Effect of the No-Flow Interval and Hypothermia on Cerebral Blood Flow and Metabolism During Cardiopulmonary Resuscitation in Dogs

Donald H. Shaffner, MD; Scott M. Eleff, MD; Raymond C. Koehler, PhD; Richard J. Traystman, PhD

Background and Purpose—We sought (1) to determine the effect of brief periods of no flow on the subsequent forebrain blood flow during cardiopulmonary resuscitation (CPR) and (2) to test the hypothesis that hypothermia prevents the impact of the no-flow duration on cerebral blood flow (CBF) during CPR.

Methods—No-flow intervals of 1.5, 3, and 6 minutes before CPR at brain temperatures of 28°C and 38°C were compared in 6 groups of anesthetized dogs. Microsphere-determined CBF and metabolism were measured before and during vest CPR adjusted to maintain cerebral perfusion pressure at 25 mm Hg.

Results—Increasing the no-flow interval from 1.5 to 6 minutes at 38°C decreased the CBF (18.6±3.6 to 6.1±1.7 mL/100 g per minute) and the cerebral metabolic rate (2.1±0.3 to 0.7±0.2 mL/100 g per minute) during CPR. Cooling to 28°C before and during the arrest eliminated the detrimental effects of increasing the no-flow interval on CBF (16.8±1.0 to 14.8±1.9 mL/100 g per minute) and cerebral metabolic rate (1.1±0.1 to 1.3±0.1 mL/100 g per minute). Unlike the forebrain, 6 minutes of preceding cardiac arrest did not affect brain stem blood flow during CPR.

Conclusions—Increasing the no-flow interval to 6 minutes in normothermic animals decreases the supratentorial blood flow and cerebral metabolic rate during CPR at a cerebral perfusion pressure of 25 mm Hg. Cooling to 28°C eliminates the detrimental impact of the 6-minute no-flow interval on the reflow produced during CPR. The brain-protective effects of hypothermia include improving reflow during CPR after cardiac arrest. The effect of hypothermia and the impact of short durations of no flow on reperfusion indicate that increasing viscosity and reflex vasoconstriction are unlikely causes of the “no-reflow” phenomenon. (Stroke. 1998;29:2607-2615.)

Key Words: cerebral blood flow ■ cerebral metabolism ■ heart arrest ■ hypothermia ■ dogs

Brain function after resuscitation from cardiac arrest depends on the duration of the no-flow period (arrest time). Unfortunately, the manual chest compressions delivered during cardiopulmonary resuscitation (CPR) in clinical practice produce peak aortic pressures of 60 to 80 mm Hg, with mean aortic pressures of 30 to 50 mm Hg. Intracranial pressure during CPR may be elevated to levels of one third of aortic pressure. Cerebral perfusion pressure (CPP; mean arterial pressure minus intracranial pressure) at low levels (<30 mm Hg) is associated with subnormal levels of cerebral blood flow (CBF) and poor outcome. With a CPP of 25 mm Hg during CPR in dogs when there is no arrest time, the level of CBF can be adequate to maintain brain oxygen utilization and ATP levels at 60% of baseline but not intracellular pH measured with MR spectroscopy. Several explanations are possible for the decrease in reflow during CPR with increasing no-flow interval, such as increased blood viscosity, perivascular swelling, and vasconstriction.

In contrast, a 6-minute no-flow interval before CPR with a CPP of 25 mm Hg produces less CBF, and CPR at a CPP of 25 mm Hg is ineffective at restoring brain oxygen utilization, ATP, and intracellular pH. In the present study we prolonged the no-flow interval from 1.5 to 3 and to 6 minutes before starting CPR with a CPP of 25 mm Hg to better define the impact of arrest duration on cerebral hemodynamics during CPR. We used these intermediate lengths of arrest duration to determine whether the resistance to reflow increases gradually or abruptly after arrest occurs. We studied regional blood flows to determine regional variations in the processes causing resistance to reflow during CPR. We also tested the hypothesis that inducing hypothermia to 28°C would protect against the deterioration in supratentorial blood flow during CPR as the preceding no-flow interval increases. Preischemic hypothermia may delay perivascular swelling or vasospastic constriction but is unlikely to reduce blood viscosity. Understanding the response at smaller no-flow intervals, the regional variations, and the response to hypothermia of resistance to reflow will help to differentiate the underlying mechanisms.
Materials and Methods

Animal Preparation

The protocol for these studies was approved by the Animal Care and Use Committee of the Johns Hopkins Medical Institutions. Thirty-six mongrel dogs weighing 10 to 15 kg were anesthetized with sodium pentobarbital (30 mg/kg IV) and fentanyl (50 μg/kg IV). The trachea was intubated, and the lungs were mechanically ventilated with 50% inspired O₂. Minute ventilation was adjusted to maintain a normal range of end-tidal CO₂ (35 to 40 mm Hg). Saline-filled catheters were advanced from the femoral vessels into the descending thoracic aorta, left ventricle, and right atrium. A midline burr hole was made in the skull, and a catheter was placed into the sagittal sinus at the level of the coronal sutures and advanced posteriorly 2 cm. Through the same burr hole, a thermistor was tunneled 1 cm between the skull and the dura. A vent with an inflatable bladder that covered two thirds of the thoracic circumference was secured snugly around the thorax with hook-and-loop fastener straps. A warm-water–perfused blanket was wrapped around the abdomen of dogs in the normothermic (38°C) group. The dogs in the hypothermic (28°C) group were covered with ice chips until their epidural and rectal temperatures were 28°C. Lactated Ringer’s solution containing no glucose (30 mL/kg IV) was infused during the surgical preparation to ensure adequate cardiac filling pressures during subsequent CPR.

Measurements

All measurements were recorded immediately before arrest and then at 5, 15, and 25 minutes during CPR. Pressures were measured in the intrathoracic aorta, right atrium, and sagittal sinus referenced to the level of the right atrium. Blood samples were obtained from the aorta and sagittal sinus for blood gas and pH analysis with the use of a Radiometer ABL3 analyzer. Blood gases and pH were corrected to body temperature and maintained within normal range after correction for body temperature. Oxygen content and hemoglobin were measured with a model OSM3 hemoximeter (Radiometer). Blood glucose concentration was measured with a model 2300A glucose analyzer (Yellow Springs Instruments Inc.).

Regional blood flows were measured with the radiolabeled microsphere technique previously validated for use during CPR.[8] Radio-labeled microspheres (15.0±0.5 μm in diameter; NEN Life Science Products) were injected into the left ventricle as blood was withdrawn from the ascending aorta. The pump withdrawal rate was 3.8 mL/min for 2 minutes during the prearrest measurement and 1.9 mL/min for 5 minutes during CPR. Before injection, the microspheres were vortexed for dispersion; ∼1.5×10⁵ spheres were injected before arrest, and ∼5×10⁶ spheres were injected at each point during CPR. The order of injection of 6 isotope labels ([⁴¹]Gd, [⁴∪]In, [¹⁰⁸]Sn, [¹⁰⁹]Ru, [⁹⁵]Nb, [⁴⁷]Sc) was randomized for each experiment. The combination of sphere doses and withdrawal rates ensured that the right heart from the femoral vein. CPR commenced after 1.5, 3, or 6 minutes of arrest. The thorax was compressed by cycling the vest pressure, as previously described.[10] The level of pressure in the vest was adjusted by varying the pressure in the reservoir chamber. The rise time to achieve a stable vest pressure was 150 milliseconds. Compressions occurred at a rate of 60/min, with a 40% duty cycle. The microprocessor also controlled a pressure-limited ventilator to deliver 100% oxygen at a variable airway pressure of 20 to 35 cm H₂O interposed after every fifth chest compression to maintain arterial PCO₂ near normal levels. All animals received a bolus 40 μg/kg of epinephrine at the start of CPR, followed by a 10-μg/kg per minute continuous intravenous infusion to maintain vascular tone without effect on cerebral metabolism.[11,12] Lactated Ringer’s was infused at a rate of 4 mL/min for 30 minutes of continuous CPR. Vest pressure was continuously adjusted to maintain a CPP of 25 mm Hg. Mean sagittal sinus pressure, which is within a few millimeters of pressure measurement of intracranial pressure during CPR in dogs,[13] was used as the downstream pressure for estimating CPP.

Statistical Analysis

All measurement variables were analyzed with 2-way ANOVA with repeated measures for the 4 groups and the 5 CPR time points. When this analysis indicated an effect of time or treatment group, 1-way ANOVA was performed within individual groups or between groups at a common time. Post hoc Newman-Keuls multiple range test was used to assess individual group differences. All values are mean±SEM. Significance was detected at the <0.05 level.

Results

The CPP (mean thoracic aortic minus mean sagittal sinus pressure) during 30 minutes of vest CPR was easily maintained at the intended level of 25 mm Hg (Table 1). The mean arterial pressure needed during CPR to generate a CPP of 25 mm Hg was similar in the normothermic and hypothermic groups despite the lower baseline arterial pressures in the hypothermic groups. The sagittal sinus pressure did not differ substantially among the 6 groups at baseline or during CPR, but it did increase above baseline during CPR in 5 of the 6 groups. The brain temperature was maintained at 38°C in the normothermic groups throughout CPR. The brain temperature fell slightly below 28°C in the hypothermic groups during CPR.

Arterial blood analysis revealed no differences between groups at the prearrest or CPR time points for carbon dioxide or hemoglobin measurements (Table 2), Glucose levels were greater and pH levels lower during CPR in the normothermic groups than in the hypothermic groups. Arterial O₂ saturation during CPR was lower in the 6-minute normothermic group, but levels were maintained above 90%.

Supratentorial blood flow before fibrillation (prearrest) was not different among the 3 normothermic groups or among the 3 hypothermic groups (Figure 1, top panel). Prearrest supratentorial blood flow in the hypothermic groups was less than that in normothermic groups (P<0.01 to P<0.001). Supratentorial blood flow during CPR was less than prearrest values in all 6 groups (P<0.0005 to P<0.0001) and varied with no-flow interval in the normothermic group. Supratentorial flow decreased during CPR as no-flow interval increased in the normothermic groups but was unaffected by the arrest duration in the hypothermic groups (Figure 1, bottom panel). In the normothermic group after 6 minutes of arrest, supratentorial flow during CPR was less than in all 5 other groups (P<0.01).
Regional blood flows showed different patterns within different structures. Prearrest brain stem blood flow (combined medullary, pontine, and midbrain blood flow) was greater in the normothermic groups than in the hypothermic groups (Figure 2) \((P<0.05\) to \(P<0.01\)). Brain stem flow after 5 minutes of CPR was lower than prearrest levels only in the group with 1.5 minutes of arrest at 38°C \((P<0.05)\). After 25 minutes of CPR, brain stem flow was below prearrest levels in all groups except for 6 minutes of arrest at both 38°C and 28°C \((P<0.05)\). Brain stem blood flow was restored to near prearrest levels early in CPR in most groups and was greater in the normothermic groups than in the hypothermic groups \((P<0.05)\). Brain stem blood flow during CPR was less after 6 minutes than after 1.5 minutes of no flow in regions of the anterior cerebral artery, middle cerebral artery, posterior cerebral artery, hippocampus, caudate, and cerebellum \((P<0.05\) to \(P<0.01)\). Flow during CPR after 6 minutes of arrest was greater under hypothermic conditions than normothermic conditions in the regions of the anterior cerebral artery, posterior cerebral artery, hippocampus, and caudate \((P<0.05\) to \(P<0.005)\).

Prearrest CMRO2 was not different among the normothermic or among the 3 hypothermic groups (Figure 4, top panel). Prearrest CMRO2 was decreased in the hypothermic compared with the normothermic groups \((P<0.01\) to \(P<0.0001)\). CMRO2 during CPR was less than that at prearrest after 3 and 6 minutes of arrest at 38°C \((P<0.005\) and \(P<0.0001)\). CMRO2 at 38°C after 6 minutes of arrest was lower than that at shorter arrest duration at 38°C \((P<0.005)\). CMRO2 during CPR decreased as no-flow interval increased at 38°C but was unaffected by the arrest duration at 28°C (Figure 4, bottom panel).

Cerebral oxygen extraction was not different among groups at baseline despite differences in temperature (Figure 5). Percent extraction increased above prearrest levels during...
Effect of No-Flow Interval and Hypothermia During CPR in Dogs

TABLE 2. Arterial Blood Analysis

<table>
<thead>
<tr>
<th>Duration of CPR, min</th>
<th>Group Prearrest</th>
<th>5</th>
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<th>25</th>
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<td></td>
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</tr>
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<td>38±0</td>
<td>36±2</td>
<td>45±3</td>
<td>42±1</td>
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<td>3.38</td>
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<td>39±2</td>
<td>40±3</td>
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<tr>
<td>6.38</td>
<td>36±2</td>
<td>49±7</td>
<td>44±8</td>
<td>35±3</td>
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<tr>
<td>1.5:28</td>
<td>39±1</td>
<td>30±2*</td>
<td>38±2</td>
<td>42±2</td>
</tr>
<tr>
<td>3.28</td>
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<td>28±2*</td>
<td>35±3</td>
<td>37±2</td>
</tr>
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<td>6.28</td>
<td>38±1</td>
<td>32±2</td>
<td>35±2</td>
<td>40±4</td>
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<tr>
<td>pH</td>
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<td>7.13±0.01*</td>
</tr>
<tr>
<td></td>
<td>6.38</td>
<td>7.35±0.01</td>
<td>7.27±0.03*</td>
<td>7.12±0.04*</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
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<td>10.0±0.4</td>
<td>11.8±0.8*</td>
<td>12.0±0.6*</td>
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<tr>
<td></td>
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<td>9.8±0.4</td>
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<tr>
<td>O2 saturation, %</td>
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<td>100±1</td>
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<td>6.38</td>
<td>100±0</td>
<td>99±1</td>
<td>98±1</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
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<td>62±3</td>
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<td>132±13*</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>162±31*</td>
</tr>
</tbody>
</table>

Definitions of groups are as in Table 1. Blood gas values are reported as corrected for body temperature. All values are mean±SEM.

*Differs from prearrest value at P<0.05.
†Differs from corresponding value in normothermic group at P<0.05.

CPR in all 6 groups (P<0.01 to P<0.0001). Extraction during CPR was greater in the normothermic groups than in the hypothermic groups (P<0.0005 to P<0.0001).

Discussion

The major new findings of this study are as follows: (1) CPR with a CPP of 25 mm Hg under normothermic conditions becomes progressively less effective in restoring supratentorial blood flow and CMRO2 as no-flow interval increases from 1.5 to 6 minutes. (2) Unlike supratentorial flow, these arrest durations have little effect on the reflow in the brain stem structures at this CPP under normothermic conditions. (3) Cooling the animals to 28°C before arrest prevents the detrimental effect of 6 minutes of arrest on the supratentorial blood flow and CMRO2 during CPR with this CPP. Remarkably, the absolute levels of blood flow in posterior and anterior cerebral artery distribution as well as hippocampus, caudate, and cerebellum in the hypothermic group were greater than those in the normothermic group during CPR after 6 minutes of cardiac arrest.

Others have shown that reflow in the brain decreases as the delay before CPR increases in cats,14 rabbits,15 and dogs.16 In these studies, unlike ours, there was a decrement in mean arterial pressure generated during CPR when the period of cardiac arrest was prolonged. As with our previous study, we were able to precisely control the level of CPP over a prolonged duration of CPR by continuously infusing epinephrine and by adjusting the vest inflation pressure. Despite the ability to hold CPP constant in both studies, we have shown a decrement in forebrain blood flow as arrest duration increases at low CPP. For example, we found that controlling CPP at 30 mm Hg during CPR and no period of arrest...
produced supratentorial blood flow of 27 ± 4 mL/min per 100 g and maintained cerebral ATP at normal levels. A slightly lower CPP of 25 mm Hg during CPR with no arrest time generated a supratentorial blood flow of 20 ± 3 mL/min per 100 g, and cerebral ATP fell to 64 ± 14% of baseline at 10 minutes of CPR. Adding a 6-minute no-flow interval before CPR with a CPP of 30 mm Hg gave a heterogeneous response of supratentorial blood flows among dogs, suggesting that a CPP of 30 mm Hg is near the threshold required for generating supratentorial blood flow sufficient to restore cerebral ATP after 6 minutes of cardiac arrest. Setting the CPP during CPR to 25 mm Hg after 6 minutes of arrest resulted in a consistently low mean supratentorial blood flow of only 7 ± 2 mL/min per 100 g at 10 minutes of CPR and an initial ATP recovery of 16 ± 5%. Thus, increasing arrest duration from 0 to 6 minutes increased cerebrovascular resistance to reflow, and a CPP of 25 mm Hg was inadequate to overcome this resistance. In contrast to forebrain and cerebellar regions, brain stem regions did not display this effect of arrest duration on reflow, consistent with our previous work.

Several mechanisms may be responsible for the increase in cerebral vascular resistance and the decrease in supratentorial blood flow as no-flow interval increases from 0 to 6 minutes. Increased viscosity of blood, constriction of blood vessels, and vascular/perivascular edema have all been implicated as increasing cerebral vascular resistance after ischemic episodes. Our present study attempts to improve our understanding of the causes of resistance to reflow after global ischemia by determining the amount and distribution of CBF after intermediate periods (1.5, 3, and 6 minutes) of arrest and the impact of preischemic hypothermia.

A potential redistribution of brain blood flow by sympathetic vasoconstriction should occur with the onset of cardiac arrest and should occur earlier than processes involving exhaustion of energy substrates and perivascular swelling. Our present findings show that under normothermic conditions, supratentorial blood flow during CPR with a CPP of 25 mm Hg progressively decreases from 18 ± 2 to 15 ± 2 to 6 ± 1 mL/min per 100 g as arrest duration increases from 1.5 to 3 to 6 minutes. CMRO₂ levels correspond with blood flows and decrease from 1.9 ± 0.2 to 1.5 ± 0.1 to 0.7 ± 0.1 mL/min per 100 g as O₂ extraction was near maximal (70% to 80%) for all 3 arrest durations during normothermia. The fall in supratentorial blood flow, as arrest duration increases, appears to be ≈ 2.8 mL/min per 100 g per minute of arrest. Estimating a y-axis intercept indicates that a blood flow of 21.3 mL/min per 100 g would be anticipated if CPR were begun without preceding arrest. This estimation is close to the 20 ± 3 mL/min per 100 g that we found after no arrest time in our previous study. Thus, the relationship of supratentorial blood flow to the preceding no-flow interval is a constant decrement over the durations tested and not an abrupt fall immediately following the onset of arrest. It is unlikely that this progressive decrement in forebrain blood flow is related to ischemia-induced sympathetic constriction of forebrain cerebral vessels.

A second explanation is that stagnant blood has an increased viscosity within the microcirculation when water shifts from plasma to the intracellular compartment and causes red cell aggregation. Increased viscosity as the sole explanation of the increased vascular resistance to a CPP of 25 mm Hg during CPR after 6 minutes of arrest seems unlikely because similar water shifts should occur in brain stem as well. In both the present and previous studies, there

Figure 1. Top, Supratentorial blood flow before and during 30 minutes of CPR. The various groups were as follows: △, 1.5 minutes of arrest at 38°C; ○, 3 minutes of arrest at 38°C; ●, 6 minutes of arrest at 38°C; ▲, 1.5 minutes of arrest at 28°C; ■, 3 minutes of arrest at 28°C; and ●, 6 minutes of arrest at 28°C. Supratentorial blood flow was less than that at prearrest in all groups (P < 0.005 to P < 0.0001). Supratentorial flow during CPR was decreased in the group with 6 minutes of arrest at 38°C compared with the group with 6 minutes of arrest at 28°C (P < 0.01). Bottom, Supratentorial blood flow during CPR plotted to show effect of arrest duration (△, 38°C; ●, 28°C).

Figure 2. Brain stem blood flow before and during 30 minutes of CPR. Symbols are defined as in Figure 1 legend. See text for statistics.
was little effect of cardiac arrest duration on brain stem blood flow. Furthermore, the lack of effect of cardiac arrest duration on reflow under hypothermic conditions, which by itself increases blood viscosity, also suggests that increased viscosity is not the major mechanism. Alternatively, hypothermia may inhibit intravascular coagulation, which could be selectively activated in forebrain and which could impede reflow.

During normothermic arrest, neuronal depolarization and shifts of water into cells would be expected to be mostly complete by 3 minutes of arrest.\textsuperscript{18–20} Thus, if cell swelling is the mechanism of poor reflow, one might expect equivalent decrements in reflow after 3 and 6 minutes of arrest. However, the ability of the mitochondria to restore ATP rapidly may become impaired as ischemic duration is prolonged.\textsuperscript{21}

Thus, another possibility is that low blood flow during CPR delivers additional water to the cells but inadequate O\textsubscript{2} to restore ATP recovery necessary to restore cell volume. Further cell swelling, particularly in perivascular astrocyte processes, could cause capillary narrowing sufficient to limit reflow at low CPP in the early minutes of CPR. However, this hypothesis does not readily explain the lack of effect of ischemic duration on blood flow to the brain stem during CPR unless swelling is delayed in brain stem during ischemia or ATP is more easily restored in brain stem. Hypothermia

\begin{figure}
\centering
\includegraphics[width=\textwidth]{brain_blood_flow.png}
\caption{Regional brain blood flow during CPR. *Difference from 38°C measurement for that arrest duration at $P<0.05$; †difference from 38°C measurement at 1.5 minutes of arrest. See text for description of changes and statistics.}
\end{figure}
decreases ATP utilization and delays the loss of ATP at the onset of ischemia. The beneficial effect of hypothermia on reflow in forebrain may be explained by delaying transcellular shifts of water during cardiac arrest and by better maintaining mitochondrial function necessary for rapid ATP regeneration.

Ordinarily, blood flow autoregulation extends to a lower CPP in brain stem than in cortex. A fourth possibility is that there are inherent differences in the regulation of arterioles in cerebral cortex and brain stem. Vasodilatory mediators such as adenosine, nitric oxide, and arachidonic acid metabolites, released during cerebral ischemia, may be further metabolized as ischemia is prolonged, and the rate of degradation may be different in different brain regions. Hypothermia could prolong the action of these vasodilatory metabolites by decreasing their rate of degradation or the degradation of vascular cAMP and cGMP evoked by these vasodilatory mediators. Degradation may be inherently slower in the brain stem.

Vasoconstrictive substances released during cerebral ischemia, such as high levels of potassium, may be accumulating after the first few minutes of circulatory arrest and be inhibited by the application of hypothermia. Neuronal depolarization under normothermic ischemia occurs in the first 90 seconds and can be delayed until approximately 4 minutes by hypothermia of this magnitude. This several-minute delay in the onset of depolarization from the metabolic protection of hypothermia probably occurs in our model. If so, an increase in vascular resistance may eventually occur with hypothermia when arrest is extended beyond the 6-minute duration used in the present study.

Hypothermia was applied to the whole animal before ischemia at a level considered moderate (28°C). Whole body, as opposed to selective, hypothermia was chosen for this model to help ensure uniformity of hypothermia. There was agreement of the rectal and brain temperatures in our hypothermic animals. Moderate hypothermia to 28°C, as opposed to mild hypothermia to 34°C, was chosen to ensure a substantial reduction in prearrest CMRO2 and ATP utilization rate without the cardiac instability seen with deep hypothermia in the dog. A considerable literature exists on the use of this level of hypothermia in the dog, and the changes in CBF, CMRO2, and cerebral vascular resistance are similar to what we observed in the prearrest state. In those studies, the mean level of hypothermia was 28.3°C (range, 26°C to 31°C), mean CBF was 28.2 mL/min per 100 g (range, 15 to 43; 48% of normothermia), mean CMRO2 was 2.2 mL/min per 100 g (range, 1.8 to 3; 43% of normothermia), and mean cerebral vascular resistance was 4.0 mm Hg/mL per minute per 100 g (range, 1.7 to 7.8; 222% of control). Our prearrest values showed a similar response to hypothermia with CBF of 28 mL/min per 100 g (range, 25 to 30; 57% of normothermia), CMRO2 of 0.9 mL/min per 100 g (range, 0.8 to 1.0; 38% of normothermia), and cerebral vascular resistance of 3.3 mm Hg/mL per minute per 100 g (range, 2.9 to 3.6; 142% of normothermia). As with these other whole body applications of hypothermia to 28°C in dogs, there was an increase in cerebral vascular resistance with decreases in CBF and CMRO2.

Our results indicate that in situations involving a period of reduced reflow, as in the clinical setting of inadequate CPR after a period of circulatory arrest, the resistance to reflow progressively increases in proportion to the length of the preceding no-flow period. This resistance to reflow at low perfusion pressures is most prominent in the supratentorial regions and may be one of the mechanisms underlying preserved brain stem function in cardiac arrest survivors.
attenuation by preischemic hypothermia of the processes during no flow responsible for resistance to reflow may explain some of the neuroprotective effects of hypothermia when applied before or during ischemia.

Acknowledgments
This study was supported by US Public Health Service, National Institutes of Health grant NS20020 and an American Heart Association Established Investigator Award (to Dr Eleff).

References
Large clinical trials have documented that as few as 27% of adults who are resuscitated successfully regain good neurological function following the event. A common clinical scenario is that the patient survives the cardiac arrest with intact brain stem function but experiences little to no cerebral recovery. Unfortunately, the actual mechanism(s) responsible for postresuscitation cerebral injury are not yet fully understood, nor is there a clear understanding of the cerebrovascular hemodynamics and metabolic alterations that occur during resuscitation.

In their article, Shaffner et al report results of an important experimental study in which they maintained cerebral perfusion pressure at 25 mm Hg with a pneumatic vest chest compression device and an intravenous infusion of epinephrine in a canine cardiac arrest model. Normothermic or moderately hypothermic (38°C) pretreated animals were randomly assigned to 1.5-, 3-, or 6-minute downtime intervals of ventricular fibrillation prior to initiating 30 minutes of CPR. In normothermic animals, supratentorial blood flow after initiation of CPR decreased as the downtime interval increased, likely due to an increased resistance to reflow at low perfusion pressure. Pretreatment with moderate levels of generalized hypothermia eliminated this effect, which may (in part) help to explain the neuroprotective actions of hypothermia during global ischemia. In contrast to the effect noted on supratentorial blood flow, brain stem blood flow after initiation of CPR was relatively unaffected by the downtime interval.

This study has several potentially important clinical implications. First, the increased resistance to reflow at low perfusion pressure seen in supratentorial but not brain stem structures helps to explain why many patients survive a cardiac arrest with only brain stem function intact. Second, the experimental model can be used to further elucidate the mechanisms responsible for the detrimental cerebrovascular and metabolic changes that occur when CPR is initiated after even a relatively brief interval of cardiac arrest. Finally, the model can be used to explore future treatments to counteract the increased resistance to reflow noted in supratentorial structures during CPR. Such therapies might be mechanical or pharmacological, but they would have to be effective when administered after the onset of resuscitation to be of clinical importance and would have to be devoid of significant deleterious hemodynamic or metabolic effects. Thus, this study offers new hope for improving the neurological outcome of cardiac arrest victims.

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Stroke. 1998;29:2607-2615
doi: 10.1161/01.STR.29.12.2607

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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