AHA and Google Life Sciences invest $50 million to transform heart health research

In an unprecedented partnership, the American Heart Association and Google Life Sciences are joining forces to reduce the global burden of cardiovascular diseases and stroke. The AHA and Google Life Sciences will each commit $25 million to the initiative, marking the largest one-time research investment in the association’s history. The organizations will blend technical, scientific and medical resources to bring new answers to fight heart disease and stroke. The AHA’s commitment is in addition to its existing research funding.

The combined $50 million investment will be used to create a single research team that will seek novel strategies to understand, reverse and prevent coronary heart disease. It was announced at Sunday’s Opening Session by AHA CEO Nancy Brown and Andrew Conrad, PhD, CEO of Google Life Sciences.

“With its devastating human impact on countless generations of families, cardiovascular disease remains the greatest and deadliest global health challenge we face today,” Brown said. “By working together, the American Heart Association and Google Life Sciences will be able to serve as the catalyst for change and transformation in reducing the impact to people’s lives from cardiovascular diseases and alleviating global burden.”

While conventional research approaches have advanced disease treatment over many decades, the advances in reducing the incidence of acute myocardial infarction and related mortality have been largely the result of specific drugs that treat people after they have the disease, or from lifestyle changes such as smoking cessation.

“Now, to make new leaps in cardiovascular health, researchers need to develop a richer, deeper understanding of what factors make someone most at risk for cardiovascular disease, what happens just before a cardiovascular problem develops and how different kinds of disease impact the body in different ways,” said Conrad, who delivered the meeting’s Opening Session.

“Life’s streams are in dire jeopardy.”

— William Osler, MD

Nitrates show no benefit on activity tolerance in NEAT-HFpEF trial

Data presented at the first Late-Breaking Clinical Trials session on Sunday suggest that nitrates, often used to improve cardiac function, may be counterproductive.

“When we did not find any strong evidence that nitrates improve symptoms, and a strong signal that they decrease activity in patients with heart failure and preserved ejection fraction,” said Margaret M. Redfield, MD, professor of medicine at the Mayo Clinic & Foundation in Rochester, Minnesota.

“Nitrates should probably be used less often in these patients.”

Redfield is lead author of “Nitrates' Effect on Activity Tolerance in Heart Failure with Preserved Ejection Fraction” (NEAT-HFpEF). The study compared changes in physical activity levels in 51 patients taking isosorbide mononitrate compared to 59 patients on placebo. On a screening questionnaire, all of the patients had identified heart failure symptoms as the primary factor limiting their activity. NEAT measured physical activity using accelerometers worn by patients throughout the 18-week study. There was no statistically significant difference in average activity between the two groups, although the nitrate group showed a numerical decrease in activity time. Patients taking nitrates also showed numerically lower quality of life scores and higher NT-proBNP, and statistically significant

Creager exhorts Scientific Sessions attendees to reduce the burden of vascular disease

About 2,500 years ago, Hippocrates called blood vessels “the sources of human nature,” comparing them to rivers that “purl through the body and supply the human body with life.”

It’s a compelling metaphor, said Mark A. Creager, MD, FAHA, as he began his address at Sunday’s Opening Session.

“Rivers are sources of life, vitality and connectivity. But when a river becomes damaged or obstructed, everything around it suffers — sometimes with grave consequences,” he said. “It’s the same situation with the rivers and tributaries that are our blood vessels. When they are damaged, everything downstream is in peril. And that is precisely the problem we, as scientists and medical professionals, are facing today — a crisis of millions of people whose rivers and streams are in dire jeopardy.”

Fast forward about two centuries to William Osler, MD, often cited as the father of modern medicine, who is quoted as saying, “Life’s tragedies are usually arterial.”

Modern research supports Osler’s observation, Creager said. Two significant vascular disorders, atherosclerosis and thrombosis, are the principal underpinnings of heart disease and stroke.

Atherosclerosis also causes peripheral artery disease, which affects about 8 million people in the U.S. and 200 million worldwide. As a manifestation of the systemic burden of atherosclerosis, PAD is strongly associated with heart attacks, strokes, life-threatening kidney and intestinal problems, amputations and other serious health issues.

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AHA President Mark A. Creager, MD, FAHA

Tuesday is “Sneaker Day” at Scientific Sessions. Everyone is encouraged to wear athletic shoes in recognition of the importance of regular physical activity.
Today is Wear Red Day, so put on your red dress, red tie, red socks or anything red to recognize the mission of the American Heart Association. We also have another outstanding day of programming lined up, including moderated posters and oral presentations on the latest advances in basic, clinical and population science.

The meeting’s second Late-Breaking Clinical Trials session begins at 10:45 a.m. in Hall D. The theme of this important session is “Decreasing the Global Burden of Disease: Breakthroughs in Prevention.” The session will include reports on the EVITA, Fifty-Fifty Program, MBCC, MI-GENES and EMPA-REG OUTCOME trials.

Two additional Late-Breaking Clinical Trials sessions highlight the afternoon program. One will feature results from the SPRINT Trial on the effects of aggressive versus less aggressive blood pressure control. Another late-breaking session this afternoon will feature results from the Severe MR trial comparing two-year outcomes of mitral regurgitation patients who received either mitral valve repair or replacement.

The day’s other program highlights include a special plenary lecture by Gary H. Gibbons, MD, director of the National Heart, Lung, and Blood Institute, and the Lasker Awardee Lecture, which will be presented by pioneering French cardiovascular surgeon Alain Carpentier, MD, PhD. Shortly after Carpenter’s lecture there will be a special presentation of the two-year follow-up of the controversial Ischemic Mitral Regurgitation Trial, sponsored and funded by the National Heart, Lung, and Blood Institute’s CT Surgery Network.

The first of the day’s two Clinical Science: Special Reports sessions begins at 9 a.m. in the Chapin Theater. “Novel Findings from Next Generation Registries” is the topic and one of the session’s presentations will review controversial findings from “Increased Incidence of Infective Endocarditis After the 2009 European Society of Cardiology Guideline Update: A Nationwide Study in the Netherlands.” Additional presentations will report findings from the SHaRe and NCDR-CathPCI registries. The session will conclude with a report on findings from the CANOA trial.

We have several plenary and special sessions throughout the day covering topics such as sex-based differences in cardiovascular disease, the role of non-statins in the “statin era,” the myocyte loss problem in heart failure, endovascular stroke therapy trials, and health disparities in African-Americans, Hispanics and rural populations.

Another special session today is devoted to the Best of AHA Specialty Conferences. We also have more joint sessions, including programs with the International Atherosclerosis Society, the American College of Cardiology, the Great Wall International Congress of Cardiology, Heart Rhythm Society and many more. The day’s second Clinical Science: Special Reports session begins at 3:45 p.m. in the Chapin Theater. The session will focus on “Cutting Edge Technologies in EP” beginning with an analysis from the Medicare ICD Registry looking at cardiac resynchronization therapy. The session will also include results from a worldwide trial looking at miniaturized transcatheter-delivered cardiac pacing, as well as a trial evaluating the impact of a guide-of-care video decision-support tool on decisions regarding CPR/ination for patients with advanced heart failure. The session will conclude with a long-awaited report on preliminary data from the EVOLUTION Registry on the real-world efficacy and safety of Watchman LAA occlusion.
**Artificial heart pioneer will present Lasker Awardee Lecture**

Alain Carpentier, MD, PhD, who has been called the father of modern mitral valve repair, will deliver the annual Lasker Awardee Lecture at 12:30 p.m. Monday in the Chapin Theater.

Carpentier made history as the surgeon who pioneered the world’s first successful, fully implantable artificial heart. After 30 years of research, Carpentier and his team have successfully implanted the first bioprosthetic artificial heart in three patients. Called CARMAT, the device differs from previous artificial hearts in several ways, Carpentier said.

“It is an electro-hydraulically-driven device whose type of contraction and auto-regulation mimics the natural heart,” he said. “Bioprosthetic hemocompatible tissues are used for all blood-contacting surfaces to potentially reduce the need for anticoagulants. Except for the batteries, all the elements, actuators, electronics, sensors and processors are incorporated into a single unit surrounded by a flexible compliance chamber.”

Carpentier will discuss results from the three implantations of the CARMAT artificial heart bioprosthesis. He will also show a video interview with one of the patients, who answers several critical questions about having an artificial heart.

“It’s really an incredible interview to watch,” Carpentier said.

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**CAREER PROGRESSION**

**MONIQUE L. ANDERSON, MD**

After her father had a heart attack when she was a child, Monique Anderson knew she’d become a doctor. But it wasn’t until she was in medical school that she realized she also wanted to conduct research:

“For me, medicine was the perfect field. I am able to see patients, implement health programs and conduct clinical research,” said Anderson, assistant professor of medicine and a cardiologist at Duke University Medical Center in Durham, North Carolina.

Anderson credits her cardiology fellowship training at Duke with providing the clinical and research training and the mentorship she needed to succeed as an academic researcher. At Duke, she also completed the American Heart Association Pharmaceutical Roundtable Cardiovascular Outcomes Fellowship program, a two-year research training fellowship.

Anderson’s research interest in cardiac resuscitation began when she was a cardiology fellow after caring for a cardiac arrest patient who survived after 55 minutes of CPR outside an exercise facility.

“Her story was miraculous and stayed in the back of my mind as I started my research fellowship,” Anderson said. “I became drawn to cardiac arrest research by its poor survival, existing health disparities and the growing impact of community-based efforts to improve survival. Whether through AHA volunteerism or my academic career, I seek to conduct the best science to decrease death and disability from heart disease.”

Anderson’s work with the AHA began in 2011 when she joined the AHA Resuscitation Science Symposium Program Planning Committee. She was later selected to serve on the Emergency Cardiovascular Care Committee and Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation’s (3CPR) Leadership Council during her first faculty year.

She’s also a member of the Early 3CPR Career Committee, the AHA Get With The Guidelines: Resuscitation Adult Research Task Force, and the AHA’s Communities and Care National Advisory Board, among other volunteer roles.

Volunteering for the AHA is a natural extension of her career as a physician and researcher.

“When I was in medical school at Harvard, I discovered I really liked the idea of building programs to serve people,” Anderson said. “I love collaborating and bringing groups together around an innovative idea. In medical school, I spent a year setting up a community education program in a church to promote lifestyle change. I still think building effective community-based prevention programs is critically important, but it is equally important to be able to critically examine and measure health outcomes.”

Anderson recently worked with the AHA to measure the outcomes and impact of its Check. Change. Control. community high blood pressure program. And if her name sounds familiar, it may be because she was featured in the Daily News last year after performing CPR on a man at Scientific Sessions in Chicago. The man had collapsed in a hotel lobby when Anderson and a group of doctors came upon him. He was unresponsive, not breathing and had no pulse.

After Anderson administered a few rounds of chest compressions, the man sat up and said, “I’m OK. I’m OK.” After undergoing tests at a local hospital, he was doing well the next day.

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**LECTURE PREVIEW**

Artificial Hearts: Lasker Awardee Lecture
12:30–1:30 p.m. Monday Chapin Theater

**SPOTLIGHT**

**Constantino S. Peña, MD**
Medical Director of Vascular Imaging, Baptist Cardiac & Vascular Institute Miami, Florida

**MEMBER SPOTLIGHT**

**How long have you been an AHA/ASA Professional Member?**
I have been a Professional Member for eight years.

**Why did you join?**
The American Heart Association is a unique organization. It represents multiple specialties and fields in the United States and internationally. It promotes patient care, basic science and clinical-based research with the common goal of heart and stroke care. It is the one organization that brings everyone together to accomplish the truly “big” goals.

**Are you involved in AHA councils?**
I am involved with the Council on Cardiovascular Radiology and Intervention. I am happy to serve as council chair this year. Personally, I enjoy both the cardiovascular imaging and the interventional focus of the council. However, some of the greatest benefits are working with the other councils in order to achieve larger and more robust goals. Specifically, I participate on the Council on Peripheral Vascular Disease and the Council on Cardiovascular Radiology and Intervention.

**What do you enjoy most about these roles?**
Working with incredibly talented and diverse scientists, physicians and clinicians from multiple fields throughout the world.

**How else are you involved with the AHA?**
The AHA offers so many ways to get involved. Personally, I have enjoyed getting involved on the local level — from Heart Walks to Heart Balls to Jump Rope challenges at my son’s elementary school. It is humbling to see how many people come out to support the AHA mission. It makes being a steward of the AHA that much more important.

**Why is membership valuable to you?**
For two reasons: 1) the ability to involve young, energetic faculty with established leaders — this interaction further motivates and inspires the future generation of clinical scientists; and 2) gaining access to state-of-the-art and innovative research.

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**American Heart Association**

**Scientific Sessions**

**2015**
Google Life Sciences CEO imagines a world where technology and healthcare intersect

Imagine if cardiologists could monitor a patient’s heartbeat every moment of the day, with a computer recording the data and detecting when something is wrong before the patient suffers a heart attack. Imagine a device that could screen for cancer cells and detect and destroy them before they cause disease. Imagine continuously monitoring blood sugar without a finger poke.

How would the world be different? That was the question posed by Andrew Conrad, PhD, CEO of Google Life Sciences, who delivered the Lewis A. Conner Memorial Lecture on Sunday. According to Conrad, the technology to make those scenarios a reality might not be as far-fetched as they sound.

“We all know the statistics on heart disease, and everyone at this meeting is probably involved and thoughtfully concerned about the fact that we’re not doing as well as we should or could,” Conrad said. “We’re spending an awful lot of money, and that cost is not manifesting itself in the results we would like. So we wondered what we could do at Google Life Sciences to improve the statistics.”

One key may be using existing tools in novel ways to make an impact on what he described as an “information problem.” And there’s no better tool for handling information than the computer, he said.

“The computer may be one of the most important new medical devices we have,” Conrad said. “It memorizes everything perfectly. It learns things, keeps them and doesn’t lose sight of them. It can help physicians and patients make better decisions by showing them things they may not have seen.”

One example of a project currently underway in the Google Life Sciences labs involves the use of nanoparticles.

“We’re talking about incredibly small spheres — 2,000 of them can fit inside of a red blood cell — and we decorate them with aptamers and antibodies and all sorts of other things,” Conrad explained. “What we hope to do eventually is put them into a pill that a person can swallow. The nanoparticles then course through the blood stream… all the while broadcasting information seamlessly up to a computer. So a physician could ask questions and see data all the time, instead of the episodic way of drawing blood every once in a while.”

In addition, Conrad described a continuous glucose monitor under development. He said the device is cheap to manufacture, disposable and much smaller than current models. It can broadcast information directly to a user’s cell phone.

He also demonstrated the watch he was wearing, another gadget under development in the Google Life Sciences labs.

“It has 17 different sensors in it, including optical perfusion and ECG.”

Conrad said, “It can measure how I walk and how I move, even my position on the Earth because it has a gyroscope and accelerometers. It can read tremors and motion and it can measure temperature both in and outside the room. It has a light sensor, a sound pressure wave and yes, it can even tell the time and the date.”

Conrad said much of the new technology being developed at Google Life Sciences represents the evolution of computer “intelligence,” noting the difference between artificial intelligence and machine learning.

“For example, putting data into a computer that can then score well on a trivia-based game show is artificial intelligence. “Machine learning is very different,” Conrad said. “That’s where we take a bunch of raw data and we ask the computer, for example, to compare two things against each other and then impart that new knowledge to us.”

What does the evolution of smarter technology have to do with improving healthcare?

“It’s all about changing healthcare from something that is reactive to something that is proactive,” Conrad said. “At Google Life Sciences, we’re looking for breakthrough technology to provide better information and then partner with experts like all of you to have an impact on the way that healthcare gets delivered.”

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**Unofficial Satellite Events**

**MONDAY, NOV. 9**

7-10 p.m. Industry-supported Symposium

Conferences in the Clinical Use of Non-Warfarin Oral Anticoagulation in Thrombosis

This activity is provided by Global Education Group. Paradigm Medical Communications, LLC is the educational partner.

Supported by an educational grant from Daiichi Sankyo, Inc.

Hyatt Regency Orlando, Ballroom C

Registration: 6:30 p.m.; www.paradigmme.com/322

7-9 p.m. Industry-supported Symposium

Anticoagulation Management and Evolving Standards of Care

Supported by Boehringer Ingelheim Pharmaceuticals, Inc.

Hyatt Regency Orlando, Ballroom C

Registration: 6:30 p.m.; www.paradigmme.com/21513

7-9 p.m. Industry-supported Symposium

An Expert Forum: Hot Topics in Stable Ischemic Heart Disease Management

Supported by Wyeth

Hyatt Regency Orlando, Ballroom C

Registration: 6:30 p.m.; www.paradigmme.com/110915

TUESDAY, NOV. 10

6:30-8:30 a.m. Industry-supported Symposium

Challenges in Cholesterol Management — What Your Patients Might Not Be Telling You: A Town Hall Symposium

Jointly provided by University of Louisville and Global Academy for Medical Education

Supported by an educational grant from Pfizer, Inc.

Hyatt Regency Orlando, Ballroom N

Registration: tinyurl.com/cholesterolmanagement

7-10 p.m. Industry-supported Symposium

Conferences in the Clinical Use of Non-Warfarin Oral Anticoagulation in Thrombosis

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• Monday, November 9 at 1:40
• Photo taken with AHA President Mark Creager, MD, FAHA
• Level 3, Chapin Theater Lobby

The government’s Precision Medicine Initiative, an effort to move precision medicine into clinical practice, will be the topic of a plenary address Monday.

Gary H. Gibbons, MD, director of the NIH’s National Heart, Lung, and Blood Institute, will discuss the NIH’s research effort to collect health data from one million or more Americans with the hope of developing personalized treatments to prevent and treat disease.

Gibbons is stepping in for NIH Director Francis S. Collins, MD, PhD, who was scheduled to give the lecture until an unexpected personal issue prevented him from attending Sessions. Before the meeting, the Daily News asked Collins about the NIH’s Precision Medicine Initiative.

“We’d like to make it possible for any American who is interested in taking part to have that opportunity in 2016,” said Collins, adding that creating partnerships between existing large-scale cohorts is another goal. The NIH is also reaching out to groups that are underrepresented in research, in part through outreach to community health centers.

“We are excited about the potential this has for identifying the risk factors that result in disease,” Collins said. “Many people have thought of the initiative as a genomics project, but it’s really much bigger than that. Certainly there will be genomics involved, and we expect the participants will have their genomes sequenced eventually.”

The initiative also calls for collection of environmental exposures data and electronic health record information.

“We’ll also have the opportunity to study many of the wearable sensors that are appearing in great numbers,” Collins said. “We hope to discover if people actually use them in a way they find helpful, and if they change health outcomes.”

One of Collins’ dreams, he said, is that wearable sensors will get “to the point where they are reliable for measuring blood pressure in the ambulatory state.”

“We’d then have a round-the-clock record of what is really happening to someone’s blood pressure. I’m certain this would change the perspective on blood pressure management in fundamental ways,” he said. Gibbons will discuss how the project may affect researchers and clinicians in the future.

“A fundamental principle of the project is that participants will be getting results back,” Collins said, noting that patients, clinicians and researchers will all have access to the data.

“If you’re a qualified researcher with a question you want to ask of the data from a million people, you’ll be able to do that,” he said. “This could become a powerful foundational platform for future clinical trials.”

If the cohort includes a million people, a lot of them will have heart disease — individuals who have agreed to be contacted for follow-up trials. This might put the research community in a position to be able to enroll and conduct clinical trials much more rapidly and cost-effectively.”

As excited as he is for these possibilities, Collins said he must also consider financial realities.

“We’ve been in a 12-year slide in purchasing power for medical research, and that has afflicted us severely since 2003,” he said. “Will that progressive loss of resources continue or will we be able to turn the corner? I am a chronic optimist. I am seeing strong bipartisan, congressional support for the NIH in general, and for precision medicine, in particular.

“However, I do have concerns that the chronic fiscal challenges and political battles facing our government may make it impossible for some of these things to happen at the pace that they could,” he said.

An executive summary of the report is available at nih.gov/precisionmedicine.

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Norman Lepor, MD, FACC

Nov 10th
10:30 AM - 11:00 AM
Efficacy, Safety, Tolerability, and Dosing Options With PCSK9 Inhibition
Paul Thompson, MD

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Yehuda Handlesman, MD, FACP, FACE, FNLA

LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9.

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Cardiovascular Genome-Phenome Studies announce project funding

The Cardiovascular Genome-Phenome Studies have added a new class of research grants to accelerate the discovery of personalized treatments and prevention for cardiovascular disease. The CVGPS studies fall under the newly created Institute for Precision Cardiovascular Medicine, which houses the AHA’s precision medicine initiatives with support from leaders in clinical medicine, federal health and the pharmaceutical industry.

CVGPS combines the power of long-term population studies with the precision of molecular analysis to unravel key distinctions between and within subgroups of patients. Discovery Grants, made possible by a generous donation from AstraZeneca, aim to increase data and research in three areas: heart failure, predicting cardiovascular disease and generating new information about HDL cholesterol.

Ten recipients will receive one-year awards of $160,000 each, American Heart Association President Mark A. Creager, MD, FAHA, announced during Sunday’s Opening Session. “The AHA continues to push ahead with new and innovative research, including the Cardiovascular Genome-Phenome Study,” Creager said. “This research integrates the precision of molecular analysis into long-term population studies to increase our understanding of cardiovascular health and disease, and direct us toward better-targeted, safer and more effective treatments.”

These grants are in addition to the Pathway Grants and Grand Challenge Awards that were announced last year. Funding for the latest grant recipients will begin in December. They are:

- Anand Rohatgi, MD, MS, University of Texas Southwestern Medical Center, Dallas; Determining the Genomic and Lipidomic Correlates of HDL Cholesterol Efflux and HDL Particle Composition
- Brian Delisle, PhD, University of Kentucky, Lexington; Genotype-Phenotype Correlations in KCNQ1 Variants from 31,000 Whole Exome Sequences Identified in a Biobank Cohort
- Sakhthivel Sadayappan, PhD, MBA, Loyola University Medical Center, Maywood, Illinois; A Polymorphic MYBPC3 Variant as a Major Risk Factor of Cardiomyopathy in South Asian Descendants
- Xue-Qiao Zhao, MD, University of Washington, Seattle; HDL Function and Residual Cardiovascular Risk
- Dhananjay Vaidya, PhD, MBBS, MPH, Johns Hopkins University School of Medicine, Baltimore; Sex-gene Interactions for Cardiometabolic Phenotypes
- Nancy Sweitzer, MD, PhD, University of Arizona, Tucson; Large-scale Discovery of Mechanistic and Predictive Biomarkers in Phenotypically Distinct Groups of Patients with Heart Failure
- Stavros Drakos, MD, PhD, University of Utah, Salt Lake City; Molecular Predictors of Favorable Myocardial Response to LVAD-induced Mechanical Unloading
- Ron Do, PhD, Icahn School of Medicine at Mount Sinai, New York; Human Genetic Approaches to Dissect the Phenotypic Architecture of Coronary Heart Disease
- Sanjiv Shah, MD, Northwestern University, Evanston, Illinois; Molecular Determinants of Hypertensive HFpEF: Genomics, Transcriptomics, and Proteomics
- David Kao, MD, University of Colorado, Denver; Characterization of Molecular Profiles in Complex Phenotypes Associated with Heart Failure with Preserved Ejection Fractions

In July, the CVGPS announced three Grand Challenge awardees. These researchers are seeking breakthroughs that lead to more targeted, safer and more effective treatments based on a deeper understanding of patients’ characteristics. Each research group received a four-year, $2 million award.

Greg Lewis, MD, will investigate whether specific tests of cardiorespiratory fitness can identify patients who may benefit from early treatment to prevent cardiovascular disease. Lewis is director of the Massachusetts General Hospital Cardiopulmonary Exercise Laboratory and director of the hospital’s intensive care unit. His research will also examine how lifestyle, genetic variations, inherited family traits and measurements of heart structure and function matches changes in metabolism during exercise.

Daniel J. Rader, MD, and Jennifer Van Eyk, PhD, will generate data on blood protein biomarkers from people of European, African-American and South Asian ancestry, and their relationship to genetic variants and risk of heart disease. Rader is professor of molecular medicine and chair of the department of genetics at the Perelman School of Medicine at the University of Pennsylvania in Philadelphia. Eyk is director of the Advanced Clinical Biosystems Research Institute and director of basic science of the Barbra Streisand Woman’s Heart Center at Cedars-Sinai Medical Center in Los Angeles.
New observational study results underline the need for proactive risk evaluation and risk-reduction programs for patients with peripheral artery disease (PAD).

In the study, which was presented Sunday at Scientific Sessions, patients with diagnosed PAD who took part in a cardiovascular risk-reduction program had significantly lower risks of all-cause mortality, stroke, myocardial infarction and amputation compared to matched patients who received standard care.

“There is a great burden of peripheral artery disease around the world,” said lead author Mohamad Hussain, MD, a vascular surgery resident at the University of Toronto. “In North America alone, about 27 million people live with PAD. The incidence has increased dramatically in recent years because of risk factors such as diabetes, high blood pressure, smoking, high cholesterol and obesity, essentially the same risk factors you have for heart disease. The problem is that these risk factors are not managed appropriately in the PAD population when you compare it to the heart disease population.”

The researchers used administrative data to follow 290 patients with diagnosed PAD who were enrolled in the Systematic Assessment of Vascular Risk (SAVR) program at Toronto General Hospital in Ontario. The SAVR patients were matched with one or two control patients from other tertiary vascular centers who were not enrolled in a cardiovascular risk-reduction program. A total of 791 patients were followed.

The primary outcomes were myocardial infarction, stroke and all-cause mortality. Secondary endpoints included lower limb amputation and revascularization procedures. Patients in both cohorts were followed for up to seven years.

Patients in the SAVR group had a significantly reduced risk of MI, stroke and death (HR=0.64, p=0.001) compared to the usual-care group. The SAVR patients were also less likely to undergo major amputation (HR=0.47, p=0.001), minor amputation (HR=0.26, p=0.001), or arterial bypass surgery (HR=0.47, p<0.001), or to be hospitalized for heart failure (HR=0.73, p=0.048). SAVR patients were also more likely to undergo peripheral angioplasty (HR=3.0, p=0.001).

“There is a significant need to develop and implement programs for improving risk-factor control in PAD just like there are for patients with coronary heart disease,” Hussain said. “Our results indicate that physicians should put a greater focus on assessing risk factors and treating them aggressively for PAD patients. These therapies would include lifestyle modifications with increased exercise, weight loss and smoking cessation, in addition to prescribing the appropriate risk-reduction therapy and monitoring on an ongoing basis.”

Hussain cited a lack of knowledge by patients and clinicians about the similarities between PAD and other forms of arterial disease as a reason for the lack of risk-reduction programs. The lack of effective risk-reduction programs accounts for the higher rates of heart attack and stroke among patients with diagnosed PAD compared to patients with recognized heart disease, he said.

“There is a significant need to develop and implement programs for improving risk-factor control in PAD just like there are for patients with coronary heart disease,” Hussain said. “Our results indicate that physicians should put a greater focus on assessing risk factors and treating them aggressively for PAD patients. These therapies would include lifestyle modifications with increased exercise, weight loss and smoking cessation, in addition to prescribing the appropriate risk-reduction therapy and monitoring on an ongoing basis.”

Hussain cited a lack of knowledge by patients and clinicians about the similarities between PAD and other forms of arterial disease as a reason for the lack of risk-reduction programs. The lack of effective risk-reduction programs accounts for the higher rates of heart attack and stroke among patients with diagnosed PAD compared to patients with recognized heart disease, he said.

If you have atherosclerotic plaque build-up in the peripheral arteries, you almost certainly have a similar build-up in the coronary arteries and elsewhere.” Hussain said. “Patients with PAD are at elevated risk for myocardial infarction, stroke and death just like anyone else with atherosclerosis. We routinely encourage cardiac patients to follow risk-reduction programs, but we do not make the same recommendations for patients with PAD. These results suggest that we should.”

Risk reduction can decrease adverse events in PAD

Mohamad Hussain, MD

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Energy drinks present cardiovascular risk, study finds

New data presented Sunday at Scientific Sessions show a striking rise in catecholamine levels after energy drink consumption in healthy young adults. These acute adrenergic changes, in turn, may potentially trigger arrhythmias or ischemia, especially in individuals with a vulnerable cardiac substrate.

“We know from prior research that energy drink consumption increases blood pressure, but the mechanisms are unclear,” said Anna Svatikova, MD, PhD, a cardiovascular diseases fellow at the Mayo Clinic in Rochester, Minnesota. “We don’t yet know much about the cardiovascular effects of these drinks, but an increasing number of young adults consume energy drinks to improve their physical and mental performance, to combat fatigue and to compensate for lack of sleep.”

Svatikova presented the new data on energy drinks during the 2015 AHA Lifestyle and Cardiometabolic Health Young Investigator Award oral abstract competition on Sunday. Catecholamine responses may play a role in increasing cardiovascular risk, she said.

In the study, Mayo Clinic researchers compared the effects of a single, 16-ounce can of a commercially available energy drink against a sham drink, measuring blood pressure and plasma norepinephrine levels before and 30 minutes after the consumption of each drink. Norepinephrine is a ‘fight or flight’ chemical, Svatikova said, that increases blood pressure and the heart’s ability to contract. It modulates heart rate and breathing in response to perceived stress.

Study participants ingested either an energy drink or a sham drink in random order on two different days. All subjects consumed the drinks in a rapid manner designed to emulate the way many young adults consume these beverages. The randomized, placebo-controlled crossover study involved 25 healthy volunteers who were non-smokers, on no medications and who had no known disease or cardiovascular risk factors.

Blood pressure and plasma norepinephrine levels more than doubled after consuming the energy drink, Svatikova reported. The energy drink elicited a nearly 70 percent increase in plasma norepinephrine levels compared to a 30 percent increase following the sham drink (p=0.003).

It is not clear how energy drinks boost plasma norepinephrine levels, Svatikova noted. Energy drinks frequently contain 100 mg to 280 mg of caffeine, while a typical cup of coffee contains 40 mg to 150 mg of caffeine. The exact amount of caffeine that may lead to adverse events and harmful side effects is unknown and may vary by multiple factors, including age, gender, body mass index, liver function and genetics, among others.

Energy drinks may also contain other stimulants, such as taurine, guarana (a seed that contains caffeine), and herbs such as gingko biloba and ginseng. Not all of the ingredients have been well studied in terms of their cardiovascular effects, although taurine, gingko biloba and ginseng have been observed to act as stimulants.

The combined effects of energy drink ingredients on cardiovascular health are also unknown. The cardiovascular responses to energy drinks in people simultaneously consuming alcohol and/or smoking, especially in people with preexisting heart disease such as high blood pressure, heart failure, rhythm abnormalities or structural heart disease, are also unknown, Svatikova said, but are likely to be significant.

“Consumers should use caution when using energy drinks because they may increase the risk of sudden heart problems, even among young people,” she said. “Asking patients about energy drink consumption should become routine, particularly when interpreting vital signs in the acute setting. Energy drinks may conceivably be silent dangers for the heart. Prior studies on cardiovascular outcomes of energy drink intake are few. The rising tide of adverse cardiovascular events associated with energy drinks calls for further research.”

Anna Svatikova, MD, PhD

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Visit participating exhibitors and get your card stamped.

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Studies analyze CPR practices, AED placement

Three abstracts presented Sunday suggest that AED placement can improve survival following cardiac arrest. New data from one of the studies suggest that extracorporeal CPR (ECCP) is more effective in patients with sustained ventricular fibrillation than in patients whose cardiac rhythm changes from ventricular fibrillation (VF) to a non-shockable rhythm during conventional CPR.

In the multicenter prospective observational study, researchers in Japan followed 457 patients with initial VF during CPR. All of the patients began ECCP after failing at least 15 minutes of conventional CPR. Patients were grouped by rhythm changes during CPR. One group had sustained VF and the other group changed from VF to a non-shockable rhythm. Significantly more patients in the sustained VF group achieved a favorable outcome, 19.7 percent compared to 3.3 percent in the group whose cardiac rhythm changed to nonshockable (p<0.001). Sustained VF during CPR was the strongest predictor for favorable outcome.

“ECCP seems to be effective in patients with sustained ventricular fibrillation during conventional CPR,” said lead author Takahiro Nakashima, MD, of the National Cerebral and Cardiovascular Center in Osaka, Japan. The AHA recommends that ECCP following out-of-hospital cardiac arrest is a class IIb indication only in cases in which the duration of circulatory arrest due to cardiac arrest is short, “but our results suggest it can be a lifesaver for the subset of patients who have sustained VF during conventional CPR,” Nakashima said.

In another study presented Sunday, videoonly CPR training was proven to be just as effective as conventional manikin-based training, at least for family members of cardiac patients. Researchers at the University of Pennsylvania compared the compression rates of individuals who were trained in CPR using a video-based program without a manikin to those trained with a video self-instruction (VSI) kit including a practice manikin. Study participants were family members of cardiac inpatients. Researchers compared the compression rates of cardiac patients.

The mean chest compression rate was 88 compressions per minute in the video-only group compared to 89 compressions per minute in the VSI group (p=0.56). Mean chest compression depth was 40 mm in the video-only group and 45 mm in the VSI group (p<0.01).

The only statistically significant difference between the two groups was the depth of chest compressions, said lead author Audrey L. Blewer, MPH, from the University of Pennsylvania Center for Resuscitation Science in Philadelphia. It is important to note that the AHA recommends that chest compressions be performed to a depth of at least 50 mm, or 2 inches.

“The purpose of this study was to develop a mechanism to get more people trained,” Blewer said. “By training more people, we hope to empower more individuals to use CPR in the typical cardiac arrest situation. This kind of video training can easily be disseminated by video-on-demand, YouTube, social media and multiple other platforms.”

Comparing the place and time of cardiac arrests with the actual availability of AEDs showed a coverage loss of approximately 21 percent. Coverage decreased by 8.6 percent during the day (8 a.m. to 3:59 p.m.), by 28.6 percent in the evening (4 p.m. to 11:59 p.m.) and by 48.4 percent at night (midnight to 7:59 a.m.).

The coverage loss during evenings, nights and weekends (when 61 percent of the tabulated cardiac arrests occurred) was 31.6 percent. The largest coverage gaps were found in schools (39.7 percent), industrial facilities (39.3 percent), recreation facilities (37.1 percent) and offices (35.7 percent). Locations that had no coverage loss included transportation facilities, long-term care facilities and homeless shelters.
Get free abstracts on USB, Booth 557. Take some science home. You can search and view abstracts presented at Scientific Sessions any time you’d like when you pick up your complimentary copy. Supported by Janssen Pharmaceuticals.

**SHOWCASE AREAS IN THE SCIENCE & TECHNOLOGY HALL**

**Emerging Science & Technology Showcase**
Stop by this area to visit companies currently in the early stages of product development or the product approval process, giving you a sneak peek at the future of cardiovascular disease prevention, diagnosis and treatment.

**Lifestyle Showcase**
Here you will find health- and nutrition-focused exhibitors. Join the AHA by calling on all people to live longer, more heart-healthy lives by supporting the products that drive health and nutrition awareness.

**Public Service Showcase**
This area features associations, non-profit service providers, universities and other organizations who strive to promote heart health.

**Research & Discovery Zone**
Visit this one-stop shop for the newest research and features from research labs around the world.

**Retail Row**
Visit these exhibitors to shop for a variety of leisure products.

**Health Tech Competition**
Watch seven medical tech startups demonstrate a broad spectrum of cardiac healthcare innovations before a panel of distinguished cardiologists, venture capitalists and industry thought leaders.

**Monday’s Theater Demonstrations**

**Booth 1601**

**Noon–1:45 p.m.**
PRALUENT® (alirocumab): Efficacy and Safety with Two Different Dosing Regimens
Sanofi Regeneron
1:15–2 p.m.
Diagnosis and Management of Atrial Fibrillation: Working Together to Reduce Stroke Risk in HFRA
Boehringer Ingelheim Pharmaceuticals, Inc.
Medtronic

**Booth 1559**

**Noon–1:45 p.m.**
A Treatment Approach for Patients With Chronic Systolic Heart Failure
Amgen
1:15–2 p.m.
A Novel Approach to the Treatment of Heart Failure
Novartis Pharmaceuticals Corporation

**Booth 163**

**Noon–1:45 p.m.**
An Update on Arterial Thrombosis Pathophysiology and Management
Merck
1:15–2 p.m.
Repatha™ (evolocumab): Product Overview
Amgen

**HeartQuarters Theater**

**Booth 859**

10:15–11 a.m.
Cardiovascular Daily
Presenters: Gail Jaeger, Medpage Today; John Poono, AHA Director, Professional Membership

11:15 a.m.–1 p.m.
Patient Education and Support
1:15–2 p.m.
Video

2:15–2:45 p.m.
Sessions OnDemand Premium Demonstration
Presenter: Diane Pernino, VP, E-Learning and Media Strategy, Adventa Technology
3–4 p.m.
Quality Team Presentation
Study finds that eating at home is beneficial to health

Men and women who prepare meals at home are less likely to gain excess weight and develop type 2 diabetes, according to a study presented at Scientific Sessions. The new data align with older studies suggesting that individuals who eat more meals out are more likely to gain weight and suffer negative health consequences.

“We now have long-term data showing that when you eat more meals prepared at home, you have a long-term lower risk for obesity and diabetes,” said lead author Geng Zong, PhD, research fellow at the Harvard T.H. Chan School of Public Health in Boston. “Based on our work, on average, if you eat 11 to 14 lunches and dinners prepared at home each week, you have a 13 percent lower risk of obesity and diabetes compared to those who eat zero to six lunches and dinners prepared at home a week.”

Zong, who is mentored at Harvard by assistant professor Qi Sun, MD, ScD, presented his study findings during an oral abstract presentation on Sunday. The results were based on accumulated data from nearly 100,000 male and female health professionals collected over 26 years.

Study participants included 57,994 women in the Nurse’s Health Study and 41,679 men in the Health Professionals Follow-up Study from 1986 to 2012. None of the participants had diabetes, cardiovascular disease or cancer at baseline. The participants submitted data on the frequencies and type (lunch or dinner) of meals prepared at home each week at baseline. Self-reported data were combined and analyzed for both cohorts.

Preparing meals at home was associated with lower weight gain during the follow-up period. After adjusting initial results for demographic and lifestyle factors, participants with 11 to 14 meals prepared at home a week had 0.42 kg to 1.25 kg lower weight gain before their average age reached 60 in 1994, as well as a pooled hazard ratio of 0.87 for the risk of developing obesity, compared to those who ate zero to six meals prepared at home.

More importantly, the former participants had 13 percent lower risk for type 2 diabetes during the follow-up period.

“We show very similar results to previous studies, but from a different angle,” Zong said. “Earlier work has shown that eating away from home, especially higher consumption of fast foods, may lead to excessive weight gain among children and young adults. The obvious problem is eating in fast food restaurants with their high-fat, high-salt, high-calorie menus. Some studies also suggest nutrient profiles of foods are not necessarily ideal if you eat at workplace cafeterias, school cafeterias or even hospital cafeterias.”

The change in eating habits over recent decades is the result of multiple socioeconomic factors, Zong noted. A growing proportion of households are headed by working parents with a higher work burden. This translates as less time to cook, less time to shop and less time to learn cooking skills. Meanwhile, restaurants of all types have increased advertising to encourage people to eat out more, he said. And restaurant portions continue to grow, increasing the calorie count of every meal eaten out.

“Encouraging patients and the general public to cook and eat more meals consisting of healthful foods at home might be important from a public health perspective,” Zong said. “The pathway seems to be having more meals prepared at home means better diet quality, less weight gain and fewer health problems secondary to obesity.”

Visit the Simulation Zone in booth 101 during scheduled sessions or drop by at your convenience to experience the devices on your own. The schedule of sessions is available for viewing in the mobile meeting guide app and in booth 101.
Negative stress echo a good sign for women and CAD

egative stress echocardiography has long been recognized as a positive prognostic sign for long-term cardiovascular outcomes, but there has been a looming question over the value of a negative stress echo in women who showed concomitant ischemic electrocardiographic changes. New data presented at Scientific Sessions suggest that a negative stress echo is the more accurate positive prognostic factor.

Mariana Garcia, MD, a cardiovascular disease research fellow at the Mayo Clinic in Rochester, Minnesota, presented new data on the prognostic value of a stress echo in women at low to medium risk for CAD during a poster session on Sunday. The poster is part of an ongoing project to expand the universe of cardiovascular disease research in women.

Researchers at the Mayo Clinic and Policlinico de Modena in Italy prospectively studied 551 women who had a stress echo with or without ultrasound contrast enhancement between 2003 and 2010. All of the women had been referred for a stress echo for the assessment of suspected coronary artery disease, and all of the women were at low to moderate risk for CAD based on an evaluation of traditional risk factors. Women with a negative stress echo were also examined using stress ECG to assess any concomitant ischemic electrocardiographic changes.

Women in the study were followed for a mean of 4.4 years. The primary endpoint was major cardiovascular events (MACE), a composite of myocardial infarction, revascularization and all-cause mortality.

Outcomes data were collected using a combination of questionnaires and phone calls. Risk models were adjusted for center, age, smoking, diabetes, dyslipidemia and hypertension. The mean age of the women at the time of their stress echo was 56.7 years.

Most of the women (85 percent) had an exercise stress echo while the remaining 15 percent had a dobutamine stress echo. A total of 89 of the women (18 percent) had concomitant ischemic electrocardiographic changes.

“The main conclusion is that with a noninvasive test such as a stress echo, a negative stress echo could be associated with a good prognosis regardless of the electrocardiographic changes over at least five years,” Garcia said. “This is in a population of women at low to intermediate risk for CAD. It is a confirmation of clinical practice, but it also underlines the need for more female-inclusive cardiovascular research.”

During the follow-up period, 23 women (15 percent) experienced MACE. Eight had myocardial infarction, four were revascularized and 11 died. MACE occurred in 15 women (3 percent) with normal stress echo results, compared to eight with ischemic electrocardiographic changes. The risk associated with a negative stress echo, despite concomitant ischemic electrocardiographic, was not statistically significant (p=0.09).

Smoking and dyslipidemia were the only factors that were significantly associated with an increased risk for MACE, with respective hazard ratios of 3.5 (p=0.01) and 2.85 (p=0.03). “Diagnostic strategies have remained controversial in women at low to intermediate risk for coronary artery disease,” Garcia said. “Compared to men, there are multiple discrepancies between chest pains, symptomology and low prevalence of obstructive coronary disease in women.

These findings underline the need to continue research in noninvasive detection strategies in the female population.”

The historical lack of cardiovascular research in women is changing, Garcia added. Recent advances in female research have resulted in at least a 30 percent decrease in female deaths from cardiovascular disease. Despite this improvement, cardiovascular disease continues to be the leading cause of death among women.

“We need clinical practices that focus on the unique aspects of cardiovascular disease in women and that support the necessary research in diagnosis, prevention and treatment of cardiovascular disease in women,” she said.
Help support the American Heart Association by signing up for the Fitbit FitForGood step challenge. Sign up at Fitbit.com/FitForGood, choose AHA as your charity, then log as many steps as possible Nov. 9 through Nov. 20. Your steps will be tracked and credited toward AHA’s step total, then the charity with the most steps at the end of the challenge will receive $500,000 from Fitbit, second place will receive $350,000 and third will receive $150,000. Those funds will go a long way in furthering the lifesaving mission of the AHA, so sign up today and get moving!
Aggressive ECMO increases survival in refractory cardiac arrest

ew data from a single-center study suggest that extracorporeal membrane oxygenation (ECMO) can be useful for out-of-hospital refractory cardiac arrest when implemented by dedicated ECMO teams supported by appropriate training.

Lionel Lamhaut, MD, an intensive care specialist at Necker Enfants-Malade Hospital in Paris, discussed the study’s findings during an oral abstract presentation on Sunday at Scientific Sessions. The retrospective, single-center observational study provides solid evidence favoring the use of ECMO by emergency medical services to treat refractory cardiac arrest, but randomized controlled trials are needed to confirm the results, he said.

“This is the first time we have seen direct evidence that prehospital ECMO can increase survival in out-of-hospital cardiac arrest,” Lamhaut said. “Before this study, ECMO was not a realistic option because of the time it takes to get to the patients and get them back to the hospital. We lost lives because of the time delay. Taking ECMO to the patient can save lives.”

The study compared two ECMO strategies. During the first part of the study period, November 2011 to December 2014, an ECMO team was alerted after 10 minutes of advanced life support failed to restart spontaneous cardiac rhythm following an out-of-hospital cardiac arrest. If an ECMO team was available, it was dispatched to the site of the cardiac arrest and began ECMO in the field. If an ECMO team was not available, the patient was transported to the hospital and ECMO was initiated on arrival.

During the second study period, January to June 2015, dedicated ECMO teams were put on alert when a basic life-support ambulance departed for a suspected cardiac arrest. Each ECMO team consisted of a physician, a nurse and a paramedic. Teams were scheduled to ensure the availability of ECMO 24 hours a day, seven days a week. Patients were assessed in real time and ECMO was started either in the field or on arrival at the hospital, depending on time and availability. Special training was given to all emergency dispatch personnel and all advanced life-support units to ensure the appropriate evaluation of patients for ECMO, and timely dispatch of ECMO teams.

The second study period with more aggressive use of ECMO showed significantly better survival, 31 percent, compared to 8 percent during the first period (p=0.014).

“When we talk about refractory cardiac arrest outside the hospital, we are used to talking about almost everyone dying,” Lamhaut said. “We know from data on in-hospital ECMO that it can save lives in refractory cardiac arrest. These results tell us that if we use very aggressive ECMO for patients with refractory cardiac arrest outside the hospital, we can save a lot of patients who now die.”

Increased survival appears to be a function of reduced low-flow time due to early implementation of ECMO, Lamhaut said. The mean low-flow period before ECMO during the second period was 73 minutes compared to 92 minutes during the first part of the study (p=0.006). The mean low-flow period was shorter during the second period for in-hospital ECMO, 83 minutes versus 101 minutes, and out-of-hospital ECMO, 63 minutes versus 80 minutes (p=0.00001).

“The more aggressive ECMO strategy, using an earlier ECMO alert, dedicated ECMO teams and ECMO training have a major impact on survival,” Lamhaut said. “The improved survival is probably a function of decreased low-flow time, especially for patients who began ECMO before they reached the hospital.”

Native T1 time and atrial fibrillation

In a poster presented Sunday at Scientific Sessions, researchers reported that there are differences in the native LV myocardial T1 time between atrial fibrillation patients with preserved LV function referred for PVI and normal controls, suggesting that native T1 time is an independent predictor of recurrence of AF after PVI in patients with paroxysmal AF.
LATE-BREAKING continued from page 1

At Sessions
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LATE-BREAKING

the Heart Failure Clinical Research Network to
in Philadelphia. This early success prompted
of medicine at the University of Pennsylvania
Failure and Transplant Program and professor
Margulies, MD, research director of the Heart
exercise and quality of life, said Kenneth B.
improved left ventricular ejection fraction,
should benefit advanced heart failure.

The study randomized 300 adults
hospitalized for an acute heart failure
syndrome to placebo or one of three doses
of liraglutide for one month. The primary
endpoint was a hierarchical rank based
on time to death, time to heart failure
rehospitalization and time-averaged change in
NT-proBNP over six months.

Liraglutide patients fared numerically
worse on nearly all measures, although
most differences failed to reach statistical
significance. Patients with diabetes showed
statistically significant weight loss, but there
was no difference for patients who did not
have diabetes.

“Liraglutide does not improve post-
hospital clinical stability in patients with
advanced heart function and reduced left
ventricular ejection fraction,” Margulies said.
“Larger studies are needed to establish the
safety of liraglutide or other GLP-1 agonists
for diabetes management or weight loss in
patients with advanced heart failure.”

A study using a combination of
telemonitoring and regular follow-up
telephone calls did not improve 180-
day readmissions for heart failure, said
Michael K. Ong, MD, PhD, associate
professor at the University of California,
Los Angeles, and lead author of “Remote
Patient Management After Discharge of
Hospitalized Heart Failure Patients: The
Better Effectiveness After Transition – Heart
Failure Study.”

A total of 715 patients hospitalized for
heart failure were given pre-discharge heart
failure education. All received telemonitoring
equipment to measure weight and blood
pressure daily, with data transferred to
monitoring nurses by cell phone. Nurses also
made nine coaching calls over the six-month
study period. A control group of 722 patients
received standard post-discharge care.

The study showed no significant difference
in 30-day or 180-day readmission rates
between the two groups, nor for 30-day
mortality. There was slight reduction in 180-
day mortality, but the differences reached
statistical significance only for patients who
completed more than half of their follow-up
coaching calls.

“High levels of call adherence seem to
make a difference,” Ong said. “We need
larger and longer studies using more current
technology to confirm these findings, which
were from post-hoc analyses.”

Two early-stage trials showed promise.
The soluble guanylate cyclase stimulator vericiguat
failed to reduce NT-proBNP compared to
placebo in patients with worsening heart failure.
But there was an increasing dose-
related benefit with higher doses, said Mihai
Gheorghiade, MD, professor of medicine
and surgery and director of experimental
therapeutics at the Center for Cardiovascular
Innovation at Northwestern University
Feinberg School of Medicine in Chicago.

Gheorghiade is lead author for “Oral
sGC Stimulator Vericiguat in Patients
with Worsening Chronic Heart Failure and
Reduced Ejection Fraction – The SOBi
Guanylate Cyclase Stimulator Study in Heart Failure
with Worsening Heart Failure Study.”

Researchers compared the physiologic
effects and pharmacokinetics of three dosing
regimens against placebo in 450 patients
for 20 weeks. The drug showed statistically
significant improvements in systolic ejection
fraction and fewer clinical events.

Finding an agent that directly improves
cardiac function has been the holy grail of
heart failure research. The phase 2 “Chronic
Oral Study of Myosin Activation to Increase
Contractility in Heart Failure (COSMIC-
HFr): Final Results from a Double-blind,
Randomized, Placebo-controlled, Multicenter
Study” suggests researchers may be moving
in the right direction.

The study explored omecamtiv mecarbil,
a novel selective cardiac myosin activator.
Lead author John R. Teerlink, MD, professor of
medicine at the University of California, San
Francisco, likened myosin activation to more
hands pulling on the rope, as it increases the
entry rate of myosin into the tightly bound,
force-producing state, increasing the duration
of systole and increasing stroke volume to
improve cardiac function.

Researchers compared the physiologic
effects and pharmacokinetics of three dosing
regimens against placebo in 450 patients
for 20 weeks. The drug showed statistically
significant improvements in systolic ejection
time, stroke volume, left ventricular fractional
shortening, and left ventricular ejection
fraction. There were also improvements in
heat rate and NT-proBNP levels.

“We believe these changes will translate
into improvements in clinical outcomes,”
Teerlink said.
Researchers discover a noncoding RNA that regulates endothelial cell function in aging tissue

It has long been recognized that endothelial cell function deteriorates with age, but the mechanisms or mechanisms responsible for this functional decline have not been clear. New data presented at Scientific Sessions suggests that at least one long noncoding RNA acts to inhibit endothelial cell proliferation and function in older tissue but not in younger tissue.

“We have found a long noncoding RNA called Meg3 that is highly expressed in endothelial cells and is increased by aging,” said Reinier Boon, PhD, group leader at the Institute of Cardiovascular Regeneration at Goethe University Hospital in Frankfurt, Germany. “The expression of Meg3 is much higher in older patients than in younger people. We see the same age-related increase of Meg3 expression in mice.”

Boon presented the findings on Meg3 during a poster session on Sunday. Meg3 is not the first noncoding RNA to show regulatory function in the vascular system, he said, but it is the first to show an association with aging and decreased endothelial function in both human tissue and in mice.

“We have found that when we inhibit Meg3, both in aging cell cultures and in older mice, the endothelial cell function improves,” Boon said. “When we remove Meg3, we see more endothelial cells, more functional endothelial cells and healthier endothelial cells in both our human cell culture models and in our animal models. This is exciting in the therapeutic sense because we might be able to do the same in patients in the future to improve endothelial cell function and vascular function. This is especially promising in older people.”

The research team has not yet fully worked out the mechanistic details of Meg3 expression and aging, but has theories about how Meg3 might work.

In human cell cultures, Meg3 localizes to the nucleus and can also be induced by hypoxia. These data suggest that Meg3 functions as an epigenetic regulator of gene expression, a feature that is not uncommon for nuclear long noncoding RNAs. Silencing Meg3 and Meg3 overexpression induce global gene expression. The team found evidence that Meg3 interacts with the epigenetics regulator complex PRC2 in endothelial cells.

When Meg3 is blocked in older cell cultures and in older mice, endothelial cells revert to a younger, more functional phenotype.

In aged mice with induced ischemia in a hind limb, blocking Meg3 induced significant recovery of perfusion compared to control mice. Silencing Meg3 also enhanced capillary and arteriole density in treated mice compared to controls.

“One of the important aspects of this work is that we are not using gene knockout mice,” Boon said. “Instead, we are using antisense oligonucleotides to inhibit Meg3. Using antisense oligonucleotides to silence RNA is a relatively new approach in this kind of research. If we can silence Meg3 in mice by simply injecting the appropriate antisense oligonucleotide, you could achieve the same effect by injecting it into humans, in theory. The translation from animal model to human is much more direct and potentially much quicker using antisense than starting with gene knockouts.”

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Tragic outcomes can also occur when veins are affected. About 900,000 people are affected by venous thromboembolism each year. Pulmonary embolism kills up to 100,000 annually.

“The burden of vascular diseases goes beyond lives lost and changed,” Creager said. “PAD and its associated complications cost over $200 billion annually in this country. That’s more than double the amount spent on all cancers.”

PAD is a health crisis that is largely unnoticed, Creager said, citing a recent survey that found that 75 percent of the public is unaware of PAD. Some physicians are similarly unaware.

“Physicians often do not look for PAD, chalk up leg pain to age, arthritis or general ailments. Physicians sometimes diagnose it, yet fail to treat it adequately,” Creager said. “Risk factor-modifying therapies and antiplatelet drugs are being prescribed for fewer than 20 percent of PAD patients who did not have previously established coronary or cerebrovascular disease. This oversight is not trivial.”

When studied in symptomatic PAD patients, antiplatelet and statin therapy each reduced the risk of heart attack, stroke and cardiovascular death by 25 percent. For symptomatic patients, supervised exercise training can double walking distance. Yet this proven therapy cannot be applied when PAD is not diagnosed.

“We have a long way to go in awareness, treatment and prevention to preserve vascular health,” Creager said. “I urge you to remember vascular diseases and their terrible toll. We can help save many lives and limbs by helping patients and healthcare professionals understand the threat that vascular diseases pose, as well as the importance of preventing, diagnosing and treating them.”
Loss of NOTCH1 may cause ascending aortic aneurysm

N OTCH1 mutations may play a role in the development of ascending aortic dilations that can result in aortic aneurysm and death, according to research presented Sunday at Scientific Sessions. Work in mouse models of ascending aortic aneurysm (AscAA) suggests that the loss of the signaling protein NOTCH1 may affect the development of the aorta and contribute to AscAA.

“There is an extremely high rate of mortality associated with rupture of AscAA,” said Sara Koenig, BA, a graduate research fellow in the Ohio State University Biomedical Sciences graduate program in Columbus. “Our work with mouse models suggests that Notch1 plays a developmental role in the ascending aorta, and an abnormal formation of the aorta may lead to aneurysm later in life.”

Koenig presented her work during a poster session yesterday. The research is based on earlier work by Koenig’s advisor, Vidu Garg, MD, director of the Center for Cardiovascular Research at Nationwide Children’s Hospital in Columbus. Garg discovered NOTCH1 mutations in two families with hereditary aortic valve disease. Multiple members of these two families were found to have ascending aortic dilation or AscAA. NOTCH1 is expressed in multiple cell lineages that contribute to the aorta, including endothelial and smooth muscle cells. The researchers found dysregulation of activated NOTCH1 in aneurysmal tissue both in patients with Marfan syndrome and those with bicuspid aortic valve, compared to control samples.

Using an existing Marfan syndrome mouse that is used to model AscAA helped advance the research. Deleting 50 percent of Notch1 in these mice resulted in an exacerbated aneurysm, characterized by a significant increase in aortic root dilation. A small proportion of the Notch1-deficient Marfan syndrome mice, about 0.5 percent, succumbed to rupture of the aorta, an event that was not observed in this mouse model.

“Notch1 is known to play a role in endothelial cells during cardiovascular development, so I deleted Notch1 specifically in endothelial cells in the Marfan syndrome mouse model,” Koenig said. “I saw the normal Marfan syndrome phenotype, but no excessive aortic dilation and no rupture.”

Deleting Notch1 from smooth muscle cells was similarly unsuccessful in producing the AscAA phenotype. But deleting 50 percent of Notch1 from second heart field cells did reproduce the AscAA phenotype. Notch1 deficiency in the second heart field-derived cells resulted in an increase in ascending aortic dilation compared to Marfan syndrome mice, and they succumbed to aortic rupture.

Second heart field cells are progenitor cells for the portion of the ascending aorta that typically dilates abnormally, then ruptures. The researchers’ current hypothesis is that lack of Notch1 alters the formation of aortic root, leaving it more susceptible to dilation and rupture. It is possible that the loss of Notch1 prevents the ascending aorta from responding to normal hemodynamic stressors in an appropriate manner and leaves tissue more susceptible to dilation and rupture, Koenig said.

The finding that loss of NOTCH1 is associated with AscAA could be clinically useful. While a great deal of translational work remains, it is possible that genetic screening could be used to identify individuals who carry potentially dangerous NOTCH1 mutations associated with AscAA, Koenig said.

Cardiac surgeons already use consecutive measurements of aortic dilation as an indication for resection of an AscAA. Specific groups of patients, including those with Marfan syndrome and bicuspid aortic valve, are considered to be at higher risk for aneurysm and have a lower threshold of aortic dilation for surgical intervention. Individuals with mutations in NOTCH1 could be at similar high risk and candidates for early surgery.

The next research steps are to screen AscAA patients for mutations in NOTCH1 and to analyze the pathway or pathways by which NOTCH1 regulates tissue formation to understand how lack of NOTCH1 can result in aortic dilation and rupture, Koenig said. This pathway analysis may produce therapeutic targets that might correct NOTCH1 signaling gone awry and prevent aortic dilation in susceptible individuals.

Go Red For Women®

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<td>Sat. at 12:00 p.m.</td>
<td>Concurrent Session: Women in Resuscitation Networking</td>
</tr>
<tr>
<td>Sun. at 9:45 a.m.</td>
<td>Heart Disease in South East Asians</td>
</tr>
<tr>
<td>Sun. at 3:45 p.m.</td>
<td>Gaps in Stroke Care for Women</td>
</tr>
<tr>
<td>Mon. at 2:00 p.m.</td>
<td>Gender Specific Issues in Physical Activity</td>
</tr>
<tr>
<td>Tue. at 9 a.m.</td>
<td>Gender, Race and Real World Practice with Stents</td>
</tr>
<tr>
<td>Tue. at 10:45 a.m.</td>
<td>Women’s Health in Congenital Heart Disease</td>
</tr>
<tr>
<td>Tue. at 2:45 p.m.</td>
<td>Improving Outcomes in Women’s Cardiovascular Health</td>
</tr>
<tr>
<td>Tue. at 5:30 p.m.</td>
<td>Symptoms, Status &amp; Gender Considerations in Valvular HD</td>
</tr>
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</table>

For more than a decade Go Red For Women® has fought for equal health opportunity for women. Check your daily planner for the latest updates on these sessions, and follow us @GoRedForWomen.

RESEARCH PARTNERSHIP continued from page 1
Introducing a new initiative designed to help health care providers and patients improve blood pressure control.

TAKE CONTROL TODAY. Visit heart.org/targetbp
HELP US FIND A WAY TO TAKE DOWN UNCONTROLLED BLOOD PRESSURE
INTRODUCING THE SPYRAL HTN GLOBAL CLINICAL TRIAL

Do you struggle with uncontrolled blood pressure, also called hypertension, despite lifestyle changes and medication?

Our SPYRAL HTN Global Clinical Trial Program is designed to study the potential of an investigational procedure called renal denervation to lower blood pressure for certain patients with hypertension.

You may be eligible if you’re between 20–80 years old, have a systolic blood pressure (upper number) reading between 150–180 mm Hg, and are struggling to manage your hypertension. Some patients who join the trial will be asked to stop taking their blood pressure medications temporarily, under their physicians’ supervision.

Talk to your doctor about the SPYRAL HTN Global Clinical Trial Program today or visit www.spyralhtntrials.com. Working together, let’s help solve our greatest healthcare challenges, one patient at a time.

Visit us at booth 945 to learn more!