader of the Women’s Nutrition Research Program. This program has been instrumental in establishing community relations by making women in the area aware of vital health related issues. Dr. Hamilton was appointed to the Pennington Biomedical Research Center in 2001 as an Associate Professor. He has contributed greatly as a physician involved in the clinical research program of the Center. Dr. Hamilton has also played an active role in translating the findings of obesity research into action in the medical community. We wish them well and thank them for their contributions to the Center.
Lifestyle Changes that Lower Blood Pressure Can Reduce the Risk of Cardiovascular Disease

Patients with high blood pressure and stage 1 hypertension who make lifestyle changes to lower their blood pressure also reduce the risk of developing cardiovascular disease, according to an article in the April 23/30 issue of The Journal of the American Medical Association (JAMA).

The article is based on a study called, "PREMIER: Lifestyle Changes for Blood Pressure Control," conducted at four clinical centers, including the Pennington Biomedical Research Center. Other centers are Duke Medical Center, Johns Hopkins Medical Center, and the data coordinating center, Kaiser Permanente Center for Health Research. The study demonstrates that an all-in-one approach to lifestyle changes, including a host of behavioral steps, have been proven to reduce blood pressure, lowering the patient’s risk for heart disease and stroke. According to the researchers, the best results were obtained when lifestyle changes included adoption of the DASH diet, which is rich in fruits, vegetables, and low-fat dairy products.

According to Dr. David Harsha, associate professor in the Division of Nutrition and Epidemiology at the Pennington Biomedical Research Center, high blood pressure (BP) is a risk factor for cardiovascular disease (CVD). Almost 50 million U.S. adults (approximately 25 percent of the U.S. adult population) have hypertension, defined as a BP of 140/90 millimeters of mercury (mm/Hg) or higher and/or currently use antihypertensive (BP-lowering) medication. Hypertension risk increases with age, and approximately half of all people aged 60 or older have hypertension, and the estimated lifetime risk for developing hypertension is 90 percent.

Lifestyle modifications that lower BP are weight loss, reduced salt intake, increased physical activity, limited alcohol consumption and a balanced diet, especially the Dietary Approaches to Stop Hypertension, or DASH diet, which emphasizes eating fruits, vegetables, low-fat dairy products, whole grains, poultry, fish and nuts and is reduced in fats, red meats and sweets.

According to Dr. Harsha, principal investigator for the PREMIER study at the Pennington Center, the researchers studied 810 patients with high blood pressure (systolic 120-159 mm Hg and diastolic 80-95 mm/Hg) and who were not taking anti-hypertensive medications. Patients who participated in this randomized trial were enrolled at one of the four clinical centers from January 2000 to June 2001, and were randomly assigned to one of three groups: (1) "established" and the DASH diet (n=268), (2) "established plus DASH," which also used the DASH diet (n=269), and an (3) "advice only" comparison group (n=273).

The researchers found that both of the behavioral interventions significantly reduced weight, increased fitness levels, and lowered blood pressure. From baseline to six months, the mean reduction in systolic BP (the top number in blood pressure) was 6.6 mm Hg in the advice only group, 10.5 mm Hg in the established group, and 11.1 mm Hg in the established plus DASH diet group.

Compared with the 38 percent prevalence of hypertension at the beginning of the study, the prevalence at six months was 26 percent in the advice only group, 17 percent in the established group, and 12 percent in the established plus DASH group. The prevalence of optimal BP (less than 120 mm/Hg systolic, and less than 80 mm/Hg diastolic) was 19 percent in the advice only group, 30 percent in the established group, and 35 percent in the established plus DASH group.

Dr. Harsha added that, in summary, the trial results demonstrate the feasibility of widespread adoption of healthy lifestyles, as promoted in the PREMIER interventions, and their beneficial effects on BP and hypertension control. “Benefits extend to both non-hypertensive individuals at risk for developing hypertension and hypertensive individuals who are not receiving medication therapy.”

“Ultimately, population-wide adoption of healthy lifestyles, as promoted in the PREMIER interventions, should substantially reduce the societal burden of cardiovascular disease and other chronic diseases.” Also, participating in the Pennington Biomedical Research Center clinical study were Catherine Champagne PhD, Phillip Brantley, PhD, Betty Kennedy, PhD, and Erma Levy MS, LD, Interventionist.
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Irene W. Pennington
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Saturday, October 4
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Conference Center
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For more information on sponsorships, booths, or details on the
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