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New Federally Funded Research Program Aims to Improve Survival from Cardiac Arrest and Severe Trauma

A young mother is unconscious and bleeding from internal injuries caused by a highway accident. A soldier is severely injured in a roadside explosion. A 50-year-old man suffers a cardiac arrest as he gets ready for work. For the "real" counterparts of these made-up case histories, the chance of survival from life-threatening injury and cardiac arrest is dismally low. Many more could survive if only they could be sustained long enough to reach a hospital alive. However, most cardiac arrest victims die before they reach the hospital, and traumatic injury is a top killer in North America. With the launch of a massive research program funded by the National Institutes of Health (NIH) and other federal and Canadian agencies, scientists hope to learn the best ways to improve survival chances from cardiac arrest and severe trauma.

The "Resuscitation Outcomes Consortium" (ROC) will conduct collaborative clinical trials of promising new treatments for cardiac arrest (the stopping of the heartbeat) and severe traumatic injury. Along with Emergency Medical Services (EMS) agencies, ROC will involve public safety agencies, regional hospitals, community healthcare institutions and medical centers in 11 regions in the United States and Canada and as many as 15,000 patients over a 3-year period. Communities involved in ROC will learn about the study in a comprehensive community education effort to be conducted over the next 6 months to a year.

"Surviving traumatic injury and cardiac arrest is a serious public health issue. Tens of thousands of Americans die each year from sudden cardiac arrest and trauma. The good news is that there is a growing body of research – basic research and small studies -- that suggests a significant number of these people can be saved," said Elizabeth G. Nabel, M.D., director of the National Heart, Lung, and Blood Institute (NHLBI) of the NIH, the lead federal sponsor of the research effort.

Other funding agencies include the U.S. Department of Defense, the NIH's National Institute of Neurological Disorders and Stroke, the Institute of Circulatory and Respiratory Health of the Canadian Institutes of Health Research, Defence Research and Development Canada, the Heart and Stroke Foundation of Canada, and the American Heart Association. The initial funding commitment to the Consortium is $50 million.

"This is the first time we have used large-scale clinical trials to improve the treatment of patients with traumatic injury and cardiac arrest. Similar studies in patients with heart attack and heart failure have answered questions about the best treatments. As a result, we've seen greatly improved survival for these disorders. That's what we want to do with cardiac arrest and traumatic injury," said Myron Weisfeldt, M.D., professor and chair of internal medicine at Johns Hopkins University and chair of the steering committee for the research effort.

All of the interventions to be tested in the new program will have been shown in smaller, single center studies to be safe and to potentially have a life-saving effect. According to Weisfeldt, the Consortium's testing of new techniques will provide the large-scale proof of effectiveness needed to support widespread adoption and use.

An important goal of the ROC will be the evaluation of interventions in terms of benefit to cognitive outcomes, as the ultimate goal of resuscitation is to return victims to their prior functional capacity.

The first treatments to be tested will be highly concentrated forms of a saline solution similar to the body's own fluids. Typically, in the crucial early minutes before blood transfusions can be safely administered in hospital, trauma patients receive normal saline solution intravenously in the field to compensate for blood loss and buy time. In the new trial, trauma patients with either signs of blood loss or severe brain injury will receive one of three saline solutions -- standard normal saline, high concentration saline, or high concentration saline with dextran, a circulation-enhancing substance. The two concentrated solutions are designed to compensate for blood loss more effectively, lessen excessive inflammatory responses and prevent brain swelling. These effects in turn could potentially lead to a reduction in organ failure for patients with major blood loss and improved function for patients with brain injury.

The second study will test a device to enhance blood flow during CPR. This device is a one-way valve that fits between the airbag used to introduce air into a person in cardiac arrest and the flexible plastic tube that goes through the nose or mouth and into the lungs to help with breathing. The valve can also be used with a facemask that goes over the patient's nose and mouth. During CPR, the one-way valve creates a small vacuum inside the patient's chest, which increases the return flow of blood to the heart.

Other possible future studies include testing of new drug approaches to aid resuscitation from cardiac arrest and evaluation of novel strategies to control hemorrhage.

There are an estimated 330,000 out-of-hospital cardiac deaths each year in the United States. Most of these are from sudden cardiac arrest, although the exact numbers are not known. In cardiac arrest, the heart stops beating effectively, blood does not circulate and no pulse can be felt. The victim collapses suddenly into unconsciousness. Heart attacks, which are caused by a blockage of a coronary artery, can sometimes lead to cardiac arrest. A common underlying cause of sudden cardiac arrest is an abrupt disorganization of the heart's rhythm called ventricular fibrillation, which can be triggered by a heart attack or can just represent a catastrophic rhythm disturbance. Unless cardiac arrest victims are treated within minutes (by defibrillation to shock an abnormally beating heart back into normal rhythm or CPR followed by or in conjunction with other procedures), they will die.

Severe injury is also a major public health problem. It is the number one killer of both children and young adults up to age 44. As a disease of young people, it is also the leading cause of life years lost. In 2002, there were over 161,000 fatal injuries in the United States. The leading causes of death following injury are brain injury, blood loss, and organ failure from excessive inflammation.

In addition to rigorous review by an NHLBI-convened independent review group, the clinical trials of the new Consortium will be conducted under strict FDA guidelines that allow for patients in life-threatening situations to participate in research without individual consent at enrollment. The guidelines specify criteria that must be followed for a study to have an exception from informed consent. These include:

- Approval by an institutional review board (IRB), a committee of experts and lay people established to review research.
- Consultation with the community.
- Public disclosure of the study's design before the study begins and when the study is over to share results.
- Notification of patients who were involved in the research.
- Oversight by an independent group of experts charged with monitoring the research for safety.

Each site's IRB will decide how best to inform the community, recommending approaches that might include town meetings, newspaper notices, random digit dialing surveys, and meetings with

groups at high risk of either cardiac arrest or trauma – such as local motorcycle clubs. In order to inform future studies involving exceptions from informed consent, the community consultation process used in ROC will be evaluated in at least one ancillary study.

“There is a high probability of benefit for patients participating in these trials,” said Joseph Ornato, M.D., the Consortium’s co-chair for cardiac arrest and chairman of the Department of Emergency Medicine at the Virginia Commonwealth University Medical Center in Richmond, VA. “Not only have these therapies been shown to be potentially life-saving, but also EMS personnel involved in the research will be trained in the most up-to-date and effective methods of emergency treatment.”

According to Tracey Hoke, M.D., Sc.M., NHLBI project officer for the ROC, “A federal exception of informed consent can only be granted when patients are in a life-threatening situation, when obtaining individual informed consent is impossible, and when current therapy is unproven or unsatisfactory. The most critical stipulation of the exception is that there must be the potential for direct benefit to the patients enrolled. In the case of ROC, this means that preliminary evidence of direct survival benefit must be shown prior to the development of any trial.”

“These initial studies, and those that follow, will change the way all providers of trauma care, military and civilian, care for the most critically injured,” said COL John Holcomb, MD, the consortium co-chair for trauma, and the Commander of the US Army Institute of Surgical Research, San Antonio, TX. “For the first time we will know, based on large and well designed studies, what interventions really make a difference.”

In a typical study scenario, a first responder will arrive at the scene of the cardiac arrest or trauma and confirm the patient’s diagnosis. The emergency medical technician (EMT) will then assess whether the patient meets the entrance criteria for the study and if so, treat the patient with the study intervention.

Since the studies will be blinded, the EMTs in the field will not know which treatment the patient receives. For example, in the first consortium study testing the concentrated saline solutions, all solutions of saline to be administered to patients will look alike, although they will be numbered for later identification and analysis by the study’s scientists.

In addition to the clinical trials, the Consortium is also currently enrolling patients into a database of all cardiac arrest and trauma events. “This is the first multi-city comprehensive database with information about how field treatment leads to patient survival,” said George Sopko, M.D., deputy project officer on the study and a medical officer with NHLBI.

The study is coordinated by investigators at the University of Washington, Seattle, Principal Investigator: Al Hallstrom, Ph.D.

The participating cities include:

- Birmingham, AL: The Alabama Resuscitation Center is coordinated through the University of Alabama at Birmingham (Central and possibly Northern Alabama). Principal Investigator: Tom Terndrup, M.D.

- Dallas, TX: The Dallas Center for Resuscitation Research is coordinated through the University of Texas Southwestern Medical Center (Dallas and surrounding cities to participate). Principal Investigator: Ahamed Idris, M.D.

- Iowa City, IA: The University of Iowa Carver College of Medicine-Iowa Resuscitation Network is coordinated through the University of Iowa (includes 10 cities throughout Iowa). Principal Investigator: Richard Kerber, M.D.

- Milwaukee, WI: The Milwaukee Resuscitation Research Center is coordinated through the Medical College of Wisconsin. Principal Investigator: Tom Aufderheide, M.D.

•Ottawa, Ontario/Vancouver, BC (counts as two regions): The University of Ottawa/University of British Columbia Collaborative RCC is coordinated through the Ottawa Health Research Institute, University of Ottawa, Ontario and St. Paul's Hospital, University of British Columbia (includes additional 20 cities). Principal Investigator: Ian Stiell, M.D., Co-Principal Investigator: Jim Christenson, M.D.

•Pittsburgh, PA: The Pittsburgh Resuscitation Network is coordinated through the University of Pittsburgh Medical Center (includes several suburbs). Principal Investigator: Clif Callaway, M.D., Ph.D.

•Portland, OR: The Portland Resuscitation Outcomes Consortium is coordinated through the Oregon Health and Science University (includes 4 counties). Principal Investigator: Jerris R. Hedges, M.D., MS.

•San Diego, CA: The UCSD-San Diego Resuscitation Research Center is coordinated through the University of California, San Diego (entire county). Principal Investigator: David Hoyt, M.D.

•Seattle and King County, WA: Seattle-King County Center for Resuscitation Research at the University of Washington. Principal investigator: Peter Kudenchuk, M.D.

•Toronto, Ontario: The Toronto Regional Resuscitation Research out of hospital Network is coordinated through the University of Toronto (includes areas surrounding Toronto). Principal Investigator: Arthur Slutsky, M.D., Co-Principal Investigators: Laurie Morrison, M.D. and Paul Dorian, M.D.

To interview NHLBI's Dr. Tracey Hoke, ROC project officer or NHLBI's Dr. George Sopko, ROC deputy project officer, contact the NHLBI Communications Office at 301-496-4236. To interview Dr. Weisfeldt, call David March, Media Relations and Public Affairs, Johns Hopkins Medicine at 410-955-1534. To interview Dr. Ornato, call 804-828-7184. To interview COL Holcomb, call 210-916-916-2720.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at: www.nhlbi.nih.gov.

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