

# Measurement of Cerebral-oxygenation Status When Commencing Cardiopulmonary Bypass in Pediatric Open-heart Surgery

Hiroomi Murayama, MD,<sup>1</sup> Shuji Tamaki, MD,<sup>1</sup> Akihiko Usui, MD,<sup>2</sup> and Yuichi Ueda, MD<sup>2</sup>

**Objective:** We hypothesize that there is a difference in the cerebral-oxygenation status between cyanotic and non-cyanotic congenital heart disease when commencing a crystalloid-primed cardiopulmonary bypass (CPB). We tested this hypothesis by using near-infrared spectroscopy (NIRS).

**Methods:** Group 1 consisted of ten patients with non-cyanotic congenital heart diseases, including atrial septal (n=4) and ventricular septal defects (n=6), while group 2 consisted of ten patients with cyanotic congenital heart diseases, including tetralogy of Fallot (n=7) and univentricular heart (n=3). Changes in cerebral-oxygenated, deoxygenated and total hemoglobin concentrations were measured by NIRS just before and every minute for the first 10 min after commencing CPB. Arterial blood analysis was performed at those same time times.

**Results:** NIRS showed a rapid fall and plateauing of cerebral-oxygenated, deoxygenated and total hemoglobin in group 1. However, although group 2 showed a rapid fall and plateauing of cerebral-oxygenated hemoglobin, a rapid fall and continuous gradual decrease in cerebral-deoxygenated and total hemoglobin were also seen. Cerebral-deoxygenated and total hemoglobin decreased more markedly in group 2 than in group 1 ( $P<0.001$ ,  $0.01$ , respectively).

**Conclusion:** NIRS revealed that the cerebral-oxygenated hemoglobin could be maintained at a similar level at the beginning of CPB in both groups. However, it showed a different distribution of cerebral-deoxygenated and total hemoglobin between the groups. An inadequate cerebral-oxygenation status may occur in the early phase of CPB in patients with cyanotic congenital heart diseases. (*Ann Thorac Cardiovasc Surg* 2006; 12: 105–12)

**Key words:** cerebral-oxygenation status, near-infrared spectroscopy, cardiopulmonary bypass, congenital heart disease

## Introduction

Crystalloid-primed nonpulsatile cardiopulmonary bypass (CPB) is now routinely employed for eligible patients in institutions worldwide. It brings about numerous changes

---

*From the <sup>1</sup>Department of Thoracic and Cardiovascular Surgery, Ogaki City Hospital, Ogaki, and <sup>2</sup>Department of Cardio-Thoracic Surgery, Nagoya University, Nagoya, Japan*

Received August 10, 2005; accepted for publication November 2, 2005.

Address reprint requests to Hiroomi Murayama, MD: Department of Thoracic and Cardiovascular Surgery, Toyohashi Municipal Hospital, 50 Aotake-cho, Hakken-nishi, Toyohashi, Aichi 441-8570, Japan.

in such patients, including excessive hemodilution, compulsory venous drainage, reduced pulmonary circulation, whole-body cooling, higher arterial-oxygenation tension, and non-pulsatile arterial pressure. These changes will affect the cerebral oxygen metabolism, and that effect will occur acutely, especially in small children. In patients with cyanotic heart diseases, the arterial oxygen status dramatically changes upon commencing CPB. We hypothesized that there is a difference in the cerebral oxygenation status between cyanotic and non-cyanotic heart diseases. Despite good clinical results from current pediatric open-heart surgery, the cerebral-oxygenation status during CPB has not been fully elucidated.

Near-infrared spectroscopy (NIRS) is a device that per-

**Table 1. Patient characteristics**

	Group 1	Group 2	<i>P</i> value
Age (yrs)	3.3±1.8	2.5±0.9	NS
Sex (m/f)	6/4	8/2	NS
Height (cm)	90.0±12.2	81.9±8.4	NS
Weight (kg)	11.8±3.4	10.3±1.8	NS
BSA (m <sup>2</sup> )	0.55±0.12	0.48±0.07	NS
Priming volume (mL)	568±50	589±92	NS
Hemodilution rate (%)	40.7±4.6	44.0±3.4	NS

All data are expressed as the mean ± standard deviation of the mean. The comparison of gender was made with Fisher's exact probability test. Other comparisons between the groups were made with unpaired *t*-test. A *P* value <0.05 was considered significant. BSA, body surface area; NS, not significant.

mits noninvasive measurements of cerebral-oxygenation status along with oxygenated and deoxygenated hemoglobin levels. In this study, we measured cerebral-oxygenation status with NIRS, focusing on the early changes that occur after CPB initiation to clarify the differences in cerebral-oxygenation status between cyanotic and non-cyanotic heart diseases.

## Methods

### Clinical profile

Twenty patients (mean±SD age: 2.9±1.4 years, body weight: 11.0±2.7 kg) undergoing open-heart surgery were included as subjects in this study (Table 1). Group 1 consisted of ten patients with non-cyanotic congenital heart diseases, including atrial septal defect (n=4) and ventricular septal defect (n=6). Another ten (group 2) had cyanotic congenital heart diseases with tetralogy of Fallot (n=7) and univentricular heart (n=3). There were no significant differences in age, sex, height, weight, or body surface area between the groups.

### Surgical management

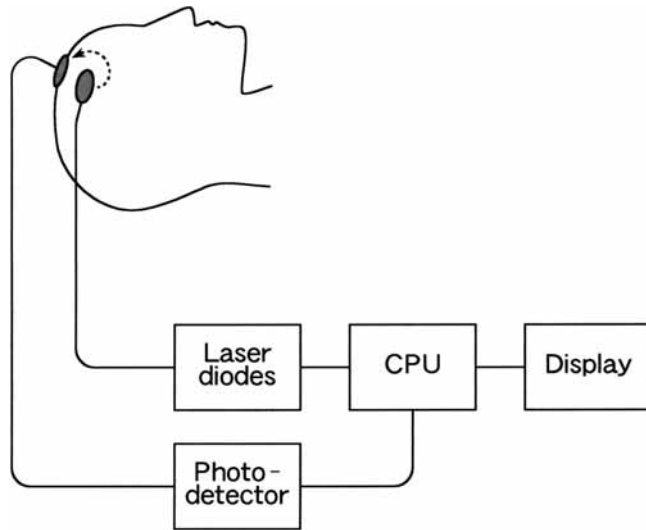
The study protocol was approved by the institutional ethics committee of Ogaki City Hospital, and written informed consent was obtained from the parents of each patient. An anatomical or functional radical operation was performed through a median sternotomy. All surgical procedures were carried out by a single consulting surgeon at a single institute. We used CPB circuits, which minimized the priming volume as much as possible. It consisted of a microporous polypropylene membrane oxygenator, a cardiotomy reservoir, and an arterial line filter. Their priming volumes were 568±50 mL in group 1 and 589±92 mL in group 2. Estimated hemodilution rates

were 40.7±4.6% in group 1 and 44.0±3.4% in group 2. These parameters revealed no significant difference between the groups (Table 1).

Anticholinergic and narcotic premedications were administered. Anesthesia was induced and maintained with fentanyl citrate (0.01 to 0.1 mg/kg) and midazolam (1.0 mg/kg). The trachea was intubated, and the lungs were mechanically ventilated with sevoflurane in 30 to 50% oxygen. The CPB circuit was primed with an asanguineous solution consisting of heparin (1,000 units), mannitol (0.5 g/kg), methylprednisolone (30 mg/kg), fentanyl (0.05 mg), vecuronium (0.2 mg/kg), and ampicillin (25 mg/kg) in Ringer's solution. Three hundred IU/kg of heparin sodium was given intravenously 3 min before cannulation. CPB was initiated with ascending aortic perfusion and superior vena caval drainage. Within the first minute following the onset of CPB, the perfusion index (PI) increased around 1.0 L/min/m<sup>2</sup>, reaching 2.0 to 2.5 L/min/m<sup>2</sup> at 5 min after CPB initiation. During the following 5 min, another venous cannula was placed into the inferior vena cava, and the PI was raised up to 3.0 L/min/m<sup>2</sup>. Mild systemic cooling was started, and the rectal temperature was maintained at around 30 to 34°C. An alpha-stat strategy was employed for acid-base management. The right or left radial arterial pressure was measured as the systemic arterial pressure by using a 22- or 24-gauge plastic cannula during the entire surgery. The mean arterial pressure (MAP) and pulse pressure (PP) were recorded. The superior vena caval pressure was measured as the central venous pressure (CVP) using a 4-Fr. central venous line inserted via the right jugular vein. The heart rate (HR) and rectal temperature (Tr) were also recorded.

### NIRS system

We used NIRS (NIRO-500; Hamamatsu Photonics,



**Fig. 1.** A schematic diagram of near-infrared spectroscopy (NIRS). Near-infrared light was carried from the laser diodes to the head by a fiberoptic bundle. The transmitted light was collected and led to the photo-detector in the spectroscope. Data were displayed on a monitor and stored on a computer disk. CPU, central processing unit.

Hamamatsu, Japan) to monitor cerebral-oxygenated hemoglobin (OxHb) and deoxygenated hemoglobin (DxHb). It relies on the relative transparency of the brain and overlying tissues in the near-infrared spectrum (700-1,000 nm).<sup>1-3)</sup> The instrument monitored the changes in absorbance at 4 different wavelengths (775, 825, 850, and 904 nm). Near-infrared light was carried from the NIRS to the head by a fiberoptic bundle that terminated in an optode (optical probe). The transmitted light was collected via another optode and a fiberoptic bundle leading to the photo-detector in the spectroscope. The two optodes, placed 4.5 cm apart, were held by an elastic bandage underneath a black cover to reduce background light. They were placed over the forehead lateral to the midline to avoid the superior sagittal sinus and above the eyebrows to avoid the frontal sinus. Data were displayed on a monitor and stored on a computer disk. A schematic diagram of the instrument is shown in Fig. 1.

OxHb and DxHb were measured by NIRS, and both measurements were added to yield cerebral-total hemoglobin (THb). The NIRS data were expressed as changing values from the baseline, which was the point at which the arterial blood was sampled for control just before CPB. They were recorded at 1-min intervals for the first 10 min after CPB initiation. Arterial blood was also collected just before CPB for control, and every minute for 10 min after commencing CPB. A blood gas analyzer (M288 Blood Gas System; CIBACORNING, Tokyo, Japan) was used for measurements of serum hemoglobin concentration (Hb), partial oxygen pressure (PaO<sub>2</sub>) and oxygen saturation (SaO<sub>2</sub>). Oxygen content (O<sub>2</sub>Cont) was calculated with the following equation:

**Table 2. Abbreviations**

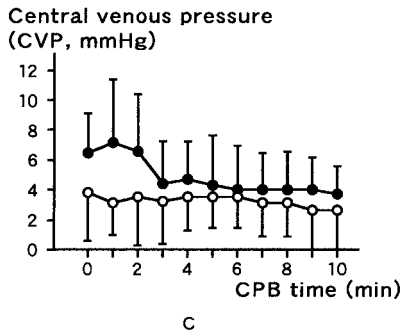
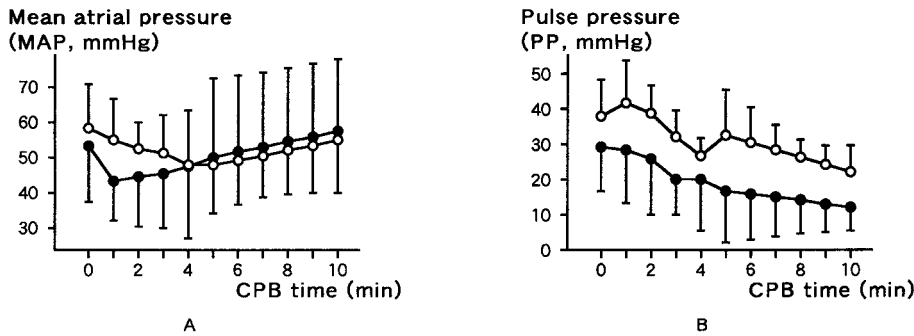
Clinical parameters		
MAP		mean arterial pressure
PP		pulse pressure
CVP		central venous pressure
HR		heart rate
Tr		rectal temperature
PI		perfusion index
Arterial blood samples		
Hb		hemoglobin concentration
PaO <sub>2</sub>		partial oxygen pressure
SaO <sub>2</sub>		oxygen saturation
O <sub>2</sub> Cont		oxygen content
NIRS measurements		
OxHb		cerebral-oxygenated hemoglobin
DxHb		cerebral-deoxygenated hemoglobin
THb		cerebral-total hemoglobin

$$\text{O}_2\text{Cont}(\text{mL/dL}) = 1.34 \times \text{Hb}(\text{g/dL}) \times \text{SaO}_2(\%) / 100 + 0.003 \times \text{PaO}_2(\text{mmHg})$$

The abbreviations of measured parameters are listed in Table 2.

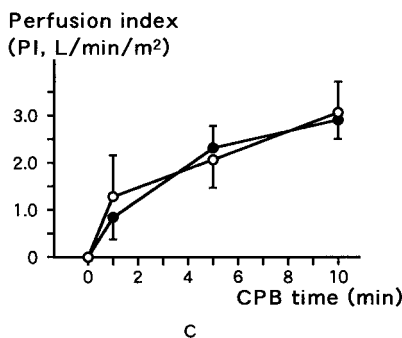
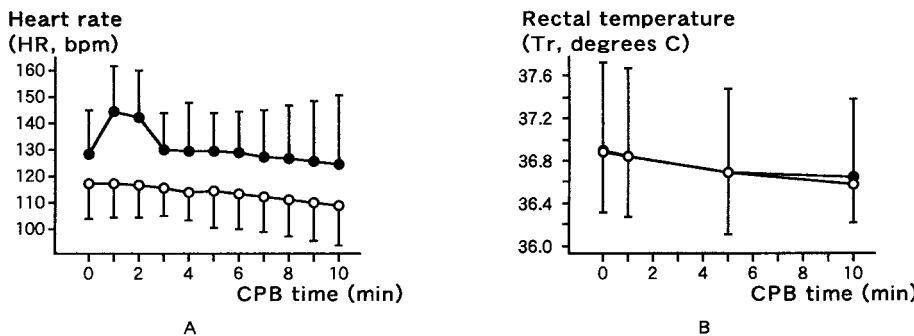
**Data analysis**

All data are expressed as the mean ± standard deviation. Changes in OxHb, DxHb, THb, Hb, SaO<sub>2</sub> and O<sub>2</sub>Cont were analyzed within and between the groups using two-way analysis of variance (ANOVA) with repeated measures. Differences in patient characteristics were tested between the groups by unpaired *t*-test for continuous variables and by Fisher’s exact probability test for categorical variables.



	Within group	Between groups
MAP	Group 1: NS Group 2: $P < 0.05$	NS
PP	Group 1: $P < 0.001$ Group 2: $P < 0.001$	$P < 0.05$
CVP	Group 1: NS Group 2: $P < 0.005$	$P < 0.05$

**Fig. 2.** Time course of the arterial mean, pulse pressures, and central venous pressure. Data represent mean values; error bars represent SD (standard deviation). MAP, mean arterial pressure; PP, pulse pressure; CVP, central venous pressure; CPB, cardiopulmonary bypass; NS, not significant.



	Within group	Between groups
HR	Group 1: $P < 0.01$ Group 2: $P < 0.01$	$P < 0.05$
Tr	Group 1: $P < 0.01$ Group 2: $P < 0.05$	NS
PI	Group 1: $P < 0.001$ Group 2: $P < 0.001$	NS

**Fig. 3.** Time course of the heart rate, rectal temperature, and perfusion index of the cardiopulmonary bypass. Data represent mean values; error bars represent SD. HR, heart rate; Tr, rectal temperature; PI, perfusion index; CPB, cardiopulmonary bypass; NS, not significant.

A  $P$  value less than 0.05 was considered significant.

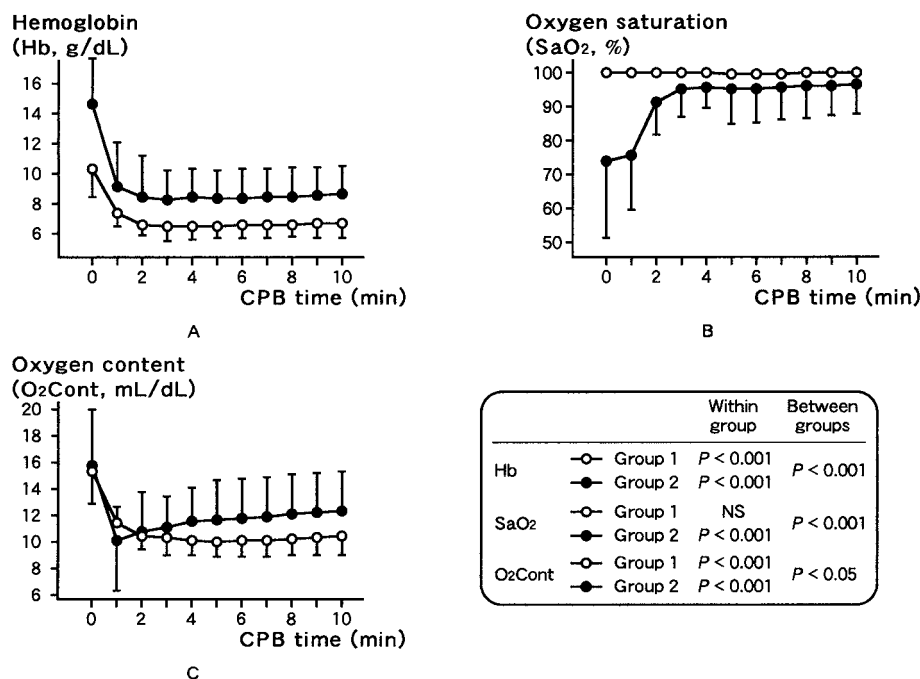
**Results**

No patients died or underwent reoperation for excessive bleeding during hospitalization, and no neurological complications were noted in any patients.

**Hemodynamics**

Changes in MAP, PP, CVP, HR, Tr, and PI are shown in Figs. 2 and 3.

MAP revealed no significant changes in group 1, while it increased significantly in group 2 during the first 10 min after CPB initiation. However, there were no significant differences between the groups. PP decreased markedly in both groups, showing significantly higher values



**Fig. 4.** Time course of the serum hemoglobin concentration, oxygen saturation, and oxygen content of arterial blood.

Data represent mean values; error bars represent SD.

Hb, hemoglobin concentration; SaO<sub>2</sub>, arterial oxygen saturation; O<sub>2</sub>Cont, arterial oxygen content; CPB, cardiopulmonary bypass; NS, not significant.

in group 1. CVP in group 2 decreased significantly in the first 3 min, but there were no significant changes in group 1. HR increased temporarily in the first couple of min, but decreased thereafter in group 2, showing significantly higher values than in group 1. PI and Tr showed similar changing curves between the groups.

#### Total body oxygenation status

Figure 4 shows the changes in Hb, SaO<sub>2</sub> and O<sub>2</sub>Cont. In group 1, Hb rapidly decreased from  $10.3 \pm 1.9$  to  $6.5 \pm 0.9$  g/dL in the first few min after CPB initiation, and remained at plateau levels thereafter. A parallel curve was presented in group 2, indicating an initial value of  $14.6 \pm 3.0$  g/dL, declining rapidly to  $8.3 \pm 2.0$  g/dL, and then remaining at plateau levels thereafter. SaO<sub>2</sub> remained unchanged at around 100% in group 1, whereas it rapidly increased from  $78.9 \pm 18.0$  to  $97.2 \pm 6.8\%$  for the first 3 min in group 2. The changes in SaO<sub>2</sub> were statistically different between the groups ( $P < 0.001$ ). Data from the arterial blood samples just before CPB showed equivalent O<sub>2</sub>Conts ( $15.3 \pm 2.4$  versus  $15.7 \pm 4.3$  mL/dL;  $P = 0.84$ ). This decreased and bottomed out 3 min after the onset of CPB in group 1, whereas in group 2 it bottomed out after 1 min and kept increasing gradually thereafter. The difference was statistically significant between the groups ( $P < 0.05$ ).

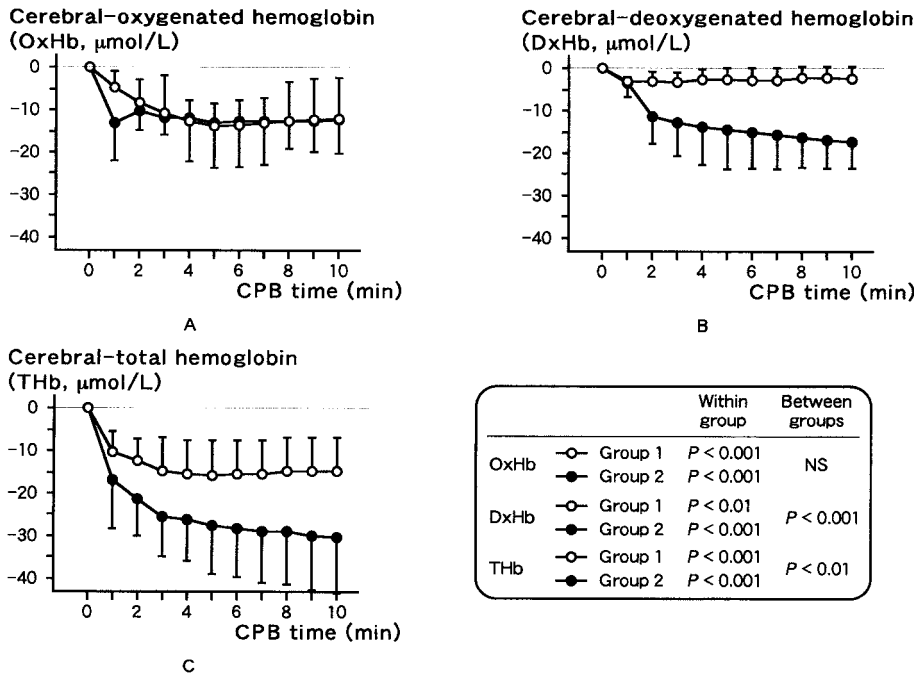
#### Cerebral oxygenation status

The changes in OxHb, DxHb and THb are shown in Fig.

5. The OxHb began to drop immediately upon the onset of CPB, and bottomed out around 5 min after CPB initiation in group 1. In group 2, it decreased rapidly in the first minute of CPB initiation, and plateaued thereafter. These changes were significant in each group ( $P < 0.001$ ,  $< 0.001$ , respectively), whereas there was no significant difference between the groups. DxHb decreased slightly and bottomed out 1 min after CPB initiation in group 1, whereas in group 2 it dropped immediately during the first few minutes after applying CPB and kept declining gradually thereafter. DxHb decreased more remarkably in group 2 than in group 1 ( $P < 0.001$ ). THb traced a similar curve to that of OxHb, falling and reaching a plateau within a few minutes after the start of CPB in group 1, while it kept decreasing gradually following a rapid fall during the first few minutes of CPB initiation in group 2. The changes in THb were also significant within each group ( $P < 0.001$ ,  $< 0.001$ , respectively), but they were more remarkable in group 2.

#### Discussion

To perform open-heart surgery safely, the cerebral-oxygenation status must be maintained above a certain level. Although we have had considerable clinical success using conventional crystalloid-primed nonpulsatile CPB, the cerebral-oxygenation status during CPB has not been completely clarified. CPB changes the serum he-



**Fig. 5.** Time course of the cerebral-oxygenation status measured by near-infrared spectroscopy (NIRS). Data represent mean values; error bars represent SD. OxHb, cerebral-oxygenated hemoglobin; DxHb, cerebral-deoxygenated hemoglobin; THb, cerebral-total hemoglobin; CPB, cardiopulmonary bypass; NS, not significant.

moglobin concentration, pulmonary circulation, body temperature, oxygen and carbon dioxide tension, venous pressure, and the arterial pressure waveform. Each factor will affect the cerebral oxygen metabolism, and inadequate perfusion may result in impairments to the central nervous system.<sup>4-7</sup> When open-heart surgery is attempted without homologous blood transfusions, patients may be exposed to excessive hemodilution. It is still unclear whether nonpulsatile perfusion may compromise cerebral circulation and adversely affect the brain.<sup>8-15</sup> Thus, in the absence of a consensus as to the specific merits of the various perfusion modalities, no “gold standard” has emerged.

Such ambiguity has been partially due to the lack of a modality that permits direct measurement of the cerebral-oxygenation status in clinical situations. We have handled CPB pragmatically with conventional monitoring of such parameters as arterial pressure, central venous pressure, serum hemoglobin level, oxygen saturation, and the perfusion index. In this situation, NIRS offers a unique way to evaluate the cerebral-oxygenation status directly and non-invasively. It provides a new monitoring modality and new information about the cerebral-oxygenation status.<sup>1-3,16</sup> In this study, it was able to detect a rapid fall and plateauing of OxHb, DxHb and THb in group 1 as well as a rapid fall and plateauing of OxHb together with a rapid fall and a gradual decrease in DxHb and THb in group 2 after the start of CPB.

During the initial period of CPB, numerous parameters also dramatically changed, i.e., Hb, PP and CVP decreased, whereas PI increased. MAP and HR showed distinctive curves from one another. Hb decreased rapidly in the first few minutes of CPB initiation and remained almost unchanged thereafter. The Hb curves of each group ran parallel. Polycythemia is a compensated status usually associated with cyanotic congenital heart diseases. Hence, the Hb curve in group 2 shifted above that of group 1. Interestingly, O<sub>2</sub>Cont was identical between the groups before CPB. Polycythemia in the patients with cyanotic heart diseases completely compensated them against low SaO<sub>2</sub> or hypoxia. O<sub>2</sub>Cont varied according with the serum hemoglobin concentration, since SaO<sub>2</sub> remained around 100% all through the procedure in group 1. In group 2, however, a rapid decrease in the serum hemoglobin level due to hemodilution occurred simultaneously with a gradual increase in SaO<sub>2</sub> as the CPB flow increased. Both together resulted in O<sub>2</sub>Cont showing a rapid fall immediately upon the initiation of CPB and a gradual increase during the following period.

The Hb curves indicated that hemodilution started as soon as CPB began, and was completed immediately in that initial phase. The gross similarity between the OxHb, THb curves and the Hb, O<sub>2</sub>Cont curves in group 1 suggested that they bore a close relationship to each other. On the other hand, OxHb, DxHb and THb were not explained solely by the changes in Hb or O<sub>2</sub>Cont in group

2. OxHb fell rapidly in the first minute but hovered around a plateau level even in the latter phase when O<sub>2</sub>Cont kept increasing gradually. There was a tendency toward a consistent decrease in THb in spite of the plateauing of Hb during this same period. This reduction in THb was mainly attributed to the decrease in DxHb. The dissociations between cerebral-oxygenation status and the arterial blood gas data in group 2 could not be clearly explained. Pre-operative exclusive polycythemia is associated with marked hyperviscosity, with hemodilution progressing rapidly in the early phase of CPB initiation. On the other hand, oxygen content is dramatically increased during that same period. Thus, we may speculate that such acute changes at the onset of CPB impact cerebral microcirculation and induce a kind of disequilibrium more remarkable in group 2 than in group 1.

Oxygen transport is defined as the movement of molecular oxygen from the atmosphere to cellular mitochondria. This movement depends mainly on the cardiac output, serum hemoglobin level, and tissue microcirculation. It is evident that hemoglobin molecules play a major role in transporting oxygen to the tissues. Cardiac output and tissue microcirculation are directly proportional to the perfusion pressure and inversely related to the total peripheral resistance. This resistance is proportional to the vascular resistance and viscosity of the perfusate. Because there is a direct relationship between the viscosity and the serum hemoglobin concentration, hemodilution produces a marked decrease in total resistance, resulting in an increase in tissue perfusion.<sup>17)</sup> Thus, hemodilution has two distinct aspects, both of which impact the cerebral-oxygenation status. While reducing oxygen content, it also provides better tissue microcirculation.

In any event, the tendency of a consistent decrease in THb indicated a trend toward decreasing cerebral hemoglobin distribution in this period. Then, we wonder whether the CPB technique is actually associated with an ideal outcome in patients with cyanotic heart diseases. Recently, Jonas and associates showed that the infants who underwent open-heart surgery with a low-hematocrit strategy might be prone to adverse neurologic developments. They compared two hemodilution protocols in open-heart surgery as to their short term and one-year outcomes, and found a significant disadvantage in the low-hematocrit group even at hemoglobin levels usually thought to be safe.<sup>7)</sup> In this study, we were able to show that cerebral-oxygenated hemoglobin was at similar level in both groups, whereas cerebral-deoxygenated and total hemoglobin were significantly different between the

groups. However, this cerebral-oxygenation status was revealed only in the early phase of CPB. It is still unclear how it changes thereafter and how it is associated with neurological and developmental outcomes. We consider that one of the next important research subjects is whether the consistent tendency of a gradual decrease of DxHb and THb in the latter phase of this study is associated with an undesirable clinical outcome. If such a relationship exists, the next issue is how to prevent the decrease in DxHb and THb, when commencing CPB.

A complex set of factors would appear to affect OxHb, DxHb and THb in patients with cyanotic congenital heart diseases. The distinctive changes in DxHb and THb in group 2 in this study were not only able to be recognized as with traditional conventional monitoring, but also to be actually induced with NIRS. Although we have had good clinical results in open-heart surgery with actual monitoring modalities, we believe that direct monitoring of the cerebral-oxygenation status during open-heart surgery is very important for patient safety, especially in those with cyanotic heart diseases.

## Summary

OxHb both in patients with cyanotic and non-cyanotic heart diseases could be maintained at a similar level upon the initiation of CPB. However, it showed a different distribution of DxHb and THb between the two groups. DxHb and THb decreased more remarkably and continuously for the first 10 min of CPB initiation in patients with cyanotic heart diseases. As the first step to clarify the differences in cerebral-oxygenation status between cyanotic and non-cyanotic heart diseases, in this study, we were focusing on the early changes that occur after CPB initiation only. Further evaluations, especially following a significant period of CPB, will be necessary to better reveal the cerebral-oxygenation status during CPB in patients with cyanotic heart diseases.

## References

1. Jobsis FF. Noninvasive infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. *Science* 1977; **198**: 1264–7.
2. Fallon P, Roberts I, Kirkham FJ, et al. Cerebral hemodynamics during cardiopulmonary bypass in children using near-infrared spectroscopy. *Ann Thorac Surg* 1993; **56**: 1473–7.
3. Wahr JA, Tremper KK, Samra S, Delpy DT. Near-infrared spectroscopy: theory and applications. *J*

- Cardiothorac Vasc Anesth* 1996; **10**: 406–18.
4. Bellinger DC, Jonas RA, Rappaport LA, et al. Developmental and neurologic status of children after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. *N Engl J Med* 1995; **332**: 549–55.
  5. Kurth CD, Steven JM, Nicolson SC, Jacobs ML. Cerebral oxygenation during cardiopulmonary bypass in children. *J Thorac Cardiovasc Surg* 1997; **113**: 71–9.
  6. Priestley MA, Golden JA, O'Hara IB, McCann J, Kurth CD. Comparison of neurologic outcome after deep hypothermic circulatory arrest with alpha-stat and pH-stat cardiopulmonary bypass in newborn pigs. *J Thorac Cardiovasc Surg* 2001; **121**: 336–43.
  7. Jonas RA, Wypij D, Roth SJ, et al. The influence of hemodilution on outcome after hypothermic cardiopulmonary bypass: results of a randomized trial in infants. *J Thorac Cardiovasc Surg* 2003; **126**: 1765–74.
  8. Matsumoto T, Wolferth CC Jr, Perlman MH. Effects of pulsatile and non-pulsatile perfusion upon cerebral and conjunctival microcirculation in dogs. *Am Surg* 1971; **37**: 61–4.
  9. Dunn J, Kirsh MM, Harness J, Carroll M, Straker J, Sloan H. Hemodynamic, metabolic, and hematologic effects of pulsatile cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1974; **68**: 138–47.
  10. Tranmer BI, Gross CE, Kindt GW, Adey GR. Pulsatile versus nonpulsatile blood flow in the treatment of acute cerebral ischemia. *Neurosurgery* 1986; **19**: 724–31.
  11. Sadahiro M, Haneda K, Mohri H. Experimental study of cerebral autoregulation during cardiopulmonary bypass with or without pulsatile perfusion. *J Thorac Cardiovasc Surg* 1994; **108**: 446–54.
  12. Frater RW, Wakayama S, Oka Y, et al. Pulsatile cardiopulmonary bypass: failure to influence hemodynamics or hormones. *Circulation* 1980; **62** (2 Pt 2): I19–25.
  13. Henze T, Stephan H, Sonntag H. Cerebral dysfunction following extracorporeal circulation for aortocoronary bypass surgery: no differences in neuropsychological outcome after pulsatile versus nonpulsatile flow. *Thorac Cardiovasc Surg* 1990; **38**: 65–8.
  14. Chow G, Roberts IG, Edwards AD, et al. The relation between pump flow rate and pulsatility on cerebral hemodynamics during pediatric cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1997; **114**: 568–77.
  15. Grubhofer G, Mares P, Rajek A, et al. Pulsatility does not change cerebral oxygenation during cardiopulmonary bypass. *Acta Anaesthesiol Scand* 2000; **44**: 586–91.
  16. Murayama H, Tamaki S, Kato N, et al. Evaluation of nearinfrared spectroscopy as a new monitoring modality during cardiopulmonary bypass: a factor analysis study. *Jpn J Artif Organs* 2000; **29**: 369–74.
  17. Cooper JR Jr., Slogoff S. Hemodilution and priming solutions for cardiopulmonary bypass. In: Gravlee GP, Davis RF, Utley JR eds.; *Cardiopulmonary Bypass: principles and practice*. Maryland: Williams & Wilkins, 1993; pp 124–37.