Halting Heart-Stopping Arrhythmias

What do vigorous exercise, shocking news and alarm clocks have in common? They all cause physical or emotional stress—which for some people can prove fatal by triggering a serious heart rhythm disturbance (arrhythmia).

Arrhythmias can occur following heart attack, heart failure, stroke or use of certain medications, but most congenital heart rhythm abnormalities are linked to inherited gene mutations. Scientists at the Montefiore Einstein Center for CardioGenetics (MECC) study these genetic underpinnings.

Some genetic glitches cause a very rapid heartbeat (for example, long QT syndrome, Brugada syndrome and catecholaminergic polymorphic ventricular tachycardia syndrome). Others (sudden infant death syndrome, hereditary heart block) can make the heart beat too slowly. All can lead to sudden cardiac arrest and death,

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I n this newsletter, we focus on a major health problem: sudden cardiac death. Often with no prior warning a person collapses, the heart suddenly stops, and they lose consciousness and appear to be dead. In fact, if he or she is not resuscitated quickly, death will be the outcome.

Sudden cardiac death can have many underlying causes. One of the most common is arrhythmia—a disturbance in cardiac rate or regularity of the heartbeat. In this issue, Dr. Tom McDonald, a member of the Wilf Family Cardiovascular Research Institute at Einstein and an internationally recognized authority on arrhythmia, describes his research in this area. He explains that arrhythmias can be caused by various genetic abnormalities and also by prior heart attacks and chronic heart failure.

We also highlight several studies by members of the Wilf Family Cardiovascular Research Institute that were recently published in medical journals. And we profile Dr. Gerald Dorros, Class of 1968, who came to campus this spring to accept Einstein’s Distinguished Alumnus Award—and who, with his wife, established the Dr. Gerald and Myra Dorros Chair in Cardiovascular Disease more than a decade ago.

Cardiovascular disease research has made enormous strides in recent decades—from the discovery of cholesterol’s many forms and functions to the development of drugs that have saved millions of lives. We hope you’ll join us in our continuing quest for heart health.

RICHARD N. KITSIS, M.D.
Director, Wilf Family Cardiovascular Research Institute
Dr. Gerald and Myra Dorros Professor of Cardiovascular Disease

**Halting Heart-Stopping Arrhythmias** (continued from page 1)

says Thomas V. McDonald, M.D. (on cover), co-director of the MECC, which also provides affected families with genetic testing, treatment and genetic counseling.

**Without Warning**

People at risk for dangerous arrhythmias usually have no symptoms until a trigger creates electrical instability in the heart’s ventricles, or pumping chambers. They may then experience a racing or sluggish heartbeat, a skipped beat, shortness of breath or fainting (syncope).

Your heartbeat—the alternating contractions and relaxations of the heart—depends on the coordinated action of ions. These electrically charged atoms of potassium, sodium and calcium flow through ion channels in the membranes of heart muscle cells, explains Dr. McDonald, who is also a professor of medicine (cardiology) and of molecular pharmacology at Einstein and an attending cardiologist at Montefiore, the University Hospital and academic medical center for Einstein.

**Genetic Origins**

Genetic defects associated with potentially fatal arrhythmias cause the proteins that help build ion channels and regulate the rate at which ions flow through the channels to malfunction. The resulting gain or loss of ion channel function affects the “action potential” of heart muscle cells—the time it takes cells to change from a resting state (when the heart relaxes between beats) to an excited state (when the heart contracts) and back again.

Dr. McDonald has studied mutations of the human ether-a-go-go-related gene (hERG) and the KCNQ1 gene. These potentially fatal mutations abnormally prolong the excited (contracting) state of heart muscle cells. This causes heart muscle to become fatigued and quiver weakly until no longer able to pump oxygenated blood to the brain.

By identifying people with these gene mutations, doctors can prescribe drugs to prevent arrhythmias from occurring. “Genetic analysis enables us to better tailor medicines and lifestyle recommendations for patients with specific mutations to reduce the risk of potentially fatal rhythm disturbances,” says Dr. McDonald.

For instance, while patients with hERG and KCNQ1 mutations can be treated successfully with beta-blockers to prevent arrhythmias from occurring, those with different mutations that cause a severe and dominant malfunction of ion channels must be treated more aggressively with pacemakers or implantable cardiac defibrillators, he says. These can help control certain heart rhythm problems and may be the best option for a patient who doesn’t respond to other interventions.

**Q&A**

Q: Sudden infant death syndrome (SIDS) is associated with accidental suffocation, but research also points to congenital defects affecting heart rhythm as factors. Should parents continue to follow SIDS prevention recommendations?

A: SIDS is not a diagnosis but rather an umbrella term for the sudden death of a seemingly healthy infant less than a year old. There are several theories about what causes SIDS, and emerging research suggests that up to 13 percent of cases could be attributable to a genetic defect that causes heart rhythm problems. To reduce the risk of avoidable suffocation, parents should continue to follow the American Academy of Pediatrics SIDS prevention recommendations: lay a baby down to sleep on his or her back; place a baby to sleep on a firm surface; don’t let a baby sleep in the parents’ bed; and remove fluffy or loose bedding and plush toys from the crib.
Stem Cells for Chagasic Heart Failure

David C. Spray, Ph.D.
Professor, Dominick P. Purpura
Department of Neuroscience
Professor, Department of Medicine (Cardiology)

Chagas disease can occur when people are bitten by bugs that carry the single-cell parasite Trypanosoma cruzi. The chronic phase of the infection can lead to heart failure. Current treatment options are limited, and heart transplant has often been the only option for people with chagasic heart failure.

Stem cells derived from bone marrow (MSCs) have anti-inflammatory properties that might help in treating this disease. Using MSCs tagged with fluorescent nanoparticles so the researchers could see them, Dr. Spray and his colleagues tagged bone marrow stem cells with fluorescent nanoparticles to make them stand out under the microscope. They then transplanted these cells into a mouse model of Chagas disease and found that the animals’ heart failure improved—suggesting that people with the disease might also benefit from transplanted MSCs. The study was published in a 2012 issue of PLOS Neglected Tropical Diseases.
Einstein alumnus Gerald Dorros was one of the first American physicians to perform coronary angioplasty.

After graduating from Einstein, he became board certified in internal medicine and eventually ended up at the Texas Heart Institute in Houston. While learning the art of cardiac catheterization there, he received a phone call from his father telling him about a new procedure called coronary angioplasty. “He’d seen this crazy thing on TV where they blew up balloons in the coronary arteries and people got better,” Dr. Dorros recalls.

In August 1978, Dr. Dorros went to the Mayo Clinic to hear a talk by Richard Myler, M.D., one of the first two American doctors to perform coronary angioplasty. “That night, I awoke and had an epiphany: ‘This is what I’m going to do,’” says Dr. Dorros.

Back then, doctors inflated their angioplasty balloons using fluid from large tanks. “I figured there was an easier way,” he says. He and a partner developed a small portable inflation device—a 3 cc plastic syringe—that inflated the balloons with a contrast solution. By the end of 1978, Dr. Dorros had used his balloon on two patients, becoming the third U.S. doctor to perform the procedure.

Soon, he and partner Simon Stertzer, M.D., formed the company Arterial Vascular Engineering (AVE) and developed a balloon catheter with improved mechanical characteristics. Then they attached a stent. Dr. Dorros subsequently performed tens of thousands of angioplasty and stent procedures and traveled the world to teach and operate. He extended balloon and stent therapy to the peripheral arteries—below the knee and in the renal, subclavian, aortic and carotid vessels.

Meanwhile, AVE had become the world’s dominant stent company; it was acquired by Medtronic in 1997. The following year, Dr. Dorros called Einstein’s then-dean, Dominick P. Purpura, M.D., to ask if he and his wife could endow a chair at Einstein. Richard N. Kitsis, M.D., now holds the Dr. Gerald and Myra Dorros Chair in Cardiovascular Disease.

Dr. Dorros remains involved with several other medical-device companies and is currently the medical director of the Isadore Feuer-William Dorros Interventional Cardiovascular Disease Foundation, Ltd. He joined the Einstein Board of Overseers in 2001 and visited campus this spring to accept the 2013 Dominick P. Purpura Distinguished Alumnus Award, presented to him by Allen M. Spiegel, M.D., Einstein’s Marilyn and Stanley M. Katz Dean.