Neurologic monitoring and outcome

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Introduction

The incidence of neurologic complications following heart surgery in children ranges from 6% to 25%.1,2 A recent retrospective report of a series of 706 children undergoing heart surgery found that 2.3% had acute neurologic complications.3 Unlike adults, who undergo heart surgery with cardiopulmonary bypass (CPB) where postoperative neurologic sequelae are largely embolic in nature,4 in children the etiology of this neurologic dysfunction is probably multifactorial.5,6 Techniques such as deep hypothermic circulatory arrest (DHCA) and low-flow bypass, which have allowed successful correction of complex cardiac defects in neonates and infants may themselves contribute to neurologic damage in this vulnerable population.7,8 Furthermore, bypass circuitry and the conduct of CPB, the management of arterial blood gas (ABG)—α-stat (not correcting ABG for temperature) vs. pH-stat (correcting ABG for temperature), hematocrit on bypass, rate and extent of cooling, and rewarming are all important contributors to potential brain dysfunction after CPB.9 In defining the extent of the problem one presupposes that these children are neurologically normal to begin with. However, studies have confirmed central nervous malformations in patients with congenital heart disease (CHD),5 specifically those with hypoplastic left heart syndrome (HLHS)9 where brain dysgenesis may approach 30%. In addition children with chromosomal defects, particularly those with microdeletions of chromosome 22, have a higher incidence of central nervous system abnormalities,10 as do neonates with coarctation of aorta.11 Hence these developmental brain disturbances add to the acquired brain injury in the perioperative setting.

During CPB, although vital organs other than the brain are routinely monitored, the brain is not monitored. The reason for this glaring omission is seldom a point of contention between the various perioperative teams managing the patient. Any strategy for cerebral rescue from the effects of CPB to the brain must be done by neurologic monitoring systems that allow easy, reliable, reproducible detection of adverse events. Despite the existence of several modalities of monitoring for almost 20 years, in these authors’ opinion neurologic monitoring during CPB still remains in its infancy. In this chapter, we review cerebral physiology during cardiac surgery in children; the current modalities for neurologic monitoring; evidence that neurologic monitoring improves neurologic outcome; and finally strategies for improving neurologic outcome.

Cerebral physiology during cardiac surgery

The experimental basis for understanding neurophysiology in infants and children undergoing cardiac surgery involving CPB with DHCA comes largely from a series of landmark clinical studies undertaken in the late 1980s through mid-1990s by Greeley, Kern, Ungerleider, and colleagues.12-16 These investigators measured cerebral blood flow by the xenon clearance method in patients during hypothermic CPB and calculated cerebral oxygen extraction by measuring oxygen saturation in the arterial blood (inflow) and in the jugular venous bulb (outflow). Cerebral metabolic rate, or 

\[
CMR_O_2 = CBF \times (C_{aO_2} - C_{jvO_2}),
\]

where \( CBF \) is cerebral blood flow, \( C_{aO_2} \) is the oxygen content of arterial blood, and \( C_{jvO_2} \) the oxygen content of jugular venous bulb blood. This method allows instantaneous assessment of the cerebral circulation from rapid changes that occur during CPB. It should be noted that in all of their studies α-stat blood gas management was used. Under deep hypothermic conditions CBF is significantly reduced, but there is an exponentially greater reduction in \( CMRO_2 \) (Fig. 8.1). A state of luxury perfusion exists with an excess of flow relative to oxygen consumption. The temperature coefficient, or \( Q_{10} \) is the ratio of \( CMRO_2 \) at two temperatures separated by 10°C, and demonstrates the exponential decrease in \( CMRO_2 \). In neonates, infants, and children, the
baseline at 37–27°C, and if cooled to 17°C, to that seen in a clinical outcome study reviewed later in calculation of a safe duration of circulatory arrest is similar 11–19 minutes at 28°C, and 39–65 minutes at 18°C. This DHCA at various temperatures. This was estimated to be these data the investigators derived a “safe” duration of reperfusion before rewarming.

In patients undergoing circulatory arrest, both CBF and CMRO₂ remain decreased after rewarming and following separation from CPB. The decreased CBF may be due to higher cerebral vascular resistance. This reduction in CBF can be ameliorated with a 10-minute period of cold full-flow reperfusion before rewarming.

The rate and manner of cooling also have significant effects on cerebral oxygenation during CPB. Kern et al. exposed infants to two different cooling strategies, aggressive or gradual. The first strategy resulted in a significantly higher \( S_jVO_2 \) (98% vs. 86%), meaning that global cerebral metabolism was more effectively suppressed than with the gradual cooling method. There was considerable patient variability, leading the authors to suggest that more precise monitoring of cerebral hypothermia was warranted. Monitoring the cerebral saturation, either with near-infrared spectroscopy (NIRS) or \( S_jVO_2 \), may provide a more accurate assessment of the state of cerebral metabolism, and CPB can be tailored to the individual. If cerebral saturation is low after the usual cooling period, additional CPB time can ensure higher cerebral saturation before a period of low-flow CPB or DHCA.

Another important factor is the question of pressure–flow autoregulation during hypothermic bypass. Using transcranial Doppler ultrasound (TCD), 25 infants were studied during normothermic (36–37°C), moderate hypothermic (23–25°C), or profound hypothermic (14–20°C) bypass. Cerebral blood flow velocity (CBFV) was measured over a wide range of cerebral perfusion pressures (CPPs), ranging from 6 to 90 mmHg. Cerebral pressure-flow autoregulation was preserved during normothermic bypass, with CBF increasing linearly until a CPP of 40 mmHg, then leveling off. In contrast, during both moderate and profound hypothermia, flow became pressure passive, increasing linearly with pressure even at a CPP of 60 mmHg.

Even though hypothermia leads to a loss of cerebral autoregulation, the CBF response to changes in arterial carbon dioxide tension is preserved in children. Hence blood gas management (α-stat or pH-stat) during CPB significantly affects cerebral physiology and may have an impact on neurological outcome. Both in vivo and ex vivo studies have demonstrated that pH-stat strategy results in greater cerebral blood flow, greater efficiency, and uniformity of brain cooling, and higher brain oxyhemoglobin saturation and less reduced cytochrome \( a,a_3 \) signifying more oxygen at the mitochondrial level than α-stat blood gas management.

Finally, using α-stat management and a xenon washout technique, Kern et al. demonstrated that, at moderate and deep hypothermia, reductions of 35–45% from conventional full bypass flow rates (100–110 mL/kg/minute for patients under 25 kg and 2.5 L/minute/m² for those over 25 kg) resulted in no change in CBF and CMRO₂ from decreasing CPB flow rates with increasing hypothermia. When flow was reduced by 45–70%, a significant decrease in CBF and CMRO₂ resulted, associated with an increase in oxygen extraction (i.e. a lower \( S_jVO_2 \)). Even at lower flows CBF and CMRO₂ decreased significantly, but oxygen extraction did not increase, suggesting an excess of flow over metabolic needs. Based on these measurements, the authors derived predicted minimal acceptable pump flow rates at various temperatures for the average pediatric patient (Table 8.1). Their prediction was validated in neonates undergoing the arterial switch operation at 18°C, who required pump flows of 10–20 mL/kg/minute to maintain cerebral blood flow, documented by TCD.

10 Q₁₀ is 3.65, meaning CMRO₂ decreases by 3.65 times from baseline at 37–27°C, and if cooled to 17°C, CMRO₂ will decrease 3.65 times from the level found at 27°C. Based on these data the investigators derived a “safe” duration of DHCA at various temperatures. This was estimated to be 11–19 minutes at 28°C, and 39–65 minutes at 18°C. This calculation of a safe duration of circulatory arrest is similar to that seen in a clinical outcome study reviewed later in this chapter. These studies confirm that hypothermia is an important factor for neuroprotection.

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Neurologic monitoring during congenital heart surgery

Electroencephalographic technologies

The standard electroencephalogram (EEG) employing between 2 and 16 channels has been utilized in congenital heart surgery. It is a rough guide of anesthetic depth, and can document electrocerebral silence before DHCA. The electro-encephalogram is affected by several factors including anesthetic agents, temperature, and CPB. Impracticalities of the use of an intraoperative EEG include electrical signal interference, complexity of placement, and interpretation. Newer devices using processed EEG technology are more user-friendly. The bispectral index (BIS) monitor (Aspect Medical Systems, Newton, MA) is currently used to guide the depth of anesthesia. Bispectral index sensor electrodes are applied to the forehead and temple producing a frontal–temporal montage, which connects to a processing unit. The device is easy to use, electrodes are easy to place, and the monitor requires no calibration or warm up time. Via a proprietary algorithm of Aspect Corporation, BIS uses fourier transformation and bispectral analysis of a one-channel processed EEG pattern to compute a single number, the bispectral BIS index. This index ranges from zero (isoelectric EEG) to 100 (awake) with mean awake values in the 90–100 range in adults, infants and children. Depth of sedation is difficult to predict using mean awake values in the 90–100 range in adults, infants and children. Bispectral index can be used to recognize EEG burst suppression, or electrical silence, which could be useful during DHCA. The monitor displays a real-time EEG waveform, but is subject to motion artifact, EMG activity and radiofrequency interference from electrical equipment in the operating room.

During CPB hemodilution and hypothermia alter pharmacokinetics and pharmacodynamics, which can lead to awareness under anesthesia. The overall incidence of awareness in adults undergoing cardiac surgery varies from 0.3% to 23.0%,31–33 which is more than in general surgical procedures. Although there are no documented reports of awareness under anesthesia in children undergoing heart surgery, BIS monitoring may still be useful to detect a level of awareness. In a cohort of children undergoing open heart surgery with an anesthetic tailored for “fast-tracking,” BIS scores increased during rewarming, a period considered at risk for awareness under anesthesia. However in this study, and in a similar study in infants less than 1 year of age,35 BIS did not correlate with stress hormone levels, a surrogate for light levels of anesthesia, nor with plasma fentanyl levels. Studies are needed that demonstrate the utility of the BIS monitor in infants undergoing DHCA.

Monitors of cerebral oxygenation

Jugular venous bulb oximetry

Jugular venous bulb oximetry (SjvO₂) has been utilized in children with CHD since the late 1980s. It is considered the gold standard of global cerebral oxygenation against which all non-invasive measurements are compared. The catheter can be placed by retrograde cannulation of the right internal jugular vein, with or without fluoroscopic confirmation of catheter tip placement. Alternatively, the catheter can be placed by the surgeon after the heart and great vessels are exposed, by cannulating the superior vena cava (SVC) retrograde and advancing it into the jugular venous bulb. SjvO₂ can be measured continuously with an oximetric catheter, or intermittent sampling for direct measurement of oxygen saturation. The drawbacks of this method include the invasive and time-consuming nature of retrograde internal jugular vein cannulation rendering it primarily a research tool. Non-invasive monitoring of cerebral oxygen saturation is more practical.

Near-infrared spectroscopy

Near-infrared spectroscopy is a non-invasive optical technique used to monitor brain tissue oxygenation. Most devices utilize 2–4 wavelengths of infrared light at 700–1000 nm, where oxygenated and deoxygenated hemoglobin have distinct absorption spectra. Commercially available devices measure the concentration of oxy- and deoxyhemoglobin, and determine cerebral oxygen saturation. The cerebral
Prototype cerebral oximeters using frequency-domain technology are under development and have the potential to measure absolute rather than calculated cerebral oxygen saturation.42

Direct comparison of the INVOS 4100 and NIRO 30039 in healthy anesthetized adults during normo-, hypo- and hypercapnia reveals a positive correlation for all data points in both absolute values, and change from baseline values (r = 0.58 and 0.85, respectively). However, application of the more sensitive Bland and Altman comparison 43 of the two methods reveals that, although the correlation was good when all 60 values were combined, individual comparison demonstrated possible large differences. The INVOS 5100 pediatric sensor tends to read significantly higher (by 14 ± 8%)41 than the NIRO 4-cm interoptode sensor (pediatric equivalent). Regardless of the device used, it is important to note that all devices measure combined arterial and venous blood oxygen saturation, and cannot be assumed to be identical to $S_jVO_2$. A corollary of this issue is that maneuvers to increase arterial oxygen saturation, i.e. increasing $FIO_2$, will increase cerebral oxygenation as measured by these devices, but the $S_jVO_2$ may remain unchanged.

In an attempt to validate the non-invasive measurement of cerebral oxygen saturation in children with CHD, $S_jVO_2$ and $rSO_2$ have been compared. In 40 infants and children 44 undergoing congenital heart surgery or cardiac catheterization, the correlation for paired measurements was inconclusive except for infants less than 1 year of age. In 30 patients undergoing cardiac catheterization, an improved correlation (r = 0.93) was found.45 All of these experimental data lead to the
appealing idea that NIRS can be used to direct therapy and influence outcome in congenital heart surgery.

**Clinical data in pediatric cardiac surgery**

Changes in cerebral oxygenation have been characterized during CPB in children with or without DHCA (Fig. 8.3). Baseline preoperative cerebral oxygen saturation (ScO₂), as measured by a frequency-domain oximeter, varies with cardiac lesion. The baseline cerebral saturation is about 70% in acyanotic patients without large left-to-right intracardiac shunts breathing room air. On room air, ScO₂ for cyanotic patients is usually 40–60%; HLHS patients receiving FIO₂ 0.17 preoperatively also have lower ScO₂, averaging 53%, vs. those receiving FIO₂ 0.21 and 3% inspired carbon dioxide, where ScO₂ averages 68%. Significant decreases in ScO₂ occur during periods of hemodynamic instability or arterial desaturation. Increases occur during cooling and vary with the rate of temperature change. Improvement in cardiac output and oxygen delivery results in an increase in ScO₂.

ScO₂ predictably decreases during DHCA to a nadir approximately 60–70% below baseline values obtained pre-bypass and the nadir is reached at about 40 minutes, after which there is no further decrease. At this point it appears that the brain does not continue the uptake of oxygen, and interestingly this time period appears to correlate with clinical and experimental studies suggesting that 45 minutes is the safe duration for circulatory arrest. The DHCA initiation at higher temperature results in a faster fall in ScO₂, reaching the nadir sooner. Reperfusion immediately results in an increase in ScO₂ levels seen at full bypass flow before DHCA.

**Relationships between low cerebral saturation (ScO₂) and adverse neurologic outcome**

There is recent clinical evidence suggesting that low cerebral saturations correlate with adverse neurologic outcome. In 26 infants and children undergoing surgery with bypass and DHCA, three with low ScO₂ had acute neurologic changes—seizures in one, and prolonged coma in two. In these three patients the increase in ScO₂ was much less after the onset of CPB and the duration of cooling before DHCA shorter. In 250 infants and children undergoing cardiac surgery with bypass, relative cerebral oxygen desaturation of more than 20% below pre-bypass baseline was observed in 58%. If left untreated 26% of them had postoperative adverse neurologic events.

There is also evidence from animal models that NIRS can be used as a guide to the safe duration of DHCA. In a study of piglets, the time of the nadir of ScO₂ values during DHCA correlated with neurologic outcome: a longer period without apparent oxygen uptake by the brain correlated with a greater chance of adverse neurological outcome. The maximum safe duration without brain oxygen uptake at 17°C was 30 minutes. In another piglet model, NIRS was used to detect cerebral desaturation when the SVC was partially or totally occluded. No other measurement (blood pressure/heart rate on bypass, SVC pressure measurements, or mixed venous oxygen saturation) predicted cerebral desaturation.
This has clinical relevance because cerebral desaturation may develop in small infants undergoing bicaval cannulation, who frequently have SVC obstruction, or patients undergoing cavopulmonary anastomosis, where the SVC is often partially occluded.\textsuperscript{50}

It is intuitive to conclude that low cerebral oxygen saturations as measured by NIRS lead to adverse neurologic outcomes and therefore should be monitored and treated. However, additional prospective outcome data in infants and children using this modality is required.

Transcranial Doppler ultrasound

Transcranial Doppler ultrasound is a sensitive, real-time monitor of CBFV and emboli during congenital heart surgery. Currently available instruments utilize pulsed-wave ultrasound at 2 MHz frequency, which is range-gated, emits a power of 100 mW, and has a sample volume length of up to 15 mm. A display of the frequency spectrum of Doppler signals is easily interpreted, and peak systolic and mean flow velocities, in centimeters/second, are displayed, as well as a pulsatility index which is equal to the peak velocity minus the end-diastolic velocity, divided by the mean velocity (Fig. 8.4). The information can be stored digitally and archived to be analyzed off line at a later date. As with cardiac ultrasound, the advantage of pulsed-wave Doppler ultrasound is that a precise sample volume can be selected which insonates only the arteries of interest, without contamination from other sources.

The most consistent and reproducible technique for clinical use in patients of all ages is to monitor the middle cerebral artery (MCA) through the temporal window, which can usually be found just above the zygoma and just anterior to the tragus of the ear (see Fig. 8.2).\textsuperscript{51} Several transducer probes are available, ranging from very small disc probes suitable for infants and children, to larger, heavier probes for adolescents and adults. The depth of the sample volume and angle of insonation is adjusted until the bifurcation of the MCA and the anterior cerebral artery (ACA) are detected. This is heralded by a maximal antegrade signal (positive deflection, toward the transducer) from the MCA, accompanied by retrograde flow (negative deflection, away from the transducer) of the same or very similar velocity and waveform, as the MCA flow (Fig. 8.4(b)). The same location should be monitored for an individual patient. Insonation at the MCA–ACA bifurcation also offers the advantage of minimizing inter-patient variability. In addition, the MCA supplies the largest volume of tissue of any of the basal cerebral arteries.\textsuperscript{52} After obtaining an optimal signal, the probe must be secured, usually by adhesive tape or clear adhesive dressing for the small disc probe, or by adjustments to a padded head ring in larger patients. Care must be taken with the latter system to thoroughly pad all pressure points and to pay particular care to the orbits. For smaller patients, securing the probe by wrapping the head with an elastic bandage is discouraged because pressure sores may develop under the area of the transducer. Also, adjustment to the probe position is often necessary during the case, so access to the transducer is important.

In infants, an alternative site for monitoring is through the anterior fontanelle, using a hand-held pencil-type probe, placing the probe over the lateral edge of the fontanelle, and aiming caudally, at a larger depth than for the temporal window, at the internal carotid artery. The depth of measurement and normal-flow velocities for the MCA are listed in Table 8.2.\textsuperscript{51} These normal velocities were determined in children without cardiovascular disease. Lesions producing large diastolic runoff, for example large patent ductus arteriosus, will have an effect on diastolic blood flow to the brain. These normal velocities were obtained in awake children under perfect examination conditions. Hemodynamic instability, less than optimal probe positioning, and general anesthesia may reduce these velocities in clinical practice. Often the clinician must accept a stable baseline for the individual patient and use it as the basis for comparison, rather than expect a perfect signal.

Transcranial Doppler ultrasound has been used extensively in pediatric cardiac surgical research to examine cerebral physiology in response to CPB, hypothermia, low-flow bypass, regional low-flow perfusion to the brain, and circulatory arrest. Hillier et al\textsuperscript{53} used TCD to study cerebrovascular hemodynamics during hypothermic bypass with DHCA in 10 infants. Cerebral blood flow velocity did not return to baseline levels after DHCA. Calculated cerebral vascular resistance (mean arterial pressure–central venous pressure/CFBV) was increased immediately after DHCA, and remained so until the end of bypass. The observed decrease in CBFV during cooling was thought to be due to decreased metabolic demand by the brain and thus less blood flow; although α-stat strategy was used. This could be explained by relative cerebral vasoconstriction during cooling in smaller arterioles downstream to the MCA and ACA, since these large arteries do not change their caliber in response to changes in P\textsubscript{CO\textsubscript{2}}.\textsuperscript{54} Transcranial Doppler ultrasound of the MCA through the temporal window was used to describe the

<table>
<thead>
<tr>
<th>Age</th>
<th>Depth (mm)</th>
<th>Mean velocity (cm/s)</th>
<th>Peak systolic velocity (cm/s)</th>
<th>End-diastolic velocity (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 mo</td>
<td>25</td>
<td>24–42 ± 10</td>
<td>46–75 ± 15</td>
<td>12–24 ± 8</td>
</tr>
<tr>
<td>3–12 mo</td>
<td>30</td>
<td>74 ± 14</td>
<td>114 ± 20</td>
<td>46 ± 9</td>
</tr>
<tr>
<td>1–3 yr</td>
<td>35–45</td>
<td>85 ± 10</td>
<td>124 ± 10</td>
<td>65 ± 11</td>
</tr>
<tr>
<td>3–6 yr</td>
<td>40–45</td>
<td>94 ± 10</td>
<td>147 ± 17</td>
<td>65 ± 9</td>
</tr>
<tr>
<td>6–10 yr</td>
<td>45–50</td>
<td>97 ± 9</td>
<td>143 ± 13</td>
<td>72 ± 9</td>
</tr>
<tr>
<td>10–18 yr</td>
<td>45–50</td>
<td>81 ± 11</td>
<td>129 ± 17</td>
<td>60 ± 8</td>
</tr>
</tbody>
</table>
with previous research done using xenon to quantitate cerebral blood flow.12

Transcranial Doppler ultrasound has also been utilized to determine the threshold of detectable cerebral perfusion during low-flow CPB. Zimmerman et al.25 studied 28 neonates undergoing the arterial switch operation with α-stat pH management. At 14–15°C the pump flow was sequentially reduced to 0 mL/kg/minute. All patients had detectable cerebral blood flow down to 20 mL/kg/minute, while one
Fig. 8.4 (cont’d)

Fig. 8.5 Arterial supply to the brain in a neonate. Transcranial Doppler ultrasound is used to measure cerebral blood flow velocity in the middle cerebral artery, ideally at its junction with the anterior cerebral artery. Reproduced with permission from Truemper EJ, Fischer AQ. Cerebrovascular developmental anatomy and physiology in the infant and child. In: Bibikian VL, Wechsler LR, eds. Transcranial Doppler Ultrasonography, 2nd edn. Oxford: Butterworth-Heinemann, 1993: 281–320.
had no perfusion at 20 mL/kg/minute, and eight had none at 10 mL/kg/minute, leading the authors to conclude that 30 mL/kg/minute was the minimum acceptable flow in this population. Finally, Andropoulos et al.\textsuperscript{55} used TCD of the MCA to determine the level of bypass flow necessary during regional low-flow perfusion for neonatal aortic arch reconstruction. They studied 34 neonates undergoing the Norwood operation or aortic arch advancement and established a baseline mean CBFV under full-flow bypass (150 mL/kg/minute) using pH-stat management at 17–22°C: 22 cm/second. They then used TCD to determine the bypass flow necessary to match this value, finding that a mean of 63 mL/kg/minute was necessary. Interestingly, this necessary level of bypass flow did not correlate with mean arterial pressure in the radial artery or cerebral saturation measured by NIRS. The necessary flow as determined by TCD varied widely, leading the authors to conclude that TCD was a valuable monitor to ensure adequate but not excessive cerebral blood flow during this complicated technique.

Cerebral emboli are a frequent threat during open heart surgery in children. Emboli are easily detected by TCD, although this is subject to artifacts such as electrocautery and physical contact with the ultrasound transducer (Fig. 8.4).\textsuperscript{56} True emboli have characteristic audio and visual signals and are designated as high intensity transient signals (HITS) which can actually be counted by the TCD software. The filtering criteria must be set to exclude artifacts, and the HITS counter can be an accurate gauge of the number of emboli detected in the artery being monitored. However the number of emboli detected in the carotid artery during pediatric congenital heart surgery did not appear to correlate with acute postoperative neurological deficits.\textsuperscript{56} Acute drops in cerebral blood flow detected by TCD can allow for adjustment of aortic cannula, which may avert neurological disaster.

One caveat when utilizing TCD clinically is that this device measures CBFV, not blood flow. Cerebral blood flow velocity is dependent on the diameter of the blood vessel whereas cerebral blood flow depends on cerebral vascular resistance, which changes in response to changes in carbon dioxide, temperature, CPP, and pump flow. Thus CBFV often correlates well with cerebral blood flow in the individual patient, particularly at deep hypothermia when autoregulation is lost and the caliber of the blood vessels is unchanged. However the clinician must always be mindful and estimate the state of the patient’s cerebral vascular resistance to translate TCD into meaningful information for clinical decision making.

**Multimodality neurologic monitoring**

With combined use of TCD to measure blood flow in the MCA/ACA, and NIRS which measures oxygen saturation of blood in the frontal lobe, it is possible to monitor up to 70% of the blood flow distribution to a cerebral hemisphere.

Simultaneous neurologic monitoring—NIRS, transcranial Doppler, and processed EEG (BIS)—may hold the greatest promise in detecting and treating neurologic abnormalities during congenital heart surgery, just as pulse oximetry combined with capnography is more effective at preventing morbidity from ventilation mishaps than either modality alone.\textsuperscript{57} A study in infants and children with CHD involving multimodality neurologic monitoring—NIRS, TCD, and four-channel quantitative EEG—showed that 70% (176/250) patients experienced a significant change in one or more parameters. When left untreated, 26% developed adverse neurologic outcomes, compared to 7% that were treated. Interestingly EEG changes were responsible for only 5% of the monitoring abnormalities, with NIRS changes responsible for 58%, and TCD 37%. This study was neither prospective, randomized, nor controlled. The 26% incidence of acute neurologic complications is greater than most other reports of neurologic outcomes after congenital heart surgery. However, to date it represents the best evidence that multimodality neurologic monitoring, particularly NIRS and TCD, in conjunction with a treatment algorithm, reduces neurologic complications following CPB.

Based on these data, and more than 4 years of experience and more than 3000 cases with multimodality neurologic monitoring at Texas Children’s Hospital, one possible algorithm for treatment is presented in Table 8.3. In infants under 1 year of age the BIS is not used because of space limitations and because of insufficient data confirming its utility in this age group. The anesthesiologist can learn to place and interpret these monitors; however, this algorithm awaits prospective validation of the potential to directly improve outcome.

For the NIRS monitor, a relative decrease of more than 20% from a stable baseline obtained pre-incision is the primary reason for treatment. Other critical values are an rs0–3 less than 30%, or greater than 95% accompanied by a significant increase in CBFV.

**Temperature monitoring**

Cerebral hyperthermia frequently develops after congenital heart surgery with CPB. The metabolic rate and oxygen consumption of neurons is raised during a period when oxygen delivery may be compromised from decreased cardiac output. This places vulnerable watershed areas or partially damaged neurons at risk for permanent cell death.\textsuperscript{58} Bissonnette et al.\textsuperscript{59} measured temperatures in the jugular venous bulb (JVBV), tympanic membrane, lower esophagus, and rectum during and after surgery in 15 infants. The patients were separated from bypass at 35°C rectal, without active warming measures. The mean JVBV was 36.9°C at the end of bypass, and this increased to 39.6°C by 6 hours postoperatively, with one patient reaching 41.4°C The authors found that the commonly monitored rectal temperature does not reflect
Preoperative care

The principles of maintaining adequate cardiac output and oxygen delivery to the brain are critically important in the immediate preoperative period. Appropriate inotropic support, avoiding hyperthermia, blood transfusion, or prompt balloon atrial septostomy when indicated will stabilize patients and improve oxygen delivery. In some centers, up to 50% of patients presenting for cardiac surgery in the newborn period have their defects diagnosed prenatally. Delivery should occur in a center experienced in the care

Improving neurologic outcome in children undergoing open heart surgery

It is clear that neurologic injury in infants and children undergoing congenital heart surgery is multifactorial in origin, and prevention remains the key to avoiding permanent central nervous system injury. A multilayer strategy for detection and prevention of neurologic abnormalities in the perioperative period is presented.

Table 8.3 Texas Children’s Hospital neurologic monitoring treatment algorithm.

<table>
<thead>
<tr>
<th>Monitor</th>
<th>Change</th>
<th>Intervention pre/post bypass</th>
<th>Intervention on bypass</th>
<th>Intervention on DHCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIRS (rSO₂ (%))</td>
<td>↓ ≥ 20% relative to pre-incision baseline</td>
<td>↑ Cardiac output, ↑ hgb, ↑ PO₂, ↑ Paco₂</td>
<td>↑ Pump flow, ↑ Paco₂, ↑ MAP, ↓ temp., ↑ hgb, √ CBFV—adjust cannulae</td>
<td>Reperfuse</td>
</tr>
<tr>
<td>DHCA: rSO₂ &lt; 30%, or at nadir &gt; 30 minutes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rSO₂ ≥ 95%</td>
<td>Rapid institution bypass; aggressive measures to ↑ O₂ delivery</td>
<td>Aggressive treatment: ↑ Pump flow, ↑ Paco₂, ↑ MAP, ↓ temp., ↑ hgb, √ CBFV—adjust cannulae</td>
<td>Reperfuse</td>
<td></td>
</tr>
<tr>
<td>rSO₂ &lt; 30%</td>
<td></td>
<td></td>
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<tr>
<td>TCD (mean CBFV, cm/s)</td>
<td>↓ ≥ 25% from pre-incision baseline</td>
<td>↑ Transducer; ↑ NIRS—if low, ↑ cardiac output, ↑ Paco₂, ↑ MAP</td>
<td>↑ Transducer; ↑ NIRS—if low: ↑ pump flow, ↑ Paco₂, ↑ MAP, adjust cannulae</td>
<td></td>
</tr>
<tr>
<td>↑ ≥ 25% from pre-incision baseline</td>
<td>↓ Paco₂, ↑ anesthetic depth, ↓ MAP</td>
<td>↓ Paco₂, ↑ anesthetic depth, ↓ MAP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emboli: more than isolated HITS</td>
<td>De-air all infusions, Trendelenburg position, stop rapid fluid boluses, search for and treat air entrainment in surgical field, look on TEE for air</td>
<td>De-airing maneuvers, Trendelenburg position, look for air on TEE, slow wean from bypass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIS</td>
<td>≥ 80 No isoelectric EEG prior to DHCA</td>
<td>↑ Anesthetic depth</td>
<td>↑ Anesthetic depth Additional cooling time; lower temperature before DHCA</td>
<td></td>
</tr>
<tr>
<td>&lt; 30 during rewarming on bypass</td>
<td></td>
<td></td>
<td>Reduce or discontinue volatile agent on pump</td>
<td></td>
</tr>
</tbody>
</table>

BIS, bispectral index; CBFV, cerebral blood flow velocity; DHCA, deep hypothermic circulatory arrest; EEG, electroencephalogram; HITS, high-intensity transient signals; MAP, mean arterial pressure; NIRS, near-infrared spectroscopy; rSO₂, regional cerebral oxygen saturation index; hgb, hemoglobin; TCD, transcranial Doppler ultrasound; TEE, transesophageal echocardiogram; √, assess parameter and adjust as necessary. Baseline rSO₂ and CBFV refer to pre-incision values during hemodynamically stable period with optimal blood gases. Frequent adjustments of TCD transducer position may be necessary to obtain the optimal signal before making interventions based on abnormally low values.
of newborns with CHD, and immediate appropriate care instituted.

Neurologic examination, cranial ultrasound, computed tomography scan, and magnetic resonance imaging have detected abnormalities related to preoperative hypoxic-ischemic injury, or malformations, including those associated with chromosomal abnormalities.60–62

Management of cardiopulmonary bypass

pH-stat vs. α-stat blood gas management

pH-stat management corrects blood gas values for temperature during CPB allowing for greater cerebral blood flow during hypothermia, greater oxygen delivery, and more even distribution of flood flow. The oxyhemoglobin dissociation curve is shifted to the right, facilitating unloading of oxygen.63 In animal models of DHCA, neurologic outcome is clearly improved when pH-stat is used. In humans (infants) this has been more difficult to demonstrate, although there were trends towards a lower death rate,20 fewer seizures, and greater hemodynamic stability. However, long-term neurologic follow-up to 4 years of age could not demonstrate a difference if pH- vs. α-stat was used.21

Low-flow bypass vs. deep hypothermic circulatory arrest

Deep hypothermic circulatory arrest, particularly if prolonged over 30–45 minutes, is associated with a higher incidence of neurologic complications. One hundred and eighty patients less than 3 months of age undergoing repair of transposition of the great arteries were randomized to low-flow CPB vs. DHCA in a landmark study at Children’s Hospital Boston.7 There was a higher incidence of seizures and elevated brain creatine kinase in the DHCA group. Seizures became more common after 30 minutes of DHCA. At 1 year follow-up a significant relationship was found between the duration of circulatory arrest and psychomotor development.64 At 4 years, the DHCA patients fared worse on examination of fine motor function. These studies provide convincing evidence that low-flow bypass is superior to DHCA in the prevention of neurologic injury.

Regional low-flow cerebral perfusion

Until recently, neonatal aortic reconstruction surgery was believed to require DHCA. The Norwood palliation for HLHS and the aortic arch advancement for repair of the interrupted or severely hypoplastic aortic arch are the most common examples. In recent years, novel perfusion techniques, such as regional low-flow cerebral perfusion,65 have been developed. Using this technique, the brain is perfused during the aortic reconstruction through a Goretex graft sewn into the base of the innominate artery, or through special small aortic cannulae advanced into the innominate artery (Fig. 8.6). Neurologic monitoring55 has demonstrated adequate cerebral blood flow and oxygenation using this technique. Utilizing this technique, DHCA to the brain can be limited to less than 10 minutes for the Norwood palliation, or eliminated altogether. This approach has theoretical advantages, and improved neurologic outcome is expected. However, prospective comparison studies have yet to be performed.

Rate of cooling and rewarming on bypass

There is evidence that brain metabolism is not adequately suppressed during cooling to deep hypothermic levels in some patients. In a study of infants undergoing cooling to 15°C, six of 17 had low jugular venous bulb saturation when this temperature was achieved, suggesting ongoing oxygen consumption that outstripped delivery of oxygen to the brain.36 Uneven or inefficient cooling of the brain may lead to neurologic deficits. Periods of cooling of less than 20 minutes...
were independently associated with lower developmental scores among newborns undergoing the arterial switch operation using DHCA. The risk of developing choreoathetosis is related to shorter periods of cooling. It appears that an insufficient perfusion period during cooling may ineffectively cool watershed areas within the brain leaving them vulnerable to ischemic injury. When low-flow or DHCA is planned the period of cooling should occur over no less than 20 minutes.

Hemodilution strategy
Classic teaching is that the hematocrit should be reduced to approximately 20 during deep hypothermia, as when blood viscosity increases. Recently, this hypothesis has been challenged with the premise that a higher hematocrit may provide greater oxygen-carrying capacity. A hematocrit of 30 provides slower decay of cerebral oxygenation vs. a hematocrit of 20 in a neonatal pig model with DHCA. In addition neurologic outcome and neuropathologic score was significantly better with higher hematocrit.

Neuroprotectant agents
At the current time, there is little evidence that any pharmacologic intervention has the potential to improve neurologic outcome in children undergoing congenital heart surgery. Corticosteroids, barbiturates, phenytoin, and aprotinin have been postulated to offer some degree of neuroprotection, but there is no current evidence to support this. One study in newborns has suggested that allopurinol may improve early outcome after congenital heart surgery. Halogenated anesthetic agents used in the bypass circuit, particularly desflurane, show promise in a neonatal pig model.

Glucose management
In the Boston circulatory arrest study hyperglycemia was not associated with worse neurological outcome and does not appear to be the concern it is in adults; in fact the probability of a perioperative seizure in the newborn is 2–3 times greater with a serum glucose less than 100 mg/dL vs. glucose greater than 200 mg/dL.

Postoperative management
Besides the basics of maintaining cardiac output and oxygen delivery, measurement of nasopharyngeal temperature and active cooling measures to limit increases in temperature may prevent neurologic injury. Consideration should be given to monitoring of cerebral oxygen saturation in certain high-risk patients. This approach also awaits prospective study of effectiveness in preventing adverse neurologic outcomes.

Conclusion
As the mortality rate for all congenital heart surgery trends downward toward 1–2% in many large, experienced centers, attention has increasingly turned to other morbidities affecting quality of life, none of which is more important than neurologic outcome. Neurologic morbidity is clearly decreasing as well, but remains a troubling problem. Basic science and clinical outcome studies have been performed in the past 15 years, but more outcome data are required. Despite clinical and experimental evidence that DHCA is detrimental to neurologic outcome, it continues to be in widespread use, and is not restricted to newborn surgery. Comparative studies with novel techniques such as regional low-flow cerebral perfusion, with long-term neurologic follow-up, need to be performed in order to address this question. The non-invasive monitors now available for cerebral oxygenation, blood flow, and EEG—do they improve outcome? Will newer technologies, i.e. frequency-domain spectrophotometers for measurement of cerebral oxygenation, prove to be more accurate? These and many other questions will be important to address as we strive to improve the quality of life for our patients.

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