Workshop Executive Summary Report: Post-Resuscitative and Initial Utility in Life Saving Efforts (PULSE)
June 29–30, 2000; Lansdowne Resort and Conference Center; Leesburg, Va

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The Post-Resuscitative and Initial Utility in Life Saving Efforts (PULSE) workshop was convened in recognition of the estimated loss of >1000 useful lives each day in the United States as a result of poor cardiopulmonary and trauma resuscitation outcomes. The purpose of the workshop was to provide an interdisciplinary forum on promising and novel life-saving therapies in settings of cardiac, hypoxic, and traumatic arrest and to identify the most promising new directions in cardiopulmonary and trauma resuscitation research. It was organized under a multiagency initiative supported by the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Child Health and Human Development (NICHD), the National Institute of General Medical Sciences (NIGMS), and the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health, together with the Food and Drug Administration (FDA), each within the Department of Health and Human Services (DHHS) and the Department of Defense (DOD). The workshop, which was held in the Lansdowne Conference Center in Leesburg, Virginia from June 29 to 30, 2000, provided the unique opportunity to convene domestic and international experts to chart a new course for future resuscitation research.

Optimism That Many More Lives Can Be Saved
Conference participants believed that the world stands at the verge of new therapies and technologies that could save thousands of lives that are currently lost after traumatic injury and circulatory or hypoxic arrest. Two broad strategies should be aggressively pursued. First, existing therapies known to restore circulation, shorten the period of ischemia, and save lives should be refined to allow more rapid and more widespread deployment. Earlier and better cardiopulmonary resuscitation (CPR), rapid defibrillation, and early control of hemorrhage will lead to immediate improvement in survival. Second, basic and applied research with the goal of identifying new therapies to minimize global ischemic insults should be expanded.

Participants were optimistic that in the near future we will develop new resuscitation strategies, devices, and therapies that will be life saving for patients who fall outside of the “effectiveness window” of current treatments. Data from human survivors of “intractable” ventricular fibrillation reveal that lives can be saved beyond the usual time limits. Cellular and tissue survival can now be significantly extended after previously “lethal” ischemia; however, the human use of such therapy awaits further research before translation into practice. Collectively, the scientific evidence suggests that new treatments will dramatically increase the number of lives saved.

We applauded earlier emphasis on focal or regional ischemia, including myocardial infarction and stroke. However, we now urge a recognition of the need to address the unique pathophysiology and options for improved treatment after global ischemia involving multiple regions and the entire body. New therapeutic interventions designed specifically to reduce ischemic reperfusion injury after the restoration of blood flow are likely to come from the frontiers of molecular medicine, basic cardiovascular sciences, neurosciences, pharmacology, and epidemiology. New diagnostic techniques and technological advances, including device development, will be critical to this effort. Diverse disciplines, including the basic sciences, clinical sciences, and biomedical engineering, should be integrated to improve our understanding of resuscitation physiology and the translation of new insights into life-saving medical practices.

To advance the science and technology of saving lives, we recommend the following specific action items, which are most likely to produce a high yield in the near future.
Specific Action Items

Expand Basic, Translational, and Applied Focused Research and Device Development

Basic, translational, and applied focused research and device development should be expanded through new research initiatives, including collaborative and integrated research projects unifying basic and applied scientists. The focus should be on mechanisms of cellular injury and options for restoring the cell to normalcy after circulatory arrest and whole-body ischemia. Novel basic science and molecular genetic approaches to resuscitation are needed to improve the understanding of critical mechanisms of injury during and after whole-body ischemia; this will lead to new therapeutic interventions.

The concept of whole-body reperfusion injury is paramount; it will prompt the development of integrated therapies and may even justify delaying defibrillation in specific ischemic settings. Subjects of special interest include the following: (1) cellular signaling processes, ionic control, and altered gene expression, induction, and regulation that lead to or are consequences of the activation of mediators of toxicity during global ischemia and in settings of reperfusion; (2) vascular control mechanisms during and after global ischemia and their pharmacological modification; (3) molecular mechanisms underlying biological models of tolerance to ischemia leading to recovery, including hibernation, arousal from hibernation, hypothermia, preconditioning, neonatal stress, and circulatory shock; and (4) an improved understanding of cardiopulmonary interactions during low flow states.

Progress in managing traumatic injuries will follow a better understanding of (1) hemostasis at the site of injury, (2) pharmacological means for regional vasoconstriction, (3) the effects of traumatic injury on cardiopulmonary function and hemodynamic responses, and (4) the effect of fluid and blood flow management on the global tolerance of tissue hypoxia.

These efforts should lead to translational research that will directly identify the optimal conditions, fluids, and drugs for use during cardiopulmonary and post-traumatic resuscitation.

Establish an International Clinical Trials Network

An international clinical trials network should be established to facilitate serial studies on out-of-hospital cardiopulmonary resuscitation and trauma and to provide centralized coordination of protocols, data management, and common endpoints. Immediate research priorities include (1) a randomized trial of the early use of amiodarone after failed defibrillation and (2) national registries on clinical cardiac and trauma research, with an emphasis on the uniformity of prehospital data collection and the characterization of injuries and their severity, initial management, and outcomes.

Other clinical studies of high priority include the following: (1) comparing vasoactive drugs such as vasopressin and epinephrine against placebo during cardiac arrest; (2) studying initial versus delayed external ventilation maneuvers; (3) determining the role of mechanical resuscitation devices and airway adjuncts; (4) examining intravascular fluid management after cardiac arrest or after the onset of the circulatory shock that follows traumatic injuries; (5) optimizing educational programs for lay and professional caregivers; and (6) beginning a multicenter trial of the rapid induction of moderate hypothermia during and after cardiopulmonary arrest based on technical advances in technologies for inducing hypothermia.

Improve Technology-Based Methodologies for Monitoring and Performing Resuscitation

Technology-based methodologies for monitoring and performing resuscitation should be improved. Such improvements would include (1) biosensors to acquire and monitor critical “real time” physiological data during resuscitation; (2) methods for rapid induction of controlled, moderate hypothermia during resuscitation; (3) methods to improve rapid vascular access; (4) cardiac arrest alert and defibrillation technologies for broad public use; and (5) new and novel devices to produce blood flow during cardiac arrest. The development of new technologies will require the participation of basic and translational scientists, biotechnology experts, creative engineering talents, and preclinical animal testing.

Promote Multidisciplinary Communications and Collaboration

Multidisciplinary communications and collaboration among investigators and federal funding agencies should be promoted to advance resuscitation research more rapidly to improve outcomes. We should thus emphasize Internet-based communications, support registries that document clinical experiences, communicate the deliberations of national organizations, and support interdisciplinary resuscitation meetings. The community of resuscitation researchers representing diverse disciplines should be identified and encouraged to communicate more broadly, including the use of the key word “resuscitation” in publications. Finally, special targeted efforts are justified to overcome administrative restraints on life-saving research.

Appendix

Planning Task Force

Chairmen: Myron Weisfeldt, MD, Columbia University, New York, NY, and Robert Wise, MD, The Johns Hopkins University, Baltimore, Md. Committee: Barbara Alving, MD, National Heart Lung Blood Institute, Bethesda, Md; Lance Becker, MD, The University of Chicago, Chicago, Ill; Jeffrey Blumer, MD, Case Western Reserve University, Cleveland, Ohio; Roberto Bolli, MD, University of Louisville, Louisville, Ky; Gerald Buckberg, MD, University of California, Los Angeles, Calif; Thomas Budinger, MD, PhD, University of California, Berkeley, Calif; Wally Carlo, MD, University of Alabama, Birmingham, Ala; Lawton Cooper, MD, National Heart Lung Blood Institute, Bethesda, Md; Richard Cummins, University of Washington, Seattle, Wash; Avroy Fanaroff, MD, Western Reserve University, Cleveland, Ohio; Henry Halperin, MD, The Johns Hopkins University, Baltimore, Md; Richard Kerber, MD, University of Iowa, Iowa City, Iowa; Karl Kern, MD, University of Arizona, Tucson, Ariz; Donald Landry, MD, Columbia University, New York, NY; David Lathrop, PhD, National Heart, Lung, and Blood Institute, Bethesda, Md; John Marler, MD, Columbia University, National Institute of Neurological Disorders and Stroke, Bethesda, Md; Graham Nichol, MD, University of Ottawa, Ottawa, Ontario, Canada; Susan Nizmeyer, MD, University of Colorado, Denver, Co; Pearl O’Rourke, MD, National Institutes of Health, Bethesda, Md; Paul Pepe, MD, University of Texas, Dallas, Tex; Jeffrey Perlman, MD,
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