

FOR RELEASE:
4 p.m. EST, Thursday
December 23, 2004

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American Heart Association 2004 year-end report:

American Heart Association's top 10 advances for 2004 include first implantable heart, heart failure pill for blacks

DALLAS, Dec. 23 –The first implantable artificial heart and a drug that dramatically improves survival in black heart failure patients are among the top 10 research advances in heart disease and stroke for 2004, says Alice Jacobs, M.D., president of the American Heart Association.

Other major milestones include the use of a less invasive angioplasty technique for stroke prevention and a pill that fights smoking and overeating.

Created in 1996, the American Heart Association's Top 10 list highlights major gains in heart disease and stroke research.

1. First implantable artificial heart approved. The United States Food and Drug Administration (FDA) approved the first implantable artificial heart, which keeps heart failure patients alive until they can receive a transplant.

A direct descendant of the Jarvik-7, implanted into dentist Barney Clark in 1982, the CardioWest Total Artificial Heart takes over a patient's failing ventricles, the heart's lower two pumping chambers and all cardiac valves. Manufactured by Syncardia Systems Inc., of Tucson, Ariz., the device is a "bridge" for people waiting for a heart transplant who do not respond to other treatments and who are at risk of imminent death from non-reversible bi-ventricular failure (left and right side heart failure).

The FDA approval was based in large part on the results of a study of the artificial heart in 81 patients at high risk for death due to irreversible biventricular cardiac failure. The rate of survival to transplantation was 79 percent, compared with 46 percent in a group of control patients who did not receive the artificial heart. The one-year survival rate among patients who received the artificial heart was 70 percent, compared with 31 percent among the controls. The one and five year survival rates among transplant recipients were 86 percent and 64 percent.

Sources: *The New England Journal of Medicine*, Aug. 26, 2004. www.nejm.org; www.fda.gov

2. Nitric oxide-boosting drug improves heart failure survival among blacks. Adding the experimental drug BiDil to standard therapy dramatically improved survival among black heart failure patients, according to the first major trial to test a drug only in Africans Americans.

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The researchers studied 1,050 blacks suffering from heart failure, a progressive breakdown of heart muscle. Patients were given either standard therapy plus BiDil or standard therapy plus placebo.

The combination treatment was associated with a 43 percent decrease in the rate of death, a 33 percent reduction in first hospitalizations for heart failures, and a significant improvement in the quality of life, compared with standard therapy alone, researchers said. Results were so overwhelming that researchers terminated the study to offer all patients the drug.

Made by NitroMed, BiDil is a combination of two older drugs, isosorbide dinitrate and hydralazine, that boost the level of nitric oxide in the blood. Nitric oxide widens blood vessels and hampers the progressive slackening of the heart muscle.

Source: American Heart Association's Scientific Sessions, November 2004.

www.scientificsessions.org: *The New England Journal of Medicine*, Nov. 11, 2004.

www.nejm.org

3. One-two punch opens blocked brain vessels faster. By itself, tissue plasminogen activator (tPA) effectively dissolves clots that can cause an acute ischemic stroke. But using ultrasonography via continuous transcranial Doppler, in combination with tPA improves the drug's clot-busting abilities, leading to even better clinical responses, a study 2004 study showed.

The researchers studied 126 stroke patients with blockage of the middle cerebral artery: Half got tPA alone and the other half received tPA plus ultrasonography, a non-invasive test that uses sound waves to measure blood flow velocity in large arteries.

Within two hours after therapy began, 49 percent of patients who received continuous ultrasound and tPA showed dramatic clinical improvement, with little or no blockage, compared with 30 percent who received tPA alone. Additionally at two hours after administration of the tPA bolus, sustained recanalization occurred in 38 percent of the tPA ultrasound group and 13 percent of the tPA only group. Bleeding in the brain — the major safety concern — was experienced by 4.8 percent of patients in both groups.

Ultrasound causes the molecules on and within clots to vibrate, which in turn creates more binding sites for tPA and improves drug transport to the clot, the researchers said. As a result, more blocked vessels open up — and open faster — than with tPA alone, they hypothesized.

Source: *The New England Journal of Medicine*, Nov. 18, 2004. www.nejm.org

4. Less invasive technique as effective as surgery for stroke prevention. Patients at high risk of stroke due to fatty blockages in the arteries leading to the brain can benefit from a refined angioplasty procedure, researchers reported in 2004.

Angioplasty, which involves inserting a balloon and installing a stent to widen the blood vessel, has not traditionally been used to widen cerebral arteries. Stents can jab against the walls

of the blood vessels, causing fatty debris to break off and enter the bloodstream. If the debris travels to and lodges in a blood vessel to the brain, the result can be a stroke or a short-term blockage of blood flow known as a transient ischemic attack.

The new technique circumvents that problem by using a small filter that catches loose bits of plaque before they have a chance to migrate to the brain.

Researchers studied 334 patients with clogged carotid arteries, the main blood vessels to the brain. About half had a standard operation to widen blocked neck arteries called carotid endarterectomy; the others underwent the refined angioplasty technique.

By one year after their procedure, the rate of death, heart attack and stroke was significantly lower in those who underwent the new procedure (12.2 percent) than in those who underwent carotid endarterectomy (20.1 percent). Only 0.6 percent of those who had received angioplasty needed a repeat procedure, compared with 4.3 percent of those who got surgery.

Source: *The New England Journal of Medicine*, Oct. 7, 2004. www.nejm.org

5. Artificial blood vessels work like the real thing. Researchers reported that this year they were able to create long lasting functional blood vessels by implanting two types of cells (endothelial cells that line the inner walls of the blood vessels and cells from the outer layer of the blood vessels), into a collagen gel, and then implanting them into mice. Prior techniques to enhance survival and growth of vascular cells has involved the use of genes that might prove oncogenic.

The blood vessels created by this technique had greater stability and formed long, branching tubes that connected with the mice's own blood vessels. As they matured, they began carrying blood. In contrast, gels that contain only endothelial cells typically fail within 60 days. This technique will help scientists create artificially grown blood vessels which can aid the further study of vessel growth and maturation, and critical factors in the workings of vascular beds.

Source: *Nature*, March 11, 2004. www.nature.com

6. Public defibrillators a lifesaver for cardiac arrest victims. Training volunteers to use defibrillators distributed in shopping malls, sports venues and other public places can double the survival rate of cardiac arrest victims, researchers reported in 2004.

Each year, about 460,000 Americans die from cardiac arrest, which usually strikes without warning. Paramedics and firefighters are trained to use defibrillators to shock victims' hearts back to normal rhythm— but emergency rescue personnel must arrive in time. With only a five- to 10-minute window of opportunity, most do not.

In the new study, defibrillators were placed in key locales at nearly 1,000 shopping centers, recreation centers, apartment complexes, entertainment complexes and community centers in 24 cities across the United States and Canada. About 20,000 volunteers were then taught to do CPR; half were also taught how to use the defibrillators.

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During the next two years, the volunteers attempted to resuscitate 235 cardiac arrest victims. Those treated by the volunteers who used defibrillators plus cardiopulmonary resuscitation were twice as likely to survive to hospital discharge (29 of 107), compared with those who were treated by volunteers who did CPR alone (15 of 128).

The results are so encouraging that they are expected to jumpstart efforts to get more defibrillators in public spaces and additional volunteers trained, researchers said.

Source: *The New England Journal of Medicine*, Aug. 12, 2004. www.nejm.com

7. Preventing birth defects — in the womb. Researchers reported this year that they can identify infants at high risk of a serious heart defect and then correct the problem — while the fetus is still in the womb.

The researchers studied 24 babies at risk of hypoplastic left heart syndrome (HLHS) due to fetal aortic stenosis, narrowing of the aortic valve that makes it hard for the heart to pump blood to the rest of the body.

In HLHS, the left side of the heart — the heart's main pumping chamber — is underdeveloped and unable to keep blood circulating after birth. Without treatment -- typically a series of surgeries -- the defect is usually fatal within the first several days after birth.

The researchers offered a procedure to open the narrowed aortic valves to all 24 mothers; 20 accepted. Of those, 14 procedures were a success and the fetal hearts continued to develop.

While the researchers must wait and see if the procedure results in normal heart function and anatomy at birth, the opportunity to save babies identified in utero as being at high risk of heart defects will be one of the most exciting fields in congenital heart disease in the coming years, specialists said.

Source: *Circulation*, Oct. 12, 2004. <http://circ.ahajournals.org/>

8. Genetic screening for heart disease a step closer to reality. This year, researchers uncovered three new mutations in MEF2A, the same gene they directly linked to heart attacks in 2003.

The MEF2A gene plays a role in protecting artery walls from building up plaque that can impede blood flow and lead to heart attacks.

In the new study, the researchers detected the three mutations in four of 207 people with coronary artery disease. In contrast, it wasn't found in any of 191 people with no signs of heart disease.

The results suggest that nearly 2 percent of people with coronary artery disease — the equivalent of hundreds of thousands of Americans — may carry a MEF2A mutation.

In the near future, genetic testing for MEF2A mutations may help to pinpoint patients at increased risk of coronary artery disease before symptoms develop, he said. That will give doctors time to offer aggressive lifestyle changes and medication to offset the risk.

Source: *Human Molecular Genetics*, October 2004. <http://www.hum-molgen.de/journals/HMG>

9. Human heart, repair thyself. Two years ago, the field of heart medicine received a shock when researchers reported that the human heart can generate new muscle cells. This year, scientists took the work a step further, reporting at American Heart Association Scientific Sessions 2004 that the human heart contains stem cells that can generate muscle cells and other cells — moreover; these cardiac stem cells can regenerate heart tissue after a heart attack.

The recognition that the human heart possesses these characteristics dramatically changes the traditional view, suggesting that the heart, like bone marrow, skin and liver, is self-renewing.

The new work shows that cardiac stem cells can be isolated from small fragments of human muscle and expanded in the lab. Theoretically, the laboratory-grown stem cells can be returned to the same patient to stimulate the growth of new heart muscle and repair the injured heart. This opens enormous therapeutic opportunities for treating heart failure, which affects over 5 million Americans.

Source: American Heart Association Scientific Sessions, November 2004. www.scientificsessions.org

10. One drug tackles two harmful habits. Researchers reported that rimonabant, the diet drug, packs a double whammy against obesity and smoking.

In one study of 787 smokers who failed in previous attempts to quit smoking, 28 percent kicked the habit for at least a month, compared with 16 percent on placebo.

In a study of 3,040 overweight patients, those who got the higher dose of rimonabant achieved and maintained a weight loss of 19 pounds, compared with five pounds in the control group.

The research also showed that the drug improves symptoms of metabolic syndrome, a group of risk factors that greatly increase the risk for heart disease and/or diabetes. For example, levels of high-density lipoprotein (HDL), or good cholesterol, rose 25 percent and triglycerides fell 10 percent in the rimonabant arm of the trial.

The pill, which will be sold under the brand name Acomplia, attacks addictive behavior by blocking a pleasure center in the brain. Manufacturer Sanofi-Aventis hopes to apply for Food and Drug Administration approval in 2005.

Sources: American College of Cardiology meeting, March 2004. American Heart Association Scientific Sessions, November 2004. www.scientificsessions.org

Statements and conclusions of study authors that are published in the American Heart Association scientific journals are solely those of the study authors and do not necessarily reflect association policy or position. The American Heart Association makes no representation or warranty as to their accuracy or reliability.

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