An Overview of Extracorporeal Membrane Oxygenation Therapy

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Abstract. A brief overview of extracorporeal membrane oxygenation and its use in infants and children is presented. The history, selection, operative procedure, daily management and complications are discussed. The international results are shown.

Key words : *Extracorporeal membrane oxygenation*

Despite recent advances in the care of neonates and children with respiratory failure, extracorporeal membrane oxygenation (ECMO) still plays a pivotal role in the care of these children. With current therapy, approximately five per cent of infants with persistent pulmonary hypertension of the neonate (PPHN) fail to respond to other modalities available, including high-frequency ventilation, nitric oxide, surfactant and liquid ventilation.[1] Despite the recent advances, mortality rates for infants and children with respiratory failure remain at 12%-75%.[2] Timmons and colleagues[3] in a retrospective review showed that children with adult respiratory distress syndrome (ARDS) had a mortality of 75%. There is also a high morbidity associated with aggressive ventilator therapy. Even with high-frequency ventilation there is an 11% incidence of chronic lung disease in neonates.[4] Therefore, there is currently a significant role for ECMO in the treatment of neonates and children with respiratory and cardiac failure of various etiologies.

History of Cardiopulmonary Bypass

John Gibbon[5] in 1937 pioneered the use of artificial circulation but it did not come into widespread use for cardiac surgery until the 1950s. Lillehei[6] proposed the use of his biological lung as an oxygenator during extracorporeal circulation because of the problems with protein denaturation in previously used systems. His oxygenator and others such as the bubble oxygenator,[7] now the mainstay for cardiac surgery, can cause damage to cells by direct exposure of blood to oxygen if used for more than a few hours. This led to research into the development of a membrane oxygenator. In 1957, Kammenmeyer[8] reported the excellent gas exchange properties of a polymer of dimethylsiloxone, now known as silicone. Once these membrane lungs and the circuit become coated with a protein monolayer, blood is no longer in direct contact with the thrombogenic foreign surface so that there is not excessive

damage to blood cells. This research led to the first human trails of prolonged extracorporeal support and forms the basis for the systems in use today.[9]

Physiology of Extracorporeal Circulation

The membrane lungs that are currently available for use in ECMO patients have two compartments divided by a gas permeable membrane of silicone. The ventilating gas (gas phase) is on one side and the (blood phase) is on the other side so that the gas and blood phases never come into contact with each other in an intact circuit. The oxygen and carbon dioxide are then free to diffuse across the membrane at a molecular level. The gradient for oxygen diffusion across the membrane is the difference between the oxygen content in the ventilating gas, generally FiO_2 is 1.0, and that in the venous blood of the patient. The inherent potential for O_2 transfer across a silicone membrane is 1210 ml O_2/ml/mil thickness at a diffusion gradient of 760 mm Hg. In addition, the actual oxygen delivery potential of the blood phase is limited by the oxygen carrying capacity of the blood with each gram of hemoglobin having the capacity to bind 1.39 ml O_2.[10,11]

Red blood cells that are nearest to the membrane wall become saturated with oxygen first and then the PO_2 locally rises. Subsequently, dissolved oxygen diffuses deeper into the blood phase, saturating more blood cells. If complete saturation of the blood phase with oxygen is to occur, then it must remain in contact with the membrane lung long enough for oxygen diffusion to the centre of the film. Oxygen transfer, therefore, increases in proportion

to the flow rate until a limitation in O_2 transfer is imposed by the thickness of the blood. When venous blood enters the membrane lung with a saturation of 75%, the flow rate needed to achieve saturation of 95% in blood leaving the membrane is termed as the rated flow and allows standardization between various oxygenators.[12] In most cases the amount of oxygen that can be delivered is dependent on blood flow available and not the capacity of the membrane to transfer oxygen to the blood.

Carbon dioxide is much more diffusible through plasma than oxygen. Thus, CO_2 transfer is limited by its diffusion rate across the membrane. The CO_2 transfer potential across the membrane lung is about four times that for oxygen. Often, carbon dioxide transfer across the membrane is so efficient that it must be added to the gas phase to decrease the diffusion gradient. Because CO_2 transfer is dependent on surface area of the membrane and not blood flow, a rising PCO_2 can be an early indicator of loss of oxygenator function, due to clot formation or water in the gas phase.

Blood flow to the membrane is limited by total circulating blood volume and the diameter of the venous catheter as well as resistance to blood return through the arterial catheter or return port in venovenous ECMO. The system must be able to flow at least at 120ml/kg/min (near total support of cardiorespiratory function). The ECMO circuit is designed to permit these flows and incorporates an oxygenator that is rated for flows above this level.

Patient Selection

Two factors are critical in determining the application of ECMO: determining the

patient population that can be helped and the best timing for instituting support. Because ECMO is an invasive procedure, efforts are made to set appropriate criteria for patient selection. The major criterion for patient selection of ECMO is that the disease process is reversible within two to three weeks, the usual time frame for ECMO support. Although, ECMO support beyond this time frame is difficult, it has been done successfully for over two months. Disease processes that lend themselves to ECMO therapy in the new born include: meconium aspiration syndrome (MAS), pneumonia, sepsis, primary persistent pulmonary hypertension of the neonate (PPHN), congenital diaphragmatic hernia (CDH), perinatal asphyxia, hyaline membrane disease, barotrauma with air leak syndrome, and peri-operative care of newborns with congenital cardiac disease. In general, cardiac defects can be identified and corrected without the need for extracorporeal support. One cardiac condition that causes PPHN and is not always recognized is total anomalous pulmonary venous return (TAPVR). ECMO can be useful in peri-operative stabilization of these seriously ill infants. In general, the use of ECMO therapy for patients with cardiac conditions has a lower survival rate than therapy for respiratory conditions.

Conditions requiring ECMO support in the non-neonatal pediatric population generally share the common terminal pathophysiology of ARDS. This disease process still carries a mortality of 50% with current intensive care therapies available for children.[9] The initiating events leading to ARDS may be one of the several, sepsis, fulminant pulmonary infections, trauma, shock, major surgery, drug-overdose, and near-drowning. Although, there was initially concern about bleeding complications in trauma patients treated with ECMO, Anderson and coworkers[13] have shown good survival in these patients. Another group of children with respiratory failure who may benefit from ECMO are children with asthma. In addition, children can also have ECMO support for a variety of cardiac conditions. This may be preoperative support, bridge to transplantation, post-cardiotomy support or cardiac support after cardiac arrest or secondary to reversible cardiac failure, such as children with infectious cardiomyopathy.[14] Again, the survival rate is lower than in children treated for respiratory failure.

TABLE 1: ECMO Selection Citeria

Alveolar-arterial oxygen gradient (A-a)DO$_2$

1. (A-a)DO$_2$ > 600 torr for 12 consecutive hours
2. (A-a)DO$_2$ > 610 torr for 8 consecutive hours
3. (A-a)DO$_2$ > 605 torr for 4 consective hours with peak inspiratory pressure > 38

Oxygenation index

Oxygenation index ≥40 on 3 of 5 post-ductal ABG's drawn 0.5 to 1 hour apart

Acute deterioration (one or both for two consecutive hours)

1. pH <7.15
2. PaO$_2$ <40 torr

Barotrauma (four of the following coexisting)

1. Pulmonary interstitial emphysema
2. Pneumothorax or pneumomediastinum
3. Pneumopericardium
4. Pneumoperitonium
5. Subcutaneous emphysema
6. Persistent air leak > 24 hours
7. Mean airway pressure > 15 cm H$_2$O

Above measurements should commence after response to conventional therapy is considered optimal.

Selection criteria for placement of patients on ECMO should ideally predict which infants and children would not do well on mechanical ventilation before life-threatening complications or irreversible lung damage ensue. Theoretically, a child should be placed on ECMO when the danger of mechanical ventilation and supportive therapies outweighs the risks of extracorporeal support. Presently, there is not a single criterion to determine these relative risks, so most institutions place children on ECMO when the expected mortality with conventional therapies is high (50%-80%). Table 1 details some of the criteria used at our institution and at many other ECMO centers around the world.

One of the criteria that was used early in ECMO centres was the (A-a) DO_2. This is defined as $(A-a)DO_2=(P_{atm}-P_{H_2O})-(PaO_2+PaCO_2)$ where P_{atm}=atmospheric pressure, P_{H_2O}=partial pressure of water vapor, PaO_2=arterial oxygen tension, and $PaCO_2$= arterial carbon dioxide pressure.[15] Many workers have found that levels over 610 torr for eight hours predict a mortality of about 80% in infants.[16,17] More recently, the oxygenation index (OI) has been used to identify patients who would have a greater than 80% predicted mortality without ECMO support. Oxygenation index is defined by the following equation: OI = (MAP x FiO_2/PaO_2) x 100% where FiO_2 = inspired concentration of oxygen, MAP = mean airway pressure, PaO_2 = arterial oxygen tension. Various workers have found that an OI ≥ 40 in candidates for ECMO predicts a mortality rate of 82% without institution of ECMO while (A-a)DO_2 in these same patients was an inaccurate predictor of mortality.[18,19] These data are all historical and each institution

should review the appropriate cut-off values to predict high mortality rate in its patient population.

In addition to strict numerical criteria, there are often clinical signs that the patient may benefit from ECMO. There are instances where a neonate or child who was previously doing well has a sudden, drastic deterioration, or there are some neonates who after birth are unstable. In these cases the patient may not survive the necessary time to calculate the OI or (A-a)DO_2. If a child has pH < 7.15 and/or PaO_2 < 40mm Hg for two consecutive hours then he should be considered for ECMO.[20]

The effect that the artificial ventilation is having on the patient is determined by looking for the signs of barotrauma listed in Table 1. If a child sustains four or more indicators of barotrauma, he is at increased risk for mortality and morbidity due to pulmonary damage and chronic lung disease. Therefore, these patients should be considered for ECMO.

Finally, if any child is in severe distress and near cardiac arrest, clinical judgment should supervene and early placement on ECMO should be considered. Besides the acute criteria for institution for ECMO, if the managing specialist feels that he has exhausted his armamentarium and the patient is not improving then ECMO is considered.

For the older pediatric patient, parameters such as the OI and (A-a)DO_2 have limited usefulness. Acute deterioration and barotrauma play a role in the selection process, but the majority of pediatric ECMO patients are selected when conventional management fails. This determination is usually a consensus judgment by the experienced critical care

providers that continued mechanical ventilation will result in the patients' death from hypoxia or acidosis or will result in such lung damage that recovery and survival would not be possible.

Contraindications to ECMO

The contraindications to ECMO are those situations that preclude either a quality outcome or a successful ECMO run. For the neonates, a weight less than two kilograms or an estimated gestational age (EGA) less than 35 weeks predicts a near 100% incidence of intracranial hemorrhage or mortality at one year when treatment with ECMO occurs.[21] Therefore, these patients are generally not considered for ECMO. The EGA seems to be the more important factor of the two. Neonates who have a chromosomal abnormality or syndrome associated with profound retardation or a fatal outcome are also excluded from ECMO. Infants with an existing intraventricular hemorrhage greater than Grade II should be excluded because of the chance for extension of the bleed with the thrombocytopenia and heparin therapy associated with ECMO.

Older children who have had a traumatic event or cardiac arrest and do not have documentation of neurologic function should not be placed on ECMO. Children with incurable diseases such as those who are immunosuppressed for cancer treatment or due to AIDS may not be candidates for support. Patients with irreversible lung disease should not be placed on ECMO unless as a bridge to transplantation, because ECMO is not a curative process and relies on the child's own body to provide lung recovery. In

general, children who have prolonged mechanical ventilation (over 10-14 days) should be offered support only after careful consideration since their lungs have sustained chronic injury. If a child has a lung biopsy with extensive pulmonary fibrosis, the chance for recovery is nil and ECMO should not be instituted. In addition, a relative contraindication to ECMO may be severe active bleeding.

Evaluation Prior to ECMO

When an infant or a child is being considered for ECMO, special attention should be directed towards the cardiovascular and neurological systems. A thorough physical examination is mandatory, especially in neonates, to screen for congenital defects incompatible with a good outcome. Baseline serum analysis are performed, with attention to platelet counts and coagulation studies.

A cardiology evaluation is obtained to rule out congenital heart disease. A two-dimensional echocardiogram is performed. The degree of ventricular dysfunction as well as any structural abnormalities are noted. In neonates, the degree of pulmonary hypertension and shunting through the patent ductus arteriosus or foramen ovale are noted. If congenital heart disease is strongly suspected and the echocardiogram is not conclusive, the patient may have an angiogram if he is stable. If a congenital lesion is found then a decision about pre-operative ECMO is arrived at by the critical care specialist, cardiologist, cardio-vascular surgeon and the ECMO physician.

Seizure activity and focal neurological deficits are often difficult to assess in this patient population due to the sedation and
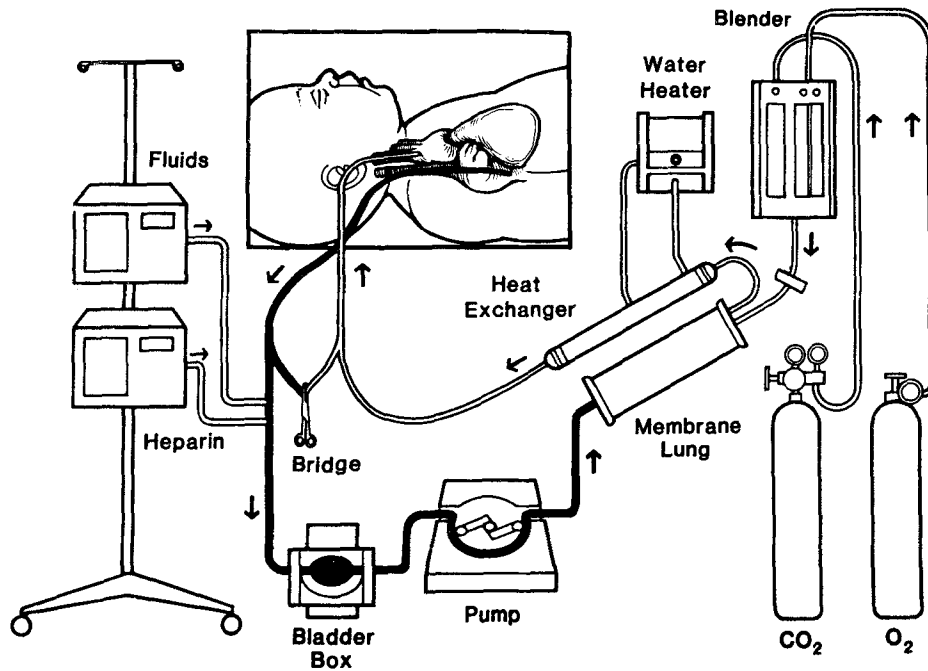
Fig. 1:   Representation of a typical, venoarterial ECMO circuit. For venovenous bypass, the circuit remains same except that venous return is into the right atrium

paralyzing agents used in this group of critically ill children. In small children, cranial ultrasound can be used as a screen for intraventricular bleeding. If the bleed is greater than Grade II, then the child is not a candidate for ECMO. Of interest, Von Allman and associates[22] recently found that children placed on ECMO with a Grade I hemorrhage were not at increased risk for major intracranial complications but those with severe edema and/or periventricular leukomalacia had a 63% incidence of associated complications. For children who do not have an open fontanelle through which to perform ultrasound and who sustain a traumatic injury or cardiac arrest,

an attempt should be made to obtain a computerized tomography (CT) scan. If the child is unstable for transport then reversal of sedation and neurologic evaluation should be performed. Seizure activity alone is not a contraindication to ECMO.

When the child appears to be a candidate for ECMO, the operating room staff and ECMO specialist, in charge of priming the circuit are put on stand-by until the final decision for ECMO is made. Blood is obtained from the child for type and crossmatch so that blood components will be available for the priming solution. Once the child meets ECMO criteria, parental consent is obtained with special attention

directed at making sure the parents are aware of the possible complications, including neurological deficits, chronic lung disease, and death. Preparation of the patient and final priming of the circuit are then carried out simultaneously.

The ECMO circuit is preassembled and sterilized. The circuit is composed of the membrane lung, a small venous reservoir, multiple ports for infusion and sampling of blood and medications, a pump, a heating device, and various monitoring devices to monitor pump flows and pressures in the system (Fig. 1). The circuit is primed with packed red blood cells and fresh frozen plasma. The pH and electrolytes of the prime solution are corrected prior to cannulation to prevent an adverse reaction during initial bypass.

CANNULATION

Venoarterial versus venovenous cannulation: Extracorporeal support can be accomplished by using two cannulae venoarterial bypass, two cannulae venovenous bypass, or the newer technique of a single double-lumen catheter for venovenous bypass. Historically, the most common cannulation technique for both infants and older children has been venoarterial, but the double-lumen venovenous technique is rapidly assuming a major role in cannulation for extracorporeal support. The only difference between the cannulation techniques for the neonate and older children is the size of the cannulae placed. There are a multitude of veins and arteries that can be used for cannulation, including the internal jugular vein, carotid artery, axillary and femoral arteries and veins, and the intrathoracic aorta, vena cava or the right atrium.

In venoarterial bypass, venous outflow is usually from the right atrium via the internal jugular vein. Blood is returned to the aortic arch via the common carotid artery. This method allows support of both cardiac and respiratory function and is, therefore, the only choice in neonates and children who need bypass for cardiac dysfunction or instability. In the majority of other patients, however, venovenous ECMO is sufficient.

For venovenous bypass using two separate veins, the right internal jugular vein is used for drainage from the right atruim and the femoral vein is used for blood return with the catheter tip advanced into the inferior vena cava. In older children there are percutaneous systems available for cannulation that are all inclusive and can be used for the drainage or return catheters (Biomedicus, Inc.). In single catheter double-lumen bypass, only the internal jugular vein is cannulated with the catheter positioned in the right atrium in such a manner so that the return port allows blood to return near the tricuspid valve. This helps to minimize the recirculation (oxygenated blood immediately flowing out of the cannula into the circuit) of blood that is present in all venovenous bypass. This form of bypass spares all arteries. A limitation to the venovenous double-lumen technique is the cannulae sizes currently available. At present the only size cannula available commercially in the USA is the 14Fr Size (Kendell, Corp.) (Figure 2). There is limited accessibility to the 12Fr and 15Fr cannulae manufactured by the Jostra Corporation in Germany. However, these cannulae are not the proper size for support of very small infants or larger children.
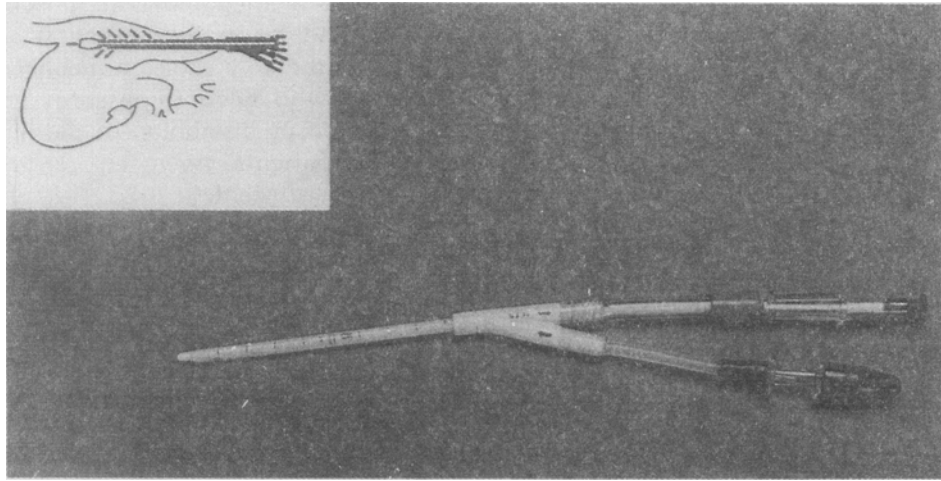
Fig. 2:   Double-lumen Venovenous ECMO cannula. Inset shows optimal position for catheter placement
in the right atrium to minimize recirculation.

Venovenous bypass supports only the pulmonary system and relies on the patient's heart to act as the pump. Therefore, these patients often require more support and are less stable initially than those on venoarterial bypass. Advantages of venovenous bypass are physiologic in addition to the anatomic sparing of the arteries. On venovenous bypass, the flow remains pulsatile and, therefore, there is less end-organ effect, especially to the kidneys. Oxygenated blood continues to flow though the pulmonary system and may decrease pulmonary hypertension. In addition, the coronary arteries do not rely on retrograde flow for a supply of oxygenated blood so myocardial perfusion and possibly performance are enhanced.

There has recently been a multicenter study (27 centers) comparing conventional venoarterial bypass (VA) to double-lumen venovenous bypass (VV) in newborns.[23] One hundred and eight patients were supported with venovenous bypass of which 10% required conversion to venoarterial bypass. Survival was 95% for VV bypass and 87% for VA bypass with a 91% survival in those infants converted from VV to VA bypass. Neurological complications were higher in the VA bypass group while the mechanical and hemorrhagic complications were similar in all groups.

Operative Procedure: The operative procedure itself is performed in the intensive care unit with operating room

Fig. 3:   Chest radiograph of a patient on venoarterial ECMO. A—Venous catheter into the right atruim
B—Arterial cannula into the aortic arch. 1-5-Chest tubes.

personnel in attendance. Surgeons use magnifying loupes, headlights, and electrocautery throughout the procedure. The patient is often placed under a radiant warmer to prevent hypothermia. If the child is not already paralyzed, this is done prior to the procedure to prevent spontaneous respiration and air embolism during venous catheter insertion. Local anesthesia or sedation with morphine or fentanyl are used.

An incision is made over the right sternocleidomastoid and the carotid sheath is exposed. The vessels are isolated from surrounding tissues, taking care not to injure the vagus nerve. The patient is given an intravenous bolus of heparin (100-200

units/kg). For venoarterial bypass, the carotid artery is ligated distally and controlled proximally with a clamp and suture ties. Through an arteriotomy, the cannula is passed a premeasured distance into the aortic arch and tied securely into position. The venous catheter is then passed into the right atrium through the internal jugular vein in a similar fashion. For the double-lumen technique only the vein is cannulated but the artery is exposed in case conversion is required. The cannula is placed so that the arterial return is near the tricuspid valve. For venovenous bypass with two catheters a separate incision is made in the groin over the area of the femoral artery and vein, about four

centimeters distal to the inguinal ligament. The femoral vein is located at the spheno-femoral junction and cannulated as described above. The tributaries are ligated sparing the deep epigastric system if possible. Additional sutures are placed to secure the cannulae to the neck and/or groin. The cannulae are connected to the circuit in a sterile fashion and flow is slowly started through the system. The wounds are closed and a sterile dressing applied. An immediate chest roentgenogram is taken to confirm cannula placement (Fig. 3). If the position is suboptimal then the cannulae are repositioned. Confirmation of catheter placement can be obtained with echocardiogram within the next 24-48 hours.

DAILY MANAGEMENT

Once the patient is on full ECMO support, the ventilator is adjusted so that the settings allow "lung rest." Typically, these settings are FiO_2 0.21 to 0.40, rate of 10-20 breaths/min, peak inspiratory pressure of 15-25 cm H_2O, and positive end-expiratory pressure (PEEP) of 10-14 cm H_2O, except in children who have an air leak or are prone to pneumothoraces. The management with higher PEEP is based on a study by Keszler and co-workers[24] which found that patients on ECMO treated with higher levels of PEEP demonstrated measurably better lung compliance in the first 72 hours on ECMO, had a shorter course on ECMO, and had less complications than the lower PEEP group.

Respiratory therapy is also done frequently without fear of an acute decompensation because of the support through the ECMO circuit. Therapy promotes alveolar recruitment and provides pulmonary toilet. The only caution is that the traumatic bleeding can occur due to overvigorous suctioning.

Activated clotting times are measured at least hourly at the bedside and are maintained at approximately two times normal (180-220 seconds) by varying the rate of the continuous heparin infusion. The usual heparin dose required is 25-50 units/kg/hr. Close correlation between activated clotting times and the blood heparin levels has been demonstrated in patients on ECMO.[25] Hematocrit is maintained over 35% by transfusion with saline-washed packed red blood cells. Platelet counts are maintained at over $75,000/mm^3$ with infusion of platelets. Recently, at our institution, the use of concentrated platelets has been discontinued because the concentration process damages the platelets and leads to more frequent infusions. The platelet count can be maintained at a higher level if the child is actively bleeding or will undergo operative intervention. Fibrinogen and clotting factors are maintained by the occasional use of fresh frozen plasma or, rarely, cryoprecipitate.

Complete nutritional support is established by standard total parenteral nutrition techniques used in other critically ill children. The insensible losses generated by the ECMO circuit must be taken into account in determining daily fluid intake. These losses can be up to 5-7 ml $H_2O/m2/$ 4 ml thickness/hr at 37°C. Electrolyte values are obtained daily and adjustments are made accordingly. Careful attention should be paid to potassium levels as hemolysis in the circuit can increase the serum potassium. In older children who are not at increased risk of necrotizing enterocolitis (NEC), the enteral route may be considered but in practice many centers

have difficulty with adynamic ileus in this critically ill patient population.[13]

During bypass prophylactic antibiotics are given, most often an aminoglycoside and ampicllin, but are varied based on pathogens found during daily cultures. Other medications are kept at a minimum. Medications to aid cardiac function such as dobutamine are kept at the lowest level necessary to maintain adequate perfusion and can often be discontinued. Dopamine is decreased to renal dose. Occasionally, the ECMO patient becomes hypertensive, due to increases in circulating renin, aldosterone and antidiuretic hormone.[26] Nitroglycerin and hydralazine are often used to decrease the pressure and lower the risk of bleeding. The child who comes to ECMO is often volume overloaded, and in addition, often requires large fluid boluses during the initial phase of bypass due to increased capillary leak. Therefore, diuretics such as furosamide are often helpful. Sedation is provided by midazolam drip and pain control by morphine or fentanyl drips. Paralysis is discontinued to allow assessment of neurological status unless the child becomes a danger to himself.

In addition to clinical evaluation of neurological status, serial ultrasound examinations are performed in those children who have an open fontanelle. Presence of an intracranial bleed greater than Grade II is an indication for cessation of ECMO, discontinuation of heparin therapy and resumption of other ventilatory techniques. Large bleeds are uniformly associated with a bad outcome. If there is a question of seizure activity, then phenobarbital is administered as an electroencephalogram (EEG) is not accurate on ECMO due to interference from the ECMO machinery. In fact, the routine use

of phenobarbital in these patients is advocated by some since these children often have cerebral edema.

Occasionally, operative intervention is necessary in a child on ECMO i.e., repair of congenital diaphragmatic hernia, patent ductus arteriosus ligation, open lung biopsy, and wound exploration. Prior to the operation, the platelet count is increased to greater than $100,000/mm^3$ and the ACT is decreased for a short time. Very careful surgical technique is followed with extra attention to hemostasis using electrocautery and suture ligation extensively.

WEANING AND CESSATION OF ECMO

Total flow through the circuit controls the patient's arterial PaO_2 by varying the relative contributions from the pump and the child's heart and lungs. Arterial oxygen content is a mixture of pump oxygenated blood and that blood oxygenated in the child's native lungs. Since the pump blood is greater than 99% saturated, an increase in the child's arterial PaO_2 is due to increased contribution by the cardiovascular system (provided pump flow is constant). Other signs of improvement are better lung aeration on chest X-ray, improved compliance while bagging the patient, and a spontaneous diuresis. Early in the run the pump provides 100-120cc/kg/min of flow. This level of bypass is reduced when the improvement in oxygenation occurs. The process continues in a stepwise fashion until the child has adequate blood gases on a flow of 20-50cc/kg/min. For venovenous bypass, the oxygen content of the pump blood is decreased until it is room air; flow remains constant since this blood will subsequently be oxygenated in the

lungs. At this point the child is excluded from the circuit and the flow is maintained through the bridge. If the child is stable and has good blood gases for one-hour minimum, the cannulae are removed and the vessels ligated. The wound is then closed. Carotid artery repair can safely be performed if there is concern about permanent ligation.[27] If prior to cannula removal the condition of the child deteriorates, he can be placed back on bypass.

RESULTS

The latest results from the ECMO registry report[28] of the Extracorporeal Life Support Organization (ELSO) are summarized in Table 2. The overall survival is 73% with a survival in neonates of 80%. The survival in all age groups is dependent on diagnosis. In the neonate, meconium aspiration syndrome is associated with a 94% survival while congenital diaphragmatic hernia is associated with a 58% survival. In the older child, the survival is highest for aspiration (64%) and lowest for bacterial or unusual pneumonias such as pneumocystis (43%).

TABLE 2: International ECMO Registry Report

(Extracorporeal Life Support Group)[28]

Group	Total reported	Number survived	Percent survived
Neonatal Respiratory	11182	8994	80
Pediatic Respiratory	1067	567	53
Cardiac Support	1650	705	43
Adult	246	114	46

COMPLICATIONS

Complications related to ECMO can be divided into mechanical or patient complications. Even though technical problems are rare, a complication can be immediately life-threatening, so continual attention of a specially trained ECMO technician is mandatory. These individuals may be physicians, nurses, respiratory therapists or perfusionists. No matter what the previous background, all need didactic and laboratory experience prior to the clinical application of ECMO. Manpower needs demand a major commitment from these individuals prior to starting a new program.

Mechanical complications occur in one to 10 per cent of patients undergoing ECMO support.[29] Cannulae problems can occur due to improper placement or damage to the vessels that they traverse. The venous cannula can be improperly placed leading to poor venous return. In venovenous bypass with the double-lumen catheters, improper placement leads to excessive recirculation. The arterial catheter can cause dissection of the aorta or if near the aortic valve can cause permanent damage to this structure. If the arterial cannula is too far into the descending aorta then coronary and cerebral perfusion can be compromised. If the cannula is in the right subclavian, then oxygenated blood goes only to the right arm and the remainder of the body remains cyanotic. Most cannula problems can be easily remedied by careful confirmation of placement on roetngenogram and echocardiogram.

Various components of the circuit can malfunction. Oxygenator failure occurs in 5% of patients. The oxygenator is changed

promptly to prevent deterioration in patient status. The pump itself can fail and handpowering of the pump temporarily allows continued flow. Tubing rupture, especially of the tubing that traverses the pump if not corrected quickly can prove fatal due to massive blood loss. Blood loss can also occur if infusion ports or stopcocks break. The circuit can have clot formation causing excessive hemolysis and necessitating a change of the circuit or individual components. One of the most concerning complications is an air embolism usually due to a tear in the tubing or oxygenator. This complication is best treated by prevention with periodic inspection of the circuit. If it does occur, the child is immediately clamped from the circuit, hopefully prior to air reaching the inflow catheter.

Patient related complications occur in 3%-16% of ECMO patients. The most common complications are related to bleeding with the most common being intracranial. This complication decreases with increasing age of the patient. Bleeding at other sites is most common at the cannulation site or other surgical sites but can occur anywhere including gastrointestinal, intrathoracic, retro-peritoneal and intrapulmonary sites. Bleeding can often be controlled with pressure and hemostatic agents. The platelet count can be increased and the heparin decreased, but a secondary complication of circuit thrombosis may occur.

Systemic hypertension is a dangerous side effect of ECMO as it can increase the risk of intracranial hemorrhage. Renal failure occurs in about 10% of children on ECMO and can be treated by hemofiltration or hemodialysis in line with the ECMO circuit. Severe cardiac dysfunction (cardiac stun) can occur rarely and is treated by increasing the bypass flows or if the patient is on venovenous bypass, by increasing inotropic support. Occasionally, the child has to be converted from venovenous to venoarterial support. There is a risk of infection, including blood borne pathogens such as hepatitis. This complication is best treated by prevention of blood product contamination and careful screening for active infection with surveillance cultures.

Long-term complications fall into two main categories: respiratory and neurological. Lung dysfunction presents as bronchopulmonary dysplasia (BPD). Prolonged periods of 100% oxygen and ventilator barotrauma are associated with an incidence of BPD of 4%-38% in infants not treated with ECMO.[30] Studies have shown a clear decrease in chronic lung disease with ECMO attributed to a protective effect of lung rest.[4] The patients treated with ECMO are also part of a group of children at high risk for developmental problems due to prolonged hypoxia, acidosis, and ventilatory support. Glass and associates[31] followed 42 ECMO patients for one year and found that 20% had suspect development, 10% were significantly delayed, and none had profound delay. There were factors associated with poor neurological outcome in these patients, including: (1) sepsis on admission, (2) chronic lung disease, (3) abnormality on CT-scan or head ultrasound. In a 10-year follow-up, Hofkosh and colleagues[32] found that school aged children, treated with ECMO, had similar cognitive scores as a matched control group and in younger children 70% had normal cognitive scores suggesting that some of the developmental delay may be outgrown in these children as they reach school age.

CONCLUSION

Extracorporeal membrane oxygenation has now been successfully used in over 10,000 patients worldwide. Even with the newer advances in the treatment of respiratory failure in children, ECMO still plays a role for those children who do not respond to other therapies. Originally limited to the neonate, ECMO now has a place in the armamentarium for the treatment of older children and adults with a variety of respiratory and cardiac diagnoses. Even as these other therapies evolve, ECMO itself advances with research underway to decrease some of the morbidity of this procedure. Therefore, ECMO should be considered as a standard therapy for respiratory and cardiac failure in the neonate and child. Prior to beginning a new program, however, a strong manpower commitment is needed from the entire staff.

REFERENCES

1. Bartlett RH. Extracorporeal Membrane oxygenation in newborn respiratory failure. In: Welch KJ, Ravitch MM et al. Pediatric Surgery, 4th ed. Chicago, Year Book Medical Publishers, 1986: 74-77.

2. Dwortz AR, Moya FR, Sabo B, et al. Survival in infants with persistent pulmonary hypertension without extracorporeal membrane oxygenation. Pediatrics 1989; 84: 1-6.

3. Timmons OD, Dean JM, Vernion DD. Mortality rates and prognostic variables in children with adult respiratory distress syndrome. J Pediatr 1991; 119: 896-99.

4. Markestad, T, Fitzhardinge PM. Growth and development in children recovering from bronchopulmonary dysplasia. J. Pediatr 1981; 98: 597-602.

5. Gibbon JH. Artificial lung maintenance of circulation during experimental occlusion of pulmonary artery. Arch Surg 1937; 34: 1105-1131.

6. Lillehei CW, Cohen M, Warden HC, et al. The result of direct vision closure of ventricular septal defect in 8 patients by means of controlled cross circulation. Surg Gyneol Obstetr 1955; 101: 447- 452.

7. DeWall R, Bartley DJ, Hrose M et al. A temperature controlling (omnithermic) disposable bubble oxygenator for total body perfusion. Dis Chest 1966; 49: 207-211.

8. Kammenmeyer K. Silicone rubber as a selective barrier. Ind Eng Chem 1957; 49: 1685-1691.

9. Dorson W, Baker E, Cohen ML et al. A perfusion system for infants. Trans Am Soc Artif Intern Organs 1969; 15: 155-160.

10. Instruction Manual-ECMO Membrane Oxygenators. AVECOR Cardiovascular Inc, Plymouth, MN, 1993.

11. Bartlett RH, Gazzaniga AB. Extracorporeal circulation for cardiopulmonary failure. Curr Prob Surg 1978; 15: 4-96.

12. Galleti PM, Richardson PD, Snider MT et al. A standardized method for defining the overall gas transfer performance of artificial lungs. Trans Am Artif Intern Organs 1972; 18: 359-368.

13. Anderson HL, Shapiro MB, Delius RE et al. Extracorporeal life support for respiratory failure after trauma. J Trauma 1994; 37: 266-274.

14. Furhman, BP, Dalton HJ. Progress in pediatric extracorporeal membrane oxygenation. Crit Care Clinics 1992; 8: 191 202.

15. Krauss AN. Ventilation-perfusion relationships in neonates. In: Thilbeault DW, Gregory GA eds. Neonatal Pulmonary Care. Reading, MA, Addison-Wesley, 1979: 54-68.

16. Ormazabol M, Kirkpatrick B, Mueller D. Alteration of alveolar-arterial O_2 gradient (A-a)DO_2 in response to tolazoline as a predictor of outcome in neonates with persistent pulmonary hypertension. Pediatr Res 1980; 14: 607.

17. Beck R, Anderson KD, Pearson GD, et al. Criteria for extracorporeal membrane oxygenation in a population of infants with persistent pulmonary hypertension of the

newborn. *J. Pediatr Surg* 1986; 21: 297-302.

18. Ortega M, Ramos A, Atkinson J *et al.* Oxygenation index can predict outcome in neonates who are candidates for extracorporeal membrane oxygenation. *Pediatr Res* 1987; 34: 462A.

19. Ortiz RM, Cilley RE, Bartlett TH. Extracorporeal membrane oxygenation in pediatric respiratory failure. *Pediatr Clin North Am* 1987; 34: 39-46.

20. Redmond CR, Graves ED, Falterman KW *et al.* Extracorporeal membrane oxygenation for respiratory and cardiac failure in infants and children. *J Thorac Cardiovasc Surg* 1987; 93: 199-204.

21. Cilley RE, Zwischenberger JB, Andrews AF *et al.* Intracranial hemorrhage during extracorporeal membrane oxygenation in neonates. *Pediatrics* 1986; 78: 699-704.

22. vonAllmen D, Badcock D, Matemoto J *et al.* The predictive value of head ultrasound in the ECMO candidate. *J. Pediatr Surg* 1992; 27: 36-39.

23. Anderson HL, Snedecor SM, Otsu T *et al.* Multicenter comparison of conventional venoarterial access versus venovenous double-lumen catheter access in newborn infants undergoing extracorporeal membrane oxygneation. *J Pediatr Surg* 1993; 28: 530-535.

24. Keszler M, Ryckman FC, McDonald JV *et al.* A prospective, multicenter, randomized study of high versus low positive end-expiratory pressure during extracorporeal membrane oxygenation. *J Pediatr* 1993; 120: 107-113.

25. Green TP, Isaham-Schopf B, Steinhorn RH *et al.* Whole blood activated clotting time in infants during extracorporeal membrane oxygenation. *Crit Care Med* 1990; 18: 494-98.

26. Sell LL, Cullen ML, Lerner G *et al.* Hypertension during extracorporeal membrane oxygenation: cause, effect and management. *Surgery* 1987; 102: 724-730.

27. Adolph V, Bonis S, Falterman K, Arensman RM. Carotid artery repair after pediatric extracorporeal membrane oxygenation. *J Pediatr Surg* 1990; 25: 867-870.

28. ECMO Registry Report of the Extracorporeal Life Support Organization, July 1996.

29. Zwischenberger JB, Cox CS. Emergencies during extracorporeal membrane oxygenation and their management, In: Arensman RM, Cornish, JD, ed. *Extracorporeal Life Support.* Cambridge, MA, Blackwell Scientific Publishing, 1992: 207-225.

30. Towne BH, Lott IT, Hicks DA *et al.* Long-term follow-up of infants and children treated with extracorporeal membrane oxygenation (ECMO): a preliminary report. *J Pediatr Surg* 1985; 20: 410-414.

31. Glass P, Miller M, Short B. Morbidity for survivors of extracorporeal membrane oxygenation: neurodevelopmental outcome at one year of age. *Pediatrics* 1989; 83: 72-78.

32. Hofkosh D, Thompson AE, Nozza RJ *et al.* Ten years of extracorporeal membrane oxygenation: neurodevelopmental outcome. *Pediatrics* 1991; 87: 549-55.