ABSTRACT  We assessed the efficacy of conventional cardiopulmonary resuscitation (CPR) in 2-
week-old piglets. We determined intrathoracic vascular pressures, cerebral (CBF) and myocardial
blood flows (MBF), and cerebral oxygen uptake during conventional CPR in this infant animal
preparation and contrasted these results with those of previous work on adult animals. We further
examined the effects of the infusion of epinephrine on these pressures and flows and on cerebral oxygen
uptake, which has not been previously evaluated in adult preparations. Conventional CPR was per-
formed on pentobarbital-anesthetized piglets with a 20% sternal displacement with the use of a
pneumatic piston compressor. Chest recoil was incomplete, leading to an 18% to 27% reduction in
anteroposterior diameter during the relaxation phase. Aortic and right atrial pressures in excess of 80
mm Hg were generated. These pressures are greater than those generally obtained in adult animals with
similar percent pulsatile displacements. CBF and MBF were also initially greater than those reported in
adult animals undergoing conventional CPR. However, when CPR was prolonged beyond 20 min,
aortic pressure fell and CBF and MBF declined to the near-zero levels seen in adult preparations. At 5
min of CPR, CBF and MBF were 24 ± 7 and 27 ± 7 ml·min⁻¹·100 g⁻¹ (50% and 17% of the values
during cardiac arrest), respectively. With the continuous infusion of epinephrine (4 μg/kg/min) in
another group of animals, MBF was significantly greater at 20 min of CPR and CBF and cerebral O₂
uptake were greater at 35 min of CPR as a result of higher perfusion pressures. At 5 min of CPR, CBF
and MBF were 46 ± 9 and 65 ± 16 ml·min⁻¹·100 g⁻¹, respectively. CBF and cerebral oxygen uptake
were maintained at prearrest levels for 20 min of CPR. Epinephrine did not appear to have an adverse
effect on cerebral oxygenation because cerebral O₂ extraction was lower in the epinephrine group. In
conclusion, we found that the infusion of epinephrine in a piglet preparation of CPR increased MBF,
CBF, and cerebral oxygen uptake by selective vasoconstriction of other vascular beds. Compared with
adult preparations, conventional CPR in infant piglets generated higher intrathoracic vascular pres-
ures, MBF, and CBF, which may be related to the change in chest shape seen in this infant CPR
preparation.

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CARDIOPULMONARY RESUSCITATION (CPR) has been extensively studied in adult animals,⁴ but
until recently,⁴ there have been no previous laboratory studies of CPR in infant animals. Recent work in adult
animals suggests that CPR may generate aortic blood flow without causing direct cardiac compression.¹ Ex-
perimental studies indicate that the increase in intrathoracic pressure caused by external chest compres-
son, pressure gradient that generates extrathoracic blood flow.¹ In
many studies of adult animals, conventional CPR pro-
duces only small changes in intrathoracic vascular pressures and correspondingly low levels of cerebral
and myocardial blood flows.⁵ However, switching to simultaneous compression-ventilation CPR in-
creases intrathoracic vascular pressures and cerebral
blood flow when conventional CPR is inadequate. 1, 3, 5, 6

The level of blood flow achieved during CPR in infant animals may not be as low as that achieved in adult animals. The chest of the infant is more deformable and chest configuration may change during CPR if chest recoil is incomplete after each compression. Vascular pressures and blood flows may not be similar in infants because differences in chest compliance, deformity, and geometry may alter the relationship between sternal displacement and the generated intrathoracic pressure. Furthermore, differences in these properties of the chest may allow direct compression of the heart to contribute more prominently to the generation of blood flow.

To study CPR in infant animals, we used 2-week-old piglets. The young piglet was chosen because of its relatively deformable chest and because the configuration of its chest is more broad than that of most other animals, including the dog. Also, the chest size, geometry, and stiffness are more similar to those of human infants than are those of most other nonprimates. The first objective of the present study was to determine if the vascular pressures and blood flows produced by conventional CPR in infant animals were greater than those in adult animals. Moreover, CPR was carried out for 50 min, a duration that is not unusual for pediatric CPR, to test whether any enhanced perfusion could be sustained over prolonged periods.

Epinephrine increases cerebral and myocardial blood flows during CPR in adult animals by increasing perfusion pressures through preferential vasoconstriction of other peripheral vascular beds. 2 The second objective of this study was to determine if epinephrine would improve cerebral and myocardial blood flows to the same extent in an infant preparation as in adults, and to determine if the drug would remain efficacious during prolonged CPR. In addition, measurements of cerebral oxygen uptake have not been reported during CPR. Epinephrine could increase cerebral O2 uptake by increasing O2 supply or by stimulating O2 demand if it crosses the blood-brain barrier in sufficient quantities. The latter effect could be deleterious if it further lowered tissue Po2. Our third objective was to determine if epinephrine improved cerebral oxygen uptake solely by increasing cerebral blood flow rather than by increasing oxygen extraction and lowering venous Po2.

Therefore, the following hypotheses were tested: (1) Higher cerebral and myocardial blood flows can be generated by conventional CPR in an infant than in an adult preparation. (2) Epinephrine further improves cerebral and myocardial blood flows for prolonged durations in infant animals undergoing CPR. (3) Epinephrine improves cerebral O2 uptake without increasing cerebral O2 extraction.

Methods and materials

Preparation. All experiments were performed on 2-week-old piglets, ranging in weight from 3.5 to 3.5 kg. The piglets were anesthetized with pentobarbital (30 to 40 mg/kg intraperitoneal) and ventilated with a Harvard ventilator at a rate of 20 to 30 breaths per minute with a tidal volume of 10 to 15 ml/kg via a tracheostomy with 30% to 50% inspired oxygen. End-tidal CO2 was monitored continuously throughout the prearrest period to maintain arterial CO2 tension (PaCO2) at 35 to 40 mm Hg. Supplemental pentobarbital was administered intravenously as needed during surgery. Saline-filled catheters were advanced via the femoral arteries and veins into the thoracic aorta, left ventricle, and right atrium, respectively. Additional catheters were inserted via axillary arteries into the proximal subclavian arteries for microsphere withdrawal and through axillary veins for infusion of fluids. A catheter was placed in the sagittal sinus with the catheter tip lying 1 to 2 cm anterior to the confluence of the sinus. This catheter was used to sample blood for determining venous blood gases, pH, and oxygen content, and to measure sagittal sinus pressure. A Cordis straight ventricular catheter was placed via a burr hole into the lateral ventricle for measurement of intracranial pressure. A No. 4F pacing catheter, was passed into the right atrium to induce ventricular fibrillation. Heparin (2000 units) was given before cardiac arrest was induced.

Measurements. To measure regional blood flows, radiolabeled microspheres were injected before arrest and at 5, 20, 35, and 50 min after ventricular fibrillation. Arterial and sagittal sinus blood samples were also obtained at these times for analysis of blood gases and pH on a Radiometer BMS3 electrode and analyzer system. Oxygen contents were measured by a Lex-O2-Con fuel cell system (Lexington Instruments). Hemoglobin levels were measured with a CO-Oximeter (Model 282, Instrumentation Laboratory, Inc.). Pressures were recorded from the intrathoracic aorta, right atrium, lateral ventricle, and sagittal sinus with Statham 23Db transducers all referenced to the level of the right atrium.

Radiolabeled microspheres (15 ± 1.5 μm diameter; New England Nuclear) were injected into the left ventricle. During all microsphere injections, reference blood samples were withdrawn from two axillary arterial catheters with a Harvard syringe pump to check for adequate mixing of microspheres. Blood was withdrawn for 2 min after the control injection and for 5 min after every postarrest microsphere injection. Use of microspheres during CPR has been previously validated. 3 In the present experiments, the error in the absolute difference between the two reference samples was 8.9 ± 5.9% (±SD) before arrest and 11.7 ± 4.6% during CPR.

The vials of microspheres were dispersed with a vortex mixer and by ultrasonic agitation. Approximately 1 × 106 spheres were injected before arrest and 5 × 106 spheres were injected for each postarrest measurement. The order of microsphere injection was assigned randomly for each experiment. The withdrawal rate was 3.8 ml/min for the prearrest injection and 1.9 ml/min for the injections during CPR. This combination of injection doses and withdrawal rates ensured that there were at least 2000 microspheres in the reference sample before cardiac arrest was induced, and at least 10,000 microspheres during CPR. Vials of blood and tissue were counted on a multichannel autogamma scintillation spectrometer (Packard, model 9042). The energy windows were (keV): 153Gd, 70 to 174; 51Cr, 280 to
The residual areas of the middle cerebral and the right ventricular free wall were cut and brain were removed and tissue samples of kidney, jejunum, facial muscle, facial skin, and tongue were obtained. The heart was cut into sections of left ventricular free wall, interventricular septum, and right ventricular free wall and atria. The left ventricular free wall and interventricular septum were sectioned into three layers, the right ventricular free wall into two layers. The brain was dissected into medulla, pons, midbrain, cerebellum, and diencephalon, the primary supply territories of the middle cerebral and posterior cerebral arteries, the watershed areas between the anterior and middle cerebral arteries and between the middle and posterior cerebral arteries, and the residual hemispheres. Cerebral oxygen uptake was calculated from the arterial-sagittal sinus oxygen content difference and blood flow to the cerebrum. Cerebral fractional O$_2$ extraction equals the arterial-sagittal sinus oxygen content difference divided by the arterial oxygen content.

**Experimental protocols.** CPR was begun 10 sec after ventricular fibrillation was induced by passing a 60 Hz alternating current through the right atrial pacing wire. Animals were randomly assigned to epinephrine and no epinephrine groups. Epinephrine was given as a 10 µg/kg bolus through the femoral vein catheter at the onset of CPR in eight piglets. An infusion of epinephrine diluted in saline at the rate of 4 µg/kg/min was continued throughout the duration of CPR. The other group of animals (n = 8) received a continuous infusion of saline without epinephrine. The rate of saline infusion was 1.7 ml/min in both groups.

At least 1 hr before beginning the experiment, 60 ml of whole blood was withdrawn over 15 min from each animal and simultaneously replaced with 180 ml of Ringer’s lactate solution. The blood pressure was stable during the exchange transfusion. The whole blood was then intravenously infused simultaneously with the arterial withdrawal of the microsphere reference sample. This was done to minimize the decrease in hemoglobin during prolonged CPR and to replace the blood withdrawn for the microsphere reference samples.

External chest compression was performed with a Michigan Instruments pneumatic chest compressor (Thumper). The Thumper pad was placed on the lower half of the sternum with the center approximately 3 to 4 cm rostral to the xiphoid. Both the Thumper and ventilator were controlled by a microprocessor. Parameters used for CPR were a chest compression rate of 100/min with a compression duration of 60% of the total cycle time (60% duty cycle). Thumper force was initially set in all animals to deliver a 20% displacement of the animal’s baseline anteroposterior chest diameter measured at the level of the xiphoid process. Piston displacement was measured from the chest position before beginning each compression cycle. Once this displacement was attained, no further adjustments of the Thumper force were made during the experiment. Force was measured via a strain gauge on the Thumper and piston displacement was measured continuously by a sliding potentiometer built into the Thumper. Ventilation was interposed between the compression phases after very fifth chest compression by a pressure-limited ventilator set at 30 to 35 cm H$_2$O peak airway pressure, as in previous adult studies. The initial four animals studied (two in each group) were ventilated with a mixture of 95% O$_2$, 5% CO$_2$ in an attempt to maintain Paco$_2$ at prearrest levels. However, since Paco$_2$ rose above baseline levels with prolonged CPR, 100% oxygen was used in the remaining 12 piglets.

**Statistical analysis.** Pressures and blood flows during CPR in the epinephrine group were compared with those in the no epinephrine group by use of two-way analysis of variance with repeated measures over time during CPR within each group. Mean values were compared by the Duncan new multiple-range test. Prearrest values for intrathoracic pressures and regional blood flows were compared between groups with the unpaired t test. Values are presented as mean ± SE, and the level of statistical significance was set at p < .05 in all tests.

**Results**

Displacement of the piston between the compression and relaxation phases, i.e., pulsatile piston displacement, was set at 20% of the baseline anteroposterior chest diameter by use of applied forces of 264 ± 54 N in the no epinephrine group and those of 279 ± 38 N in the epinephrine group. This pulsatile displacement was sustained over the 50 min duration of CPR in both groups of piglets (figure 1). In neither group did the chest completely recoil during the relaxation phase. This reduced the diameter of the relaxed chest by 19% after 5 min of CPR and by 27% after 50 min of CPR, with no alteration in applied force. This loss of recoil combined with the 20% pulsatile displacement decreased the chest diameter during the compression phase to 61% of the initial anteroposterior diameter at 5 min and to 54% at 50 min of CPR in both groups (figure 1). Despite this change in chest shape, chest compression did not fracture the ribs.

**Heart.** Intrathoracic vascular pressures of approximately 100 mm Hg were achieved in both the treated

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**FIGURE 1.** Piston position during chest compression and relaxation phases of the cycle, and net piston displacement expressed as a percent of prearrest anteroposterior chest diameter (12.0 ± 0.3 cm). Note that displacement was essentially unchanged over the 50 min duration, but that marked deformation occurred during the relaxation phase by 5 min and continued to further deform over the 50 min period in both the epinephrine (solid line) and no epinephrine (dashed line) groups.
and untreated groups during the compression phase (figure 2). Right atrial systolic (compression phase) and diastolic (relaxation phase) pressures remained stable in the epinephrine group throughout 50 min of CPR. The variance was greater at 5 and 20 min in the untreated group as a result of right atrial systolic pressures of approximately 200 mm Hg in three of eight animals. Thereafter, systolic pressures in these three animals declined to the range observed in the epinephrine group. These very high pressures may have been due to compression causing isolation of a subcompartment, such as the right atrial appendage. Aortic systolic and diastolic pressures decreased after 20 min of CPR. There was a net positive gradient for forward coronary blood flow (figure 2) during diastole in the no epinephrine group and during both systole (for 20 min) and diastole in the epinephrine group. In comparing the two groups, there was no statistically significant difference in systolic or mean aortic pressure (p < .10) or in systolic or mean right atrial pressure. Epinephrine significantly increased diastolic aortic pressure. Moreover, with epinephrine, the aortic-to-right atrial pressure gradient was higher during both systole (30 ± 14 mm Hg with epinephrine vs −12 ± 14 mm Hg without epinephrine) and diastole (28 ± 7 vs 15 ± 6 mm Hg) (5 min values). When the three animals with excessive right atrial pressure were excluded from the untreated group, the systolic gradient was still not different from zero (5 ± 13 mm Hg).

Before cardiac arrest was induced, total myocardial blood flow was 188 ± 38 ml·min⁻¹·100 g⁻¹ in the no epinephrine group and 189 ± 16 ml·min⁻¹·100 g⁻¹ in the epinephrine group. During CPR without epinephrine, myocardial blood flow was 27 ± 7 ml·min⁻¹·100 g⁻¹ at 5 min, then decreased to near-zero levels as CPR progressed (figure 3). Epinephrine substantially increased myocardial blood flow at 5 and 20 min of CPR, but with more prolonged CPR myocardial blood flow decreased as perfusion pressure declined. In the epinephrine group blood flow to the right ventricle, left ventricle, and interventricular septum were similar in magnitude and decreased in parallel during CPR (figure 3). In the no epinephrine group, however, blood flow to the right ventricular free wall was greater than that to the left ventricular free wall and septum at 5 min of CPR (both in ml·min⁻¹·100 g⁻¹ and as a percent of

**FIGURE 2.** Aortic (AO) and right atrial (RA) systolic (compression phase) and diastolic (relaxation phase) pressures during 50 min of conventional CPR with (right) and without (left) epinephrine infusion. Shaded areas illustrate magnitude of positive aortic-to-right atrial pressure gradients for forward coronary blood flow. Note that a positive gradient occurs during systole in the epinephrine group.

**FIGURE 3.** Top, Total myocardial blood flow during CPR with (solid line) and without (dashed line) epinephrine. Asterisk indicates significant difference between groups at 5 and 20 min. Bottom, Blood flow to right ventricular free wall (RV, circles), left ventricular free wall (LV, squares), and interventricular septum (triangles) in the epinephrine group (solid lines) and no epinephrine group (dashed lines). SE bars omitted for clarity, but least significant difference bar (LSD, derived from Duncan multiple-range test) shown for comparisons among heart regions within an animal group. (Means must differ by height of bar for p < .05.) LSD for comparing means between groups is twice that shown for within-group LSD. Asterisk indicates that RV blood flow was greater than LV and septal blood flows at 5 min in the no epinephrine group. Flows in all three regions in the epinephrine group were greater than those in the respective regions in the no epinephrine group at 5 and 20 min.
The ratio of subendocardial to subepicardial left ventricular blood flow fell from 1.46 ± 0.13 before cardiac arrest to 0.76 ± 0.14 at 5 min of CPR in the no epinephrine group, and from 1.18 ± 0.09 to 0.85 ± 0.18 in the epinephrine group. The ratio did not significantly differ between groups.

**Brain.** Intracranial pressure and sagittal sinus pressure were higher than prearrest levels and remained unchanged during 50 min of CPR (figure 4). The two pressures were similar before arrest and during the first 20 min of CPR; however, sagittal sinus pressure exceeded intracranial pressure by 6 ± 2 and 7 ± 1 mm Hg at 35 and 50 min in the no epinephrine group (difference in hydrostatic height was equivalent to 1 mm Hg). There was no difference in intracranial or sagittal sinus pressures in treated and untreated groups. Epinephrine increased the estimated cerebral perfusion pressure (mean aortic pressure minus the higher of intracranial or sagittal sinus pressure) (figure 4).

In the untreated group, total cerebral blood flow was 50% of the prearrest level at 5 min, but then decreased as perfusion pressure diminished (figures 4 and 5). Epinephrine treatment maintained cerebral blood flow at prearrest levels during the first 20 min of CPR and at 69% of the prearrest level at 35 min and 24% at 50 min. Epinephrine infusion significantly increased cerebral blood flow during the first 35 min of CPR.

During CPR without epinephrine treatment, the fraction of O₂ extracted across the brain increased to approximately 0.85, which was insufficient to maintain baseline O₂ uptake beyond 5 min of CPR (figure 5). Fractional O₂ extraction was significantly less in the epinephrine group at 20 min, but then increased as cerebral blood flow fell with prolonged CPR. When epinephrine was infused, cerebral O₂ uptake was maintained throughout 35 min of CPR and O₂ uptake was greater than that without epinephrine.

Blood flow to the primary cerebral arterial territories and to the watershed areas between these territories was similar on a percentage basis in both CPR groups. However, during CPR some of the caudal regions had significantly greater blood flow, as a percent of control, than did the whole cerebrum. For example, at 20 min of CPR in the epinephrine group, blood flow was greater in medulla, midbrain, and diencephalon than in cerebrum (figure 6). In the no epinephrine group midbrain blood flow was also greater than that to cerebrum.

**Other organs.** Blood flows to cephalic muscle, cephalic skin, tongue, jejunum, and kidney are listed in table 1. Blood flow to these tissues was too small to allow detection of significant differences between groups given the level of interanimal variability. However, as a percent of prearrest levels, blood flow to cephalic tissues was higher relative to cerebral blood flow in the no epinephrine group than in the epinephrine group. This was especially true during prolonged CPR when aortic pressure and cerebral blood flow fell, tongue and skin blood flow remained nearly unchanged, and muscle blood flow significantly in-

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**FIGURE 4.** Mean aortic pressure (MAP, circles), mean sagittal sinus pressure (SSP, squares), and mean intracranial pressure (ICP, triangles) before cardiac arrest and during 50 min of CPR in the no epinephrine (left) and epinephrine groups (right). Shaded area illustrates magnitude of mean cerebral perfusion pressure during CPR.

**FIGURE 5.** Total cerebral blood flow, cerebral fractional O₂ extraction, and cerebral O₂ uptake before cardiac arrest and during 50 min of CPR in the no epinephrine (dashed lines) and epinephrine groups (solid lines).
increased above the 5 min value. In the epinephrine group, noncerebral cephalic blood flows were in general lower as a percent of prearrest levels, and muscle blood flow did not increase during prolonged CPR.

Blood analyses. There were no significant differences between animal groups with respect to Pao2, Paco2, pH, hemoglobin level, oxygen saturation, or oxygen content during CPR (table 2). Sagittal sinus oxygen content was lower in the no epinephrine group at 5 and 20 min of CPR. During the course of CPR, Paco2 rose and arterial pH and oxygen content declined in both groups. The decreased oxygen content was the result of a decrease in hemoglobin level and, in some animals, a decrease in oxygen saturation (table 2). In those animals in which saturation decreased, it usually did so at only one time point as a result of a transient drop in Pao2 below 100 mm Hg together with an acidic Bohr shift.

Discussion

The major findings of this study are first, that in an infant animal preparation, conventional CPR produces relatively higher intrathoracic vascular pressures and cerebral and myocardial blood flows than in most previous adult preparations; second, that epinephrine further improves cerebral and myocardial perfusion pressures and blood flows for more prolonged periods of conventional CPR; and third, that epinephrine enhances cerebral O2 uptake by increasing cerebral blood flow and not by increasing cerebral O2 extraction.

Comparison with conventional CPR in adult preparations. In piglets conventional CPR was initially more effective in providing cerebral and coronary perfusion than it was in large adult dogs.3,5 Cerebral and coronary blood flows were less than 10 ml·min−1·100 g−1 in dogs, while we found these blood flows to be greater than 20 ml·min−1·100 g−1 at 5 min of CPR in piglets not receiving infusions of epinephrine. These higher initial flows were related to the greater mean aortic pressures achieved in these piglets (61 ± 8 mm Hg at 5 min) compared with those in large dogs (27 ± 2 mm Hg).3 This difference was not simply due to a species difference because conventional CPR in older pigs also generates poor perfusion pressures. Moreover, conventional CPR in young, 6 to 12 kg dogs6 and in young 17 to 23 kg pigs10 also appears to provide relatively high cerebral and coronary perfusion during the first few minutes of CPR.

Several explanations can be offered to account for these differences between infant and adult animals. Endogenous humoral systems, including circulating catecholamines, may be more effective in sustaining peripheral arteriolar tone during the first 5 min of CPR. The rise in cephalic muscle blood flow observed when CPR was prolonged supports this explanation. However, humoral factors do not account for the relatively high right atrial pressures during chest compression. A second major difference between the infant and adult animals that may contribute to the high intrathoracic vascular pressures is the change in shape of the chest that occurs in the infant preparation. The infant chest wall is more compliant and requires less force to achieve a 20% sternal displacement of the anteroposterior diameter, as prescribed by the Guidelines for CPR and Emergency Cardiac Care.11 However, despite the lower applied force, chest recoil was incomplete, leading to a change in the relaxed diameter that was reduced approximately 20%. The chest wall of the human infant is also relatively deformable and similar changes in shape could occur during CPR.

One possible mechanism for this loss of thoracic recoil is a decrease in pulmonary compliance. Decreased compliance could result in decreased lung volume and atelectasis, which could account for the gradual rise in Paco2. We do not believe this is a major factor, however, because major areas of atelectasis were not evident at autopsy and because the rise in Paco2 was much slower than the major change in recoil that occurred within the first few minutes of CPR. The gradual rise in Paco2 is more likely related to a rise in mixed venous PO2. Moreover, the change in chest diameter is too large to be solely accounted for by a change in lung compliance. Rather, the inherent mechanical properties of the infant chest wall are probably the predominant factor.
TABLE 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Before arrest</th>
<th>5 min</th>
<th>20 min</th>
<th>35 min</th>
<th>50 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalic muscle</td>
<td>I 6.9±2.3</td>
<td>0.9±0.5</td>
<td>2.8±1.1^</td>
<td>3.2±1.1^</td>
<td>2.8±1.2^</td>
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<tr>
<td></td>
<td>II 12.1±4.0</td>
<td>0.7±0.5</td>
<td>0.8±0.2</td>
<td>1.2±0.6</td>
<td>0.9±0.3</td>
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<tr>
<td>Cephalic skin</td>
<td>I 2.6±0.5</td>
<td>1.0±0.6</td>
<td>1.0±0.4</td>
<td>1.1±0.4</td>
<td>0.4±0.2</td>
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<td></td>
<td>II 4.9±1.4</td>
<td>0.5±0.2</td>
<td>0.4±0.2</td>
<td>0.3±0.1</td>
<td>0.2±0.1</td>
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<tr>
<td>Tongue</td>
<td>I 5.5±0.9</td>
<td>3.9±2.1</td>
<td>3.0±1.1</td>
<td>2.8±0.8</td>
<td>2.3±1.1</td>
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<td></td>
<td>II 8.4±2.2</td>
<td>1.7±0.4</td>
<td>1.4±0.3</td>
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<td>Jejunum</td>
<td>I 38±9</td>
<td>8.7±6.8</td>
<td>6.9±3.4</td>
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<td>II 30±4</td>
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<td>3.6±0.8</td>
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<td>2.7±0.9</td>
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<td>Kidney</td>
<td>I 189±24</td>
<td>21.1±12.5</td>
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<tr>
<td></td>
<td>II 188±25</td>
<td>4.3±3.6^</td>
<td>1.1±0.6</td>
<td>0.7±0.4</td>
<td>0.2±0.1</td>
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</table>

Group I, without epinephrine; group II, with epinephrine. Prearrest values were not significantly different by unpaired t test.

The consequences of this loss of recoil are twofold: first, higher intrathoracic pressures may be generated because of the reduced relaxed diameter, and second, the possibility of direct cardiac compression between the sternum and vertebral column is enhanced. Our data do not distinguish between direct cardiac compression, which has traditionally been presumed to be important in infant CPR, and intrathoracic pressure as the predominant mechanism for the generation of peripheral blood flow in this preparation. However, the high systolic right atrial pressure, exceeding 80 mm Hg, is consistent with the intrathoracic pressure mechanism for pumping blood. It should also be pointed out that the positive aortic-to-right atrial systolic pressure gradient in the epinephrine group does not necessarily imply direct cardiac compression. Epinephrine, by causing peripheral vasoconstriction, may increase the time constant for discharging blood through the arterial system. In this case, the change in aortic pressure with each compression, i.e., pulse pressure, will approach the pulsatile change in intrathoracic pressure. Therefore, it is possible to explain our observations by the intrathoracic pump mechanism.

Effect of epinephrine. The infusion of epinephrine substantially augmented cerebral and myocardial blood flows during both the initial and prolonged phases of CPR. Furthermore, cerebral blood flow could be maintained at prearrest levels during the first 20 min of CPR. In previous studies using either conventional or simultaneous compression-ventilation CPR in dogs it was found that epinephrine caused

TABLE 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Before arrest</th>
<th>5 min</th>
<th>20 min</th>
<th>35 min</th>
<th>50 min</th>
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<td>Paco_2 (mm Hg)</td>
<td>I 125±10</td>
<td>180±37</td>
<td>161±42</td>
<td>147±44</td>
<td>118±36</td>
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<tr>
<td></td>
<td>II 165±14</td>
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<td>123±30</td>
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<tr>
<td>Paco_2 (mm Hg)</td>
<td>I 40±2</td>
<td>21±4^</td>
<td>37±8</td>
<td>48±19^</td>
<td>55±27^</td>
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<td></td>
<td>II 43±3</td>
<td>34±6</td>
<td>39±6</td>
<td>46±5</td>
<td>47±7</td>
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<td>Arterial pH</td>
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<td>7.52±0.07</td>
<td>7.19±0.08</td>
<td>7.07±0.11^</td>
<td>6.99±0.12^</td>
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<tr>
<td></td>
<td>II 7.35±0.03</td>
<td>7.38±0.07</td>
<td>7.15±0.06^</td>
<td>6.98±0.04^</td>
<td>6.90±0.05^</td>
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<tr>
<td>Arterial hemoglobin (g/dl)</td>
<td>I 9.4±0.4</td>
<td>8.8±0.3</td>
<td>7.6±0.5^</td>
<td>7.2±0.5^</td>
<td>6.1±0.5^</td>
</tr>
<tr>
<td></td>
<td>II 11.2±0.6</td>
<td>10.9±0.7</td>
<td>9.6±0.7^</td>
<td>8.5±0.7^</td>
<td>7.1±0.5^</td>
</tr>
<tr>
<td>Arterial O_2 saturation (%)</td>
<td>I 100±0</td>
<td>99±1</td>
<td>83±10</td>
<td>75±14^</td>
<td>73±14^</td>
</tr>
<tr>
<td></td>
<td>II 100±0</td>
<td>97±2</td>
<td>88±5</td>
<td>84±9</td>
<td>85±9</td>
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<tr>
<td>Arterial O_2 content (ml/dl)</td>
<td>I 13.4±0.6</td>
<td>12.9±0.6</td>
<td>9.3±1.4^</td>
<td>7.8±1.6^</td>
<td>6.4±1.4^</td>
</tr>
<tr>
<td></td>
<td>II 16.2±0.7</td>
<td>15.0±1.1</td>
<td>11.6±0.6^</td>
<td>10.0±0.9^</td>
<td>8.6±1.0^</td>
</tr>
<tr>
<td>Sagittal sinus O_2 content (ml/dl)</td>
<td>I 6.0±0.4</td>
<td>2.3±0.5^</td>
<td>1.3±0.4^</td>
<td>1.3±0.4^</td>
<td>1.3±0.5^</td>
</tr>
<tr>
<td></td>
<td>II 8.7±1.8^</td>
<td>4.8±1.2^</td>
<td>3.4±0.8^</td>
<td>2.1±0.6^</td>
<td>1.2±0.1^</td>
</tr>
</tbody>
</table>

Group I, without epinephrine; group II, with epinephrine.

^p < .05 vs prearrest value; ^p < .05 vs group I values.
selective vasoconstriction in noncerebral peripheral vascular beds. This maintained higher aortic systolic and diastolic pressures for perfusing heart and brain without markedly altering right atrial or intracranial pressures. Our results in piglets are consistent with these studies. We found that without epinephrine, blood flow to some peripheral tissues was maintained (cephalic skin and tongue) or actually increased (cephalic muscle) as CPR was continued beyond 5 min. This occurred despite declining aortic pressures, which implies further peripheral vasodilatation and suggests that part of the decline in aortic pressure resulted from the loss of neurohumoral vasoconstrictor tone. With the administration of epinephrine, vasoconstrictor tone was apparently higher because peripheral blood flows were lower at higher aortic pressures. Thus, our data support the concept that epinephrine benefits cerebral and myocardial perfusion by selective vasoconstriction of noncerebral peripheral vascular beds, thereby raising perfusion pressure for the brain and heart.

An alternative explanation is that aortic pressure was elevated in the epinephrine group because intrathoracic pressure may be greater as a result of a greater lung inflation after every fifth compression. This explanation seems unlikely. A greater ventilation should be associated with a lower PaCO₂. We found no difference in PaCO₂ between groups, and the 5 min values tended to be in the opposite direction.

Epinephrine did not sustain high cerebral or myocardial blood flow beyond 35 min of CPR, which differs from results of a similar study of prolonged CPR in adult dogs. The reason for this difference is unclear, but several possibilities can be offered. It could potentially be attributed to the effects of hypovolemia caused by intracellular and extracellular fluid shifts with prolonged CPR, to central hypovolemia with large amounts of fluid sequestered in peripheral compliance vessels, or to arterial hypovolemia caused by obstruction of central blood vessels due to chest deformation. Alternatively, the efficacy of epinephrine may not be sustained in the presence of acidosis in young piglets. Whether this loss of efficacy occurs in older pigs or is specific to infant pigs is unknown.

The elevated myocardial blood flow at 5 and 20 min of CPR in the epinephrine group was associated with an elevated aortic diastolic pressure. These results are consistent with those in dogs and have led to the use of the diastolic pressure gradient as an indicator of changes in coronary blood flow during CPR. However, our data suggest that forward coronary blood flow may occur during the compression phase of CPR with epinephrine infusion because of the positive systolic aortic-to-right atrial pressure gradient. A positive systolic gradient can also occur in dogs with epinephrine. Therefore, the diastolic gradient as an index of coronary flow may be an incomplete indicator for comparing different interventions during CPR.

It has been suggested that epinephrine may worsen subendocardial ischemia in fibrillating hearts at constant coronary blood flow. We found that the ratio of subendocardial to subepicardial blood flow fell from prearrest levels during CPR, but that it was not lower after administration of epinephrine. Others have also observed this ratio to decline with the onset of fibrillation in pump-perfused hearts. Therefore, unless epinephrine increases oxygen demand selectively in the subendocardium, selective subendocardial ischemia is unlikely with epinephrine infusion in this preparation.

Cardiac arrest in children is often the result of asphyxia leading to bradyarrhythmias and asystole or to fibrillation. We have not evaluated the efficacy of epinephrine after cardiac arrest with a prior hypercarbic hypoxic episode in an infant preparation. However, in adults, epinephrine is effective in raising perfusion pressure after asphyxia or after a 5 min delay in the onset of CPR after ventricular fibrillation when tissue anoxia is significant.

Cerebral oxygen uptake. Cerebral oxygen uptake has not previously been measured during CPR. Samples of sagittal sinus blood are assumed to represent pure cerebral venous blood. While this is a reasonable assumption at normal levels of cerebral blood flow, some extracranial venous blood may enter the cavernous sinuses from a retrograde direction during chest compression at a low cerebral blood flow. However, this error should have little bearing on our conclusions because cerebral oxygen uptake is necessarily extremely low at near-zero blood flow.

The brain normally extracts 40% to 50% of supplied oxygen. If cerebral blood flow decreases by more than 50%, an increase in oxygen extraction will not be capable of maintaining oxygen uptake. We found that without epinephrine, cerebral oxygen extraction was nearly maximal (84%) by 5 min of CPR. As cerebral blood flow continued to fall below 50% with prolonged CPR, cerebral oxygen uptake necessarily fell because oxygen extraction was near maximal.

The infusion of epinephrine increased cerebral oxygen uptake and maintained it at prearrest levels for over 20 min of CPR. Epinephrine may directly stimulate cerebral oxygen uptake when the blood-brain barrier is disrupted, which may occur during CPR. This potential stimulation of oxygen demand could
adversely affect tissue oxygenation if cerebral blood flow is limited. However, we found higher sagittal sinus oxygen contents at 5 and 20 min of CPR and a lower fractional oxygen extraction at 20 min in the epinephrine group. Only when cerebral blood flow declined with the loss of perfusion pressure during prolonged CPR did oxygen extraction become maximal. This indicates that the benefit of increasing oxygen supply with epinephrine outweighs any potential metabolic stimulation in terms of tissue oxygenation.

This conclusion is based on global venous measurements; regional heterogeneity at the microcirculatory level cannot be excluded. We did not observe gross differences between primary supply area and watershed border areas of the major cerebral arteries. However, blood flow was better sustained in thalamic and brainstem regions with epinephrine. Similar observations have been made in adult dogs in which the onset of CPR was delayed. Whether this represents regional metabolic or vascular effects of epinephrine, or simply a greater regional vasodilator reserve that emerges with the higher perfusion pressure is not clear.

Arterial oxygen content fell progressively during CPR in both groups as a result of decreased hemoglobin concentration and, in some animals, decreased oxyhemoglobin saturation. Thus, with near-maximum cerebral oxygen extraction, the decrease in arterial oxygen content may also force cerebral oxygen uptake to decline in our preparation. However, even if arterial oxygen content was maintained with prolonged CPR, the blood flows achieved at these times would still have exhausted the oxygen extraction reserve and oxygen uptake would still have declined. Therefore, the progressive hemodilution probably affected the results quantitatively to some extent during prolonged CPR, but not the conclusion that cerebral oxygen uptake was better preserved with epinephrine over 35 min of CPR.

In conclusion, we found that conventional CPR in 2-week-old piglets generates high intrathoracic vascular pressures and high levels of myocardial and cerebral blood flows. These pressures and flows are higher than those generally found in adult animals and may be related to the change in shape of the highly compliant chests. Without epinephrine, these high blood flows are not sustained during prolonged CPR. With the continuous infusion of epinephrine, higher levels of myocardial and cerebral blood flows are achieved for more prolonged periods as a result of elevated systolic and diastolic perfusion pressures. Moreover, the infusion of epinephrine enhances cerebral oxygen uptake by increasing cerebral blood flow and not by increasing cerebral oxygen extraction.

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