

Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass

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INTRODUCTION

The technology to provide artificial oxygenation of the blood to supplement or entirely take over the gas exchange functions of the lungs was conceived and developed in animals in the 1930s and 1940s, first used in humans in the 1950s, and has been available for clinical use since the 1960s. When coupled with a blood pump to support cardiac output, this technology has two major medical applications: cardiopulmonary bypass (CPB) and extracorporeal membrane oxygenation (ECMO). CPB is fundamentally a technique in anesthesiology to take over blood circulation and oxygenation so that surgery can be performed on a nonbeating, bloodless heart and great vessels. In pediatrics, CPB is required to perform surgical repairs of a wide range of congenital heart disease, malformations of the great vessels, transplantation of thoracic organs, and other thoracic surgery. On the other hand, ECMO is an aggressive supportive care intervention used in the intensive care unit to support critically ill patients when conventional ventilatory support, circulatory support, or both have failed. In pediatrics, ECMO has applications in the neonatal intensive care unit for newborns with severe lung disease, in the cardiac intensive care unit for patients with severe heart failure, including complications after cardiothoracic surgery, and in the general pediatric intensive care unit for other causes of very severe circulatory or pulmonary failure.

Since both techniques involve large extracorporeal circulatory volumes in critically ill patients, CPB and ECMO programs depend heavily on support from the

blood bank to provide blood products both at the time the extracorporeal circuits are first established, through the duration of the “run,” and during the recovery period. This chapter will first review the basic layout of CPB and ECMO circuits. Then, because CPB and ECMO are used in different clinical situations, it will review the uses and outcomes of the two techniques separately. Their impact on the blood bank will be discussed at the end of each section.

CIRCUIT FOR ECMO AND CPB

The fundamental elements of the extracorporeal circuit for CPB or ECMO are cannulae, the pump, a blood reservoir, the oxygenator, and a heat exchanger. There are many additional components that provide for safety and monitoring. The cannulae are the connections of the patient’s circulation to the extracorporeal circulation, drawing deoxygenated blood from the patient’s venous circulation and returning oxygenated blood to either the arterial or venous side of the patient’s circulation. The pump drives the blood through the components of the extracorporeal circuit, and if the blood return is to the arterial side of the circulation, the pump also delivers systemic arterial blood flow to supplement or replace the cardiac output. The oxygenator provides a large surface area over which gas exchange between the blood and an exogenous mixture of oxygen, air, carbon dioxide, and possibly anesthetic agents can occur. The heat exchanger permits manipulation of the temperature of the blood returned to the patient.

Cannulae

Access to the patient's circulation for CPB or ECMO must be large enough to support blood flow equivalent to the patient's entire cardiac output, as much as 5 L/min in an adult. A cannula is placed in a jugular or femoral vein by direct surgical cut down or within the superior vena cava or right atrium when placed for CPB during cardiothoracic surgery. To return oxygenated blood, the common carotid is used most commonly for arterial access for veno-arterial (VA) ECMO and an aortic cannula is placed at surgery most commonly for CPB. ECMO support can be delivered entirely through venous access (veno-venous [VV] ECMO is described further), in which case the return cannula may be in the femoral vein, the contralateral jugular vein, or in the second lumen of a double lumen venous cannula (Foley 2000). In many cases, the jugular vein and carotid arteries used for ECMO access are sacrificed (ligated) when ECMO support is discontinued.

Pump

A roller pump is most commonly used to move blood through the extracorporeal circuit and to provide arterial pressure for the patient. An alternate technology is a centrifugal pump. The roller pump consists of a disk that rotates within a semicircular raceway and moves rollers, which compress the flexible tubing against the inside wall of the raceway, propelling the blood forward. The adjustable rate of rotation of the pump determines the flow rate of blood through the pump and ultimately the amount of arterial flow contributed by the circuit. This flow is not pulsatile. The pump must have a mechanism to detect elevated pressure related to occlusion anywhere in the return side of the circuit downstream of the pump and to reduce or stop flow before the elevated pressure leads to a catastrophic disconnection in the circuit.

Blood Reservoir

Blood is drawn through the venous cannula into the extracorporeal circuit by gravity, entering a collection reservoir located well below the level of the access cannula. The reservoir provides a volume of blood that acts as a buffer to allow for discrepancies between the rate of blood coming from the patient and the pump rate. The reservoir must be equipped with a sensor to detect emptying. This sensor is part of a servo control mechanism that will slow or stop the pump to ensure that the pump flow rate does not exceed the rate at which blood comes from the patient. This helps prevent introduction of air in the circuit by cavitation and air embolism in the patient.

In an ECMO circuit, this reservoir is small, typically 30 mL, while in a CPB circuit the reservoir is larger with a capacity of a liter or more of blood. The reservoir in the CPB circuit serves other functions, including collection of the large volume of blood that is in the heart and vessels after CPB flow is established and salvaging blood removed from the surgical field by suction. The large blood reservoir provides a margin of safety (10 to 15 seconds of blood flow) in case the return side of the CPB circuit should leak or become dislodged. However, returning the red cells in the large volume of blood from the reservoir to the patient at the end of the CPB run presents a problem, as will be discussed.

Oxygenator

The oxygenator is the central component of the CPB or ECMO circuit since it performs the function of the lungs, which is to saturate the hemoglobin of the venous blood with oxygen. The oxygenator provides a large surface area for an interface between blood and the gas phase, either with hollow fibers or a folded silicone membrane. An oxygen rich gas mixture is passed through the oxygenator in the direction opposite to blood flow, establishing a countercurrent that promotes diffusion of oxygen into the blood. The total surface area, and therefore the capacity of the oxygenator, is selected based on the size of the patient and the blood flow that must be fully oxygenated. Exposure of blood to this large artificial surface is also thought to be responsible for many of the coagulation and inflammatory abnormalities associated with ECMO and CPB.

Heat Exchanger

Since flow rates equivalent to the entire cardiac output are involved, the infusion of blood at a temperature below normal body temperature would rapidly result in hypothermia. Thus, a heat exchanger is a necessary component of an ECMO circuit to ensure that the temperature of the blood returning to the patient is at 37°C. In some cardiothoracic surgery, controlled hypothermia is used to reduce the metabolic demands of the brain and other organs, especially if a period of circulatory arrest is planned. The heat exchanger can be used to cool the body temperature and, at the end of the procedure, to restore it to normal.

Extracorporeal Volume and Priming

The components of the ECMO or CPB circuit and the filters and tubing that connect them combine to form a large extracorporeal volume. The extracorporeal volume of the smallest circuit is 400 to 500 mL, about

twice the blood volume of a neonate for whom it could be used. For larger patients, the extracorporeal volume of the circuit may be larger, principally because a larger oxygenator is required. However, the ratio of circuit volume to patient blood volume is greatest for neonates and generally decreases with larger patients.

The large extracorporeal volume of ECMO or CPB circuits means that, for many pediatric patients, these circuits must be primed with red cells before they are connected to the patient. A “bloodless” prime may be used if the patient is large enough and the hemoglobin high enough to tolerate a dilution effect. The red cells are typically combined with a buffer solution and may also be combined with 5% albumin solution or fresh frozen plasma (FFP), and the pH and electrolyte concentrations of the circuit prime are checked before initiation of support. In some situations, whole blood may be used as the priming fluid. Several considerations go into the decision for how the extracorporeal circuit will be primed, as listed in Table 17.1. These considerations are among the major determinants of how blood bank support for the ECMO or CPB program will be organized.

Anticoagulation

Because of the large area of artificial surface in contact with the blood in the oxygenator, patients on ECMO and CPB circuits experience activation of coagulation factors and platelets, and therefore must receive aggressive anticoagulation. This is usually accomplished using infusions of unfractionated heparin with dose adjustments based on whole blood activated clotting time (ACT) measurements. The typical target value for the ACT is 180 to 200 seconds for a patient on ECMO support, and >500 seconds for a patient on CPB. The typical protocol calls for hourly monitoring using a “point of care” instrument, at the bedside or in the operating room. Since the ACT is a less sensitive assay than the activated partial thromboplastin time (aPTT), the doses of heparin and level of anticoagulation for ECMO and CPB are typically higher than for medical

TABLE 17.1 Physiological and Medical Considerations in Priming of ECMO and CPB Circuits

Level of urgency
Ratio of patient blood volume to circuit volume
“Cardiac stun”—related to pH, potassium, calcium, electrolytes
Desired hematocrit—degree of hemodilution
Pre-existing coagulopathy
Renal function
Number of blood donor exposures

anticoagulation therapy. For this reason, patients on ECMO support are at risk for hemorrhagic complications (ELSO Registry 1995). At the end of a surgical procedure using CPB, the heparinization is reversed using protamine, in order to promote postoperative hemostasis.

ECMO

Indications

ECMO is a complex, risky, and expensive life-support measure that is usually reserved for patients whose underlying disease process is associated with a mortality of >80%, which has not responded to conventional ventilatory support and medical therapies, but that is still potentially reversible (Bartlett et al. 2000). Among term neonates, respiratory failure due to severe meconium aspiration syndrome or persistent pulmonary hypertension and among premature infants, severe respiratory distress syndrome are the most common indications for initiation of ECMO support (Table 17.2). In the ELSO database, these three indications accounted for 60% of reported ECMO for neonates (ELSO Registry 1995; Shanley et al. 1994). ECMO support limits the barotrauma associated with aggressive conventional or high frequency ventilation and provides a period of “lung rest” during which inflammatory processes in the lung may subside. Respiratory failure from lung hypoplasia with congenital diaphragmatic hernia (CDH) accounts for another 20% of ECMO utilization in neonates, but it is less clear that “lung rest” provided by ECMO has a net beneficial effect on the outcome of CDH.

TABLE 17.2 Indications for ECMO support

Neonatal	Pediatric
Meconium aspiration	Bacterial pneumonia
Respiratory distress syndrome	Viral pneumonia
Persistent pulmonary hypertension	Acute respiratory distress syndrome (ARDS)
Congenital diaphragmatic hernia	Burns
Sepsis	Inhalation injuries
	Near drowning
	Sepsis
	Myocarditis—bridge to transplantation
	Failure to wean from CPB after surgery
	Arrest or heart failure after cardiac surgery

The decision to place a patient on ECMO support is a complex medical and ethical judgment. The ELSO guidelines for neonatal ECMO listed in Table 17.3 demonstrate that the patient must be both ill enough to warrant the risks of ECMO, including heparinization, and also free of irreversible complications and lethal disease processes so that the potential benefit of ECMO may be realized. There are calculated indices of severity of lung disease (Kim and Stolar 2000), which can be used to predict mortality and eligibility for ECMO support. The criterion that places a limit on the duration of conventional ventilation is intended to exclude patients who have already been exposed to prolonged barotrauma and have already developed bronchopulmonary dysplasia.

Beyond the neonatal period, in the pediatric intensive care unit, the indications for ECMO are more varied and include respiratory failure associated with sepsis, pneumonia, acute respiratory distress syndrome (ARDS) or systemic inflammatory response syndrome (SIRS), burns, inhalation injury, drowning, complications of bone marrow transplantation, and complications of cardiothoracic surgery, as listed in Table 17.2 (Bartlett et al. 2000; Montgomery et al. 2000; Green et al. 1996). Overall survival to hospital discharge is dependent on the initial diagnosis (ELSO Registry 1995) and is better if respiratory failure is not complicated by multiorgan system failure or infection or a protracted period of conventional ventilation (Masiakos et al. 1999). In cardiothoracic surgery, survival from post-operative ECMO is also better if the course is not prolonged and not complicated by infection (Montgomery et al. 2000; Aharon et al. 2001). ECMO support has been successfully used in patients with sickle cell disease with severe acute chest syndrome (Trant et al. 1996; Pelidis et al. 1997).

Veno-arterial Versus Venovenous ECMO

When the primary indication for ECMO support is respiratory failure and the patient's cardiovascular function is preserved, it may be preferable to use VV

ECMO support rather than VA ECMO. The VV ECMO circuit returns oxygenated blood to the venous circulation rather than the arterial side and relies on the heart to provide all systemic arterial blood flow. This strategy has the advantages of not sacrificing a carotid artery; avoiding the risk of arterial embolization, of air or particulates; providing better perfusion to the lungs and coronary arteries; and providing pulsatile blood flow from the heart, which improves renal function. Since VV ECMO relies on the native cardiac function, there is no ready mechanism to compensate for loss of cardiac function by "turning up" the level of support from the ECMO circuit pump. This feature of VV ECMO is especially critical for the startup phase if there is an acute reduction of cardiac output related to pH or electrolyte abnormalities in the priming fluid, a phenomenon referred to as "cardiac stun."

VA ECMO is required when both pulmonary and cardiac function must be supported by the ECMO circuit. This applies when the underlying indication for ECMO support is primary heart disease or when cardiovascular failure is a prominent feature of the disease process, as in septic shock.

Course and Outcomes

Once initiated, a course of ECMO support can be continued for days to weeks although the chance of survival from prolonged courses is diminished (Masiakos et al. 1999). ECMO support is weaned by incremental reduction of the pump flow rate while monitoring oxygenation, acidosis, and lung compliance (Kim and Stolar 2000; Hirschl 2002). Survival rates for patients on ECMO vary from 40% for adults to 80% for neonates (ELSO Registry 1995). The survival rates for neonatal ECMO for meconium aspiration syndrome (MAS), respiratory distress syndrome (RDS), persistent pulmonary hypertension (PPH) are in the range of 83% to 94%. For CDH, there was no difference in survival rates before and after ECMO support became available in one institution (Keshen et al. 1997) and no difference in survival in a study that compared two institutions caring for CDH patients, one with ECMO and one without. The overall survival rates of 53% with no ECMO support and 44% survival with ECMO (Wilson et al. 1997; Azarow et al. 1997) are similar to the 58% survival rate noted in the ELSO registry for infants with CDH. In older children, one study demonstrated a mortality of 28.6% in pediatric intensive care unit patients with a predicted mortality of 50% to 75% when supported with ECMO as compared to 71.4% in similarly high-risk patients who were not treated with ECMO (Green et al. 1996).

TABLE 17.3 ELSO Guidelines for Neonatal ECMO (1997)

Gestational age ≥ 34 weeks and birth weight ≥ 2000 g
No significant coagulopathy or bleeding complications
No major intracranial hemorrhage
Mechanical ventilation less than 10–14 days and reversible lung disease
No uncorrectable cardiac lesions
No lethal congenital anomalies
No evidence of irreversible brain damage

Blood Bank Support for ECMO Programs

The blood bank plays two roles in supporting the needs of ECMO patients: providing blood products for the initiation of ECMO support and providing blood products for the ongoing needs of a patient on ECMO. As discussed previously, the initiation of ECMO support for a pediatric patient usually requires red blood cells (RBCs) for priming the circuit and often plasma. Patients on ECMO support also have ongoing consumption of coagulation factors and plasma and may have ongoing bleeding and thus require frequent transfusions of FFP, cryoprecipitate, platelets, and booster transfusions of packed red blood cells (PRBCs).

Blood Products for Priming

Under ideal circumstances, the typical ECMO priming protocol would use one to two units of ABO and Rh group-specific and crossmatch-compatible PRBCs, depending on the extracorporeal volume (ECV) of the ECMO circuit, and possibly one unit of group-specific FFP. PRBCs should also be negative for sickle hemoglobin, since the red cells may be exposed to hypoxia and severely abnormal metabolic conditions. Since the ECV of an ECMO circuit is often a significant fraction of the total blood volume of the pediatric patient, the red cells used for the prime would ideally conform to guidelines for massive transfusion, including avoidance of PRBC units in additive solutions and use of relatively fresh red cells (Luban et al. 1991). Additional considerations include provision of cytomegalovirus (CMV)—safe blood products for low birth weight neonates and for thoracic organ transplant candidates who will be immunosuppressed.

In practical application, the single most important determinant in providing blood product support for ECMO is the level of urgency or the amount of time available for preparation. Extreme urgency may require compromise of the ideal blood product preparation as previously described. Examples of clinical scenarios for which ECMO circuits might be started are shown in Table 17.4. Provisions for the most extreme degrees of urgency require storage of group O, Rh(D)-negative PRBCs in a monitored refrigerator in the intensive care unit. These units may be somewhat older than ideal and will be transfused uncrossmatched. For a neonate transferred to a tertiary care center for consideration of ECMO support, there may be several hours of forewarning before the arrival of the patient, permitting time to find fresher PRBCs. However, the ABO/Rh blood group of the patient may not be established, and the PRBCs may not be crossmatched before the circuit is initiated. For the least urgent scenario in which a patient is electively transferred to ECMO support, preparation of the ideal blood product may be possible.

Blood Products for Coagulopathy and Ongoing Needs

The coagulation complications of ECMO are significant: since the patient is heparinized, a prolongation of the aPTT and a tendency to bleeding are expected complications of ECMO support. The Extracorporeal Life Support Organization (ELSO) registry gives an incidence of 15% intracranial hemorrhage and 7% other bleeding for neonates on ECMO (ELSO Registry 1995). Patients on ECMO circuits who also have chest tubes or recent surgery may have significant ongoing blood loss from those sites. Despite this aggressive

TABLE 17.4 Examples of Blood Product Protocols for ECMO Startup

Clinical Scenario	Urgency	Products	Blood Group	Storage*	Crossmatch
Cardiac arrest in cardiac ICU	5–10 minutes	2 units PRBCs	O-neg PRBCs	Additive solution, stored in ICU, <14 days	Retrospective
Disruption of ECMO circuit	5–10 minutes	2 units PRBCs	O-neg PRBCs	Additive solution, stored in ICU, <14 days	Retrospective
Progressive septic shock, not neonatal	30 minutes	2 units PRBCs	O-neg PRBCs	<10 days old, any preservative	Immediate spin
Neonate transferred for ECMO	1–2 hours	2 units PRBCs 1 unit FFP	O-neg PRBCs AB plasma and platelets	<10 days, CPD or CPDA	Retrospective
Cardiac ICU	30–60 minutes	2 units PRBCs	Type specific	<7 days old, additive solution	Immediate spin or full
Gradual respiratory or cardiac failure on conventional support	Hours to days	2 units PRBCs	Type specific	<10 days, CPD or CPDA for neonate, otherwise any	Full

*Based on the protocols of The Children's Hospital of Philadelphia.

anticoagulation, there is activation and consumption of platelets and procoagulant factors related to exposure of blood to artificial surfaces. Clotting within the ECMO circuit occurs frequently, with an incidence of 25% of ECMO circuits for neonates. Fibrin deposition within the oxygenator and other parts of the circuit may reduce its efficiency for gas exchange and may obstruct flow. During prolonged ECMO "runs," fibrin may accumulate within an ECMO circuit to a level that requires transferring the patient to a new, freshly primed circuit. The rate at which fibrin accumulates may be influenced by the materials used in the circuit (Grossi 2000) as well as the patient's underlying disease process.

Surveys of blood product utilization for pediatric patients on ECMO support generally report more frequent transfusion of platelet concentrates than plasma or PRBCs and also a wide range of transfusion requirements for individual patients. The number of transfusions will vary significantly with the transfusion trigger employed in the ECMO support protocol (Minifee et al. 1990). For example, the transfusion trigger for platelets for patients on ECMO is reported from 50,000 to 110,000/ μ L (Minifee et al. 1990; Chevuru et al. 2002). One survey of 91 neonates on ECMO support for a mean of 4.6 days found that these patients received 0.6 to 1.0 red cell transfusions, 0.1 to 0.3 FFP transfusions, and 1.8 platelet transfusions per day on ECMO (McCoy-Pardington et al. 1990). However, the range of numbers of transfusions per ECMO patient was wide: 0 to 17 transfusions for red cells, 0 to 8 for FFP, and 1 to 32 for platelets. Another survey reported a mean of 1.3 platelet transfusions per day on ECMO, with variation related to institution and ECMO technique (VV versus VA) (Chevuru et al. 2002). Sepsis while on ECMO clearly increases the platelet requirements (Chevuru et al. 2002; Zavadil et al. 1998). For comparison, mean daily blood product requirements for adults on ECMO were 4.6 units of red cells, 0.5 units of FFP, 15 units of random donor platelet concentrates, and 1.0 units of cryoprecipitate (Butch et al. 1996). The numbers of blood products required for an ECMO program for adults are predictably greater than for pediatric patients.

Although not described in these surveys, cryoprecipitate is commonly used to supplement the fibrinogen level in pediatric patients on ECMO circuits, with a transfusion trigger to maintain the fibrinogen above 100 mg/dL.

CPB

CPB is used to facilitate heart surgery by supporting the systemic blood flow and oxygenation artificially,

permitting the heart to be asystolic and drained of blood. In pediatric cardiothoracic surgery, CPB is necessary for surgical correction of congenital heart disease that requires opening the ventricles or great vessels. This includes lesions of low complexity such as atrial septal defect and ventricular septal defect, as well as more complex lesions such as tetralogy of Fallot, transposition of the great vessels, single ventricles, hypoplastic left heart syndrome, and cardiac or pulmonary transplantation. The patient population varies widely in age, physiology, and complexity and includes cyanotic newborns undergoing arterial switch procedures and stage 1 Norwood procedures to school-age children undergoing elective repairs. In some centers, the patient population may also include young adults who have developed late complications of cardiac operations in childhood and adults with symptoms related to long-standing unrepaired congenital heart disease. In some cases, cardiac malformations are corrected in stages, with a palliative procedure first and a definitive correction later. In addition, there are patients who require surgical revision of previous repairs because of incompetent valves or vascular stenosis. Patients in the latter two categories will undergo second or third cardiac operations with CPB.

Overview of CPB Run

The CPB circuit is typically primed with red cells shortly before the start of surgery and the pH, hematocrit, potassium, and calcium levels of the circuit prime checked. The circuit is also heparinized. The cannulae for CPB are placed in the vena cava and aorta by the surgeon and handed from the surgical field to the bypass perfusionist to be connected to the CPB circuit. CPB support is initiated after the surgical field is exposed, just as the intracardiac portion of the surgical procedure is begun. A cardioplegia solution containing a high concentration of potassium is administered. Time on CPB is kept to a minimum because risk of bleeding and neurological complications are correlated with the duration of the CPB run (Menache et al. 2002). The actual time may vary from 20 minutes to over 60 minutes depending on the complexity of the repair and the patient's anatomy. Additional anesthesia techniques such as hypothermia, cooling of the head, and periods of circulatory arrest may also be used. Transfusions, fluids, and medications may be administered via the CPB circuit, depending on the amount of blood loss, and red cell salvage techniques can also be incorporated into CPB. CPB is discontinued when the repair is complete, cardiac function has been re-established, and surgical hemostasis is obtained. Before the patient leaves the operating room, the CPB circuit may be used for addi-

tional manipulations as discussed later. After the use of the CPB circuit is complete and the cannulae have been removed, the patient receives a dose of protamine calculated to reverse the heparin received during CPB.

Postoperative Hemorrhage

Transient mediastinal bleeding is an expected result of cardiac surgery, and chest tubes are routinely left in place to decompress the mediastinum and facilitate measurement of blood loss. Chest tube drainage varies widely from 16 to 110 mL/kg/24 hours (Manno et al. 1991) but is a cause for re-exploration of the surgical site in about 4% to 9% of cases (Williams, Bratton, and Ramamoorthy 1999; Chambers et al. 1996). CPB has multiple effects on the coagulation proteins, platelets, and inflammatory cytokines, causing both activation and consumption, which may contribute to postoperative bleeding (Williams, Bratton, and Ramamoorthy 1999; Williams et al. 1999; Williams et al. 1998; Despotis and Hogue 1999; Dietrich 1996). The factors associated with bleeding following cardiothoracic surgery with CPB are many and include the patient's age, preoperative condition, the type of procedure, whether the procedure is a first or repeat sternotomy, the length and number of suture lines, the duration of CPB, type of blood product support, anesthesia techniques used, adequacy of reversal of heparin, adequacy of surgical hemostasis, platelet counts, platelet function, coagulation tests for procoagulants and fibrinolysis, and thromboelastogram parameters (Williams, Bratton, and Ramamoorthy 1999). Because of this complexity, controlled studies of bleeding after CPB are difficult to perform in order to isolate, for example, the relative effect of blood product support on postoperative bleeding.

Blood Bank Support for CPB Programs

Fresh Whole Blood

A well-controlled, although not strictly randomized study of the effect of using fresh whole blood in the immediate post-bypass care of children undergoing cardiothoracic surgery with CPB was conducted by Manno et al. (1991). This study compared three blood products: very fresh whole blood, stored at room temperature for less than 6 hours after donation; fresh whole blood, stored refrigerated for 24 to 48 hours; and reconstituted whole blood, consisting of one unit each of PRBCs stored less than 5 days, plasma, and whole blood-derived platelets. These blood products were administered following the CPB run. The study found a significant reduction in postoperative blood loss for very fresh

and fresh whole blood versus reconstituted whole blood for the entire group of 161 patients. The mean postoperative blood loss was approximately doubled for patients younger than 2 years and for patients undergoing complex procedures who received reconstituted blood versus fresh whole blood. No hemostatic advantage was noted for patients older than 2 years or for simple procedures. There was no advantage of the 6-hour fresh whole blood versus the 24- to 48-hour fresh whole blood. The most significant laboratory finding correlated with the use of fresh whole blood compared to reconstituted whole blood was an improvement in platelet function, and the overall superiority of fresh whole blood was attributed primarily to better preservation of platelet function in the fresher product and therefore better restitution of platelet function in vivo after CPB.

Fresh whole blood has advantages beyond improved hemostasis in the care of children after surgery with CPB. Using whole blood to replace acute blood loss as measured by chest tube drainage is logistically simpler than component therapy and may therefore be safer in a busy intensive care unit. The leak of potassium from red cells into plasma during storage is primarily a function of storage age, and the potassium concentration in the supernatant of whole blood is lower than in packed cells of the same storage age (Michael et al. 1975). These features of fresh whole blood may also be safety advantages for patients who have recently undergone cardiac surgery and whose transfusions may be administered rapidly through the CPB cannulae or other central lines.

Providing fresh whole blood less than 48-hours old is a logistic challenge for blood centers, transfusion services, and the cardiac anesthesia and surgery services, and it is not universally available. Since it contains both red cells and plasma, whole blood must be type specific—there is no “universal donor” type. A reliable supply of fresh whole blood requires a commitment from the blood supplier to retain a portion of the daily collections of at least the common ABO and Rh blood groups types as whole blood, to perform the infectious disease testing of those units on an expedited schedule, and to facilitate delivery of those units to the transfusion service such that they can be crossmatched and made available within 48 hours of collection. The blood center must also be willing to recruit blood donations for less common blood types. Family members of the patient may be valuable committed donors for this program (Manno et al. 1991). The transfusion service must be in frequent contact with both the cardiothoracic surgery service and the blood center with updates on changes in the surgery schedule, adequacy of specimens for crossmatch, unanticipated serologic findings such as maternal

isohemagglutinins in newborns, and difficulties with blood availability. The costs associated with the use of fresh whole blood include the loss of plasma and platelet components that would otherwise have been made from units retained as whole blood, the labor costs of expedited processing, and the cost of repeated blood ordering for the same patient because of inevitable last-minute changes in the operating room schedule for this critically ill patient population. The transfusion service must also develop mechanisms to manage the untransfused whole blood in its inventory. Despite these difficulties, providing fresh whole blood for pediatric cardiothoracic surgery is feasible (Kwiatkowski and Manno 1999), and the costs associated with it may be viewed as a part of the total cost of caring for this group of patients.

Ultrafiltration and Aprotinin

Two recent developments in cardiac anesthesia offer the possibility of reducing complications after cardiac surgery with CPB. Conventional ultrafiltration (CUF) involves the incorporation of a device with a permeable membrane with a defined pore size into the CPB circuit, allowing removal of water and solutes, and small molecules from the CPB circuit with retention of the cellular elements of the blood. This technique serves as a hemoconcentration step, removing fluid introduced during priming and raising the hematocrit of the bypass circuit, but may have additional benefits in reducing postoperative edema, improving immediate postoperative cardiac function, improving cerebral metabolic recovery after CPB, and possibly removing soluble inflammatory mediators generated during CPB (Ramamoorthy and Lynn 1998; Montenegro and Greeley 1998; Gaynor 2001). Modified ultrafiltration (MUF) (Friesen et al. 1997; Quattro et al. 2002) is a variation of this technique in which the ultrafiltration is performed after discontinuation of CPB rather than during, with blood flow through the CPB circuit reversed, that is, drawing from the arterial side and returning to the venous side. MUF prolongs the duration of the surgical procedure by 5 to 20 minutes (Ungerleider 1998) but may be more efficient in removing fluid. MUF also permits concentration and return of blood in the CPB reservoir to the patient. One study comparing CUF and MUF in pediatric cardiothoracic surgery patients found no difference in a variety of outcomes including postoperative hematocrit, hemodynamics, and blood product use (Thompson et al. 2001), but the study design may not have employed MUF to its fullest advantage. The value of MUF in CPB for pediatric cardiac surgery is still under debate (Ramamoorthy and Lynn 1998; Gaynor 2001).

Aprotinin is a nonspecific serine protease inhibitor that has effects both in blocking fibrinolysis and attenuating contact inhibition as measured by inhibition of kallikrein (Mossinger and Dietrich 1998). These actions of aprotinin might serve to counteract the activation of coagulation proteins and inflammatory mediators generated during CPB (Dietrich 1996). The use of aprotinin during and/or immediately following CPB has beneficial effect in adults undergoing coronary bypass surgery, and some studies have suggested that aprotinin may improve surgical closure time, blood product utilization, and postoperative hemostasis in pediatric patients (Costello et al. 2003; Mossinger et al. 2003), while others have not (Davies et al. 1997).

Blood Product Utilization

The overall blood product requirements for pediatric cardiothoracic surgery patients are difficult to estimate because of the many factors that come into play, including age of patients and complexity of procedures attempted (Manno et al. 1991; Chambers et al. 1996), priming volume of the equipment in use, CPB technique (Friesen et al. 1997; Davies et al. 1997), availability of fresh whole blood, target hematocrit for the end of CPB, and the multiple factors that affect postoperative bleeding and the algorithms that are used to manage it (Despotis and Hogue 1999). One survey from an institution that used whole blood less than 48-hours old and intraoperative cell salvage but not CUF, MUF, or aprotinin and that had defined transfusion guidelines, which were not monitored for the study, reported that pediatric cardiothoracic surgery patients received a mean of 3.1 whole blood or red cell units, 1.4 platelet units, and 1.1 plasma units, for a total of 5.6 +/- 5.1 donor exposures (Chambers et al. 1996). Total blood product utilization may be reduced by practices such as dividing whole blood units when the CPB circuit can be primed with half of a unit.

SUMMARY

Blood support for CPB and ECMO programs places special demands on a pediatric transfusion service because of the variety and critical nature of the disease processes involved, the time-sensitive demands for specialized blood products, and the absolute requirement for blood products to initiate these therapies in small children.

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