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## Pediatric Perfusion Techniques for Complex Congenital Cardiac Surgery

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### HISTORICAL CONSIDERATIONS

Motivated by the inadequacy of nonsurgical therapy in ameliorating congenital cardiac disease, surgical pioneers in the 1940s and 1950s began to develop techniques that would allow for the intracardiac repair of congenital heart disease. The first operation on the open human heart under direct vision—closure of an atrial septal defect (ASD) in a 5-year-old girl—was performed at the University of Minnesota by Dr. F. John Lewis on September 2nd, 1952 (1). This

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operation was performed using inflow stasis and moderate total body hypothermia. Within 1 year, Lewis reported closure of 11 ASDs with only 18% mortality (2). This success, however, could not be extended to more complex defects without a system of extracorporeal oxygenation and perfusion. On May 6, 1953, John Gibbon used his extracorporeal oxygenation system to successfully close an ASD in a young woman (3). Despite this success, initial attempts at mechanical cardiopulmonary bypass (CPB) were uniformly dismal; of 18 reported cases between 1951 and 1954, using a variety of methods for total CPB (film oxygenators, bubble oxygenators, and monkey lungs), only those with ASDs survived (4–10). Faced with these results, alternative methods of perfusion were pursued, and on March 26, 1954, C. Walton Lillehei and colleagues successfully closed a ventricular septal defect (VSD) in a 12-month-old infant using controlled cross-circulation with the patient's father functioning as the extracorporeal oxygenator (11). From the late 1950s to well into the 1980s, bubble oxygenators were utilized in most extracorporeal oxygenation circuits. However, the high amount of embolic materials that were released by these devices led to the development of membrane oxygenators, which are now the gold standard for extracorporeal oxygenation (3).

### CONGENITAL HEART SURGERY AT NEW YORK PRESBYTERIAN HOSPITAL/COLUMBIA CAMPUS

Pediatric congenital heart surgery has been performed for over 30 years at New York Presbyterian Hospital's Columbia Campus, which is located in upper Manhattan. The Morgan Stanley Children's Hospital of New York (CHONY) is the children's hospital of the Columbia Campus, and is currently the largest congenital heart surgical center in New York State, performing over 500 congenital heart surgeries on CPB per year.

The following chapter outlines general considerations for the pediatric perfusionist, including many of the policies and procedures currently used at CHONY.

### CHALLENGES OF CARDIOPULMONARY BYPASS IN THE PEDIATRIC POPULATION

Perfusionists who specialize in pediatric perfusion are challenged to prepare for different sized patients; therefore, they need to employ a variety of oxygenators and circuitry to accommodate children who could be as small as 1 kg or as large as an adult.

### *Circuits*

A current trend in bypass surgery is toward decreasing the overall prime volume that the patient encounters during CPB. Moreover, utilizing the lowest prime possible for neonates and infants is especially important because of their particularly high extracorporeal circuit prime volume/patient blood volume ratio. This ratio can be decreased by employing small diameter, and therefore low prime, tubing (Table 1). Cardiac indices of 2.2–2.5 can be utilized to calculate extracorporeal flow, thereby providing appropriate full flow bypass, while avoiding overcirculation (Table 2). For children less than 5 kg, a circuit that primes with 220 cc is possible; this can be accomplished by utilizing 1/8 in. tubing for the arterial line and 3/16 in. in the venous line. The raceway and sump tubing for this circuit are 3/16 in. and the vent tubing is 1/8 in. Small diameter vent and sump tubing decreases the overall surface area and requires less steal from the total circulating volume when actively filled. An additional 40 cc of prime volume can be saved if the arterial filter is excluded, making the prime 180 cc. This circuit has been successfully used (no arterial filter) to perform a bloodless arterial switch on a 3.4-kg Jehovah's Witness. Even though the necessity of arterial filtration for neonates is debatable, Sorin Group (Mirandola, Italy) has recently developed a low prime arterial line filter (D 130 kids®, 16 cc). Certainly the development of even lower prime arterial filters is merited.

For children who weigh between 5 and 13 kg, a perfusion circuit that primes with 270 cc is available. This system utilizes the standard 3/16 × 1/4 loop and a 1/4 raceway. The use of low prime, high-flow oxygenators, such as the Baby-RX™ by Terumo®, has given the perfusionist the opportunity to offer a bloodless prime to some children who

Table 1  
Common Tubing Diameters and Their Associated Prime Volumes Per  
Inch of Tubing

<i>Tubing Diameter in Inches</i>	<i>Cc/inch</i>
1/2	3.5
3/8	1.8
5/16	1.3
1/4	.82
3/16	.45
1/8	.20

**Table 2**  
**Appropriate CI Per Patient Temperature**

<i>Core temp °C</i>	<i>Cardiac index M<sup>2</sup></i>	<i>*Approx DHCA</i>
37–35	2.2–2.5	5 min
<35–32	2.0–2.2	
<32–28	1.8–2.0	
<28–24	1.6–1.8	20 min
<24–20	1.0–1.5	
<20	0.5–0.8	45 min

\*90% probability of absence of structural or functional damage.

(Source: Kirklin JW, Barratt-Boyes GB, eds. Cardiac Surgery. Churchill-Livingstone, New York, 1993:61–127.)

would previously have required exogenous packed red blood cells; it can be particularly useful for children in the 10–15-kg range.

The Sorin D 100 Kids oxygenator® primes with 31 cc and is now available for neonates, and hopefully even lower prime devices will be developed.

A 1/4 × 3/8 in. A–V loop and pediatric oxygenator are used for children between 15 and 30 kg (some centers report the use of 5/16 in. venous line tubing in place of 3/8 in. for this patient population). From 30 to 55 kg, a 3/8 × 3/8 in. A–V loop and 3/8 in pump boot are routinely utilized, also with a pediatric oxygenator, and all patients over 55 kg receive an adult setup (Table 3).

**Table 3**  
**CHONY Bypass Circuits**

<i>Circuit FLOW</i>	<i>cc/L per min</i>	<i>OXYGENATOR</i>	<i>LOOP</i>	<i>PRIME*</i>	<i>FILTER</i>	<i>BOOT</i>
A.	<650 cc	<b>Baby-RX™</b>	1/8–3/16	220 cc	AF02	3/16-
B.	>650 cc–1.3 L	<b>Baby-RX™</b>	3/16–1/4	270 cc	AF02	1/4-
B1.	>1.3 L–1.5 L	<b>Baby-RX™</b>	1/4–3/8	375 cc	AF02	1/4-
C.	>1.5–2.5 L	<b>SX10R®</b>	1/4–3/8	610 cc	AF02	3/8-
D.	>2.5–3.5 L	<b>SX10R®</b>	3/8–3/8	850 cc	AL-8	3/8-
E.	>3.5 L	<b>SX18R®</b>	3/8–1/2	1150 cc	AL-8	1/2-

\*Represents the minimum dynamic prime at the onset of CPB, excluding the cardioplegia prime.

In addition to constructing extracorporeal circulation systems that are honed to the varying sizes of a pediatric population, other factors must be considered, including degree of hypothermia, acid–base management strategy, cardiopulmonary and cerebral protection, and techniques to manage bypass-induced inflammation.

### *Hypothermia*

In 1950, Bigelow first demonstrated the linear relationship between falling temperature and falling metabolic rate when anesthesia was used to control shivering and the increased muscle tone generated in response to cold (12). These findings were applied by Lewis et al. during their first open intracardiac repair in 1953 (1). After the development of the pump oxygenator, CPB and hypothermia were combined by Sealy, and some degree of hypothermia became common practice in the conduct of cardiac surgery (13).

#### **USE OF HYPOTHERMIA IN CONGENITAL HEART SURGERY**

The degree of hypothermia used during congenital heart surgery depends primarily on the reduction in flow required to perform an accurate repair. Mild (34–30°C), moderate (<30–25°C) or deep hypothermia (<25°C) may be employed. Mild hypothermia can be used in many simpler procedures, where the period of myocardial ischemia is relatively short. For more complex repairs, moderate hypothermia allows for longer aortic cross-clamp times and temporary periods of lower flow with maintenance of adequate myocardial protection (Table 2). The maintenance of a bloodless operative field in infants and neonates can be particularly challenging for several reasons, including aortopulmonary collaterals, increased pulmonary venous return and anomalous anatomy. Furthermore, the arterial and venous cannula themselves may make adequate exposure difficult. The use of deep hypothermia enables low flow CPB or circulatory arrest, which mitigates all of these problems. CPB may be initiated with a single atrial venous cannula that can be removed (along with the arterial cannula) during the circulatory arrest portion, thereby providing a bloodless and cannula-free operative field. The following chart represents a basic CPB temperature guideline for many congenital heart anomalies. (Table 4).

#### ***CO<sub>2</sub> Management: Alpha-Stat Versus pH-Stat***

One of the most studied aspects of hypothermia is its effect on the acid–base balance during CPB. In humans, the extracellular fluid pH

Table 4  
CHONY Hypothermia Chart

<i>Procedure</i>	<i>Temperature °C</i>
ASD secundum	36
ASD Sinus Venosus	34
VSD	32
Sub Aortic Stenosis	32–35
Tetralogy of Fallot	28–32
TAPVR	18
PAPVR	34
Norwood	18
Bidirectional Glenn	32–35
Hemi-Fontan	18
Fontan (lateral tunnel)	18–32
Fontan (extra cardiac)	34
Atrioventricular Septal Defect	28–32
Ross Procedure	28–32
Arterial Switch-VSD	18
Arterial Switch-ASD	18–24
MVR/AVR/TVR	32
Interrupted Aortic Arch	18
Ebstein's Anomaly	28–32
Truncus Arteriosus	18–24
RV-PA conduit	28–32

( $pH_e$ ) is maintained within a narrow range between 7.36 and 7.44 at normothermic temperatures. Intracellular pH ( $pH_i$ , which is more difficult to measure, but of significantly more importance to optimal intracellular enzymatic functions), is maintained at around 7.1, which is close to the pH of neutrality (pN) of water where the hydroxyl/hydrogen ion ratio approaches unity (14,15). Maintenance of the intracellular environment at a pH close to pN ensures that enzymatic processes occur at an optimal rate (15). As temperature falls, the dissociation constant of water increases, resulting in a decrease of both hydrogen and hydroxyl ions. Thus, maintenance of neutrality requires a rise in pH (decrease in hydrogen concentration).

In ectothermic (i.e., cold-blooded) animals, blood pH increases to maintain intra- and extracellular pH close to the pN of water. To do this, ectotherms allow  $PaCO_2$  to fall by maintaining normothermic ventilation despite the decreased  $CO_2$  production that occurs with falling temperature (16,17). This method of pH management is called

alpha-stat because the ratio (termed “alpha”) of dissociated-to-nondissociated imidazole groups (the primary blood buffer at hypothermic temperatures) remains constant (16). Although a full discussion of the biochemistry of alpha-stat pH management is beyond the scope of this chapter, it appears to offer biochemical stability in the setting of falling temperature (16). The other method of acid-base management is termed pH-stat; in this method, despite the rising pN of water, blood pH is maintained at a constant 7.40 through the addition of CO<sub>2</sub>. This method lowers pH<sub>i</sub> resulting in loss of intracellular electro-chemical neutrality. Heterothermic (ie. hibernating) animals use a predominantly pH-stat method of acid-base management during hibernation. However, certain active tissues (e.g., heart and liver) actively extrude H<sup>+</sup> across their cell membrane, resulting in the maintenance of pH<sub>i</sub> near values predicted by alpha-stat management (18). Furthermore, during awakening, animals begin to hyperventilate, reverting to overall alpha-stat pH management and regaining optimal enzymatic function.

### CHOICE OF ACID–BASE MANAGEMENT STRATEGY

The traditional preference for the pH-stat method in the 1960s and 1970s was predicated on two theories: (a) hypercarbia would ameliorate the leftward shift of the oxyhemoglobin dissociation curve which occurs with hypothermia, thereby increasing tissue oxygen availability, and (b) cerebral vasodilation in response to elevated CO<sub>2</sub> would selectively increase cerebral blood flow during the period of CPB (18,19). However, the leftward shift of the dissociation curve is balanced by the increase in oxygen dissolved in plasma during hypothermia, and the dissolved oxygen may be sufficient to fully support cerebral metabolism at hypothermic temperatures (20,21). Although pH-stat management does appear to enhance distribution of extracorporeal perfusate to the brain, and thereby improve the speed and distribution of brain cooling, it is also associated with impaired metabolic recovery after circulatory arrest (22–24).

Most evidence suggests that, in adults, the management strategy does not matter, or there may be benefit to the use of alpha-stat management (25–27). In children, however, the data is more controversial. Although some studies do report improved outcomes using alpha-stat, others have demonstrated shorter recovery of electroencephalographic activity, decreased incidence of electroencephalographic seizures, and improved postoperative developmental scores using pH-stat (28,29). The heterogeneity of results has led some authors to recommend a combined strategy where 10 min of pH-stat management is used to

promote brain cooling, followed by alpha-stat management to return the cerebral milieu to electrochemical neutrality (23,30). This crossover method or pH-stat management alone may be the best method in pediatric patients, particularly those in whom large aortopulmonary collaterals impair cerebral cooling (31–33).

The perpetual debate between alpha- and pH-stat blood gas management is ongoing, with many centers reporting good results utilizing either strategy. Therefore, intercenter differences in intraoperative patient management may create a multifactorial milieu that favors one method over another. Therefore, the alpha-stat management strategy has always been utilized at CHONY for all congenital heart surgery. However, current low prime oxygenators are capable of transferring CO<sub>2</sub> over a large range of patients ranging from less than 2 to 15 kg. These units tend to be too efficient for neonates, so low sweep rates are necessary to avoid hypocapnea, especially when cooling to and warming from DHCA and, most importantly, during procedures where aortopulmonary collaterals are present.

A 1995 CHONY study, which used ultrasound to interrogate the middle cerebral artery (MCA) during DHCA and hypothermic low flow bypass, found that patients who underwent deep hypothermia had lower cerebral blood flow velocities after rewarming than those who only experienced moderate hypothermia (34). It was also noted anecdotally, that middle cerebral artery flow could be used to predict low pCO<sub>2</sub> levels. At a given mean arterial pressure with obvious detectable MCA flow, pCO<sub>2</sub> was above 30 mmHg; in contrast, marked decreases in MCA flow velocity were associated with a pCO<sub>2</sub> that was less than 20 mmHg.

### ***Myocardial Protection***

Despite the increased tolerance for hypoxia and ischemia in experimental evaluation of the immature myocardium, in clinical practice, immature myocardium appears to be more susceptible to injury than the adult heart (35–37). Both the hypoxia and the volume and pressure overload common with congenital heart defects result in increased preoperative myocardial stress and susceptibility to perioperative injury (35). Several conditions, including left-to-right shunts, single ventricle with mixed circulation, and atrioventricular valve insufficiency, may lead to volume overload, and then to ventricular hypertrophy and dilatation; similarly, outflow tract obstruction or elevated vascular resistance may result in elevated ventricular pressures and, ultimately, to hypertrophy (36,38,39). Ventricular compensation in both cases leads to



myocardium that may be more susceptible to ischemic insult during operative repair (38,40–42).

Proper management of  $pO_2$  is also important for neonatal myocardial protection, especially in the setting of cyanotic lesions (43). To avoid excessive hyperoxygenation, a slightly hyperoxic blood gas strategy can be utilized by maintaining a  $pO_2$  goal in the high 200 s.

### *Cardioplegia*

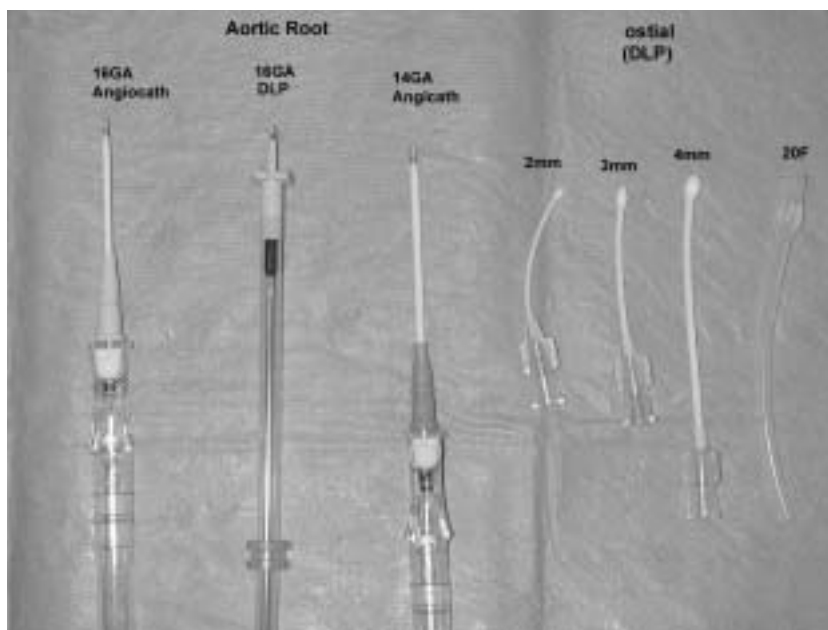
There are a variety of recipes for cardioplegia solutions and circuit configurations for their delivery. For patients less than 30 kg, a potassium solution of 60 Meq/L with a low prime circuit (75 cc) has proven reliable. This method allows for a quick dose of 15 cc/kg, followed by subsequent doses of 5–7 cc/kg at 20–30-min intervals. The cardioplegia delivery system utilizes a 1:1 blood/clear solution with a 3/16 over 3/16 raceway, the Sorin Vanguard™, and a 1/8-in. delivery line. The cardioplegia solution consists of: 900 cc D5W, 60 Meq KCL, 30 Meq  $NaHCO_3$  and 12.5 g of Mannitol. Even lower cardioplegia prime volumes are possible by using 1/8-in tubing in the raceway and smaller conductors. For children over 30 kg, a 4:1 blood cardioplegia system can be used. With this configuration, a high dose of 120 Meq/L is delivered until 7 cc per kg is administered, and then the low dose of 60 Meq/L is given until an additional 8 cc/kg (for a total of 15 cc/kg) is achieved.

There are a variety of cannulae available for pediatric cardioplegia delivery, including Angiocaths®, DLP® aortic root cannulae, and DLP® balloon tip cannulae for individual coronary ostial cardioplegia delivery (Fig. 1). It is possible to perform most pediatric congenital heart surgery without the use of retrograde cardioplegia.

### *Systemic Responses to CPB*

#### **PULMONARY DYSFUNCTION**

The lungs are at risk for injury during CPB from two perioperative processes: ischemia/reperfusion and the systemic inflammatory response; these are exacerbated by the frequent coexistence of varying degrees of preoperative pulmonary hypertension. With the onset of total CPB, the lungs become dependent on the bronchial arteries for nutrient and oxygen delivery; where these are not adequate, ischemic injury may occur (44–47). The inflammatory response to CPB contributes to postoperative pulmonary hypertension, leading to increased



**Fig. 1.** Cardioplegia Cannulae (Angiocath®, DLP®).

right ventricular work in the postcardiotomy heart and, more importantly, results in pulmonary edema with its attendant decrease in functional residual capacity, compliance, and gas exchange (48–52). The relative impact of and interaction between these processes is complex, as illustrated by the fact that low-flow CPB appears to cause worse lung injury than does circulatory arrest (53,54).

Several strategies have been proposed to limit pulmonary injury during and after CPB. Steroid treatment mitigates the systemic inflammatory response and improves pulmonary compliance and vascular resistance (55). Ultrafiltration also appears to limit post-CPB pulmonary dysfunction (56–59). Experimentally, liquid lung ventilation appears to improve postoperative pulmonary function, but the application of this technique awaits human trials (60–62).

In the post-CPB phase, pulmonary hypertension may be ameliorated through the use of inhaled nitric oxide (NO), and the use of NO may facilitate weaning from CPB, making it an essential tool for pediatric congenital heart surgery (63). The intraoperative administration of NOi can be managed by the respiratory therapists, perfusionists, and/or the

anesthesiologists. The respiratory therapists should supply the NO delivery system (INOvent®). After delivery of the system to the operating room, the perfusion or respiratory teams can purge it of nitrogen dioxide, ensure that the system is running smoothly, and then set the requested dose (usually 20 PPM). Anesthesiologists then connect the NOi system in-line with their ventilator tubing.

## NEUROLOGIC INJURY

**Mediators of Neurologic Injury.** The conduct of CPB in neonates, infants, and children exposes these patients to biological extremes far in excess of those present in most adult operations: deep hypothermia, hemodilution, low perfusion pressures, and wide variations in pump flow rates are common (64). In addition, variability in glucose supplementation, cannula placement, the presence of aortopulmonary collaterals, patient age and predilection for neurologic damage, prior episodes of severe hypoxia, and brain mass may all affect the neurological response to and morbidity from CPB (64). Because of difficulties with neurological and cognitive assessment in infants and children, accurate estimates of the long-term neurological impact of CPB in the pediatric population are difficult to obtain (65). However, estimates of acute neurological morbidity approach 25% (66). Such morbidity may take many forms including stroke, diffuse hypoxic-ischemic lesions, intracranial hemorrhage, delayed choreoathetoid syndrome, spinal cord lesions, cerebral infarction, diffuse cortical atrophy and seizures (65). Several potential mechanisms have been proposed for these injuries (65):

1. Unrecognized preoperative neurological abnormalities;
2. Hypoxic insults;
3. Altered cerebral blood flow and cerebral metabolism with hypothermia;
4. Embolic events; and
5. Low cardiac output states following cardiac surgery.

Unrecognized preoperative neurological abnormalities complicate the analysis of postoperative neurological defects in children. Up to 1/3 of patients may have abnormal preoperative magnetic resonance brain imaging without neurological symptoms or deficits (67). The natural history of such lesions cannot be known for certain, given that many of these patients present with cardiac defects requiring emergent repair. However, clearly many patients have abnormal cerebral blood flow even before being subjected to CPB (68).

With decreasing temperature, cerebral blood flow decreases linearly due to autoregulation, but cerebral metabolism decreases exponentially, resulting in ample cerebral oxygen delivery at low temperature, despite minimal pump flow rates (Table 2) (69). However, even with deep hypothermia, cerebral metabolism continues at a low level, leading to hypoxia and ischemia when the pump is turned off for circulatory arrest. As noted above, hypothermia has additional protective effects on the ischemic brain that help mitigate the resultant damage. Nonetheless, prolonged circulatory arrest time is associated with an increasing risk of neurological injury regardless of the techniques of neuroprotection used (70). Methods that may help limit ischemic injury during DHCA, in addition to hypothermia, include intravenous methylprednisolone (55) and the use of aprotinin (68,71). Other methods, including blockade of thromboxane A<sub>2</sub> receptors, free radical scavengers, and platelet-activating factor inhibitors, remain experimental at this time.

Although less frequently the cause of neurological morbidity in children than in adults, microembolic events occur commonly and may contribute to end-organ injury. Air embolism may be particularly likely where operative repair necessitates opening the left side of the circulation to the air (68). The use of membrane oxygenators and arterial filters has minimized but not eliminated the risk of air embolism (72,73). When cerebral air embolism does occur, both reestablishment of hypothermic CPB and hyperbaric O<sub>2</sub> therapy may reduce the size of microbubbles, allowing them to pass through capillary beds, and thereby reduce tissue damage (74). Furthermore, the risk of neurological injury does not end with the termination of CPB; in the postoperative period, factors that increase brain metabolic demand (hyperthermia), or decrease substrate and oxygen delivery (low cardiac output or hypoglycemia), may lead to brain injury (64).

Traditionally, DHCA was used for most cardiac repairs in the pediatric population. While its use has enabled technically successful cardiac repairs, DHCA in the format used in the 1980s and early 1990s did not provide adequate protection for the brain (75). Improvements in technology have made it feasible to use bicaval cannulation and continuous low-flow perfusion even in neonates (75). Although neurological outcomes, including stroke rates and long-term developmental outcomes, were improved using continuous low-flow perfusion (76), evidence continues to accumulate that this method may result in increased soft tissue edema, poor pulmonary function, and

**Table 5**  
**Common Strategies for Limiting Neurologic Injury with the Use of Deep Hypothermic Circulatory Arrest**

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Prebypass treatment with steroids and aprotinin (71,78)
Adequate duration of cooling ( $\geq 20$ min) to ensure more uniform and homogeneous brain protection (79,80)
Maintenance of higher hematocrits during the cooling phase
**Using pH stat blood gas management strategy during the cooling phase (23,28,81)
**Use of intermittent hypothermic cerebral perfusion for 1 to 2 min at 15–20 min intervals (77,82)
**Use of MUF after CPB (83)
Attention to postoperative cerebral metabolic demand and substrate delivery through limitation of hyperthermia and maintenance of adequate cardiac output I (64,75)

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DHCA, deep hypothermic circulatory arrest; CPB, cardiopulmonary bypass.  
 Recommendations based on ref. 75.

\*\*Not used at CHONY.

substantial cerebral edema and neuronal Golgi apparatus damage (53,54,75,77,78). In addition, the inability to remove the cannula during low flow bypass may make a technically accurate repair more difficult. Where DHCA is required, current research suggests a variety of modifications that mitigate the risk of neurological injury (Table 5<sup>23,28,64,71,75,77–83</sup>) (75). Safe and appropriate application of DHCA is essential to ensuring the best cardiac repair, as well as the best neurological outcomes.

### SYSTEMIC INFLAMMATORY RESPONSE

Modern CPB leads to a systemic inflammatory and immunological response through injury of specific blood elements, embolic events, and the activation of complex systems designed to protect the body against bleeding, thrombosis, and invasion by foreign organisms (84). In most patients, these processes are well tolerated; however, they pose an additional risk to patients at the extremes of age where the accompanying morbidity may increase mortality (84).

**Antiinflammatory Strategies.** Several therapeutic strategies have been promulgated to attenuate the CPB-induced inflammatory process. Corticosteroids have been used for years to moderate the inflammatory cascades. Most of the powerful effects of steroids occur through

inhibition of signal transduction and gene transcription in inflammatory cells; because these processes take time, administration of high-dose steroids is most effective when it occurs several hours before CPB (55). Other potential pharmacologic strategies include: serine protease inhibitors (aprotinin) (85), phosphodiesterase inhibitors (milrinone and pentoxifylline), NO donors (sodium nitroprusside), antioxidants (superoxide dismutase and *N*-acetylcysteine), and complement inhibitors (86). Unfortunately, despite encouraging experimental results, most of these strategies have yielded equivocal results in clinical trials (86). Mechanical techniques including hemofiltration, circuit miniaturization to reduce priming volumes and oxygenator exposure, leukocyte filters, the use of DHCA to mitigate postbypass edema and heparin-bonded circuits have generally been more successful, particularly in the pediatric population (68,86).

A successful strategy for reducing postoperative inflammation uses a combination of the aforementioned techniques. The overall conduct of perfusion should be based on the idea that low prime volumes, and therefore diminished surface areas, are essential to mitigating postoperative inflammation. Other strategies employed to reduce excessive postoperative inflammation include: (a) the use of  $\alpha$ - and  $\beta$ -antagonist sodium nitroprusside for DHCA procedures at 3–5 mcg/kg/min for vasodilatation during cooling and rewarming, (b) the administration of aprotinin (Trasylo<sup>®</sup>) during all DHCA procedures, as well as most cases with average bypass times exceeding 1.5 h, and (c) the liberal use of intraoperative hemoconcentration, including postbypass modified ultrafiltration, when indicated (*see* Hemodilution). These techniques may minimize the requirement for delayed postoperative sternal closure.

Concerning the use of aprotinin, a modified half dose protocol that is based on the patient's weight may be efficacious (87). Anecdotaly, using aprotinin on all DHCA procedures has not resulted in clots in the bypass circuit, a disruption in graft flow or any significant renal dysfunction (88,89). The protocol consists of (a) a test dose that is given by the anesthesiologist after heparinization, (b) a loading dose that is also administered by the anesthesiologist, (c) a pump prime dose which the perfusionist adds 5 min after the infusion of the test dose (except when clear prime replacement is utilized, in which case the aprotinin (Trasylo<sup>®</sup>) pump prime dose is added to the prime after the clear has been removed), and (d) a continuous infusion that is maintained by the anesthesiologist until the patient leaves the operating room (Table 6).

Table 6  
Trasylol®

**TEST DOSE**

Administered by anesthesia after heparinization

<15 Kg = 0.3 cc

15–30 Kg = 0.6 cc

>30 Kg = 1 cc

**PATIENT DOSE**

**LOAD-** Administered by anesthesia after heparinization

<51 Kg ————— 20,000 KIU/Kg (2 cc/Kg)

>50 Kg ————— 100 cc

**PUMP-** Added to the pump prime after the load is started.

<21 Kg ————— 40,000 KIU/Kg (4 cc/Kg)

21–50 Kg ————— 80 cc

>50 Kg ————— 100 cc

**MAINTENANCE**—RUN BY ANESTHESIA UNTIL THE PATIENT LEAVES THE OR

25% of the Pump Prime dose in cc/h

## TECHNIQUE FOR CARDIOPULMONARY BYPASS IN THE PEDIATRIC POPULATION

### *Prime/Hemodilution*

The small size of infants and neonates in comparison to the extracorporeal circuit significantly complicates several aspects of the conduct of CPB. In adults, the priming volume accounts for only 25–33% of the patient's blood volume; in neonates, the priming volume may exceed the blood volume by 200–300% (common pediatric pump circuits have total volume between 500 and 1200 mL). This inevitably leads to significant hemodilution with the onset of extracorporeal circulation (Table 7). Hemodilution reduces plasma proteins and clotting factors (contributing to interstitial edema and coagulopathy), produces electrolyte imbalances, results in a release of stress hormone, and activates inflammatory pathways. The optimal hematocrit will vary from case to case and depends on the diagnosis, degree of functional impairment, and planned surgical procedure; for example, those patients in whom a palliative procedure will result in postoperative mixed circulation with cyanosis will be poorly tolerant of a low hematocrit and may require physiologic normal hematocrit at the termination of the procedure (90).

Table 7  
Prime Constituents

Circuit	Albumin	FFP	PRBCs	Heparin	CaCl	NaHCO <sub>3</sub>	^Mannitol^	Total prime
A <3kg	coat circuit with 50 cc of 25%	60 cc	125 cc	500 U	75 mg	(10mEq + 1 mEq/kg)/2	(250 mg/kg)/2	220 cc
A	50 cc of 25%	none	125 cc	500 U	50 mg	(10mEq + 1 mEq/kg)/2	(250 mg/kg)/2	220 cc
B	50 cc 25%	none	#180 cc	700 U	*75 mg	(10mEq + 1 mEq/kg)/1.5	(250 mg/kg)1.5	270 cc
B1	75 cc 25%	none	#250 cc	1,000 U	*100 mg	(10mEq + 1 mEq/kg)/1.5	(250 mg/kg)1.5	375 cc
C	100 cc 25%	none	*350 cc	1,200 U	*100 mg	10 mEq + 1 mEq/kg up to a total of 25 mEq	250 mg/kg	640 cc
D	150 cc 25%	none	*350 cc	1,700 U	*100 mg	25 mEq	250 mg/kg	850 cc
E	200 cc 25%	none	*350 cc	2,200 U	*100 mg	25 mEq	250 mg/kg	1,150 cc

All circuits are initially primed with Plasmalyte<sup>®</sup>, which is partially chased out by the albumin, blood, or FFP, and then the drugs are added; therefore, the balance of all prime volumes is Plasmalyte<sup>®</sup>.

#A blood prime is often not necessary; \*Calcium is added only if blood is used; ^An equivalent dose is given at cross clamp removal.



$$V_{\text{blood}} = \frac{[\text{Hct}_d \times (V_{\text{pt}} + V_{\text{circuit}})] - [\text{Hct}_{\text{pt}} \times V_{\text{pt}}]}{\text{Hct}_{\text{blood}}}$$

$V_{\text{blood}}$  = volume of blood needed in prime

$\text{Hct}_d$  = desired hematocrit on CPB

$\text{Hct}_{\text{pt}}$  = patient hematocrit prior to CPB

$\text{Hct}_{\text{blood}}$  = hematocrit of blood to be added to prime

$V_{\text{pt}}$  = patient's circulating blood volume

$V_{\text{circuit}}$  = extracorporeal circuit volume

**Fig. 2.** Estimating blood needed for priming.

The level of hemodilution at the initiation of bypass is determined by the addition of donor blood to the prime solution (otherwise consisting mainly of crystalloids and colloids). Given the risks associated with the use of donor blood (viral particle transmission; complement activation; transfusion reaction; lactate, potassium, citrate-phosphate-dextrose, and glucose infusion) (91–93), attempts have been made to minimize the priming volume required as well as the need for transfusion. Following determination of the desired hematocrit, blood is added to the prime according to the following formula. (Fig. 2). The blood added to the prime may be either packed red blood cells (PRBCs) or whole blood. The use of fresh PRBCs has been advocated, although concerns about using stored blood may be overstated (94). Where PRBCs are used, colloid is also usually added to increase the oncotic pressure of the perfusate and decrease edema formation; maintenance of normal osmotic pressure has been associated with improved survival in infants after CPB (95). Other additives to the prime solution include: variable levels of electrolytes, buffer, calcium (though hypocalcemic primes are generally preferred to mitigate the risk of calcium during ischemic arrest), glucose, and lactate. More controversial is the use of mannitol, both as an osmotic diuretic and free-radical scavenger, and the addition of steroids to reduce the systemic inflammatory response to CPB and ischemia.

## HEMODILUTION

Although previously thought to be safe, bypass strategies employing hemodilution to a hematocrit of less than 25% have been associated with poor perioperative hemodynamics and adverse psychomotor outcomes (96); therefore, an on-bypass hematocrit of 28–35% is a reasonable goal. To achieve this hematocrit goal, small circuits, clear

Table 8  
Common Cannulae and Associated Flows

CHONY VENOUS CANNULAE							
DLP® single stage straight	Max Flow cc/min	Venous line	Biomedicus®	Max Flow Cc/min	Aug flow	Bi-caval Angled DLP® or Angled Edwards®	Max Flow cc/min
14 Fr	300		8 Fr	300		12 Fr	500
16 Fr	450		10 Fr	600		12	750
18 Fr	800		12 Fr	900		12	1000
18 Fr	1000	3/16	14 Fr	1200		14	1000
20 Fr	1200	1/4	15 Fr	750	2000	14	1200
22 Fr	1600	1/4	17 Fr	1100	2600	16	1500
22 Fr	1800	3/8	19 Fr	1500	3500	16	1800
24 Fr	2200	3/8	21 Fr	2000	4500	18	2100
28 Fr	2800	3/8	23 Fr	2500		18	2500
30 Fr	3100	3/8	25 Fr	3000		20	2800
32 Fr	3500	3/8	27 Fr	3500		20	3200
32 Fr	4000	1/2	29 Fr	4500		24	4000
34 Fr	4400	1/2				24	5000
36 Fr	5000	1/2				28	6000
38 Fr	5500	1/2					
40 Fr	6000	1/2					

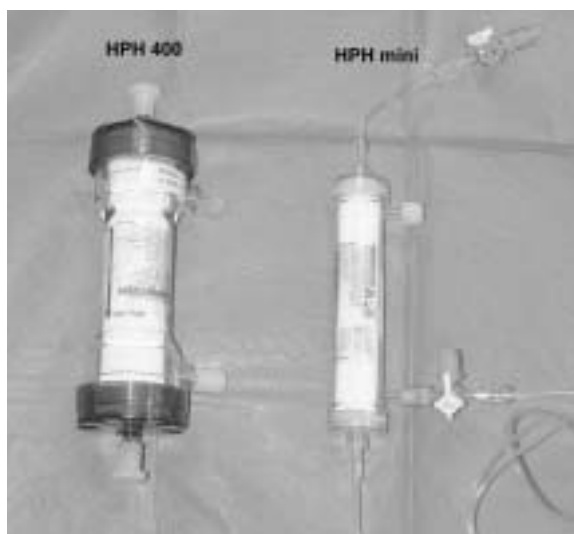
CHONY ARTERIAL CANNULAE			
DLP® wire	Max Flow Cc/min	Biomedicus®	Max Flow Cc/min
6 Fr	400	8 Fr	650
8	650	10	1100
10	1100	12	2200
12	2200	14	2900
14	2900	15	3000
16	4000	17	4000
		19	5500
		21	6500
		23	8000

prime replacement, hemoconcentration, and PRBC transfusions can be utilized. Certain procedures, including short bypass runs, such as during subaortic stenosis resections and ASD closures, may merit lower hematocrits (in the mid 20s).

If a blood prime is not indicated, then pre-CPB prime replacement can be accomplished (clear prime replacement). First, remove any extra circuit volume over that necessary to make the connection to the arterial cannula. Next, with a clamped arterial line, drain the patient via the venous line into a transfer bag—thereby chasing out the prime. If the connection to the transfer bag is on the venous line, then gravity draining into the bag will suffice (although only the venous volume can be removed). In contrast, if the transfer setup is connected on the arterial line, then all of the volume up to that point may be translocated by running the arterial head and controlling the speed of removal with a venous line clamp. Blood pressure during the exchange can be augmented with  $\alpha$ -agonists. However, only the available extra fluid may be removed, so an overaggressive removal strategy is not recommended. Often, much of the fluid that is removed is ultimately transfused back to the patient during the procedure, especially during rewarming. While this would appear to nullify the effect of the replacement procedure, there is evidence that intraoperative fluid shifts can be minimized if a mostly autologous prime is encountered by the patient at the onset of CBP (97).

Hemoconcentration, either conventional or post-bypass, is an important tool for managing excess circuit volume, removing proinflammatory mediators and controlling excess potassium levels. To manage excess circuit volume during pediatric congenital heart surgery, 8 and 27 cc prime hemoconcentrators are available. The 8 cc (Hemocor Junior®) is primarily used on circuits where the prime is 270 cc or less, and the 27 cc (Hemocor 400®) on all others (Fig. 3).

Extended bypass times are associated with increasing expression of proinflammatory mediators (98). Therefore it is helpful to use hemoconcentrators for all cases with expected bypass times exceeding 1.5 h, even in the absence of extra circuit volume requiring removal. This is accomplished by adding a balanced electrolyte solution to the circulating volume and then removing that same amount of volume with the hemoconcentrator. Also, excess potassium levels can be safely managed with aggressive ultrafiltration using normal saline to “wash out” the excess potassium. Normal saline is relatively acidotic, so serial blood gasses are necessary when employing this technique.



**Fig. 3.** Hemoconcentrators (HPH 400®, HPH mini®).

### MODIFIED ULTRAFILTRATION

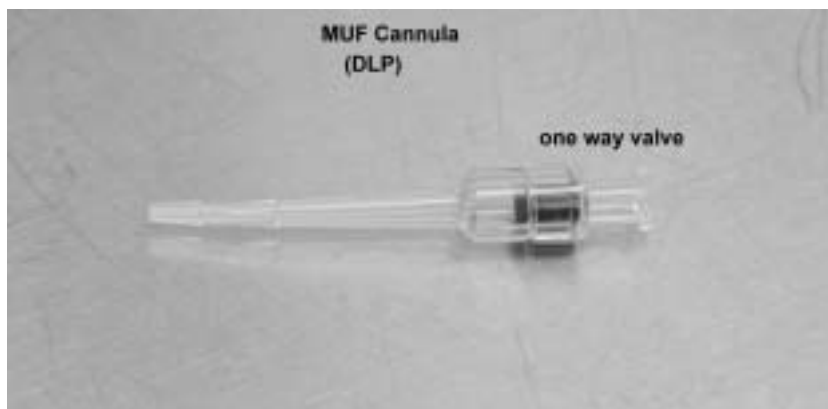
At CHONY there are three reasons that we do not routinely use modified ultrafiltration (MUF). First, when using very low prime circuits (180–270 cc), it is difficult to use MUF because there is very little excess circuit volume left in the reservoir after the cessation of CPB. Therefore, flushing the MUF circuit usually requires the addition of volume to the bypass circuit. Second, in larger children (over 25 kg), the amount of time necessary to remove enough volume to effect a significant change reduces the positive effects of MUF. Finally, there is evidence that utilizing conventional hemoconcentration for the removal of pro-inflammatory mediators is as effective as MUF (99). However, children between 14 and 20 kg are subjected to a circuit with a relatively high prime volume compared to their blood volume. Therefore, MUF can effectively increase postbypass hematocrit and remove proinflammatory mediators. For these patients, we utilize a simple arterial-venous MUF circuit. The MUF access line is connected to the arterial manifold sample port, then threaded through a small twin pump and connected to the Hemocor 400® hemoconcentrator. Next, the MUF tubing exits the hemoconcentrator and is connected, via a lucred connection, to the cardioplegia set, ultimately terminating in the right atrium. A stopcock is connected to the lucred site so that flow can be

diverted to the venous reservoir for priming and to create a continuous circuit for intraoperative hemoconcentration. A DLP® vessel cannula with a one way valve is placed on the end of the cardioplegia line and, after flushing the system, the right atrium is cannulated via the venous cannula site (the venous cannula has been removed). (Fig. 4). This system is easy to set up, simple to de-air (via the bypass line which runs to the venous reservoir), is protected by a one way valve, and, since it utilizes a vacant twin pump, does not compromise circuit integrity by necessitating the removal of a pump sucker or cardioplegia tubing to attain flow. (Fig. 5)

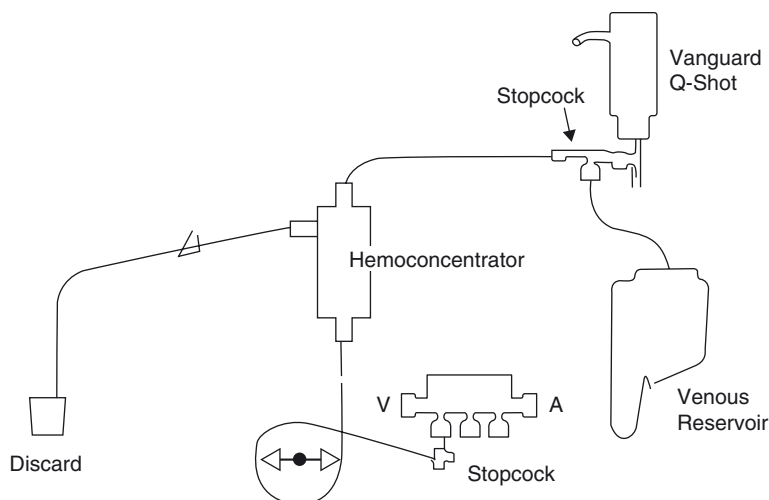
### PRIME SOLUTIONS

Priming of the bypass circuit is undertaken with a mixture of crystalloid and colloid solutions, as well as PRBCs (when needed) and additives. The crystalloid component is Plasmalyte® and the colloid is 25% albumin. When a child is less than 3kg, fresh frozen plasma can be included in the prime to avoid excessive fibrinogen and clotting factor dilution.

As a general rule, most patients less than 10kg require PRBCs in the prime. For neonates and infants, the target hematocrit for the procedure can usually be achieved by utilizing one unit of washed packed red blood cells with part of the unit given in the prime and the remainder transfused while on CPB. All PRBC units should be leukodepleted and, for children under 4 months old, they should also be irradiated and CMV negative. To ensure a physiologic potassium level in the prime, a cell saver is utilized to wash all donor blood with a balanced electrolyte solution.



**Fig. 4.** DLP® MUF cannula.



**Fig. 5.** MUF setup with Sorin Vanguard®.

Mannitol, sodium bicarbonate, heparin, and calcium chloride are also routine pump prime additives. (Table 7. Prime constituents)

### ***Pumps***

Both centrifugal and roller pumps have been used for pediatric CPB. The main advantages of using roller pumps for all neonatal and infant bypass procedures are lower prime when 1/4 in. and 3/16 in. tubing are used in the raceway and more accurate low-flow capabilities. However, the priming volume of centrifugal heads has decreased significantly in recent years, making them a viable alternative for larger patients. Centrifugal pumps have several potential advantages, including reduced priming volumes over 3/8 in. and 1/2 in. tubing, diminished damage to formed elements in the blood, and enhanced air removal (70). In addition, these pumps are capable of delivering pulsatile perfusion, which may improve microcirculatory flow (24).

### ***Cannulation***

The art of connecting the CPB circuit to the patients' circulation is governed by cannula selection and placement. The goal of cannulation is to use the lowest profile cannula with the best flow dynamics for the patient's calculated blood flow, combined with optimal placement for the prescribed corrective procedure. (Table 8. Cannulae flow) Pediatric bypass procedures are commonly associated with a variety of cannulation schemes. Table 9 gives a general cannulation site guideline,

Table 9  
Pediatric Cannulation

<i>Procedure</i>	<i>Venous Location/Type</i>	<i>Venous Location/Type</i>	<i>Arterial Location</i>	<i>Arterial Location</i>
ASD secundum	SVC/Rt ang	IVC/Rt ang	Asc Aorta	
ASD Sinus Venosus	SVC/Rt ang	IVC/Rt ang	Asc Aorta	
VSD	SVC/Rt ang	IVC/Rt ang	Asc Aorta	
Sub Aortic Stenosis	RA/Str		Asc Aorta	
Tetralogy of Fallot	SVC/Rt ang	IVC/Rt ang	Asc Aorta	
TAPVR	RA/Str		Asc Aorta	
Norwood	RA/Str		PDA	Neo aorta
Bidirectional Glenn	RA/Str	SVC/Rt ang	Asc Aorta	
Hemi-Fontan	RA/Str		Asc Aorta	
Fontan (lateral tunnel)	RA/Str or SVC/Rt ang	IVC/Rt ang	Asc aorta	
Fontan (extra cardiac)	RA/Str		Asc aorta	
Artrioventricular Septal Defect	SVC/Rt ang	IVC/Rt Ang	Asc aorta	
Ross Procedure	SVC/Rt ang	IVC/Rt Ang	Asc aorta	
Arterial Switch	RA/Str		Asc aorta	
MVR/AVR/TVR	SVC/Rt ang	IVC/Rt ang	Asc aorta	
Interrupted Aortic Arch	RA/Str		Pre interruption	Post interruption
Ebstein's Anomaly	SVC/Rt ang	IVC/Rt ang	Asc aorta	
Truncus Arteriosus	RA/St		Asc aorta	
RV-PA conduit	RA/St		Asc aorta	
Rastelli	SVC/Rt ang	IVC/Rt ang	Asc aorta	
AVR	RA/Str		Asc aorta	

RA, right atrium; SVC, superior vena cava; IVC, inferior vena cava; Rt ang, right angled; Str, straight.

however, consideration must be given to intercenter differences of bypass technique. For example, whether DHCA will be used for an arterial switch operation (a current trend in pediatric congenital heart surgery is toward the elimination of circulatory arrest) or whether certain procedures will be done off bypass (BDG, Fontan). Moreover, cardiopulmonary bypass may become unnecessary or relegated to a back-up roll for the repair of some congenital heart lesions due to the emergence of hybrid cardiology techniques. (Table 9. cannulation site summary) Vacuum assist has been used to augment venous return in the piglet model, mainly as a means to decrease priming volumes, although this technique is not widely used for neonatal surgery (100).

Cannulation for multiple reoperations can be challenging, especially when immediate bypass is necessary. For larger children, the femoral artery is a common cannulation site; however, in infants it is very difficult to cannulate the femoral artery, so the auxiliary and carotid arteries are possible alternative sites. Venous cannulation can also be achieved in the associated veins of the alternative arterial cannulation sites. It is a safe practice to establish both arterial and venous cannulation before attempting sternotomy when there is a high likelihood of injuring the heart or great arteries. However, it is also common to use the bypass suckers to provide venous drainage until an adequate venous cannula can be inserted into the heart.

## CONCLUSION

The use of CPB in congenital heart surgery requires specialized techniques and attention to the specific age-dependent physiologic differences of this diverse patient cohort. Considering the technical and physiologic complexity of conducting successful CPB for these patients, they should ideally be managed by perfusionists who specialize in a primarily congenital heart disease caseload. Delivery of the best possible care is likely to occur when children with congenital heart disease are treated at centers that see large numbers of these patients. Of further interest, approximately 80–85% of these children will survive to become adults with congenital heart disease. This distinct group of patients presents unique challenges to health care providers; therefore, they may be best managed within specialized adult congenital heart disease centers (101).

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