SCA 2013 PBLD  Anesthetic Management for Deep Hypothermic Circulatory Arrest
James M. Anton, MD
Assistant Professor and Fellowship Program Director, Division of Cardiovascular Anesthesiology
Texas Heart Institute, St. Luke’s Episcopal Hospital, Houston, Texas

Marc Kanchuger, MD
Associate Professor, Department of Anesthesiology
New York University School of Medicine, New York, New York

Learning Objectives
After this educational activity participants should be able to:
1. Understand and identify the anesthetic considerations for patients undergoing cardiac surgery requiring Deep Hypothermic Circulatory Arrest (DHCA).
2. Understand and identify cannulation strategies and options for providing selective cerebral perfusion during cardiac surgery requiring DHCA.
3. Understand indications, options, and relative advantages and disadvantages for the different modalities of intraoperative neurologic monitoring available for patients undergoing cardiac surgery requiring DHCA.

Case Presentation
A 62 year-old female (65 kg) was found to have a large aneurysm of the ascending thoracic aorta (5.0 cm) and the aortic arch (6.0 cm), with associated moderate aortic regurgitation. Past medical history was positive for hypertension and tobacco use. Baseline creatinine was 0.68 and other pertinent lab values were normal. Transthoracic echocardiogram showed moderate, eccentric aortic regurgitation, preserved biventricular systolic function and a dilated ascending thoracic aorta. Left heart catheterization revealed no significant coronary artery disease.

The patient was scheduled to undergo total replacement of the ascending aorta and the aortic arch as well as exploration of the aortic valve with planned DHCA.

Case Questions
1. What are the perioperative risk factors for this patient undergoing DHCA?
2. What are the surgical indications for DHCA?
3. What is the purpose of DHCA? What is the basic physiology of DHCA?
4. What are the anesthetic considerations for this patient prior to DHCA?
5. What, if any, monitors should be used to evaluate neurologic status during DHCA?
6. Are there any procedures that can be used to augment neuroprotection prior to DHCA?
7. Are there any pharmacologic agents that should be used prior to DHCA? If so, why?
8. At what point of surgery should cooling of the patient occur?
9. What are the physiological changes of hypothermia?
10. To what degree should cooling occur? Where should temperature be measured?
11. How do alpha-stat and pH-stat differ? Which one would you use to manage this patient?
12. What is the target glucose during DHCA? Would you treat a blood glucose of 200 mg/dL? How?
13. The cerebral oximeter on the left side drops 30 points in comparison to the right side. With what techniques (if any) do you respond?
14. Over what period of time should rewarming occur? What temperatures should be reached?
15. How does rewarming effect coagulation? How would you prepare for post-DHCA coagulopathy?

Discussion
Purpose of DHCA
DHCA theoretically uses induced hypothermia (nasopharyngeal temperatures less than 24° C) to protect the brain during cessation of flow to the brain, in order to provide a bloodless surgical field for visualization of the great vessels. DHCA allows the surgeon to have good visualization for complex cardiac procedures. It can be used also in pulmonary embolectomy and neurovascular surgeries. The theory is to cool the patient, cease blood flow to the brain, and rely on the hypothermic protective effects of decreased cerebral metabolic rate of oxygen (CMRO$_2$). CMRO$_2$ decreases significantly with hypothermia; there is a 6-7% decrease in metabolism per 1° C decreased. At 25° C, CMRO$_2$ is decreased to 37%; at 15° C, CMRO$_2$ is decreased to 15%. Hypothermic protection of the brain cannot be explained only secondary to a decrease in CMRO2; the protective effects of hypothermia on brain tissue is not completely understood.

**Indications for DHCA**

DHCA is used for open heart procedures where the ability to perfuse the brain through the head vessels is not possible with standard proximal aorta cannulation. Repairs of the aortic arch, congenital repairs involving the aortic arch, repairs to the head and neck great vessels, or neurosurgical and pulmonary endarterectomies may require DHCA. Inability to clamp the distal arch, secondary to severe aortic atheromas, may also require DHCA to minimize stroke risk.

**Duration of DHCA**

The duration of DHCA considered safe is controversial. One retrospective analysis showed the risk of stroke increases when the length of DHCA is longer than 40 minutes. Acceptable duration is considered to be around 30-40 minutes due to the increase in risk of cerebral injury. Animal studies suggest significant cerebral tissue damage with greater than 45 minutes.

**Temperature Considerations during DHCA**

Bladder temperature is used to measure core body temperature. Although cerebral temperature can be measured using the tympanic membrane, this measurement is obviously difficult to obtain accurately and is unreliable during DHCA. Differences between core (bladder) and peripheral (nasopharyngeal) temperatures are approximately 2-4° C. Both nasopharyngeal and jugular venous bulb temperatures can be used as surrogates for cerebral temperature. Typically 2° C difference exists between core and cerebral temperatures.

**Cooling/Rewarming during DHCA**

Rapid cooling of cerebral tissue can lead to heterogeneous temperatures and cerebral hypoxia. Slow cooling to ensure homogenous hypothermia of the cerebrum is important. External cooling by packing the head in ice is also utilized to help inhibit secondary rewarming during the duration of DHCA. Hemoglobin oxygen affinity increases with hypothermia; thus rapid cooling may increase the risk of cerebral hypoxia. Cerebral CMRO$_2$ is decreased to 16% at 15°C and 37% at 25°C, thus it is suggested that acceptable cooling is between 15-25°C accomplished over 30-60 minutes. Cerebral silence with EEG is only predictable at nasopharyngeal temperature of 12.5°C or cooling longer than 50 minutes. In one review, cooling to 18°C over 30 minutes showed only 60% of patients had electroencephalographic silence on EEG. Rewarming should be accomplished over a similar time period to a temperature of 34-35°C prior to weaning from CPB. Significant institutional variance exists in the cooling and rewarming of patients undergoing DHCA. Temperatures should be maintained between 35-37°C and post-operative hyperthermia avoided in patients at risk for cerebral ischemia.

**Perioperative Neurologic Risks of Deep Hypothermic Circulatory Arrest**

Circulatory arrest causes hypoxic injury to all organs; however, the most serious and feared by clinicians is damage to the neurological system. Cerebral dysfunction post-cardiac surgery is a real and worrisome side effect. Neuropsychological dysfunction has been reported anywhere between 33%-83% of individuals undergoing cardiopulmonary bypass (CPB). The incident of stroke post-DHCA is approximately 10%. The
etiology of cerebral injury post-DHCA is not completely defined; however, it is thought to be due to an impairment in cerebral autoregulation, which is disrupted in hypothermic circulatory arrest. Cerebral autoregulation is the ability of cerebral blood flow to stay constant between MAP of 50 mmHg and 150 mmHg. During normal CPB conditions, cerebral autoregulation is thought to be maintained; however during deep hypothermia (<22°C), pH stat management, and circulatory arrest, cerebral autoregulation is disrupted. Risk factors reported to be associated with post-surgical cerebral injury include:

- Age
- MAP (intraoperative hypotension)
- Emboli
- Temperature
- SjVO2 (higher SjVO2 during DHCA has been associated with increased cognitive decline, the thought is possibly due to increased flow, not necessarily the increase in O2, which may transport more emboli)
- Cerebral hypoperfusion during CPB
- Cerebral oxygenation desaturation during rewarming

Anesthetic Monitoring Considerations
Monitoring for DHCA should include standard ASA monitors, central venous access, and bilateral radial arterial lines are often placed as the right axillary artery or inominate artery may be used for antegrade cerebral perfusion cannulation. Pulmonary artery catheters with continuous cardiac output capabilities and intraoperative TEE may also be used, to guide hemodynamic management, arterial and venous cannulation, and post-aortic repair evaluation. Blood gas and electrolyte management is crucial during DHCA and evaluation should be done often. Several options for neurologic monitoring exist. EEG monitoring, BIS monitoring, transcranial Doppler ultrasound, cerebral oximetry and jugular bulb oxygen saturation (SjVO2) have all been used to monitor neurological status during DHCA.

Neurologic Monitoring
1. EEG Monitoring – EEG is used to predict cerebral injury, as neuronal activity is altered prior to cellular death occurs. Ischemic EEG changes (loss of amplitude, loss of fast-frequency activity, increase slow-frequency activity) occur when cerebral blood flow is around 20 mL/100 g/min, while isoelectric activity occurs at 12 mL/100 g/min. Detection of changes may represent lack of perfusion, hypotension and initiation of CPB. At EEG silence, CMRO2 is predicted to decrease to 50%.4
2. BIS Monitoring – The BIS monitor uses an algorithm that incorporates EEG parameters and gives a single number to range. It is important to note that the EEG does not decrease on a linear 1-100 scale as does the BIS. With DHCA temperatures (<18°C), the BIS has been shown to decrease to 0.
3. Transcranial Doppler Ultrasound (TCD) – Doppler of the middle cerebral artery can be measured and velocities depicting blood flow can be measured. TCD can detect embolic phenomenon. The embolic matter causes changes in the sound of the Doppler signal from scattering.
4. Cerebral Oximetry (Near Infrared Spectrophotometry) – Near infrared spectrophotometry works on the premise of light penetrating the skull and being absorbed or reflected by brain tissue. Two signals – deep brain signal vs. superficial brain signal are used. The deep brain signal is calculated by subtracting the superficial signal from the total signal. Normal range is around 50-75%.
5. Jugular Bulb Oxygen Saturation (SjVO2) – Jugular bulb venous oximetry reflects the balance between cerebral oxygen supply and demand. Normal SjVO2 is between 65-70% and is dependent on cerebral blood flow. The absolute value of SjVO2 may not be as important as a trend. Decreased SjVO2 levels may signify hypotension, increased cerebrovascular resistance, and hypocapnia, while levels greater than 75% may signify cerebral hyperemia, hypercapnia or presence of an AV malformation.
Retrograde/Antegrade Cerebral Perfusion
Normal mean cerebral blood flow at 37°C is 750 mL/min, which is 16% of total cardiac output. During circulatory arrest, selective perfusion of the head vessels can be performed. Flow is diverted to the head vessels at a rate slow enough to provide adequate hypothermia. Drawbacks to selective cerebral perfusion are the risk of embolic events, complications of cannulation and inadequate surgical experience. Retrograde cerebral perfusion (RCP) uses bicaval cannulation and diverts flow through arterial line flow divergence through the SVC cannula. Flow through RCP is maintained between 300-1000 mL/min. Pressure is measured in the SVC and with target goals less than 20 mmHg. RCP allows the brain to receive hypothermic blood and may provide homogenous hypothermia. The benefits of RCP are debated. RCP in some studies has been shown to provide oxygen to brain tissue, however, whether this provides protective effects is unknown. Embolic phenomenon and tissue edema may be associated with RCP; however the use of RCP is suggested during complex aortic repairs in the literature. RCP is thought to provide the most protection by washing out debris and metabolites. Antegrade Cerebral Perfusion (ACP) is another mechanism thought to provide cerebral protection during DHCA. ACP is often accomplished by right axillary artery cannulation and requires skilled surgical techniques. Perfusion through the innominate artery depends on a competent Circle of Willis to perfuse the left hemisphere of the brain. Flow rates with ACP are approximately 10-20 mL/kg/min.

Pharmacologic Neuroprotective Agents
Standardization of neuroprotective agents during DHCA is lacking. Use of agents such as barbiturates and propofol vary from institution to institution. It is proposed that neuroprotective effects of such drugs may decrease any cerebral metabolic activity that remains at temperatures less than 18°C. In the past, when thiopental was available, doses of 20 mg/kg were administered prior to DHCA to provide EEG silence. Recent reports investigating the use of propofol in DHCA have not demonstrated neuroprotective effects, but do show effect EEG burst suppression. Isoflurane does provide EEG suppression, but does not decrease cerebral blood flow. Steroids do provide anti-inflammatory and spinal cord protection during CPB, but neuroprotection during DHCA has not been proven. Other agents such as etomidate, lidocaine, and mannitol have also been suggested.

Metabolic Considerations
During circulatory arrest, cessation of oxygen and glucose causes ATP depletion (which causes lactate accumulation and acidosis), loss of Ca+ homeostasis, free radical production, inflammation, leukocyte production, and cerebral edema. At normal temperatures (37°C) and cardiac output, oxygen consumption is 2.90 mL/g/min (20% of total body oxygen consumption) while at 20°C, oxygen consumption drops to 0.90 mL/g/min. It is theorized hypothermia provides the neurologic protective effect, by decreasing CMRO2, reducing oxygen free-radical production, diminishing intracellular Ca+ influx, and decreasing glutamate toxicity.

Alpha Stat vs. pH Stat
During hypothermia, the solubility of both O2 and CO2 increases while the partial pressure of O2 and CO2 decrease. Two different techniques to manage acid-base status exist: alpha-stat and pH-stat. During alpha-stat (not temperature corrected), there is an alkaline shift during hypothermia. Normal pH is maintained at normal temperature (37°C). pH stat management (temperature corrected) involves adding CO2 to the oxygenator, in order to keep CO2 and O2 values at normal in the hypothermic blood. Proponents of pH-stat argue that adding CO2 causes cerebral vasodilatation, which may cause faster and more homogenous cooling. Those in favor of pH stat management propose this technique counteracts the leftward shift of the oxygen dissociation curve which results in increasing oxygen delivery, tissue oxygenation and cerebral blood flow. Proponents of alpha-stat argue that it promotes cerebral protection by maintaining cerebral autoregulation. Arguments in favor of alpha-stat state that by maintaining cerebral autoregulation, cerebral protein function and membranes are maintained. A
recent meta-analysis of the 206 articles on alpha vs. pH-stat showed that pediatric literature supports pH-stat, whereas alpha stat may be better in the adult population.\textsuperscript{11}

**Glucose Management**
During CPB, there is increased insulin resistance secondary to cytokine release. With hypothermic CPB, glucose, glucagon, growth hormone, and catecholamine levels increase while insulin levels decrease. Glucose levels continue to increase during rewarming. Hyperglycemia during DHCA has been associated with worsening neurological outcomes.\textsuperscript{12} Tight glucose control is important during the entire procedure. Blood glucose levels of less than 140 mg/dL are suggested, and insulin drips often needed throughout the entire procedure.\textsuperscript{13}

**Coagulation and Bleeding**
Hypothermia causes significant coagulopathy. Platelets and other factors are often needed during weaning from cardiopulmonary bypass. Prolonged cardiopulmonary bypass times, significant suture lines, and disruption of coagulation all are causes for increased blood loss. Close detail to coagulation monitoring is imperative. Blood transfusion and the use of antifibrinolytic therapy may be warranted in the post-bypass period. The use of antifibrinolytic therapy pre-DHCA and used throughout DHCA has been associated with fatal thrombosis.\textsuperscript{14}

**References**
14. Fanashawe MP, Shore-Lesserson L, Reich DL. Two cases of fatal thrombosis after aminocaproic acid therapy and deep hypothermic circulatory arrest anesthesiology 2001;94:4-10.