Section

1

# Fundamental Aspects

Chapter

1

# Past, Present and Future of Pediatric Cardiac Anesthesia

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The practice of pediatric cardiac anesthesia has remarkably developed over the past years into a speciality to provide complex intensive care.

However, pediatric cardiac anesthesia began in 1938 when Gross first time successfully ligated a patent ductus arteriosus on a 7-year-old girl.[1]

After the first successful ligation of patent ductus arteriosus, surgery involved the extracardiac great vessels advanced rapidly. Chief among these achievements was the development of the Blalock–Taussig shunt.[2]

In 1946, Harmel and Lamont reported their experience of anesthetizing 100 patients undergoing Blalock–Taussig shunts performed by Alfred Blalock at Johns Hopkins Hospital for palliation of pulmonic stenosis.[3] Patients ranged in the age group of 10 weeks to 20 years, but majority were less than 8 years. All had disabling cyanosis, erythrocytosis, and poor cardiac function. The most frequent anesthetic agent used was cyclopropane, supplemented with ether and morphine. Assisted spontaneous ventilation was carried out in all patients. In an era of limited choice of anesthetic drugs, where there existed no muscle relaxants, no mechanical ventilators, and rudimentary monitoring, in order to provide the anesthetic care for pioneering surgical procedures on sick children required courage and innovation.

Also, the cardiopulmonary bypass (CPB) was developed and applied to clinical settings in the 1950s. After that the field of pediatric cardiac anesthesia has undergone impressive development, and now it is characterized by a speciality that requires complex clinical and intensive care skills.

In 1958, Arthur Keats, who became a pioneer among the cardiac anesthesiologists in the second half of the 20th century and reported the anesthetic challenges encountered during 200 open heart procedures utilizing CPB at Baylor University/Texas Children's Hospital.[4]

Anesthetic drugs used were cyclopropane or thiopental for induction and ether for the maintenance of anesthesia. Muscle relaxants were used in this series (succinylcholine infusion prior to CPB and tubocurarine during CPB), assisted spontaneous ventilation or manual positive pressure ventilation were utilized. In less than 10% of patients who were unable to be extubated at the end of the procedure, tracheostomy was performed to facilitate ventilator support and removal of the tracheal secretions. The mortality rate was 23%, with most of the deaths occurring during or immediately after the operation.

The mortality rate among the infants was 48% in less than 1 year of age and was significantly higher. During the ensuing decades, mortality rates associated with cardiac surgery and anesthesia decreased, but it was appreciated that patients with congenital heart disease (CHD) continued to have a higher perioperative mortality than the general population.

Baum studied the incidence of death associated with noncardiac surgical procedures in hospitalized children with CHD in 1990s.[5] Examination of a large, multi-institutional database revealed that children with CHD had a significantly greater mortality incidence than children without CHD within both 1 and 30 postoperative days. Mortality rates were incrementally greater in infants <1 year of age and in neonates.

Odegard and colleagues at Boston Children's Hospital demonstrated that both the incidence of cardiac arrest and the mortality associated with cardiac arrest in patients with CHD could be reduced to remarkably low rates.[6] In their review of over 5000 anesthetics for cardiac surgical procedures, the incidence of cardiac arrest was 0.79%. About one quarter of these cardiac arrests was associated with anesthetic factors, and all of these patients were successfully resuscitated. The remainder of the cardiac arrests was deemed to be "procedure related", and the mortality rate among these patients was 7.5%. These incidences are among the lowest ever reported for patients with CHD. The authors attributed their success to the adoption of dedicated cardiac anesthesia team that provided anesthetic care to this population of patients in their hospital. This concept is important because it described the success associated with implementation

of an anesthetic delivery model—the dedicated cardiac anesthesia team—that has been adopted by most leading pediatric cardiac centres today.

The safety of pediatric cardiac anesthesia was also improved by the development of newer anesthetics and increased knowledge of the cardiovascular effects of anesthetics.

During the 1980s, Hickey and colleagues at Boston Children's Hospital conducted a series of studies of the hemodynamic effects of several anesthetic drugs in children with CHD. Their subjects were incubated infants receiving ventilatory support during the first postoperative day following open heart surgery. They had invasive intravascular monitors in place, so direct measurement of atrial and pulmonary artery pressures (PAP) and cardiac output (CO) was obtainable.

The first paper in this series reported a study of bolus administration of fentanyl 25 μg/kg.[7] Synthetic opioid in high doses had become an important component of pediatric cardiac anesthesia[8] and by demonstrating lack of effect on HR, systemic blood pressure (MAP), PAP, systemic and pulmonary vascular resistances (SVR and PVR), and CO, this study confirmed the hemodynamic safety of fentanyl use in infants with heart disease.

A similar study on the hemodynamic effects of ketamine followed by a bolus dose of 2 mg/kg was associated with no significant change in systemic or pulmonary hemodynamics, HR, and CO.[9] These results confirmed the supportive role that ketamine can have in children with CHD and that PVR is unaffected in mechanically ventilated infants.

Williams, in a study of children with CHD undergoing cardiac catheterization[10] demonstrated the hemodynamic effects of propofol. Propofol had minimal pulmonary vascular effects but caused a marked decrease in SVR. This drastic decrease in SVR can lead to hypotension and reduced coronary artery perfusion pressure.

*In vitro* studies, demonstrated that the anesthetics depressed myocardial contractility, is mostly in a dose-dependent fashion.[11,12] The development of echocardiography enabled non-invasive *in vivo* measurement of ventricular contractility, and Barash conducted a pioneering study of halothane's depressant effect on myocardial contractility in children.[13] Echocardiography was subsequently used to demonstrate the advantages of newer volatile anesthetics over halothane in this regard[14] and the lack of depression of contractility by high-dose opioid in children with CHD.[15,16]

The most comprehensive hemodynamic study of children with CHD was carried out by Rivenes,[17] using echocardiography and invasive monitoring, the effects of halothane, isoflurane, and sevoflurane were documented, including the changes in HR, MAP, SVR, CO, and measurements of ventricular contractility. This study supports the continued use of sevoflurane and isoflurane as components of a balanced anesthetic in this population. In addition to hemodynamic changes, the stress response to anesthesia and cardiac surgery was investigated.

In a seminal paper, Anand and colleagues demonstrated that the neonate responded to surgical stimuli associated with thoracotomy for ligation of the ductus arteriosus with a marked hormonal and metabolic response and that was significantly attenuated by the inclusion of a fentanyl bolus in the anesthetic regimen.[18]

Subsequent studies demonstrated that this stress response could not be completely blocked by a variety of anesthetic drugs used during the procedures involving CPB[19] but an association with outcomes has been difficult to demonstrate.

As understanding of systemic and pulmonary hemodynamic increased, it became obvious that control of PVR was of utmost importance in the safe management of infants and children with CHD. Significant increases in PVR in children with pulmonary hypertension could lead to pulmonary hypertensive crisis and right heart failure, contributing to high perioperative incidence of cardiac arrest.[20] On the other hand, significant decrease in PVR in patients with left-to-right intracardiac shunts could cause pulmonary over-circulation.

In a classic investigation, Rudolph and Yuan demonstrated that PVR increased significantly during either hypoxia or acidosis and that the combination of the two resulted in a more marked increase.[21]

Subsequent clinical studies demonstrated that PVR and PAP could be manipulated by altering pH by changing either $PCO_2$ or hydrogen ion concentration.[22,23] Hickey documented that in patients with pulmonary hypertension, elevations of PVR were exacerbated by noxious stimuli including tracheal suctioning caused a 70% increase in PVR and PAP that was prevented by pretreatment with fentanyl.[24] The pulmonary hemodynamic effects of the inhalational anesthetics have not been studied extensively, but changes in the PVR are probably similar to those of SVR, as pulmonary to systemic blood flow ratio (QP:Qs) did not change significantly in children with septal defects.[25]

The development of palliative procedures for infants with single ventricle physiology led to recognition of the need to maintain a relatively high PVR in those patients to achieve QP: Qs balance prior to surgical palliation.

Low PVR is associated with pulmonary over circulation and systemic hypotension leading to low CO and impaired coronary perfusion, so inspiration of either subambient oxygen or hyperbaric gas mixtures was employed to maintain high PVR.

Ramamoorthy and colleagues demonstrated that, while both methods successfully maintained high PVR, the use of hypercarbia resulted in higher MAP and diastolic blood pressure and greater systemic and

cerebral oxygen saturations.[26] CPB is associated with defects in coagulation that are exaggerated in infants due to the greater amount of hemodilution associated with relatively large pump prime volumes. Kern[27] demonstrated that the concentrations of coagulation factors and platelets decreased by 50–70% with the onset of CPB in neonates.

Treatment of this dilutional coagulopathy following CPB has generally required transfusion of blood products. Using thromboelastography (TEG), Miller and colleagues identified fibrinogen and platelets as the chief deficiencies in small children and recommended platelet and cryoprecipitate transfusions.[28] Fresh (<48-hour-old) whole blood was more effective in achieving hemostasis than reconstituted blood components, probably due to the better functioning of the platelets.[29] Transfusion requirements were reduced by attenuating the dilution of coagulation factors with modified ultra-filtration or infusion of autologous fresh whole blood following the conclusion of CPB.[30,31] The later development of miniaturized CPB circuits significantly reduced pump priming volume, hemodilution, and transfusion requirements.[32]

The use of TEG allowed effective detection and monitoring of post-CPB coagulopathy, but traditional TEG required bulky apparatus and was time-consuming. However, modifications to TEG have transformed it to a rapid, point-of-care monitor. By activation of blood samples with either celite or tissue factor, TEG results were realized much more rapidly while retaining their accuracy.[33] Furthermore, when heparin was added to a sample obtained during rewarming on CPB, the resulting activated thromboelastogram could be initiated earlier[33] and displayed on the computer screen at the anesthesia work station at the time of separation from bypass.

Advances in surgical techniques were associated with great strides in the treatment and palliation of infants with complex CHD. One such technique was the wide spread adoption in the 1970s of deep hypothermic circulatory arrest (DHCA), which gave the surgeon unobstructed access to a still heart. As mortality rates associated with cardiac anesthesia and surgery declined, it was appropriate that attention turned to morbidity.

Perhaps, no other topic has captured more interest of investigators in the field of pediatric cardiac anesthesia, surgery, and critical care for the past quarter century as that of neurological injury and developmental delay associated with increasingly complex surgical repairs of CHD.

Investigators at Boston Children's Hospital, among others, have led clinical investigation of this topic in an ongoing series of studies. In 1988–1992, a study of infant's undergoing repair of transposition of the great arteries concluded, 31% had neurological abnormalities by examination and up to 50% had low psychomotor test results at 1 year of age.[35] Multiple factors have been demonstrated by these studies to be associated with neurodevelopmental impairment following cardiac surgery. Longer duration of DHCA correlated with worse postoperative neurodevelopmental outcome[34] More aggressive cooling of the patient prior to DHCA resulted in more complete cerebral cooling as assessed by higher jugular venous oxygen saturation.[35] Management of pH during hypothermic CPB made a difference, with pH-stat being associated with better cerebral oxygenation and blood flow and better developmental outcomes than the more alkaline alpha-stat management.[36,37] Better out comes were observed when hematocrit was maintained above 24% during hypothermic CPB in infants.[38]

Perioperative care and management of CPB are not the only contributors to neurodevelopmental impairment in infants. Neonates with complex CHD were shown to have a significant incidence of brain abnormalities prior to any surgical or anesthetic intervention. Kurth observed that neonates with CHD had significantly lower regional cerebral oxygen saturation preoperatively than did neonates without CHD and that increasing complexity of CHD was associated with lower cerebral oxygen saturation.[39] Furthermore, brain magnetic resonance imaging (MRI) evidence of neurological injury was present preoperatively in a significant number of neonates undergoing surgical CHD repair.[40] Andropoulos demonstrated that both preoperative MRI evidence of brain injury and preoperative low regional cerebral oxygen saturation were associated with poorer neurodevelopmental outcomes at 1 year of age.[41]

The description of the Norwood procedure for palliation of infants with hypoplastic left heart syndrome (HLHS) led to the adoption of a logical series of staged palliative operations—Norwood,[42] Glenn[43,44] and Fontan[45] for babies with HLHS and was a significant advancement in the treatment of infants who previously would not have survived. The challenges associated with the greater complexity and risk of single ventricle patients, however, led to the further development of new treatments and monitors that was accompanied by an overall decrease in perioperative mortality rates. For example, the extensive reconstruction of the aortic arch within the Norwood procedure necessitated a prolonged period of DHCA, so the technique of low flow regional cerebral perfusion was developed to provide ongoing perfusion of the brain.

Pediatric cardiac anesthesiologists have been in the forefront of investigations of both newer surgical techniques and monitors of brain perfusion.

Hoffman and colleagues described the utility of near infrared spectroscopy (NIRS) monitoring of regional oxygen saturation and demonstrated that two site (cerebral and somatic) monitoring contributed to goal-directed therapy with improved outcomes during the perioperative period.[46,47] Cerebral oxygen saturation levels following separation from CPB during neonatal

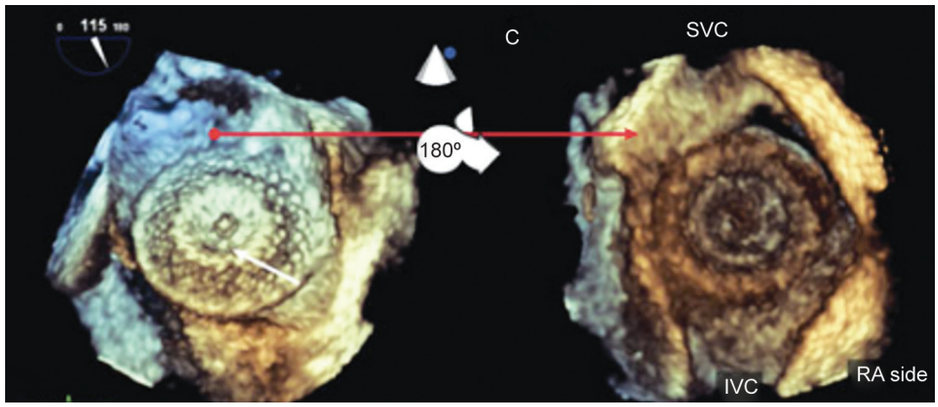


**Fig. 1.1:** 3D TEE showing ASD device after deployment

operations correlated with the neuro developmental test results and brain MRI findings at 1 year of age.[48]

Transcranial Doppler ultrasonography (TCD), a monitor of cerebral blood flow velocity, was used to determine the minimum pump flow rate to ensure cerebral blood flow during low flow CPB.[49] While, employing a combination of TCD and cerebral NIRS monitoring during regional cerebral perfusion, Andropoulos demonstrated the higher flow rates than previously were required to maintain adequate cerebral perfusion.[50]

The accumulated knowledge of the factors contributing to neurodevelopmental impairment in infants undergoing CPB and the development of advanced monitoring and surgical techniques led to great strides in reducing the severity of postoperative neurodevelopmental deficits. Using a technique that combined regional cerebral perfusion during CPB with multimodal brain monitoring using NIRS regional cerebral oxygen saturation and TCD, Andropoulos and colleagues demonstrated remarkably good neurodevelopmental outcome in neonates undergoing complex surgical procedures. Bayley Scales of Infant Development III testing at 1 year of age revealed normal cognitive scores and language and motor scores that were only 0.8–0.9 standard deviation below normal controls.[51]

TEE expertise was in the domain of cardiologists prior to 1990s. Transesophageal echocardiography (TEE) has become an integral part of perioperative care during pediatric cardiac surgery. The intraoperative use of TEE has remarkably improved the outcome of surgery from neonate to children. The evolution has resulted in dramatically reduction in reexploration surgeries after CHD operations. Preoperative transthoracic echocardiography (TTE) deals with diagnostic aspects of the congenital anomalies. However, the objectives for performing Preoperative TTE evaluation of complex congenital conditions may not be identical with those of intraoperative TEE. Apart from confirming the preoperative diagnosis and finding additional lesions, intraoperative TEE focuses on monitoring hemodynamic parameters and ventricular function, assisting conduct of cardiopulmonary bypass (CPB), evaluating surgical results and detecting surgical complications.[52]

TEE is also useful in percutaneous device closure of congenital septal defects in cath lab **(Fig. 1.1)**.

The continual innovations and improvements in the surgery and anesthetic management has resulted in the better survival outcome in this vulnerable cohort to adulthood. A combined approach and dedicated cardiac intensive care unit has further improved the survival. In near future, now the day is not far when intrauterine correction of congenital cardiac disease will be done routinely.

The time has come when cardiovascular anesthesia should assume leadership within the health system through its contribution in perioperative echocardiography, and take a leadership role in the point of care coagulation laboratory in addition to intensive care and postoperative cardiac surgical care.

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