Persistent low cerebral blood flow velocity following profound hypothermic circulatory arrest in infants

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Acute neurological morbidity following repair of congenital heart disease (CHD) in infancy is well recognized, particularly with the modalities of hypothermic cardiopulmonary bypass (CPB) and profound hypothermic circulatory arrest (PHCA). Reduced O_2 delivery (perfusion defect) during rewarming following PHCA has been shown in the operating room. This reduction in cerebral blood flow coincides with disordered cerebral metabolism and oxygen utilisation after PHCA. The objective of this study was to extend the period of investigation of cerebral blood flow velocity (CBFV) behaviour in infants following PHCA to determine if hypoperfusion persisted in the paediatric intensive care unit (PICU). Ten patients undergoing CHD surgery were divided, based on the pump modality employed, into either mild hypothermic CPB or profound hypothermic CPB with circulatory arrest. Following admission to the PICU, sequential recordings of the mean CBFV in the middle cerebral artery, anterior fontanelle pressure, haemodynamic variables, tympanic membrane temperature, haematocrit and $PaCO_2$ were performed. The PHCA group had a consistently reduced CBFV compared with the control group ($P < 0.05$). The CBFV values at one, two and four hours were 60 ± 11, 51.8 ± 11.4 and 52.6 ± 11.9 respectively in the mild hypothermic CPB group. The CBFV values at one, two and four hours were 26.6 ± 6.8, 32.6 ± 10 and 34 ± 8 respectively in the PHCA group. There was no difference in cerebral perfusion pressure between both groups. Tympanic temperature, haematocrit and $PaCO_2$ did not vary between groups at any interval. This study demonstrates a sustained reduction in the CBFV pattern following PHCA into the postoperative period despite adequate cerebral perfusion pressures. This abnormality correlates with electroencephalographic aberrations documented after PHCA. It supports the concept of a prolonged unreactive cerebrovascular bed which could potentially contribute to the acute neurological morbidity following PHCA in neonates.

La morbidité neurologique infantile attribuable aux malformations cardiaques congénitales (MCG) opérées sous circulation extracorporelle (CEC) en hypothermie et sous arrêt circulatoire en hypothermie profonde (ACHP) est bien connue. En salle d'opération, on a déjà démontré une diminution de l'apport en oxygène (insuffisance de perfusion) au cours du réchauffement pendant l'ACHP. Cette réduction de la perfusion cérébrale coïncide avec un bouleversement du métabolisme cérébral et de l'utilisation de l'oxygène après l'ACHP. L'objectif de ce travail était d'étendre la durée de l'examen du comportement de la vélocité du débit sanguin cérébral (VDSC) après un ACHP chez les enfants pour déterminer si l'hypoperfusion persistait à l'unité des soins intensifs pédiatriques (UPSI). Après l'admission à l'UPSI, des enregistrements séquentiels de la VDSC moyenne de l'artère cérébrale moyenne, de la pression de la fontanelle antérieure, de l'hématocrite et de la $PaCO_2$ ont été effectués. Le groupe ACHP avait une VDSC diminuée comparativement au groupe contrôle ($P < 0,05$). Les valeurs de la VDSC à la première, deuxième et quatrième heure étaient de 60 ± 11, 51,8 ± 11,4 et 52,6 ± 11,9 respectivement dans le groupe de la CEC légèrement hypothermique. On n'a pas trouvé de différence pour la pression cérébrale de perfusion entre les deux groupes. La température tympanique, l'hématocrite et la $PaCO_2$ n'ont varié en aucun moment entre les groupes. Cette étude montre une réduction soutenue dans l'évolution de la VDSC après une ACHP pendant la période post-

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opératoire malgré des pressions de perfusion adéquates. Cette anomalie concorde avec les changements électroencéphaliques trouvés après l'ACHP. Elle confirme le concept de non réactivité du lit cérébrovasculaire qui pourrait contribuer à la morbidité neurologique après l'ACHP chez le nouveau-né.

The use of deep hypothermic circulatory arrest during cardiopulmonary bypass facilitates surgical repair of complex congenital cardiac lesions in infants. As improved myocardial protection strategies reduce the risk of serious cardiac morbidity, the obligatory global ischaemic insult imposed by profound hypothermic circulatory arrest (PHCA) focuses attention on central nervous system morbidity. Adverse neuropsychological sequelae following congenital heart surgery in infants and children are well documented. Ferry[1] described a 2–25% incidence of acute neurological morbidity from six major paediatric centres in North America undertaking congenital cardiac surgery using hypothermic cardiopulmonary bypass with or without PHCA. Newburger,[2] in a single centre, prospective analysis of infants undergoing arterial switch repair for transposition of the great arteries reported an increased acute neurological risk imposed by the use of PHCA, compared with continuous low-flow cardiopulmonary bypass. Burrows *et al.* documented transient neurophysiological dysfunction, coinciding with an increase in anterior fontanelle pressure, which occurred after PHCA.[3]

Extensive investigation has focused on the aetiology of this neurological dysfunction. Alterations in blood flow and distribution, "mechanical" injury from macro and microembolization and systemic inflammatory responses related to cardiopulmonary bypass (CPB) are the primary perioperative factors thought to be involved.[4,5] The exclusive noxious factor associated with the use of PHCA, (and perhaps occasional low-flow hypothermic cardiopulmonary bypass interventions[6]) involves complete cessation of blood flow for a variable interval. Abnormalities in the magnitude and pattern of cerebral blood flow following a period of PHCA have been demonstrated. These include a sustained reduction associated with loss of autoregulation following recovery from hypothermic cardiopulmonary bypass and PHCA using xenon clearance techniques.[7] Subsequently this group reported altered cerebral metabolism and oxygen utilization following PHCA, despite adequate hypothermic suppression of cellular metabolism.[8] This evidence of a sustained reduction in cerebral blood flow and altered metabolism following recovery from PHCA has been corroborated by other groups using similar methodology (xenon clearance global cerebral blood flow and sagittal sinus sampling) or transcranial Doppler sonography.[9,10]

These perfusion and metabolic abnormalities following PHCA have all been observed while the patient remained anaesthetized in the operating room during the rewarming phase of cardiopulmonary bypass and following discontinuation of the extracorporeal circulation. Recently an animal model has been used to compare PHCA with continuous low-flow CPB and a reduction in cerebral blood flow and an increased cerebral vascular resistance up to at least four hours after PHCA was demonstrated by radioactive microsphere determination.[11] In contrast, van der Linden using transcranial Doppler sonography studied the characteristics of the peak systolic cerebral blood flow velocity of the middle cerebral artery in ten infants (age 7.3 ± 1.3 mo) undergoing congenital heart surgery using PHCA and reported no difference between the pre- and postoperative *systolic* flow velocities in the middle cerebral arteries.[12] Despite the absence of flow variability, a metabolic aberration manifested by an increase in cerebral lactate production was observed exclusively in the PHCA group.

This paper reports a study of the behaviour of cerebral blood flow velocity in neonates and infants following PHCA. Transcranial Doppler was used in the Paediatric Intensive Care Unit (PICU) to measure the mean cerebral blood flow velocity in the M_1 segment of the middle cerebral artery for a period of at least six hours following PHCA.

Methods

With the approval of the Research Ethics Board of the Hospital For Sick Children, Toronto, and written informed parental consent, ten patients aged less than 19 mo (month) undergoing congenital heart disease surgery were studied after their admission to the PICU. The patients were divided into two groups in accordance with the modality of extracorporeal support used. Randomization was determined by the surgical requirements of the operative procedure. The study group underwent deep hypothermic CPB with PHCA whereas the control group had mild hypothermic CPB only. Patients were excluded from the study if neurological dysfunction had been clinically identified before surgery.

Anaesthesia was standardized in both groups. Induction and maintenance were achieved with fentanyl 50–100 $\mu g \cdot kg^{-1}$ *iv*. Pancuronium 0.15 $mg \cdot kg^{-1}$ *iv* was administered to facilitate tracheal intubation and subsequent intermittent positive-pressure ventilation with an air/oxygen mixture. Supplemental doses of fentanyl and pancuronium were given as required. Cerebrovasodilator therapy was used to facilitate temperature fluxes while on pump and following weaning from CPB was employed primarily for haemodynamic manipulation. Rectal, oesophageal and myocardial temperatures were monitored continuously.

Following anticoagulation with heparin 300 IU · kg^{-1}, non-pulsatile CPB was established with a standard roller pump (Cobe Canada Ltd., Scarborough, Ontario) and a 0.8 or a 1.6 m^2 hollow fibre membrane oxygenator. The CPB circuit was primed with packed red blood cells, a balanced salt solution (PlasmaLyte 148, Baxter Corporation, Toronto, Ontario), 25% albumin, mannitol 1 g · kg^{-1}, sodium bicarbonate, calcium chloride, heparin and cefazolin, with the objective of maintaining the haematocrit between 20–30% during CPB. Cardiopulmonary bypass flows were calculated as normal between 2.4 and 3.2 L · m^{-2} · min^{-1}. Alpha-stat acid-base management was used where temperature correction of measured pH and $PaCO_2$ was not performed, with desired end-points of pH between 7.35 to 7.4 and $PaCO_2$ between 35 to 45 mmHg.

All study measurements were performed in the PICU, at intervals of one, two and four hours after the admission of the patient. Real-time haemodynamic variables (heart rate, invasive mean arterial pressure and central venous pressure) were recorded on a Hewlett-Packard M1106B (Hewlett Packard, Mississauga, Ont.) and downloaded onto a Macintosh locally developed system (Apple Corporation, Cupertino, Ca.) for storage and subsequent retrieval. Cerebral perfusion pressure was defined as mean arterial pressure minus intracranial (anterior fontanelle) pressure or central venous pressure, whichever was greater. Anterior fontanelle pressure – an accurate estimation of intracranial pressure[13] – was measured by a pre-calibrated Albin-Bunegin fontanometer and displayed and recorded on a single channel recorder. Tympanic membrane temperature (CORE · CHECK 2090, IVAC Corporation, San Diego, Ca.), a non-invasive estimate of hypothalamic temperature, $PaCO_2$ and haematocrit were documented at each measurement interval. At the time of recording, sodium nitroprusside was the sole vasodilator agent being therapeutically employed in either group. Two patients in the control group, and four patients in the PHCA group, were receiving sodium nitroprusside therapy during the mCBFV readings. The doses ranged from 0.5 to 3 μg · kg^{-1} · min^{-1}.

Cerebral blood flow velocity (CBFV) was measured non-invasively by transcranial Doppler sonography with the Medasonics CDS MP218 (Medasonics Inc., Fremont, Ca.). This monitor had the following characteristics: an emitted ultrasonic frequency of 2 MHz; an emitted area of 1.5 cm^{-2}; an effective depth range of 25–120 mm; a resolution of 3 cm · sec^{-1} and an emitted clinical ultrasonic power of 100 mW. The frequency spectra of the Doppler signals were displayed on a real-time spectrum analyzer (Compaq 420, Houston, Texas) which allowed clear aural and visual separation of flow for unambiguous interpretation of the CBFV waveform.

The transducer probe was placed over the temporal window of the skull just cephalad to the zygomatic arch approximately 1–2 cm anterior to the tragus to insonate the M_1 segment of the ipsilateral middle cerebral artery (MCA). The gate depth was set to 30–35 mm initially depending on the size of the patient and according to the recommendations of Gillard *et al.*[14] The Doppler signal was optimized for clear and accurate measurements by adjusting the gate depth, angle of insonation, power and dynamic range. A reproducible window was ensured by stipulating that retrograde anterior cerebral artery flow (A_1 segment) accompanied all M_1 segment, MCA signals. The mean CBFV was obtained from the calculation of the area under ten CBFV profiles obtained during steady-state haemodynamics. This area was then multiplied by the elapsed time of ten consecutive velocity envelopes, the result being divided by ten to yield the mCBFV. This estimation represents the intravascular volume of flow which is the closest approximately of the real cerebral blood flow.

Statistical analysis

Demographic and parametric data were expressed as mean ± standard deviation. Intragroup analysis was performed using repeated-measures ANOVA with Student Newman Keuls test for multiple comparisons. The unpaired Student's t test was used for between group analysis at each measurement interval. The Fisher-exact test was used to analyse nonparametric data. Statistical significance was accepted as $P < 0.05$.

Results

Demographic data and CPB variables are presented in Tables I and II respectively. Patients in the control group were maintained on normal flow CPB throughout the repair or palliation of their congenital heart defect. The interval between cessation of CPB in the operating room and the first CBFV recordings in the PICU was documented for all patients. One patient in the PHCA group did not survive the perioperative course and died five days after her initial surgery secondary to her residual anatomical cardiac disease (repaired truncus arteriosus type II with bilateral branch pulmonary artery hypoplasia). All other patients recovered fully from their surgical interventions.

The mean cerebral blood flow velocity of the PHCA group was decreased at one, two and four hours following admission to the PICU compared with the control group (Figure 1). The cerebral perfusion pressure did not vary either within or between groups at any of the measuring intervals (Figure 2). There was no difference between haematocrit, tympanic temperature and $PaCO_2$ at any of the measuring time intervals between the control and

TABLE I Patient demographics

PHCA Patient #	*Age (days)*	*Weight (kg)*	*Diagnosis*	*Procedure*
1	208	4.5	AVSD	Repair
2	57	2.62	AVSD	Repair
3	9	2.4	IAA,TRUNC,VSD	Repair
4	99	3.91	AVSD	Repair
5	4	3.59	TGA	ASO
Mean (±SD)	75.4 (±84)*	3.4 (±0.88)*		
Control Patient #				
1	282	9.8	Previous ASO	Repair AS
2	245	6.4	COR Triatriatum	Repair
3	455	9.68	TAT	Redo BCPS
4	285	9.5	TAT	BCPS
5	132	6.44	HLHS	BCPS
Mean (±SD)	280 (±115)	8.4 (±1.8)		

*$P < 0.05$ compared with control.
Abbreviations: PHCA – profound hypothermic circulatory arrest; AVSD – atrioventricular septal defect; IAA – interrupted aortic arch; TRUNC – truncus arteriosus; VSD – ventricular septal defect; TGA – transposition of the great arteries; ASO – arterial switch operation; AS – aortic stenosis; TAT – tricuspid atresia; BCPS – bidirectional cavopulmonary shunt; HLHS – hypoplastic left heart syndrome.

TABLE II Cardiopulmonary bypass variables

	Control	*PHCA*	*$P < 0.05$**
Lowest temperature (°C)	30 (±3.4)	16.6 (±3.1)	*
CPB (min)	75.6 (±16)	79.8 (±20)	NS
PHCA (min)	NA	56 (±29)	
CPB off to 1st CBFV (min)	169 (±32)	152 (±25)	NS

Data are mean (±SD); NS = not significant; NA = not applicable. CPB = cardiopulmonary bypass. PHCA = profound hypothermic circulatory arrest.

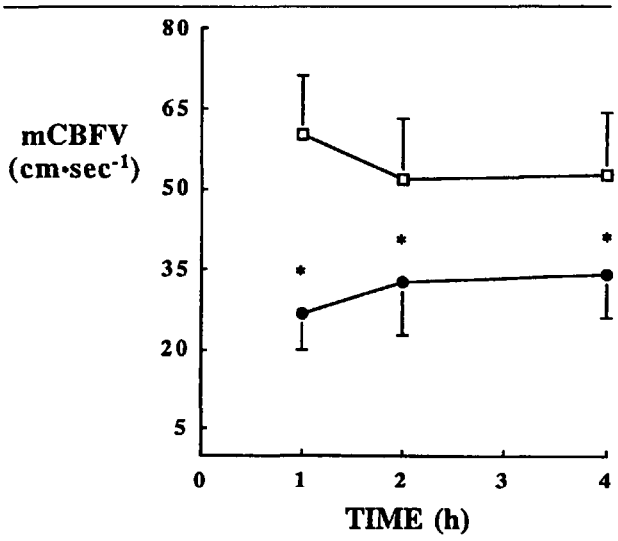

FIGURE 1 The mean cerebral blood flow velocity (mCBFV ± SD) was different at all measurement intervals between the PHCA (profound hypothermic circulatory arrest) group (●) and the normal flow CPB (cardiopulmonary bypass) group (□). Time 0 coincides with PICU (Paediatric Intensive Care Unit) admission. *P < 0.05.

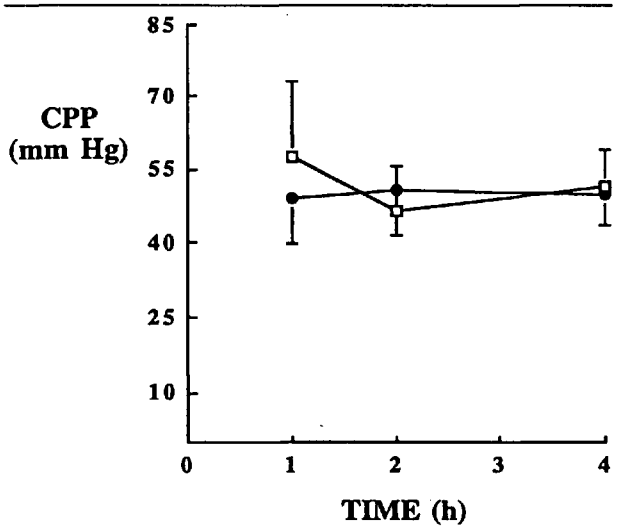

FIGURE 2 The cerebral perfusion pressure (CPP ± SD) did not differ between groups at any measurement interval. (● profound hypothermic circulatory arrest, □ normal flow cardiopulmonary bypass). Time 0 coincides with PICU (Paediatric Intensive Care Unit) admission.

PHCA groups (Table III). Blood glucose management was similar in both groups and there were no differences noted between groups perioperatively. Although cerebrovasodilator and inotropic interventions were more common in the PHCA group compared to the control group, this difference did not reach significance.

Discussion

This prospective, observational study demonstrated that a reduction in mean cerebral blood velocity (mCBFV) following PHCA continues for at least six hours after cardiopulmonary bypass compared with a group of patients with similar cerebral perfusion pressure and mild hypothermic CPB. The mCBFV values of both groups were different at all three measurement intervals. Between two to three hours after cessation of CPB (the first measurement) this reduction of mCBFV in the PHCA group was most pronounced. Although it remained lower than in the control group the difference declined with time. Cerebral perfusion pressures were similar at all times in both groups. The presence or absence of cerebral auto-

TABLE III Influence of cerebral blood flow determinants at each measuring interval

Time (hr)	*Control*	*PHCA*	*$P < 0.05$*
	Haematocrit		
1	0.3 ± 0.04	0.36 ± 0.12	NS
2	0.3 ± 0.06	0.39 ± 0.1.	NS
4	0.31 ± 0.03	0.40 ± 0.08	NS
	Temperature (° C)		
1	37.3 ± 1.4	36.6 ± 1.25	NS
2	38 ± 1.4	37.4 ± 0.8	NS
4	37.4 ± 1.2	37.8 ± 0.95	NS
	$PaCO_2$ (mmHg)		
1	40.6 ± 5.7	38.6 ± 12.4	NS
2	40.4 ± 5.4	37.4 ± 12	NS
4	42.2 ± 7.7	35.8 ± 9.5	NS

Data are mean (±SD); NS = not significant; h = hour. PHCA = profound hypothermic circulatory arrest.

regulation cannot be confirmed since no attempt was made to modify the systemic perfusion pressure or the cerebrovascular resistance.

Examination of the results of this study leads to three potential interpretations. Firstly, the reduced cerebral blood flow velocity could be appropriate for the resting metabolic activity of the rewarmed brain. A review of the literature shows only two studies addressing the post-PHCA flow-metabolic coupling of the brain in the hours following the discontinuation of CPB.

Mezrow *et al.*, using a dog model, studied cerebral blood flow and metabolism after 45 and 90 min of PHCA.[15] Cerebral blood flow was measured using a radionuclide-labelled microspheres whereas cerebral metabolic rates for oxygen and glucose were calculated after sampling arterial and sagittal sinus blood. A reduction in cerebral blood flow with elevated cerebrovascular resistance was observed at four hours after PHCA despite normalization of oxygen and glucose consumption. Compensation was achieved by an elevated substrate extraction, which demonstrates uncoupled flow-metabolism.

Van der Linden *et al.* studied both cerebral blood flow and cerebral metabolic variables in 17 children (mean age 7.5 mo) undergoing either low-flow continuous CPB or PHCA (mean duration 39 min).[12] Systolic cerebral blood flow velocity in the middle cerebral artery returned to preoperative levels within two hours following CPB. However, a cerebral metabolic deficit manifested by an increase in lactate release was measured for up to six hours following PHCA, suggesting either inadequate substrate (i.e., oxygen and glucose) delivery or cellular utilization by the rewarming brain. Again flow-metabolism uncoupling is evident, although the dynamics of the uncoupling are not the same. It is worth noting that the cerebral blood flow reported in their study is based on *peak* systolic flow velocity which is more inclined to reflect changes in red cell velocity than volumetric flow. We believe that the best correlation between CBF and CBFV in the M_1 segment of the middle cerebral artery is most accurately reflected by the mean CBFV ($AUC^*t_2-t_1$) (AUC corresponds with area under the velocity curve and t_2 represents the time at the end of recording, t_1 is the initial time). They also reported the absence of diastolic flow velocity for a period of up to six hours after PHCA.[16] This could be due to either a persistently elevated intracranial pressure[3] or the expression of the higher critical-opening pressure required after PHCA.[6] The absence of diastolic flow observed by van der Linden was repeatedly identified during this study. Impaired cerebral metabolism and blood flow in the immediate post-CPB period has been demonstrated by two other groups. However, these results are not specifically comparable with the data from this study because of the differing study periods.[8,17,18]

Secondly, the mCBFV observed in the control group could be increased suggesting luxury perfusion or elevated cerebral metabolic activity. Bode[19] reported mCBFV values in the order of 74 $cm \cdot sec^{-1}$ in awake infants aged 3–12 mo. Previous studies in this and other institutions have shown that mCBFV in the range 50–60 $cm \cdot sec^{-1}$ are usual following the induction of anaesthesia and at the conclusion of CPB in infants and children undergoing similar procedures as in this study.[20,21] Therefore, the postulation that the mCBFV observed in the control group was relatively hyperaemic is also doubtful.

Finally, the most plausible interpretation for the mCBFV observed with the PHCA patients is the presence of inadequate cerebral perfusion. The validity of this statement is supported by Mezrow[18] who, using a dog model and a microsphere technique determination of cerebral blood flow, revealed reduced flow in a magnitude very similar to that reported in this study. The persistence of reduced cerebral blood flow continued until eight hours after PHCA which concurs with the results reported in this clinical study where a persistence of reduced flow lasted up to six hours after PHCA. Mezrow showed that this reduction in flow correlated directly with an elevated cerebrovascular resistance. Other groups, using varied methods of cerebral blood flow determination in infants undergoing PHCA, have documented reduced cerebral blood flow in the operating room, following discontinuation of CPB.[7,9] The purpose of this study was to take their intraoperative observations further and demonstrate

if a persistent reduction in cerebral blood flow in the PICU occurred.

There are some limitations and methodological considerations in this study that need to be addressed. The two groups were not matched for age. This occurred because the design of this study was dictated by the CPB temperature level used. The necessity to have a mild hypothermic and severe hypothermic group resulted in a series of control patients predominantly undergoing bidirectional cavopulmonary shunts, a procedure usually performed in the older infant and child. However, the age-corrected CBFV results (based on the normal values as described by Bode[19]) demonstrate a persistent difference between the two groups.

Because of the nature of this observational study pharmacological therapy administration was not controlled. The use of sodium nitroprusside was biased in favour of the study group versus the control group. This agent is a cerebrovasodilator that increases intracranial pressure in humans, presumably by increasing intracranial blood volume.[22] However, during hypothermic CPB, sodium nitroprusside does not dilate cerebral resistance vessels.[23] Thus, although its effects are controversial the consequences for this study are that it has either made no difference or artefactually increased the cerebral blood flow velocities of the study group and hence reduced the observed difference between the two groups. Therefore, the use of sodium nitroprusside should not bias the results of this study.

Cardiac output changes have little impact on cerebral blood flow. Bouma *et al.* found no correlation between changes in cardiac output and changes in cerebral blood flow in head-injured patients, even in the absence of autoregulation.[24] Cerebral perfusion pressures and inotropic interventions were similar in both groups. Although no comment can be made about the actual cardiac output, the cerebral perfusion pressures were similar in both groups so it is unlikely that it accounted for the observed differences in mCBFV.

The use of mCBFV as an index of cerebral perfusion is based on previous data that demonstrated that the basal cerebral arteries in children remain constant in calibre despite variation in either $PaCO_2$ or cerebral perfusion pressure.[25,26] The site of major cerebrovascular resistance appears to be downstream from these conductance vessels. A second assumption is that changes in CBFV are proportional to changes in CBF. This conjecture has been validated by two adult studies demonstrating good correlation between changes in cerebral blood flow and CBFV.[27,28] Thirdly, we assume that the angle of insonation remains constant between measurements. In this study inter-observer error was eliminated by ensuring that a single investigator performed all data measurements. Consistency of positioning was optimized by standardizing the fixation technique between both sequential readings and subjects, and ensuring muscle relaxation persisted for the study interval. Previous investigators have shown that the angle between the ultrasound beam and the flow of blood must be $<30°$ to minimize the error in velocity measurement.[29] Because the velocity of blood flow is proportional to the cosine of the angle of insonation, as the angle of insonation approaches 0° the cosine approaches 1.0. The maximum error that can be attributed to the change in the angle of insonation is 13% at an angle of 30°. Blood flow in the M_1 segment of the middle cerebral artery is oriented toward the ultrasound probe and therefore if the vessel diameter, the angle of Doppler insonation, and the flow characteristics within the vessel are constant, the changes recorded will reflect changes in CBF. As the conduct of cardiopulmonary bypass and the anaesthetic management were similar between both groups it is assumed that these factors did not influence the flow velocity observed. Finally, the blood glucose concentrations did not vary between both groups during the course of cardiopulmonary bypass.

What is the importance of this study? A persistent reduction in mCBFV in infants undergoing PHCA into the postoperative period is reported. This is the first clinical study suggesting this observation, although it has been reported in an animal study.[11] This reduction in mCBFV following PHCA remains when compared with the control group, even with age correction. This phenomenon could be a consequence of what has been termed cold-induced "vasoparesis."[30] A future study to validate previous suggestions that this reduced flow is associated with disordered metabolism is justified. Also the mCBFV behaviour in the PICU following continuous low flow CPB is unknown. A high incidence of acute neurological morbidity has been reported after repair or palliation of congenital heart lesions when PHCA is used as a therapeutic strategy.[1,31] Postoperatively the "excitotoxins" liberated during the intraoperative course in infants undergoing CPB and PHCA may contribute to the high incidence of early seizures.[2,32] However, this data examined the consequences of PHCA. The potential root cause of the cerebral perfusion defect despite apparently normal cerebral perfusion pressures remains to be elucidated.

In conclusion, a cerebral oxygen delivery defect for up to six hours following PHCA in neonates and infants is suggested by this study. This may be a contributing factor to, or a result of, the observed association of acute neurological morbidity and PHCA. It supports Greeley's contention that the prudent use of PHCA should be combined with emphasis on improvement of cerebral protection both during and after the arrest period.[33]

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