

Perioperative Management of a Child with Hypoplastic Left Heart Syndrome of the Jehovah's Witness Faith Presenting for Hybrid Comprehensive Stage II Procedure

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Abstract: Over the years, there has been a growing recognition of the potential negative sequelae of allogeneic blood products on postoperative outcomes following cardiac surgery. In addition, followers of the Jehovah's Witness (JW) faith have a religious restriction against receiving blood or blood components. Advances in perioperative care, cardiopulmonary bypass (CPB), and surgical technique have minimized the need for allogeneic blood products. Specific blood conservation strategies include maximizing the preoperative hematocrit and coagulation function as well as intraoperative strategies, such as acute normovolemic hemodilution and adjustments of the technique of

CPB. We report a 7-month-old patient whose parents were of the JW faith who underwent a comprehensive stage II procedure for hypoplastic left heart syndrome without exposure to blood or blood products during his hospital stay. Perioperative techniques for blood avoidance are discussed with emphasis on their application to infants undergoing surgery for congenital heart disease. **Keywords:** bloodless surgery, bloodless pediatric surgery, Jehovah's Witness, cardiac surgery, acute normovolemic hemodilution, retrograde autologous prime, venous antegrade prime, pediatric cardiac surgery. *J Extra Corpor Technol. 2016;48:141–147*

Hypoplastic left heart syndrome (HLHS) is a complex congenital heart condition, which includes abnormal development of left side cardiac structures, resulting in left ventricular outflow tract obstruction (1,2). Traditionally, HLHS and other obstructive lesions have been thought to result from low flow through the embryonic heart. However, a growing body of evidence has postulated a genetic component to HLHS. Recent investigations have linked multiple genetic loci to this disease, which accounts for approximately 1–3.8% of all congenital cardiac lesions (3,4). There are multiple surgical strategies available for the management of HLHS including the classical staged procedures of Norwood, Glenn, and Fontan; heart transplantation, and more recently, the hybrid approach which involves a hybrid stage I, comprehensive

stage II, and Fontan completion (5,6). The hybrid approach in managing children with HLHS has been pioneered and established as the preferred approach for treating these neonates and infants at our institution (Nationwide Children's Hospital, Columbus, OH). The first stage of the hybrid pathway includes bilateral pulmonary artery (PA) banding through a median sternotomy and a patent ductus arteriosus (PDA) stent. The stent is placed through a sheath inserted directly into the main PA with a multidisciplinary approach involving the surgeon and an interventional cardiologist in the hybrid operating room suite. The hybrid palliation avoids cardiopulmonary bypass (CPB) and virtually eliminates concerns regarding the need for allogeneic blood products. Prior to discharge, 1–2 weeks after the initial procedure, balloon atrial septostomy (BAS) is performed to ensure adequate mixing at the atrial level. At 4–6 months of age, the second stage, the comprehensive stage II, is performed. The comprehensive stage II includes removal of the bilateral PA bands, closure and removal of the PDA stent, reconstruction of the aortic arch, and the creation of a superior cavopulmonary anastomosis (Glenn procedure). At 2 years of age, the Fontan procedure is completed in the same manner as the Norwood pathway for HLHS.

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Followers of the Jehovah's Witness (JW) faith have a religious restriction against receiving blood or blood components, even in life-threatening emergencies. During the consent process, families are asked if albumin usage is acceptable; most families accept the usage of albumin as it is acellular and therefore, not considered a foreign blood product. Traditionally, the repair of complex congenital cardiac lesions in infants and young children either required or carried a high incidence for the transfusion of allogeneic blood products. Advances in perioperative care, CPB, blood avoidance techniques, and surgical techniques have minimized this need especially with the use of the hybrid technique as palliation during infancy. Evidence suggests that blood conservation techniques in pediatric cardiac surgery reduce the complication rate, minimize perioperative morbidity, mortality, and the overall financial burden (7–10).

Specific blood conservation strategies include maximizing the preoperative hematocrit and coagulation function as well as intraoperative strategies and techniques. The latter includes acute normovolemic hemodilution (ANH), retrograde autologous priming (RAP), venous antegrade priming (VAP), use of miniaturized CPB circuits, and manipulation of the coagulation cascade. As a referral center for patients of the JW faith, these strategies are routinely used to avoid the need for allogeneic blood products during surgery for congenital heart disease. We report a 7-month-old patient of the JW faith who underwent a comprehensive stage II procedure for HLHS without exposure to blood or blood products during his perioperative course. Perioperative blood avoidance techniques are discussed with emphasis on their application to infants undergoing surgery for congenital heart disease.

DESCRIPTION

Institutional review board approval is not required for publication of isolated case reports at Nationwide Children's Hospital. A 7-month-old, 8-kg male infant with parents of the JW faith presented for a comprehensive stage II surgical procedure. He was prenatally diagnosed with HLHS (mitral stenosis/aortic stenosis subtype). Surgical history included balloon aortic valvuloplasty (BAV) and hybrid stage I procedure on day of life 3. At 1 month of age, he underwent repeat BAV and a BAS for residual aortic stenosis and poor left ventricular growth. The hospital course following this cardiac catheterization was complicated by a stroke and seizures. After outpatient follow-up and monitoring by cardiology, he was considered to be a poor candidate for a two ventricle repair. Patient weight, height, and body surface area were 8 kg, 67 cm, and .367 m², respectively. Preoperatively, he received intramuscular injections of erythropoietin (Amgen Inc., Thousand Oaks, CA) (500 µ/kg) every day for a week,

5 mg/kg oral ferrous sulfate (Boca Pharmaceutical, LLC, Coral Springs, FL) two times a day for a week. He was also maintained on his baseline medication regimen of 10 µg/kg per day digoxin (DSM Pharmaceuticals, Inc., Research Triangle Park, NC) and 20 mg/kg (in two doses per day) levetiracetam (UCB, Inc., Smyrna, GA). On physical examination, he was in no acute distress. There was a grade III systolic ejection murmur heard at the left lower sternal border. His preoperative hematocrit and hemoglobin were 57% and 19.7 gm/dL, respectively. Coagulation studies, serum electrolytes, and blood glucose levels were all within normal limits. Preoperative transthoracic echocardiogram showed hypoplastic left ventricle with aortic and mitral stenosis, ostium secundum atrial septal defect, mild aortic insufficiency, trivial tricuspid and pulmonary insufficiency, PDA stent, and normal right ventricular function.

The patient was held nil per os for 6 hours for solids and 2 hours for clear liquids. He was transported to the operating room and standard American Society of Anesthesiologists' monitors were placed. ASA monitors include inspired oxygen monitoring, continuous electrocardiogram (ECG), pulse oximeter (finger probe), non-invasive blood pressure, continuous temperature (nasopharyngeal and rectal), and end-tidal carbon dioxide. After the inhalational induction of general anesthesia with sevoflurane in air and oxygen, two peripheral intravenous cannulas were placed, and endotracheal intubation was facilitated with rocuronium (1.2 mg/kg). The right radial artery was cannulated with a 22-gauge catheter under aseptic precautions using ultrasound guidance. Maintenance anesthesia included fentanyl (total dose of 10 µg/kg), a dexmedetomidine infusion at .2 µg/kg/h, and sevoflurane titrated to maintain hemodynamic stability. After establishing arterial access, ANH was initiated by removing 20 mL/kg blood, as per our institutional protocol with the administration of minimal crystalloid to avoid hemodilution (10–12). Using our previously described setup, the patient's blood was kept in a contact with him through continuous loop throughout the procedure at room temperature. Anticoagulation of the blood was achieved by the addition of 8 mL of anticoagulant citrate dextrose solution USP (ACD; Fenwal Inc, Lake Zurich, IL) to every 52 mL of whole blood. The blood was kept in the operating room at room temperature. Tranexamic acid (Pfizer Australia Pty Ltd, West Ryde, New South Wales, Australia) (100 mg/kg) was administered prior to incision, while on CPB, and after separation from CPB and reversal of heparin with protamine administration. The pre-CPB period was unremarkable and CPB was initiated after RAP and VAP. Patient stability was assessed during ANH, RAP, VAP, and through the procedure by monitoring arterial blood pressure, near-infrared spectroscopy (NIRS), and continuous electrocardiography (Figure 1). Changes in arterial blood pressure and

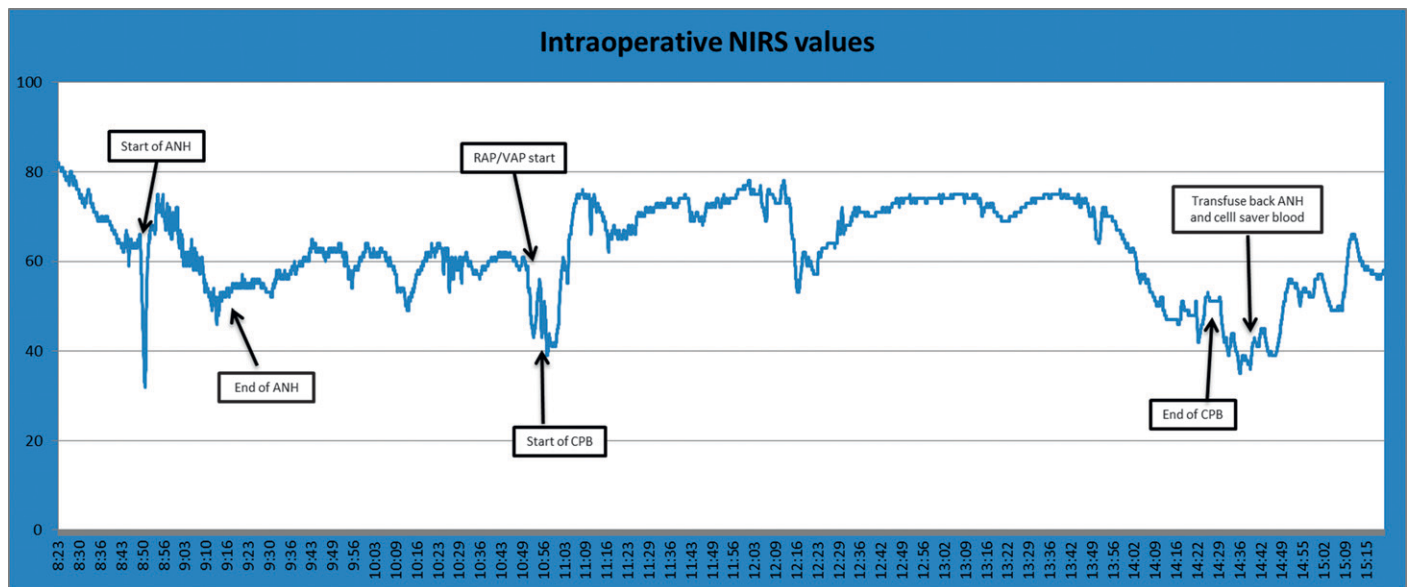


Figure 1. Cerebral oxygenation as measured by NIRS over the course of the case.

cerebral NIRS were treated by the administration of incremental doses of 1–2 $\mu\text{g}/\text{kg}$ phenylephrine or .2 $\mu\text{g}/\text{kg}$ epinephrine. The total volume of RAP and VAP was 150 mL, making the total crystalloid volume in the circuit prime only 75 mL. A low prime volume was achieved by using a CPB circuit with A Terumo FX0[®] oxygenator (Terumo Cardiovascular Systems Corporation, Ann Arbor, MI), 1/8-inch arterial line, 3/16-inch venous line, 3/16-inch arterial boot, and 3/16-inch suckers were used for the primary circuit. The CPB circuit was a modification of our typical neonatal circuit. The major alteration of the circuit was that the roller pump was angled to face the oxygenator allowing nearly 10 inches of our normal arterial boot to be removed, thereby decreasing prime volume by nearly 40 mL. In addition, a Minntech[®] Hemocor[®] HPH MINI hemofilter (Minntech, Minneapolis, MN) and a Sorin Cobe CSC-14 Custom 1:1 cardioplegia delivery system (Sorin Group USA Inc., Arvada, CO) were also used. A Maquet (Maquet, Hirrlingen, Germany) level sensor was placed at the manufacturer's suggested minimum operating level and a bubble detector was placed on the arterial line post oxygenator. A CDI 500 (Terumo Cardiovascular Systems Corporation) was used to monitor in-line blood gases during bypass and was calibrated to an iStat[®] blood gas analyzer (Abbott Point of Care, Inc, Princeton, NJ) The prime volume of all the circuit constituents was 140 mL. The circuit was primed with Normosol-R[™] (Hospira, Inc., Lake Forest, IL), 7 mEq sodium bicarbonate 8.4% (Hospira, Inc.), 1200 IU sodium heparin (Sagent Pharmaceuticals Schaumburg, IL), 7.2 mL mannitol 25% (Hospira, Inc.), and 50 mL albumin 25% (CSL Behring AG, Bern Switzerland). The target flow rate for this patient at our institution is a 2.2 L/min/m² cardiac index,

which equates to 100 mL/kg/min. During CPB, the patient was cooled to 24°C (flow rate was decreased to 1.8 L/min/m² during hypothermia) and selective cerebral perfusion was achieved through carotid artery cannulation. Our standard protocol for heparin administration and reversal is based on HDR using heparin management system (HMS) (Medtronic Inc, Minneapolis, MN). In an effort to minimize blood draw, we empirically dosed heparin at 400 units/kg prior to initiating CPB. We only run activated clotting times (ACTs) on the HMS machine during bypass to reduce the amount of blood loss. Total CPB time was 217 minutes with a selective cerebral perfusion time of 77 minutes. The procedure was performed under a beating heart condition with the coronary blood flow being maintained through a side port from the aortic cannula into the ascending aorta proximal to the cross clamp. This technique was accomplished through the leuc port off the arterial cannula through a 1/8-inch line attached to a 2-mm olive tip cardioplegia catheter (Medtronic Inc.). During cooling, the patient had one episode of ventricular fibrillation which was successfully treated by internal paddle defibrillation. During rewarming, the flow rate was increased back to full flow (2.2 L/min/m²). At the conclusion of CPB, a 25 $\mu\text{g}/\text{kg}$ bolus of milrinone was administered during rewarming, followed by an infusion at .25 $\mu\text{g}/\text{kg}/\text{min}$. The surgeon placed two right atrial lines for monitoring and infusion of medications. The total intraoperative time was 506 minutes. After successful separation from CPB, modified ultrafiltration (MUF) was performed for 10 minutes, with a target blood flow rate of 5 mL/kg/min. Total ultrafiltrate volume removed during MUF was 250 mL. Residual heparin effect was empirically reversed with protamine (5 mg/kg). Following this, 140 mL (20 mL/kg) of

ANH blood was transfused back to the patient and recombinant factor VIIa (90 µg/kg) was administered. In addition, a total of 105 mL of cell saver blood was transfused. After ensuring adequate hemostasis and stability, the chest was closed. At the completion of the surgical procedure, residual neuromuscular blockade was reversed and the patient's trachea was extubated prior to departure from the operating room. The lowest hematocrit on CPB was 24% and the final hematocrit at the end of the procedure was 39%. The highest lactate during the case was 2.8 mmol/L. The total urine output during the case was 219 mL. The patient was transported to the cardiothoracic intensive care unit (CTICU) with a nasal cannula at 2 L/min with standard ASA monitoring. Postoperative pain management was achieved with acetaminophen (Johnson & Johnson Consumer Inc., New Brunswick, NJ) (12.5 mg/kg) intravenously every 6 hours and nurse controlled analgesia of fentanyl at .5 µg/kg basal dose and .5 µg/kg every 12 minutes (13). No blood or blood products were transfused intraoperatively or postoperatively. The postoperative course was unremarkable and the patient was transferred to the inpatient ward on the third postoperative day and discharged home on postoperative day 14.

COMMENT

When attempting to establish a blood conservation strategy, there are many questions that need to be answered and standards that need to be met to guarantee the safety of patients and the ability to consistently reproduce the results. As a referral center for patients of the JW faith, we have tailored many of these approaches to limit the need for allogeneic blood products for these patients. These techniques can also be applied more broadly to all patients presenting for surgery for congenital heart disease. Factors that impact the need for allogeneic blood products may involve the preoperative, intraoperative, and postoperative period (Table 1).

Preoperatively, maximizing hematocrit and ensuring adequate coagulation profile are important especially in patients with cyanotic congenital heart disease who may have baseline coagulation dysfunction (14). Identification and treatment of anemia are simple components of perioperative blood avoidance. Simple maneuvers such as the treatment of iron-deficiency anemia may result in significant increases in the hematocrit prior to surgical intervention (15). Augmentation with erythropoietin may be used to increase the hematocrit to supranormal values and thereby prepare the patient for intraoperative phlebotomy to provide autologous blood for later transfusion (14,15). The latter may be particularly beneficial in patients of the JW faith as they will generally accept ANH provide the blood remains in contact with their

Table 1. Potential perioperative blood avoidance techniques.

Preoperative
Preoperative hematocrit with treatment of anemia with iron ± erythropoietin
Correction of abnormal coagulation function
Intraoperative
Anesthetic management to inhibit physiologic stress response
Preoperative phlebotomy (ANH)
RAP
VAP
ZBUF
MUF
Anticoagulation management and heparin dosing
Pharmacologic modification of coagulation cascade (tranexamic acid)
Heparin reversal with protamine
Recombinant factor VIIa
Postoperative
Limitation of postoperative phlebotomy
Team approach to postoperative hemoglobin management

body through tubing or other devices. It also offers a cost effective alternative to preoperative autologous donation which may be problematic in small children with limited venous access.

Our intraoperative protocol can be divided into three phases. The first phase, pre-CPB period, starts with the induction of anesthesia and ends with the commencement of CPB. Goals during the pre-CPB period are to minimize the physiological stress of the induction of general anesthesia, endotracheal intubation, and placement of invasive vascular catheters (arterial and central venous access). Intravenous fluid administration is tightly controlled during this phase to avoid hemodilution which may result in a lower than needed hematocrit prior to the initiation of CPB which results in a secondary hemodilution. Infusion pumps are used to deliver a set quantity of crystalloid in an attempt to avoid over expansion of the blood volume and dilution of the hematocrit. Based on the predicted hematocrit on CPB, ANH is used during this time to provide fresh, whole blood for reinfusion after CPB. During ANH, 10–20 mL/kg for children weighing less than 5 kg or 10–20% of the blood volume for patients weighing more than 5 kg is slowly removed via the arterial line. As opposed to surgeries which do not use CPB in which the removed blood is replaced in a 3:1 ratio of crystalloid to blood, during this time, fluid replacement is limited based on physiological parameters.

Table 2. Perioperative trend of hematocrit and lactate levels.

	Hematocrit (%)	Lactate (mmol/L)
Baseline	57	1.2
Post-ANH	58	1.3
Last on CPB	24	2.2
Post-MUF	33	1.8
24 hours postoperative	44	.8

Although referred to as ANH, the technique is primarily preoperative phlebotomy and fluid is administered only as needed to maintain heart rate, blood pressure, and cerebral NIRS. During this time, incremental doses of phenylephrine and epinephrine may be used instead of fluid. If excessive fluid is administered, the secondary hemodilution that occurs during CPB may result in an excessively low hematocrit and the need to use allogeneic blood products. Hematocrit has been reported to be an important factor influencing neurocognitive outcomes in neonates and infants undergoing cardiac surgery (16–20). Although the lowest hematocrit has been debated as a possible culprit for worsening of long-term developmental and neuropsychological outcome, the evidence available to guide clinicians on the minimum safe hematocrit during CPB is not universally agreed upon (8–10,21). Additionally, it may be that hematocrit has limited impact as there is growing evidence that the most influential factors influencing outcome are preoperative, genetic, and socioeconomic factors (Table 2).

A continuous looped IV circuit can be used to eliminate waste of blood during phlebotomy for laboratory samples and to keep the ANH blood in continuous contact with the patient to remain in accordance with the patient's religious beliefs (10,11). In the event that the patient is not tolerating the ANH process and is not responding to interventions, ANH is aborted and CPB initiated. The ANH blood provides replacement of not only packed red blood cells, but also platelets and coagulation factors that facilitate correction of the coagulopathy after CPB. The blood should be kept at room temperature to maintain normal platelet function. In our patient, a total of 140 mL (20 mL/kg) was removed during the ANH process with an only transient drop in cerebral NIRS of approximately 20% from pre-ANH level which returned back to baseline with incremental doses of phenylephrine and epinephrine (Figure 1).

Another important technique that can be used to minimize hemodilution during CPB is the process of RAP and VAP. After placement of the aortic and venous canulas and prior to initiation of CPB, crystalloid in the arterial limb is pushed out as blood is allowed to fill the arterial cannula (RAP). Blood is then allowed to flow into the venous limb and displace the crystalloid in the CPB circuit (VAP). This process may also result in hemodynamic instability and it may be necessary to support physiologic parameters with incremental doses of epinephrine and phenylephrine, guided by arterial blood pressure, ECG, and cerebral NIRS changes. If the patient does not tolerate the process, RAP and VAP are aborted and CPB initiated. In our patient, the RAP and VAP process resulted in the removal of 150 mL with only a transient decrease in the cerebral NIRS that returned to baseline with the initiation of CPB as noted in the figure.

The second phase, CPB period, includes the time from the start of CPB to the end of CPB. The use of miniaturized circuits is a major factor that minimizes the prime volume of the circuit, limits hemodilution, and decreases the need for allogeneic blood products. This is accomplished by not only decreasing the length of the tubing by moving the perfusionist closer to the surgical site, but also decreasing the diameter of the tubing. These modifications also serve to minimize exposure of the blood to a larger surface area of tubing which may help decrease the inflammatory response and thereby improve the post-CPB coagulation profile and decrease bleeding (22). During CPB, zero-balance ultrafiltration (ZBUF) is used to remove excess crystalloid and water from the CPB circuit and the patient during CPB. This process also helps by continually filtering free fluid and inflammatory mediators from the patient. ZBUF removes inflammatory mediators that are generated during CPB, decrease total body water, lung water, and improves postoperative physiological parameters including the coagulation profile (22–24). ZBUF was initiated immediately after administration of the first dose of cardioplegia and maintained at approximately 80 mL/min throughout the case. Normosol-R™ (Hospira, Inc.) was used as our ZBUF solution and was buffered with 20 mEq/L sodium bicarbonate and 200 mg/L calcium chloride was also added to prevent hypocalcemia.

Another factor that affects the perioperative need for allogeneic blood and blood products is the management of anticoagulation during CPB. In common clinical practice, heparin is dosed based on changes in the ACT. However, recent data suggest that strategies may result in inadequate heparin dosing with ongoing thrombin formation, enhanced activation of the inflammatory cascade, and increased perioperative bleeding (25,26). A heparin concentration-based management protocol has been shown to more effectively provide anticoagulation and limit ongoing thrombin formation (25,26). These issues may be particularly relevant in neonates and infants (27). In addition to heparin management strategies, the use of anti-fibrinolytic agents has been shown to improve coagulation function and decrease perioperative bleeding (28). In our patient, our standard dosing regimen for tranexamic acid was used to inhibit fibrinolysis and augment coagulation function.

Finally, the third phase, the post-CPB period, starts after separation from CPB and lasts until the end of surgery and transport to the CTICU. Immediately following the termination of CPB, MUF is used to further remove free water and inflammatory mediators. The process also results in hemoconcentration of the CPB circuit and ultimately an increase in the hematocrit. During MUF, the patient's blood is circulated from the aorta, retrograde down the arterial cannula into the CPB circuit through a filter that allows additional removal of free water. The concentrated blood is then returned back to the patient,

into the right atrium. After MUF is completed, heparin activity is reversed with protamine, and the ANH blood is transfused back to the patient.

Recombinant factor VIIa usage in pediatric cardiac surgery may reduce intraoperative bleeding, decrease postoperative chest tube drainage, and potentially decrease the re-operation rate (29). For JW patients, our protocol is to administer an intraoperative dose of 90 µg/kg immediately after administering the ANH blood. Given its cost, the lack of prospective, randomized trials demonstrating its efficacy, and the potential for a pro-thrombotic effect, the routine use of recombinant factor VIIa in patients having surgery for congenital heart disease is not advocated (30). The consent form for this patient population includes the possibility for the administration of recombinant factor VIIa and families are made aware of the potential risks of this clinical practice. We believe the anecdotal data support the use of recombinant factor VIIa when other products cannot be used; however, there is no evidence-based medicine to support its use.

DDAVP is a manufactured analogue of the hormone, vasopressin. It improves platelet aggregation by augmenting the release of von Willebrand factor (vWF) from endothelial cells. It may effectively augment platelet/coagulation function in patients with uremia, those on antiplatelet agents and GP IIa/IIIb inhibitors presenting for emergency cardiac surgery, and those who are genetically deficient in the quality or quantity of vWF or factor VIII. Although we do not routinely administer postoperative, our protocol includes its use in JW patients who have ongoing bleeding in the CTICU following cardiac surgery.

During the postoperative period, simple maneuvers to limit perioperative blood loss and the need for allogeneic transfusions include limiting postoperative phlebotomy and a protocolized approach regarding postoperative transfusion thresholds. Although time-honored thresholds of ≥ 8 gm/dL have been suggested, there is limited evidence-based medicine on which to determine an absolute transfusion threshold. Recent evidence suggests that patients with HLHS do not necessarily benefit from higher hematocrit values (31). More importantly physiologic parameters should be evaluated and end-organ oxygen delivery assessed using serum lactate levels. In many cases, hemoglobin values down to 6–7 gm/dL are well tolerated (32,33). Our institution uses a policy for obtaining a court order to allow for transfusion of a child in the event of life threatening anemia.

Our case illustrates the potential of the possibility of safely performing surgery with CPB for an infant with complex congenital heart disease without the use of allogeneic blood or blood products. As patient advocates, we should strike a balance between respect for the beliefs of the JW parents and the safety and well-being of our

patients. Achieving this goal requires proper planning and a multidisciplinary team approach that starts in the preoperative period and continues through discharge from the hospital. As summarized in Table 1, various techniques and interventions can be used in the preoperative, intraoperative, and postoperative period to limit the need for blood and blood products.

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