INTRODUCTION

Permanent brain damage caused by ischemia and reperfusion that results from disease processes such as stroke and cardiac arrest (CA) with resuscitation has been estimated to affect approx 200,000 patients in the United States annually (1). Neuronal damage from stroke and CA occur by different mechanistic models of injury. In ischemic stroke, only a portion of the brain is at risk, and the ischemia is only complete in the center of the vulnerable area. This central area of dense ischemia is surrounded by a penumbral zone in which blood flow is diminished but not completely lost. As opposed to CA with resuscitation, flow ceases altogether and the entire brain is at risk for a transient period of complete ischemia followed by reperfusion (2).

Neuronal impairment after ischemia and reperfusion from CA is determined by many elements, including arrest (no-flow) time, resuscitation (low-flow) time, reperfusion (no-flow, hyperemic phase, and global and multifocal hypoperfusion) severity, and temperature. The enormous significance of the postresuscitation phase for long-term outcome is often underestimated. Nevertheless, the time from onset of cardiopulmonary arrest (CPA) until restoration of an effective spontaneous circulation is, probably the single most vital determinant of long-term, neurologically intact survival from CPA. The majority of neuronal-injuring processes occur not during the actual CA or resuscitation but throughout reperfusion.

The idea of cerebral resuscitation was first introduced by Peter Safar in the 1970s and started with the concept of “brains too good to die” after cardiac standstill (3). Despite
all the marvelous and exciting improvement in resuscitation techniques in the last few decades, neurological recovery continues to be the major limiting factor in acquiring a meaningful quality of life postresuscitation. Cerebral injury occurring after CA and resuscitation becomes a primary focus in the management priorities in the postresuscitation phase of care. Unfortunately, recent estimates show that only 3–10% of cardiopulmonary resuscitation (CPR) attempts outside of the hospital setting result in survival without brain damage (4,5). The poor tolerance of neurons to global ischemia accounts for much of the morbidity and mortality associated with CA. Additionally, in the last two decades, research focused on amelioration of neuronal injury has been extensive but at best frustrating, principally because the mechanisms responsible for the injury caused by cerebral ischemia and reperfusion are extremely complicated and multifactorial in nature and not yet entirely understood.

In addition to cerebral dysfunction following global ischemia, other factors contribute to the morbidity and mortality after CA, which may hinder recuperation from neuronal injury. These include cardiovascular and hemodynamic derangements, respiratory insufficiency, and hyperthermia, all of which are common after the return of spontaneous circulation (ROSC (6,7)). Although the multiorgan dysfunction syndrome from other causes such as hemorrhagic or septic shock has been linked by an intermediary state termed systemic inflammatory response syndrome (SIRS), there is limited evidence for a clear relationship between that syndrome and the postresuscitation syndrome (8,9). Instead, it appears more likely that protracted derangements of hemodynamic and respiratory function, many of which may be iatrogenic in nature, in the postresuscitation period are fundamentally responsible. The postresuscitation syndrome proved to affect primarily the brain, but also to some extent the extracerebral organs, even when systemic blood pressure, arterial blood gases, and blood volume were normalized. This syndrome is identified by protracted tissue acidosis and reduced cardiac output and tissue perfusion.

Shortly after resuscitation, patients may display a wide range of physiological conditions. Patients may regain normal hemodynamic and cerebral function. On the other hand, many remain comatose with cardiopulmonary insufficiency. All patients require meticulous, repeated assessments to establish the status of their neurologic and cardiopulmonary systems. Postresuscitation goals include preservation of brain function and optimization of respiratory, cardiovascular, metabolic, renal, and hepatic function in order to arrest secondary organ injury. Additionally, it includes an assessment and treatment for the cause of the CA.

To improve on the survival after ROSC, one fundamental objective is the complete reestablishment of regional cerebral perfusion. In normal circumstances, cerebral blood flow is autoregulated such that it is independent of perfusion pressure over a wide range of blood pressures, usually between a mean arterial blood pressure (MABP) of 50 to 150 torr (10). After global brain ischemia, however, autoregulation is lost, and perfusion becomes contingent on arterial pressure primarily. Consequently, the occurrence of postresuscitation hypotension, a common phenomenon, can reduce cerebral blood flow severely and result in further brain damage (11). Therefore, after restoration of spontaneous circulation, MABP should be at least normalized, and attaining a blood pressure higher than pre-arrest values by administration of fluids or vasopressors may be even more beneficial (2).

A consistent problem in the postresuscitation phase is counting on simple vital signs to indicate adequate resuscitation. Simple restoration of blood pressure, even in the presence of excellent coronary perfusion alone and improvement in tissue gas exchange do not necessarily correlate with better survival (12). However, if spontaneous ventila-