# Extracorporeal Membrane Oxygenation in the NICU

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*The purpose of this article is to provide an overview of extracorporeal membrane oxygenation in neonatal patients.*

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## ABSTRACT

Extracorporeal membrane oxygenation (ECMO) was developed for adults but has been used in neonates as a life-saving rescue therapy for infants with respiratory failure and/or cardiac collapse as a result of congenital diaphragmatic hernia, meconium aspiration syndrome, persistent pulmonary hypertension, or systemic sepsis. ECMO has been proven to increase the survival rate for these diseases. This article provides an overview of neonatal ECMO: the history and development of neonatal ECMO, patient selection criteria, clinical management, the ECMO circuit, weaning from ECMO, and possible complications of ECMO.

**Keywords:** extracorporeal membrane oxygenation; neonatal; life support

Extracorporeal membrane oxygenation (ECMO) has improved the survival of patients after more conventional therapies have failed. ECMO utilizes a mechanical oxygenator and a blood pump as substitutes for the respiratory and cardiovascular systems to deliver oxygen, remove carbon dioxide, and assist the heart. It is basically a long-term, modified heart-lung bypass machine.

## HISTORY

Seventeenth century physiologists conducted experiments proving oxygenation of the blood was not dependent on lung inflation and deflation.[1] These experiments gave rise to artificial perfusion and oxygenators, which were developed in the late 19th century. Bubble oxygenators were the first extracorporeal oxygenators, where oxygen was directly bubbled through blood to oxygenate it.[1] This original bubble oxygenator accomplished the oxygenation by shaking the blood and air within a balloon device. But, when the blood and air come into direct contact during oxygenation, there can be damage to the red blood cells and the platelets.[1] Many scientists developed improvements in the actual methods used to oxygenate the blood, with various types of membranes and devices that allowed diffusion of oxygen and carbon dioxide. In 1916, the discovery of heparin was key to preventing coagulation of the blood.

John Gibbon developed a device that was successfully used on the first adult open-heart surgery patient in 1953.[1,2] In 1971, Dr. Donald Hill performed the first successful ECMO treatment on an adult patient in respiratory failure.[3] By 1975, the use of ECMO in the adult population was increasing, but, because survival rates were very low, most institutions had stopped using ECMO therapy to treat adult patients with respiratory failure.[3] The low survival rate in adults was due to the extensive damage already done to the lung from years of respiratory failure or ventilation insults. This resulted in a very high mortality rate in adults.

Dr. Robert H. Bartlett, a thoracic surgeon, began his work on extracorporeal circulation during his residency training in 1965, with a goal to improve the efficiency of the




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membrane oxygenators. His primary motivating factor was that many of the pediatric patients with congenital heart defects died during postcardiac surgical repair due to low cardiac output and respiratory failure. Dr. Bartlett initially worked with ECMO therapies on sheep in the research lab using a semipermeable membrane oxygenator. These membrane oxygenators were similar to the heart-lung bypass machines used in cardiac failure patients, but the heart-lung bypass machines could only be used for short periods before damage or hemolysis of the blood cells occurred and caused death. Therefore, Dr. Bartlett worked on oxygenators that could be used for longer periods of time for the pediatric cardiac surgery patients.[1,4]

In 1975, a pregnant immigrant woman crossed the Mexico-California border to deliver her daughter in the United States.[3] Her baby was born with meconium aspiration syndrome (MAS) and developed persistent pulmonary hypertension (PPHN). At that time, the only option for treatment was conventional ventilator therapy. The baby was deteriorating rapidly with a $PO_2$ of 12 when, as a last resort, Dr. Bartlett placed the infant on ECMO. The infant had developed severe pneumonitis secondary to meconium aspiration and was managed on ECMO for three days, allowing her lungs time to heal. The infant survived neurologically intact and was adopted following discharge (Figures 1–3).[3,4]

By the early 1980s, ECMO was more widely used in the neonatal population and became a tool for treating newborn respiratory failure when other less invasive measures were not successful. In 1980, Dr. Bartlett moved back to the University of Michigan to continue his work and began ECMO training for other centers around the country. By 1986, 18 NICUs were using ECMO in practice.[3] It is interesting to note that ECMO therapy for pediatric and neonatal patients was introduced despite the low success rate seen with adult patients. With most neonatal disorders, the neonatal lung is able to repair itself with a period of rest from high-ventilatory treatment. Mortality rates are higher for infants with diaphragmatic hernia than for those with a strictly respiratory diagnosis (e.g., MAS or PPHN).

There was much controversy over the use of ECMO as a treatment for respiratory failure during the late 1970s and early 1980s because of the lack of a randomized, controlled trial.[1,3] The high survival rate of patients given the treatment

**FIGURE 1 ■ Esperanza, the first neonatal ECMO survivor, 1975.**

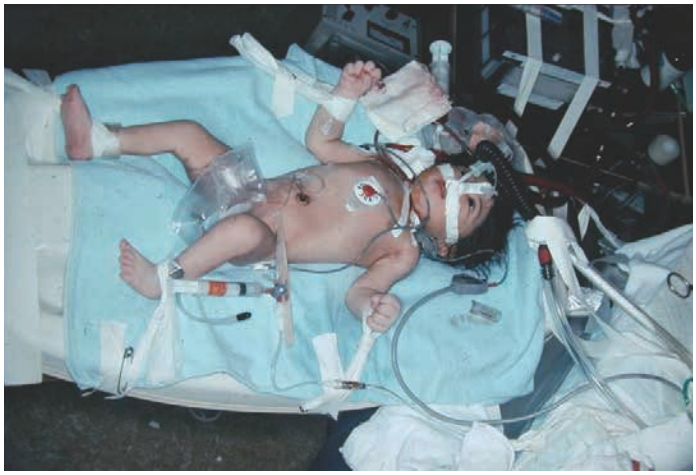


**FIGURE 2 ■ Esperanza, 6 months.**

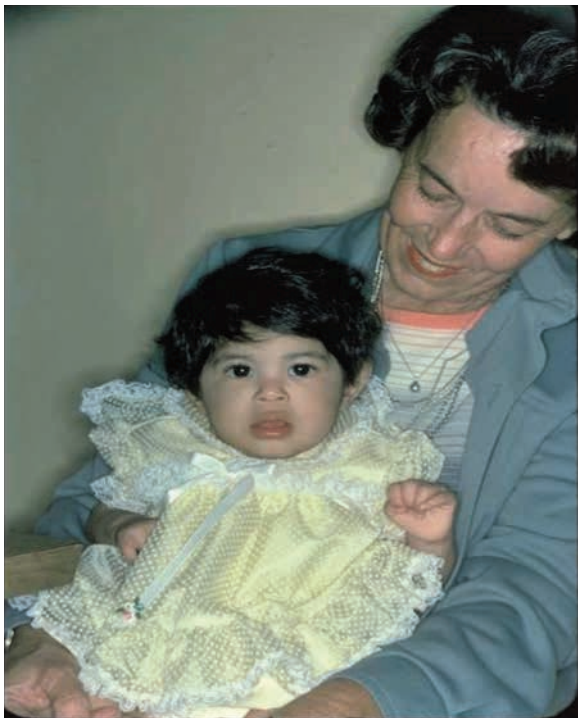


**FIGURE 3 ■ Esperanza, age 21.**

also caused many physicians to question the ethics of not providing this intervention. The controversy persists even today, following the development of other therapies like high-frequency ventilation, nitric oxide, and surfactant, which have made ECMO treatment nearly nonexistent for neonatal respiratory disorders.

The Extracorporeal Life Support Organization (ELSO) was founded in 1989. ELSO consists of physicians, nurses, perfusionists, and other health care providers who share their outcomes with each other and provide ECMO guidelines for all practicing facilities.[5] ELSO still provides resources and training for credentialing personnel and maintains a current database of participants who received ECMO treatment.

## NEONATAL PATIENT SELECTION

Infants who meet the criteria for ECMO will usually have some type of severe respiratory failure or cardiovascular collapse despite being on maximum conventional therapy. Maximal conventional therapy consists of surfactant administration, inhaled nitric oxide, cardiovascular medication, and high-frequency ventilation. Several disease states in the newborn period may cause respiratory failure or cardiovascular collapse, including PPHN, respiratory distress syndrome, MAS, and congenital diaphragmatic hernia (CDH). Surgery for congenital heart disease can also be an indication for ECMO therapy. ECMO may be required after surgery to accommodate the infant's adjustment to a postsurgical cardiovascular state.[5]

When selecting patients, it is imperative to determine if the infant's disease is reversible. ECMO is a supportive process, highly invasive, and associated with many risks. Only extremely ill infants with a high prediction of mortality (greater than 80 percent) should be selected for ECMO therapy.[6] Calculating the oxygenation index and alveolar-arterial (A-a) oxygen difference are ways used to determine eligibility for ECMO treatment.[6,7] Specific neonatal criteria used to determine eligibility are listed in Table 1.

Certain patients are excluded from ECMO treatment because of the increased chance of complications. Infants weighing less than 2 kg are not candidates for ECMO therapy because current cannula sizes are too large for small infant vessels.[5] Infants with active bleeding problems are usually not considered for treatment due to the high risk of increased bleeding while on ECMO. The ECMO circuit is primed and maintained with heparin to prevent coagulation of the blood during treatment. Heparinization of the blood and circuit increases the risk for intraventricular hemorrhage (IVH) in premature infants or infants with an existing hemorrhage. Infants who have a lethal anomaly are also excluded from treatment. Exclusion criteria are listed in Table 2.

Infants who are asphyxiated in utero or who meet criteria for head or body cooling can also meet ECMO criteria. The cooling guideline can be altered to prevent further coagulation complications caused by the cooling process and heparinization.[5]

**TABLE 1 ■ ECMO Criteria**

| Test | Calculation | Criteria for Treating |
|---|---|---|
| Oxygenation index (OI) | (mean airway pressure $\times$ $FiO_2$ $\times$ 100)/ postductal $PaO_2$ | Greater than 40 |
| Alveolar-arterial (A-a) oxygen difference ($AaDO_2$) | (713 $\times$ $FiO_2$) $-$ ($pCO_2$/0.8) $-$ ($PaO_2$) | Greater than 600 mmHg |

**TABLE 2 ■ ECMO Exclusion Criteria**

| |
|---|
| Weight < 2,000 g (2 kg) |
| Active bleeding |
| Existing intraventricular hemorrhage |
| Lethal birth defects or anomalies |

## NEONATAL CANNULATION AND MANAGEMENT

Once the decision is made to place the infant on ECMO, three personnel teams are notified: the medical team, the surgical team, and the circuit specialists. The medical team consists of neonatologists, intensive care nurses, and respiratory therapists. The neonatologist notifies the surgical team and the circuit specialists that an infant meets ECMO criteria. The circuit specialists include a cardiovascular perfusionist, respiratory therapist, and registered nurses. Once the patient is placed onto the pump, the circuit specialists are responsible for priming the pump and managing ECMO, in collaboration with the attending ECMO physician.[5]

Preparing the environment and infant prior to cannulation is a priority. The team clears the room of excess equipment to make space for the ECMO circuit. A Replogle-type nasogastric (NG) catheter and a Foley bladder catheter are placed prior to heparinizing the infant to prevent traumatic bleeding. The team keeps 1 to 2 units of packed red blood cells (RBCs), fresh frozen plasma, and platelet concentrate at the bedside.[5] It is important to use packed RBCs that are less than 5 days old to ensure RBC viability, low potassium levels, and a higher hemoglobin concentration.[5] Baseline lab work is obtained: blood type and screen; electrolyte panel including ionized calcium, blood urea nitrogen (BUN), creatinine, and glucose; complete blood count including hemoglobin, hematocrit, and platelet count; and coagulopathies including prothrombin time (PT), partial thromboplastin time (PTT), and disseminated intravascular coagulation screen.[5]

Extracorporeal life support or ECMO is obtained by cannulation of the venous system and the arterial system. Two methods of cannulation are commonly used: the

veno-venous (VV) and veno-arterial (VA) methods. VV bypass maintains pulmonary blood flow but with less effective cardiac support. With VV bypass, a double-lumen catheter is placed within the right atrium via the internal jugular vein to drain and infuse the blood. VA bypass is typically used to allow the heart to heal after cardiovascular collapse.[5] The VA approach requires placement of two catheters with cannulation of the right carotid artery and the right internal jugular vein. During VA ECMO, blood exits the body from the venous catheter in the right atrium, is oxygenated, and then reenters the body through the carotid artery. VA is the most widely used method in the neonatal population even though there is obliteration of the carotid artery upon decannulation. The reason for its wide use in neonates is that it provides support for the cardiac circulation. The VV method provides no support for the circulation and less oxygenation of the blood due to immediate mixing of the blood in the right atrium.[3]

After the teams are ready to begin cannulation, the infant is prepared. Most centers do not incorporate the use of an anesthesiologist during the procedure because general anesthetics are not used. Before the procedure, the infant is given a systemic narcotic for pain control, a short-acting muscle relaxant, and a local anesthetic at the site of cannulation.[5] Once the vessels for cannulation are located, the infant is heparinized. Heparin is administered at 50 to 100 units/kg and allowed to circulate a few minutes prior to obtaining an activated clotting time (ACT). The normal ACT in the neonate is somewhere between 70 and 180 seconds, but it varies widely. The ACT goal when treating a neonate with ECMO is 200 to 250 seconds to prevent catheters from clotting during the procedure.[5] Maintenance heparin is adjusted to maintain an ACT less than 300 seconds while the infant is on ECMO. Usual maintenance dosing is infused at approximately 20 to 50 units/kg/hour.[5]

Once the infant is placed on the ECMO pump, the initial pump flow setting is 50 mL/minute.[5] After a few minutes, the pump flow is increased to maintain the venous pressure greater than −25 cm $H_2O$.[5] During the flow adjustment, systemic vasopressors can be weaned since the ECMO pump now supports the infant's blood pressure and perfusion. Infants can experience hypertension after initial placement on the pump due to improved cardiac support; therefore, weaning of inotropes is required to prevent hypertension and subsequent hemorrhagic complications.[5]

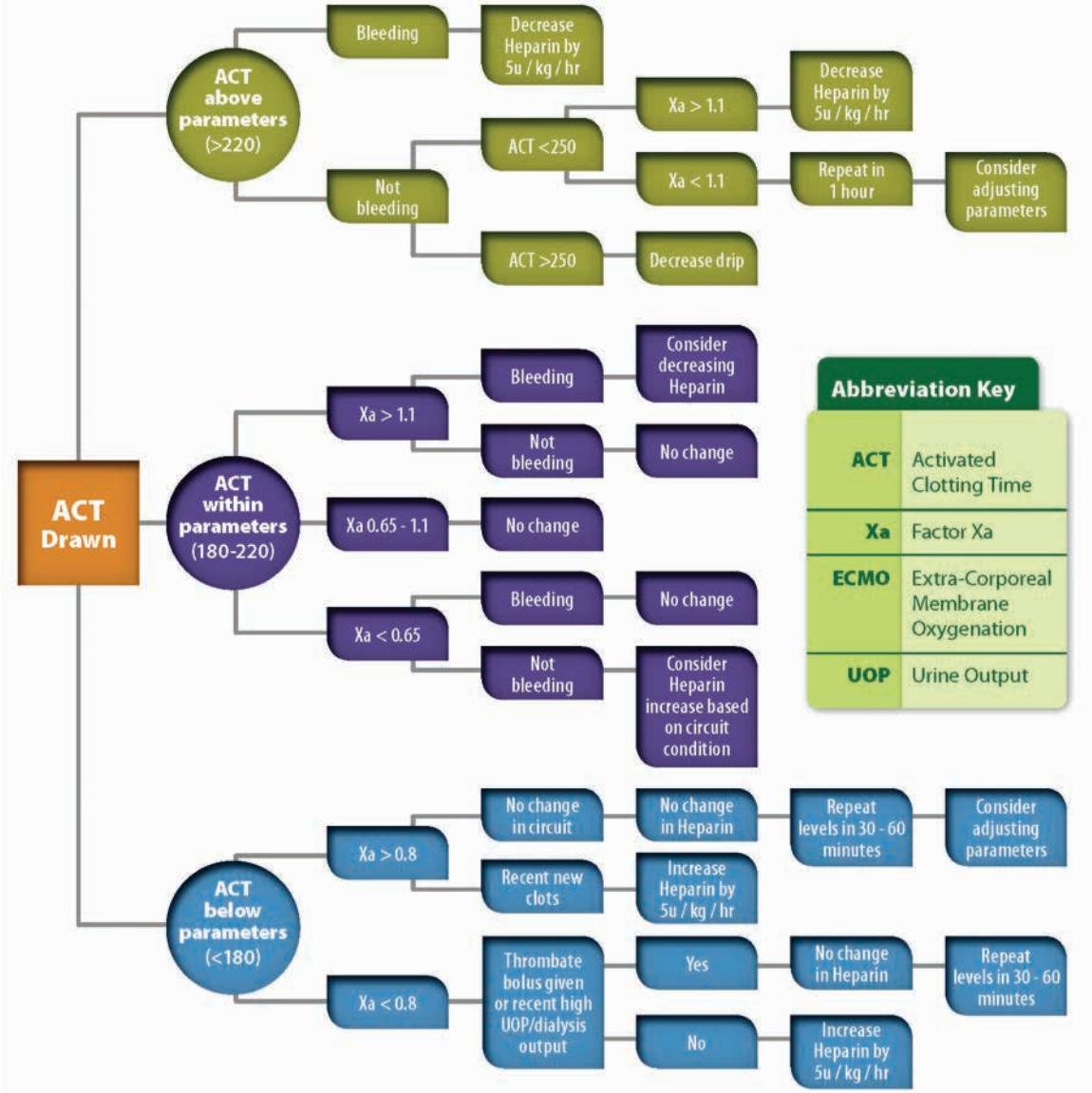
Because oxygen delivery and removal of carbon dioxide is being provided by the ECMO circuit, the ventilator can be weaned to "rest settings." Minimal ventilator settings are used. The goal for mechanical ventilation during ECMO is to prevent atelectasis and maintain lung expansion.[5]

The patient is monitored very closely while on the ECMO pump. The circuit specialists monitor the pump and pump parameters, while the registered nurse and respiratory therapist monitor the infant and provide routine care. Vitals signs are documented hourly. An ACT is obtained hourly to monitor coagulation status. The heparin infusion is adjusted based on the results (Figure 4). The tubing of the ECMO system inherently consumes platelets (platelets stick to tubing), and the flow of blood through the tubing and pump causes hemolysis of the RBCs (the mechanical process of the pump can compress and break the RBCs).[5] A basic metabolic panel of electrolytes (Na, K, $CO_2$, Cl) with BUN and creatinine is obtained every 4 hours along with platelet count, hematocrit, and a lactate to monitor the level of hemolysis and acidosis. To monitor for bleeding, a PT, PTT, and fibrinogen are obtained every 8 hours. An arterial blood gas from the ECMO circuit and from the infant are obtained periodically as needed but at least every 12 hours. Daily lab work includes a coagulopathy evaluation of thromboelastography, a comprehensive metabolic panel (basic metabolic panel with liver function studies), and an anti-thrombin III.[5]

## MONITORING OF THE ECMO CIRCUIT

The goal of ECMO is to support the patient while allowing the injured organs time to rest and heal. The venous cannula drains deoxygenated blood from the right internal jugular vein. The blood enters the ECMO circuit by passing through compliance chambers. The compliance chambers are an essential part of the system. Monitoring of the compliance chambers allows the perfusionist to quickly assess the volume level of the patient and circuit.[5] Hypovolemia or low volume levels in the chambers causes an increase in negative pressure on the venous tubing and right atrium. Causes of low volume include kinking of the tubing or cannula or loss of fluid or blood. Blood is pulled from the patient into the compliance chamber using either a roller pump or occlusive pump. The blood is then pushed forward into the oxygenator, and oxygenated blood is eventually pushed back into the arterial system through the right carotid artery into the aorta. Gas exchange occurs in the oxygenator. The oxygenator is made of silicone rubber sheets that are wrapped around plastic screens, which prevents blood from coming in direct contact with the gas.[5] Oxygen is added by adjusting the $FiO_2$ from the flow meter to the oxygenator. The flow of the circuit determines how fast the blood is pushed through the ECMO pump and how fast it returns to the infant. This is measured in mL/kg/minute through the oxygenator. Average flow settings are 100 to 200 mL/kg/minute depending on the carbon dioxide and oxygen levels.[5] However, the greatest oxygenating factor is the hemoglobin content of the blood. Desired hematocrit levels are kept higher than 35 percent for greater oxygen delivery to the tissues.[5] Increasing the hemoglobin improves oxygen delivery to the tissues. Blood within the ECMO circuit cools quickly, so it is important to regulate the heat exchanger to maintain the temperature of the blood at 37°C.[5]

**FIGURE 4 ■ ECMO coagulation algorithm.**




Infants frequently demonstrate transient acute tubular necrosis (ATN) once placed on ECMO. It is unclear if ECMO is the sole cause of ATN, but hypoxia, hypovolemia, and acidosis are known causes of end-organ damage.[8] A hemofiltration device can easily be added to the circuit to clear renal by-products from the circulating blood. This hemofiltration removes these toxins from the blood while retaining blood cells and proteins.[5]

Weaning of the ECMO flow is based on many factors. Improvement in the chest x-ray, arterial blood gases, and saturations must occur prior to weaning. The pump's lowest flow setting is 50 mL/kg/minute. Once the infant is stable on the lowest flow, a trial without ECMO may be attempted.[5] The ventilator settings are increased, and the circuit bridge is opened. The circuit bridge allows the pump to continue running blood through the circuit in case the infant fails to come off ECMO. Decannulation of the infant occurs after he has met defined institutional criteria.[5]

## COMPLICATIONS

The circuit specialist team constantly monitors the ECMO circuit and pump for complications. Many complications can be prevented if caught early. If a complication does arise and the infant needs to be removed from the ECMO pump, the circuit is clamped and unclamped in this order: venous line, bridge, and arterial line.[5]

Inadvertent decannulation is a preventable complication. Light sedation of the infant prevents him from dislodging the cannulas. During routine turning of the infant, the team must communicate movements with each other and move in unison. Another common complication is clot formation in either the circuit or the baby. Clots form from stagnation of blood or cell lysis caused by turbulent blood flow. Small clot formation is not damaging to the system or the infant, but monitoring for larger clot formation is imperative.[5] During ECMO, air embolism may occur secondary to a leak in the circuit. As reported by the ELSO registry, air embolism accounts for about 4 percent of all complications.[5] Tubing rupture and infection are other documented cannula complications.

Extra personnel must be readily available in case of an emergency such as pump failure or rupture. Additional personnel are needed if pump failure occurs. Pump failure can be due to power failure or mechanical failure. One individual would be needed to hand-crank the pump, while the other person problem-solves the issue and monitors the patient.[5] Because the infant is heparinized, bleeding in the lungs, gastrointestinal system, or brain (IVH) can be life threatening. Oozing or bleeding can also occur following nasal suctioning, intravenous catheter placement, heelsticks, or other nursing care. Bruising may become apparent while on ECMO.

Overall, neonatal outcomes have been relatively good for newborns treated with ECMO. Survival rates are better (approximately 80 to 90 percent) for respiratory disorders than for cardiac defects or CDHs (approximately 50 percent).[3] Outcomes are dependent on the initial diagnosis, length of time on conventional ventilation prior to institution of ECMO, incidence of chronic lung damage, incidence of cardiac or respiratory arrest, and complications during ECMO treatment.

## CONCLUSION

Advances in neonatology continue to improve medical management of the neonate. The use of inhaled nitric oxide, surfactant replacement therapy, and high-frequency ventilation have decreased the need for the highly invasive therapy of ECMO. Yet even with these past advances, infants continue to develop pulmonary hypertension and CDH. When necessary, ECMO still remains a rescue therapy for many of these neonatal diseases with an overall survival rate greater than 80 percent.[6]

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