Extracorporeal Life Support

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CHAPTER 1

Mechanical Ventilation

Efforts to support the respiratory system significantly predate the introduction of extracorporeal life support (ECLS). Before there were oxygenators and centrifugal pumps, pulmonologists had been supporting patients with artificial respiration. Ventilatory support evolved from the early use of bellows for ventilation.

I. History

A. 1555
Vesalius used bellows ventilation to keep animals alive while demonstrating his experiments.

B. Early 20th Century
Numerous tubes, masks, and positive-pressure ventilatory apparatus were developed for resuscitation and for delivering anesthesia.[1]

C. Early 1900s
Automatic artificial ventilators were developed by Fell,[2] and then made available commercially by Draeger[3] in 1907.

D. Late 1920s
"Iron Lung" was developed to provide mechanical ventilation for victims of poliomyelitis by a negative pressure system. The polio epidemic of 1952 stimulated further research into mechanical ventilation: the Danish experience with hand ventilation in polio patients led to a fall in mortality from 80 to 23% (Fig. 1.1).

E. 1940s
Bennett developed a portable machine to deliver oxygen to aircrew during the WWII. The first large scale production of reliable ventilators stemmed from designs by Blease.[4] These were used primarily for anesthesia. Other ventilators included pressure-cycled devices developed by Bennett and Bird.

II. Current Modes of Ventilation

A. Assist Control Ventilation
Tidal volume (V_T), F_iO_2, and minimal ventilator frequency are set, but additional breaths are provided whenever the patient initiates an inspiratory effort of sufficient magnitude. The control or backup respiratory rate assures a baseline minute ventilation. Preferred mode of ventilation for a patient with a normally functioning brainstem and respiratory center.

B. Control-Mode Ventilation (CMV)
Ventilator breaths are time-cycled and either volume-limited or pressure-limited. In this mode the patient is not allowed to participate in any phase of respiration. Appropriate for patients under anesthesia, paralyzed, heavily sedated, or suffering from brain-stem injury.

C. Intermittent Mandatory Ventilation (IMV)
Time-cycled controlled mechanical ventilation. Respiratory rate and tidal volume are preset. Additional spontaneous breaths are patient generated

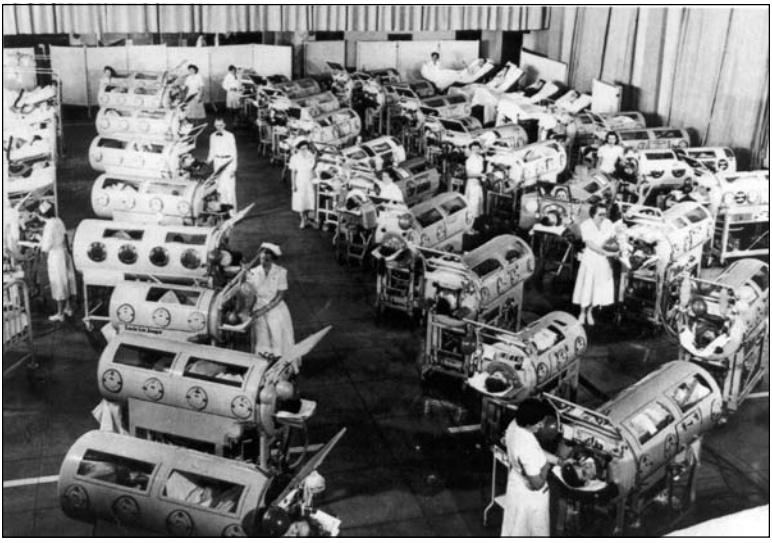

Fig. 1.1. Caring for patients with polio at Rancho Los Amigos Hospital in Los Angeles, circa 1950. Reprinted with permission from March of Dimes.

and may be of small volume. Developed to minimize the mean intrathoracic pressure by allowing the patient to perform some of the work of breathing.

D. Synchronized Intermittent Mandatory Ventilation (SIMV)
Modification of IMV in which the controlled V_T is delivered at the time of spontaneous inspiratory effort (i.e., effort cycled).

E. Over time, other modes were developed and functions added to the commercial ventilators (Fig. 1.2). Ventilatory modes were diversified to adapt to an expanding range of pulmonary conditions. A common goal is to maintain lung volume which may in turn decrease sheer stress, recruit functional residual capacity (FRC) and increase surfactant production (Table 1.2).
   1. Pressure Support Ventilation (PSV)
   Adds a pressure-cycled component to the basic volume-cycled mechanism. Allows airflow to occur until a preset pressure threshold is reached. This pressure is a function of the inspiratory flow rate, the impedance of the machine's delivery system, and the patient's respiratory system, all of which are in series. The patient initiates all breaths. The primary purpose of PSV is to overcome the resistance of the circuitry during the weaning period.
   2. Pressure Control Ventilation (PCV)
   Inspiratory time is set in this feature. A preset system pressure is rapidly achieved and maintained throughout inspiration by adjusting

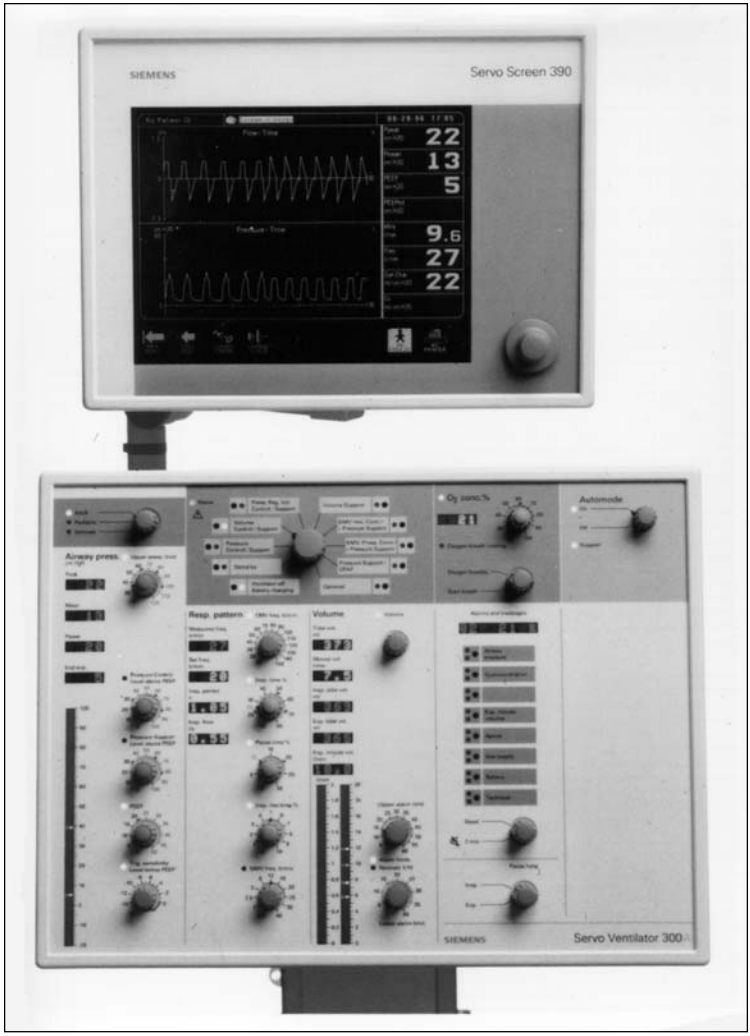

Fig. 1.2. The current Siemens servo 300 series ventilator.

machine inspiratory flow. The resulting decelerating flow pattern avoids overdistension and may provide better distribution of gas.

3. Inverse Ratio/Pressure Control Ventilation (IRV)
   Provides a relatively long inspiration time and a short expiratory time with the result that mean airway pressure is increased without a con-

comitant rise in peak airway pressure. Often used in severely hypoxic patients. Intrathoracic pressure is usually higher than with conventional inspiratory/expiratory ratios, which may adversely effect venous return.

4. Airway Pressure Release Ventilation (APRV)
   Adds a periodic pressure release mechanism that allows a spontaneously breathing patient to exhale a lower volume. This mode allows ventilation to be assisted without causing increases in already high inspiratory airway pressures.
5. Permissive Hypercapnia (Protective Ventilation)
   A ventilatory strategy for adult respiratory distress syndrome (ARDS), this technique limits airway pressure and tidal volume while permitting hypercapnia. In theory, by minimizing distension of the alveoli, the incidence of lung injury will be reduced and recovery may be improved. However, a prospective study[5] randomizing 120 patients to this technique (peak inspiratory pressure (PIP) at <30 cm H_20,V_T <8 ml/kg) or conventional ventilation (PIP allowed to rise to 50 cm H_20, V_T 10-15 ml/kg) showed no difference in mortality, incidence of barotrauma or organ failure. In another study, efforts toward limiting the inspiratory pressures of mechanical ventilation was performed in a group of 53 patients with early ARDS.[6] Patients were randomly assigned to either conventional ventilation (maintain lowest possible positive end expiratory pressure (PEEP) for adequate SaO_2, V_T 12 ml/kg, normal $PaCO_2$) or protective ventilation (low PEEP, V_T 6 ml/kg, PIP <20 cm H_2O, permissive hypercapnia). Early survival was better in the protective-ventilation group (62% vs. 29%, p<0.001) as was success in weaning from mechanical ventilation (66% vs. 29%, p = 0.005). However, no significant difference in survival to hospital discharge was found (55% of the protective-ventilation group survived, as compared with 29% in the conventional-ventilation group, p = 0.37).
   Another report, from the Acute Respiratory Distress Syndrome Network,[7] demonstrated an improvement in survival in patients with ARDS by adopting a ventilator strategy of lower V_T. These investigators showed that in a multicenter, randomized trial of patients with ARDS, a lower V_T (6 ml/kg) and a plateau pressure of 30 cm H_20 or less, was associated with decreased mortality (31% vs. 39.8%, p = 0.007) and increases in the number of days without ventilatory support (12+11 vs. 10+11; p = 0.007), when compared to traditional ventilator settings (V_T 12 ml/kg) and a plateau pressure of 50 cm H_20 or less.

F. Advanced Ventilatory Support
   Treatment of more neonatal and pediatric maladies contributed to the development of various types of high frequency modes of ventilation.

Table 1.1. Disease processes associated with respiratory failure

Diffuse Homogenous Lung Disease

Conditions: Respiratory distress syndrome (RDS) in premature infants, and pneumonia (especially Group B *streptococcus*), pulmonary hemorrhage and ARDS in the term infant.
Pathophysiology: The pathophysiology includes edema, atelectasis, decreased lung compliance and ventilation/perfusion mismatch.
Goals: Specific goals of ventilator management are to improve lung inflation, compliance, and ventilation/perfusion matching while avoiding barotrauma or negative effect on cardiac inotropy.
Results: Survival profile not as favorable as that of meconium aspiration syndrome. Data conflicting regarding nonconventional forms of respiratory support versus routine mechanical ventilation. Some etiologies of respiratory failure may be more amendable to successful treatment with ECMO.

Nonhomogeneous Lung Disease

Conditions: Meconium aspiration syndrome (MAS) is the most common process in this category, and the most common process requiring ECMO.
Pathophysiology: MAS results from the presence of meconium within the airways, leading to postnatal airway obstruction, inflammatory reaction and surfactant inactivation. Pulmonary hypertension and/or myocardial dysfunction may also be present.
Goals: Support gas exchange until the component of airway obstruction is resolved. Hemodynamic support may be necessary early in course.
Results: Response of patients with MAS to HFO is low (only 30% patients responded to HFO with an increase in oxygenation), but those that did respond were able to avoid the need for ECMO. The vast majority of patients that did not respond to HFO required ECMO for adequate gas exchange. As HFO does not promote airway clearance of meconium or mucus plugs, air trapping may ensue and lead to barotrauma.
Because of the maintenance of lung volumes and sometimes elevated intrathoracic pressure, decreased venous return may ensue, reducing cardiac output. In patients with limited reserve, ECMO may still be required. A subset of patients with MAS appears to simulate RDS. These patients may respond better to HFO support.

Lung Hypoplasia Syndromes

Conditions: Includes neonates with congenital diaphragmatic hernia (CDH).
Pathophysiology: Combination of ipsilateral lung hypoplasia and persistent fetal circulation.
Goals: The goal of therapy in this group of patients is to provide maximal oxygenation at the lowest possible mean airway pressure while supporting the patient during periods of persistent fetal circulation. A complex protocol is required to manage this disease process, with the major emphasis on avoiding overinflation. HFO ventilation often used in this setting prior to use of ECMO.
Results: These patients typically have not had a great response to HFO, although in a series of 15 patients with CDH who were candidates for ECMO, 27% responded to HFO and did not require ECMO.[7] Management of these patients with HFO is difficult, and ready access to ECMO is critical.

continued on next page

Table 1.1. continued

Airleak Syndromes

Conditions: Pulmonary interstitial emphysema (PIE) is the most common airleak disease process requiring ECMO.
Pathophysiology: PIE is manifested pathologically by dilated distal bronchioles and diffuse alveolar collapse.
Goals: The goal of management is to improve lung inflation, while avoiding overinflation that may cause rupture of the dilated distal airway and exacerbate the underlying condition. An important aspect of the management of these patients involves transition from HFO to CMV, again requiring extensive experience in ventilator management.
Results: With the emergence of HFO, the need for ECMO in this population has decreased significantly. HFO provides adequate ventilation and oxygenation at lower peak and/or mean intrapulmonary pressures than conventional ventilation, allowing the airleak to be controlled and sealed.

1. high frequency positive-pressure ventilation (HFPPB) at rates of 60-110 per minute;
2. high frequency jet ventilation (HFJV) at rates of 110-400 per minute;
3. high frequency oscillatory (HFO) ventilation at rates above 400 and up to 2400 per minute.

The goal of these modes is to limit airway pressures. These techniques, used in an increasing number of patients,[8] have enabled the avoidance of ECMO for some conditions (Table 1.1) including: (1) diffuse homogeneous lung disease, (2) nonhomogeneous lung disease, (3) lung hypoplasia syndromes, and (4) airleak syndromes. Conditions associated with severe airleak, pulmonary hypertension and poor cardiac performance may respond poorly with all forms of ventilation, and may still require ECMO. The goal of therapy, whether mechanical ventilation or ECMO, is to support the infant while the pathophysiologic state is reversed.

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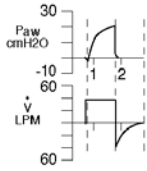
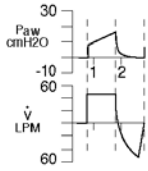
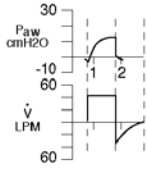
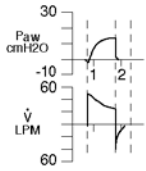
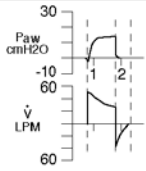
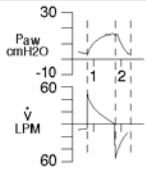
Table 1.2.

Mode	Airway Pressure / Airflow Pattern	Primary use	Benefits
CMV		Abnormal respiratory drive (under anesthesia, sedated, brain stem injury).	Preset V_T delivered regardless of inspiratory effort.
AC		Normal brainstem and respiratory center. Versatile mode used in postoperative patients and to rest patients.	Preset V_T activated by patient effort. Insured minimum respiratory rate.
SIMV		Recovering, awake patients. Weaning mode.	Commonly available. Assisted set V_T. Not dependent on compliance. Patient-ventilator synchrony. Patient allowed to take spontaneous breaths.
PSV		Weaning mode.	Best support of V_T during each breath Decreased work of breathing. Patient controls depth and timing of inspiratory flow. Patient comfort on ventilator.
PCV		Severely hypoxic. Hemodynamically stable.	Peak airway pressure precisely controlled. V_T supported during each breath. Inspiratory phase ends when the preset pressure limit is achieved.
PCV-IRV		Profound hypoxia. Adequate hemodynamics.	May increase mean airway pressurewithout significantly increasing peak airway pressure.

tory machines. In: Atkinson RS, Boulton TB, eds. The History of Anaesthesia. London: Royal Society of Medicine 1987:386-93.
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Extracorporeal Support

I. Cardiopulmonary Bypass

A. First Extracorporeal Perfusion

While early investigators reported experiences with experimental extracorporeal perfusion (Brown-Sequard 1848-58) and functioning oxygenator (Von Frey and Gruber 1888), it was John H. Gibbons Jr. (1937) who reported the first successful experimental heart-lung bypass circuit, and developed an experimental method of managing the otherwise fatal complication of pulmonary emboli.[1] After a career designing the technology, he developed an apparatus and techniques to a point where 12 of 20 dogs survived the closure of a surgically created ventricular septal defect (VSD) for 1 week to 6 months.[2]

B. The first attempt to use a heart-lung machine to repair intracardiac defect was by Dennis and colleagues, April 5, 1951 at University of Minnesota Hospital.[3] The first two patients operated upon within one week's time both died in the operating room. The first patient had a misdiagnosis of what preoperatively was thought to be a secundum atrial septal defect. At operation, this was actually a partial atrioventricular canal lesion, which at that time, could not be repaired. The second patient did have a secundum atrial septal defect (ASD) repaired but died intraoperatively of a massive air embolism.[4]

C. Although his first patient died, Gibbon reported the first successful clinical use on May 6, 1953, for the successful treatment of an atrial septal defect in an 18-year-old woman. Gibbon's next 2 patients both died using cardiopulmonary bypass (CPB), and he became discouraged, never again performing open-heart surgery.

II. Cross-Circulation

A. Dr. C. Walton Lillehei at the University of Minnesota introduced the concept of cross-circulation as an alternative means of into circulatory support for cardiac surgery. Cardiopulmonary bypass was felt to be associated with major physiologic disturbances that were poorly understood at the time. Much of the rationale for this work was based upon the azygous flow principle, a realization that the body could tolerate periods of lower flow. Volume of blood needed to be pumped decreased, allowing improved visualization because of less blood volume returning to the heart. Moreover, the cannulas could be positioned completely out of the operative field by using a separate donor animal for oxygenation (cross-circulation) (Fig. 2.1).

B. On March 26, 1954, a VSD was repaired by Dr. Lillehei.[5] The technique was used in 45 cases, with 28 (62%) of the patients surviving to hospital discharge. Twenty-two patients (49%) were still alive after 30 years. None of the donors died. By 1955, improved oxygenators were developed and cross-circulation was replaced by cardiopulmonary bypass.

III. Oxygenators

A. Early biologic oxygenators attempted to utilize both canine lungs[6] and monkey lungs[7] as oxygenators. Only a minute fraction of these patients survived.
B. 1955: Mayo-Gibbon screen oxygenator[8] (Fig. 2.2).
C. 1955: DeWall-Lillehei bubble oxygenator[9] (Fig. 2.3).
D. Membrane Oxygenators
   1. 1956: 1st successful membrane oxygenator (a device allowing blood to interface with gas over a large, thin, surface area) built by Clowes et al.[10]
   2. 1956: Kolff and associates described the use of a disposable membrane oxygenator. These had advantages over bubble oxygenators for longer cardiopulmonary bypass runs (>6-8 hours), with better biocompatibility manifested by a lesser degree of thrombocytopenia, complement activation, postoperative bleeding and microemboli.[11]
   3. The ease of use and lower cost of membrane oxygenators compared to the bubble oxygenators have led to their dominance in the market for routine open heart procedures (Fig. 2.4).

IV. ECMO–Acute Support

A. General
   1. 1971: First successful human clinical use of ECMO reported by Hill.[12]
   2. An early trial failed to show efficacy, due to patient selection.[13]
   3. Despite this, use of technology rose, peaking in 1992 with over 1,500 cases reported.
   4. Today, neonatal ECMO is decreasing in frequency due to the availability of other technologies such as high frequency oscillating ventilation (HFOV), inhaled nitric oxide (NO), and surfactant therapy. In general, patients undergo ECMO for some complex disease processes as evidenced by the increase in the ECMO duration per patient in some studies. There has been a shift away from straightforward neonatal cases and toward more complex pediatric and cardiac cases. More patients with CDH and less neonates with RDS are undergoing ECMO therapy. Consequently, there has been an increase in the incidence of patient complications on ECMO.
   5. Results have been good, but have varied with age of patient and underlying condition. There has also been a significant decrease in the overall survival rate for patients treated with ECMO.[14] However, a recent report showed that when corrected for the relative increase in neonates with CDH, this trend disappeared.[15]

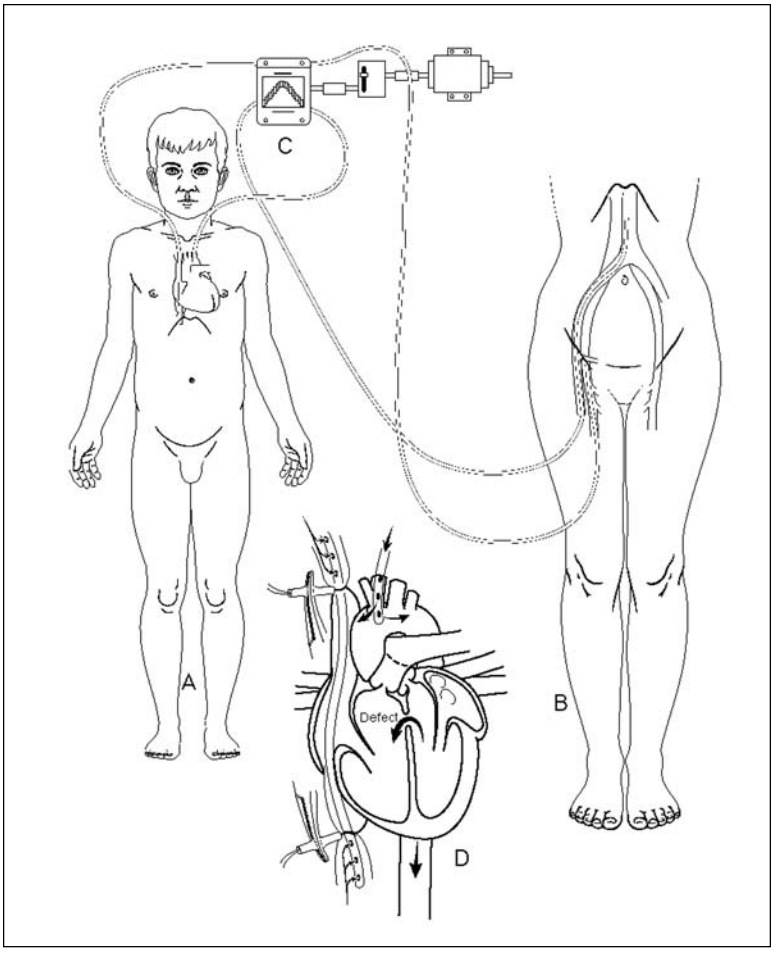

Fig. 2.1. Cross-circulation support technique for repair of an intracardiac defect.

6. Whichever therapeutic modality is selected when caring for these patients, if they are not responding appropriately, reassess the accuracy of the diagnosis.

B. Neonatal
   1. 1972: Initial research efforts in the laboratory of Dr. Robert Bartlett at the University of California at Irvine/University of Michigan targeted towards the management of respiratory failure in neonates led to the initiation of clinical trials of ECMO.
   2. 1975: The first successful clinical application of ECMO for the management of neonatal respiratory failure by Bartlett et al.[16] The initial

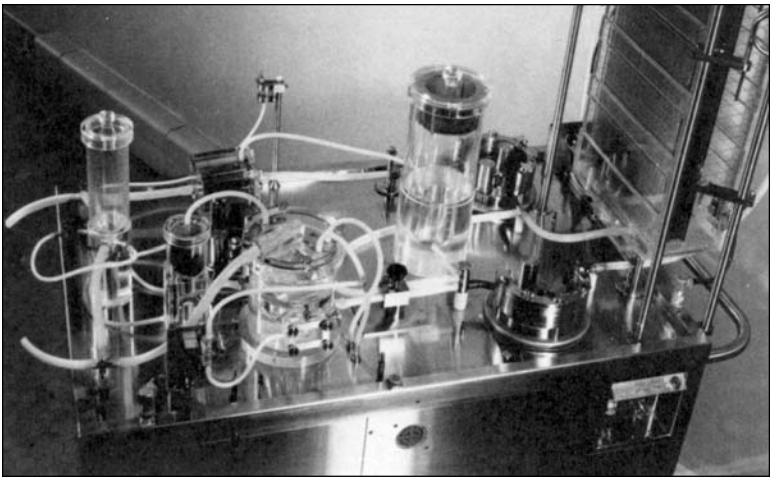

Fig. 2.2. The Mayo Clinic-Gibbon screen oxygenator. Used by Dr. John W. Kirklin and colleagues at the Mayo Clinic in 1955 (with permission).

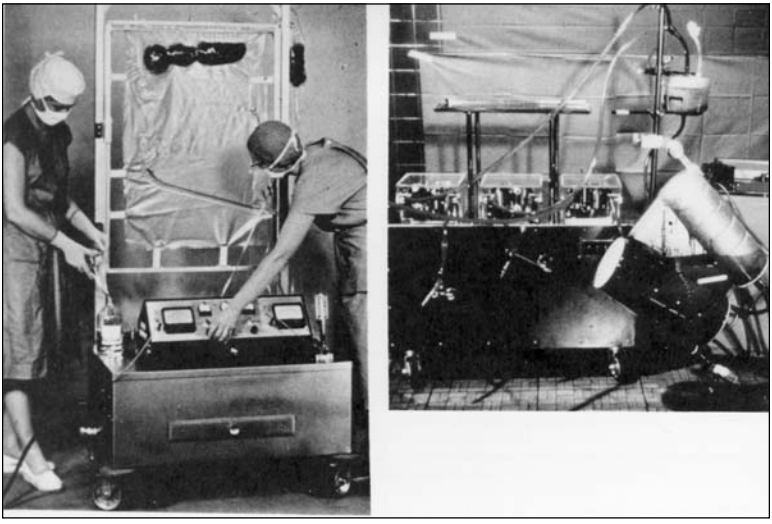

Fig. 2.3. The DeWall-Lillehei plastic sheet oxygenator (left panel). Disposable bubble oxygenator with built-in heat exchanger, shown here during a perfusion (with permission).

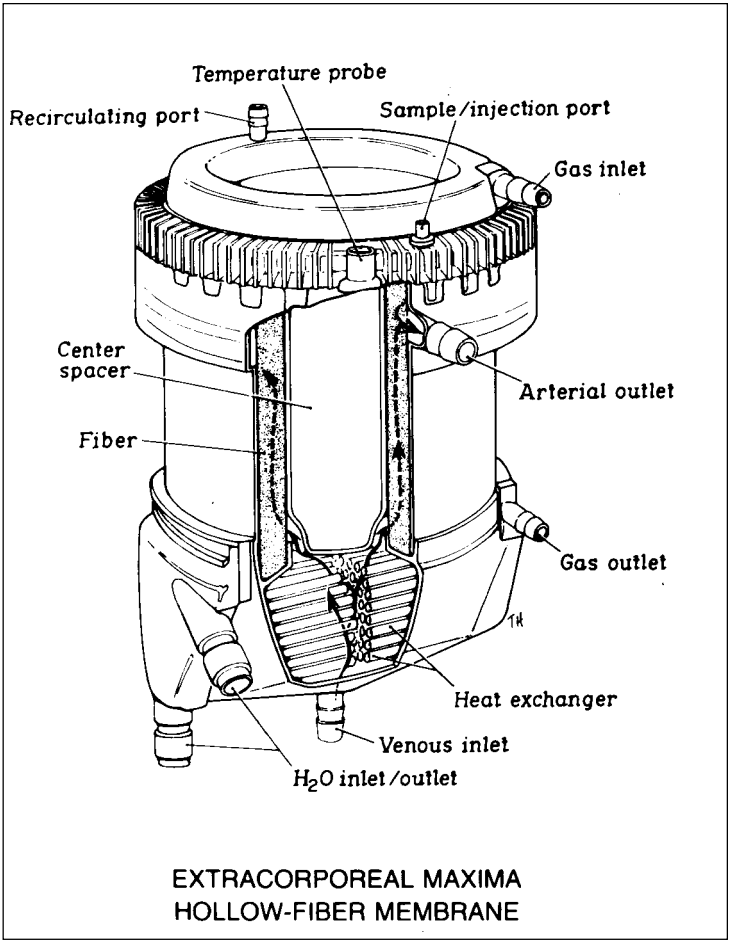

Fig. 2.4. The Maxima hollow-fiber membrane oxygenator. Used for short-term ECMO support, commonly in adults.

series of patients consisted of 45 newborns with 25 survivors, proving the efficacy of this technology. Predicted mortality in this group of patients without ECMO approximated 80-90%.

3. Currently, ECMO remains the treatment of choice for neonatal respiratory failure secondary to meconium aspiration syndrome, congenital diaphragmatic hernia,[17] primary pulmonary hypertension/persistent fetal circulation, and selected cases of hyaline membrane disease, pneumonia/sepsis, and air leak syndrome (Fig. 2.5).

C. Pediatric ECMO

In the pediatric population, use of ECMO is less extensive, with most

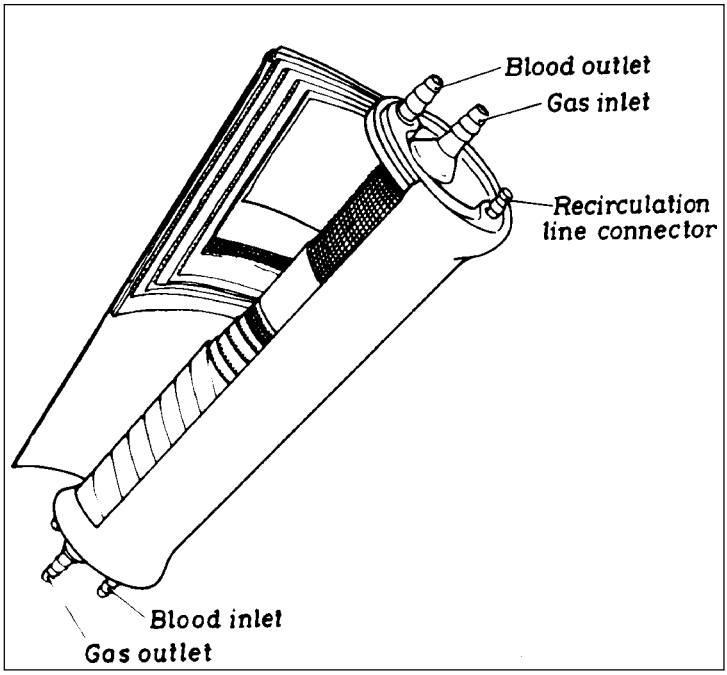

Fig. 2.5. The Avecor silicone rubber membrane oxygenator. The standard oxygenator used in neonatal ECMO and long term adult support.

reports detailing its application in respiratory failure from bacterial, viral, and pneumocystis pneumonias, aspiration, ARDS, intrapulmonary hemorrhage. Survival rate of ECMO in children has been between 40% and 70%, compared to 10% without this modality. Pediatric cases have the same problems experienced in adult populations: the diffuse, often irreversible disease processes in the pulmonary system.

D. Adult ECMO

1. Initially limited to use in neonates, applications expanded to include the pediatric population and adults with acute respiratory failure. In these latter groups, ECMO is much less well accepted. A National Institutes of Health (NIH)-funded study completed in 1979 and published in 1980 by Zapol and colleagues,[13] failed to demonstrate an advantage of ECMO over conventional mechanical ventilation for the management of ARDS. The survival rate with ECMO was 9.5%, compared with 8.3% using conventional treatment. These findings led many centers to limit use of this modality to the neonate with respiratory failure.
2. Gattinoni et al[18] used a modified ECMO technique of extracorporeal carbon dioxide removal ($ECCO_2R$) in adult acute respiratory failure.

Their new application of extracorporeal life support followed several principles. First, the purpose of ventilation is to excrete CO_2. Oxygenation can be achieved by inflation and airway oxygenation alone. Second, progressive lung injury in ARDS is caused in part by trauma from high ventilatory pressures or over distension injury of the more normal alveoli. Third, if the emphasis should be on CO_2 removal to eliminate the need for high pressure ventilation, this could be done with venovenous ECMO. Fourth, this system would allow for normal pulmonary blood flow, even if the lung was severely injured with large amounts of transpulmonary shunting. Used in adults in venovenous extracorporeal gas exchange with low frequency positive pressure ventilation in a variety of adult patients. In 1986, they reported 21 survivors in 43 patients (49%).

3. Morris and associates[19] compared use of extracorporeal CO_2 removal and pressure-controlled inverse ratio ventilation in patients with severe ARDS. A computerized protocol dictated the management of those patients randomized to the control, mechanical ventilation limb of the study. Survival was not significantly different in the 19 mechanical ventilation (42%) and the 21 extracorporeal (33%) patients ($p = 0.8$). The authors did not advocate ECMO for therapy for ARDS, and recommended its use be restricted to controlled clinical trials.
4. Recent experience with adult ECMO from European centers[20] has given some support to limited use of this technology in extreme situations for both children and adult patients. In a series of 14 patients with ARDS that did not respond to conventional ventilation, extracorporeal life support (ECMO) application resulted in survival in 9 (64%).

V. ECMO–Prolonged Support

A. General
   1. Use is mostly limited to adult applications, specifically, ARDS. Success with this technique, although not supported by controlled studies, has been used extensively in Europe, where adults with respiratory failure are supported for an average of 21 days.
   2. Survival in some series[20] has approached 60%, compared with 10% for patients receiving conventional therapy. Despite these results, its use in the U.S. has been infrequent.

B. Specific Studies
   1. A significant experience is that of Lennartz and colleagues[20] from University of Marburg, Germany. From August 1984 through December 1995, 182 patients were placed on ECMO. Mean duration of ECMO in recent cohort was 21 days. One-hundred-six patients (58%) survived. There was a trend toward increased survival in the group treated with heparin coated circuit (47.6 vs. 64%). Survival was also better in the younger age groups: 65.8% in patients less than 20 years, 63.6% in patients 20-40 years old, and 41% above 40 years.

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Principles of ECMO

I. General

A. Physiologic Changes on ECMO
   1. Given the closed ECMO circuit, the volume of blood removed by the cardiopulmonary bypass device is exactly equal the volume of blood reinfused. Therefore, there is no net effect on central venous pressure, right or left ventricle filling, or hemodynamics.
   2. One response is an initial fall in blood pressure with initiation of ECMO related to peripheral vasodilatation as a response to the blood contacting the synthetic surfaces, stimulating the complement cascade and other inflammatory pathways (Fig. 3.1).

B. Specific Types of ECMO
   1. Venoarterial (VA) ECMO
      a. Cardiopulmonary bypass circuit takes over the functions of both heart and lungs.
      b. Venous blood is drained and oxygenated, with the blood returning to the patient via the arterial system.
   2. Venovenous (VV) ECMO
      a. Venous blood is drained and oxygenated, as would occur in VA ECMO, but is returned to the venous circulation.
      b. Differs from VA ECMO in that the oxygen content of the blood in the right atrium is increased, as mixing occurs.
      c. Patient must be relatively stable hemodynamically, as the heart still provides primary support in this mode of ECMO. Some oxygenated blood is passed into the right ventricle, lungs, and into the systemic circulation, while some is returned to the ECMO circuit (recirculation). As the lungs improve, the oxygen content and CO_2 in the patient's arterial blood also improve because of ongoing pulmonary blood flow (Fig. 3.2).

II. Gas Exchange on ECMO

A. Oxygen Delivery
   1. Membrane Factors
      a. Factors related to adequate oxygenation
         i. membrane diffusion characteristics (thickness, materials)
         ii. membrane surface area
         iii. oxygen concentrations in sweep gas and blood
      b. Thickness of the Blood Path Layer
      c. FIO_2 on the ventilator

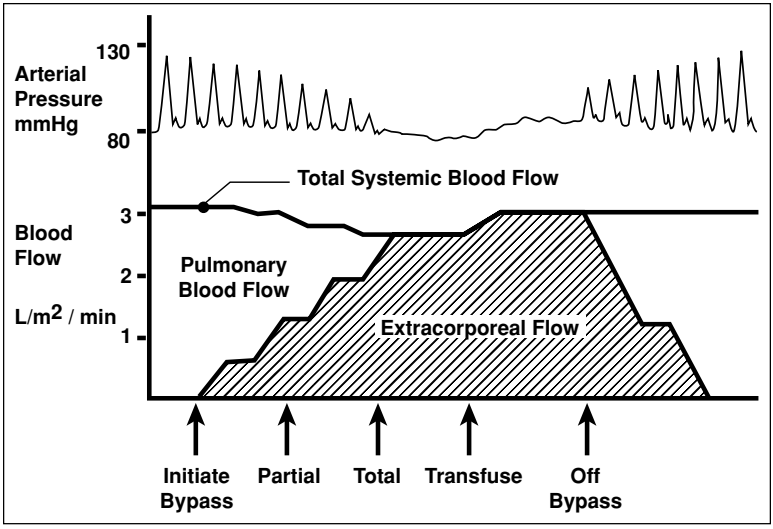

Fig. 3.1. Hemodynamic changes during ECMO (initiate ECMO, partial bypass/total bypass, off bypass)

d. Independent of Sweep Gas Flow Rate

2. Circuit Factors

Early during ECMO, most of the oxygen delivery is via the membrane oxygenator. While CO_2 elimination is dependent on gas flow, oxygen delivery relies on blood flow rate.

a. ECMO flow rate

Transit time of the red cells in the oxygenator

i. Relationship to rated flow of oxygenator. Rated flow of a membrane oxygenator is the pump flow rate at which maximal oxygen delivery is achieved (Fig. 3.3).

The geometry of the 0.8 m^2 membrane is such that the rated flow is 1000 ml/min, corresponding to an actual oxygen transfer of 50 ml/min. This information is important in choosing a specific oxygenator for a specific patient (Table 3.1). As long as the rated flow for the oxygenator is greater than the ECMO blood flow, the lung will be fully saturated and the amount of systemic oxygen delivery via the ECMO circuit is controlled by blood flow and the oxygen uptake capacity.

ii. When a membrane oxygenator is used below its maximal rated flow, the amount of oxygen delivery is inversely related to the saturation in venous blood.

iii. The driving gradient of oxygen into the blood layer is great and therefore the rate at which oxygen diffuses across the

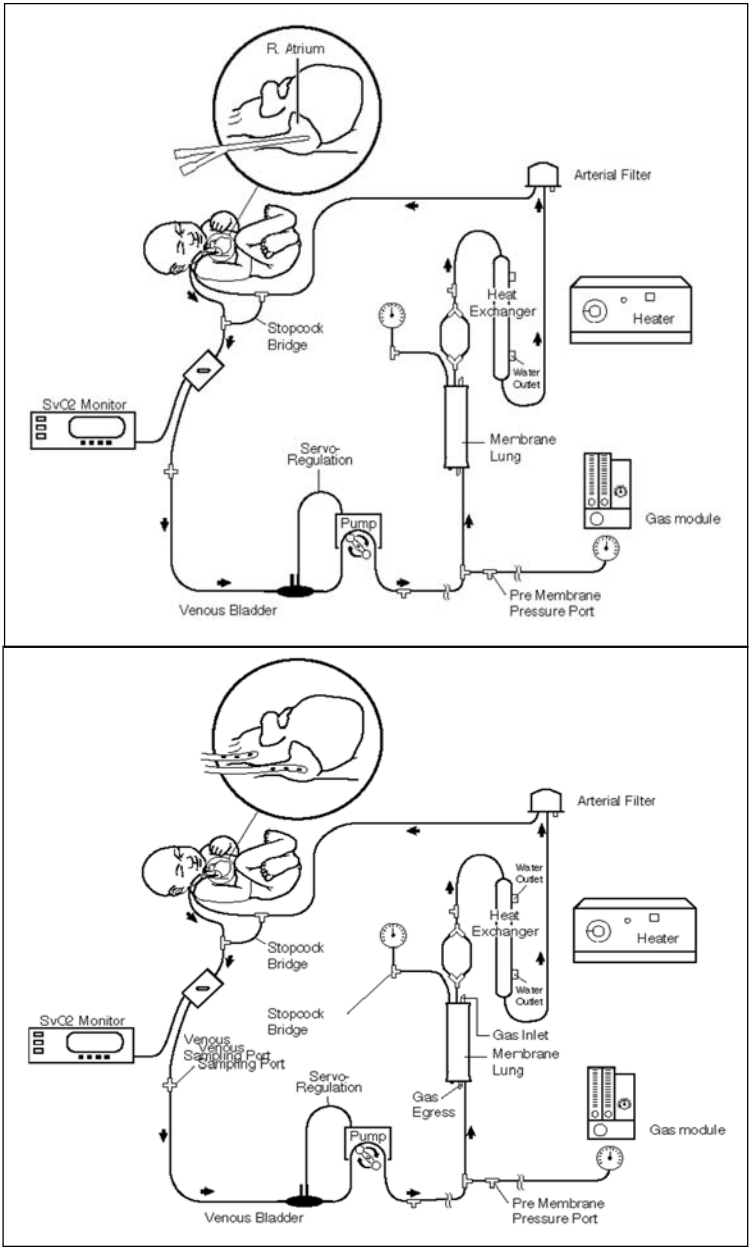

Fig. 3.2. Neonatal ECMO Cannulation options. A, top panel, Venoarterial ECMO; B, lower panel, Venovenous ECMO

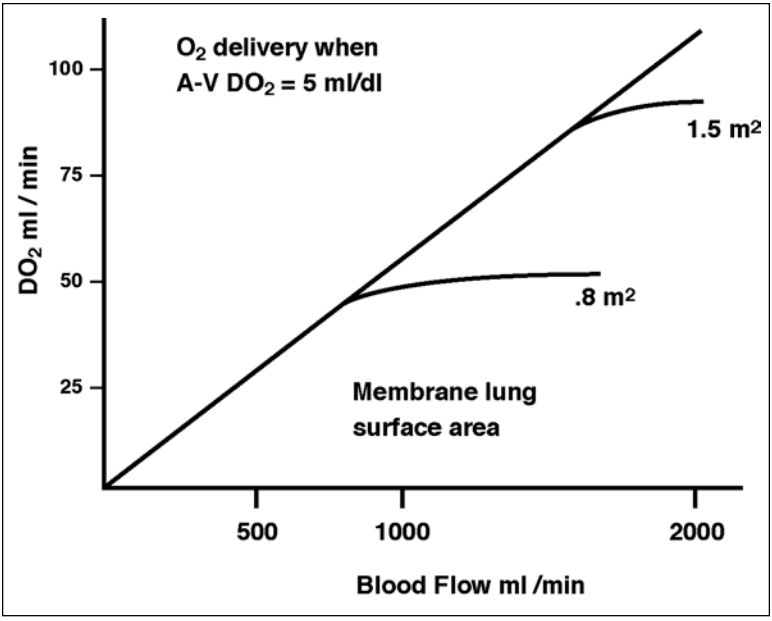

Fig. 3.3. The amount of oxygen delivered as a function of the surface area of the membrane. (Assuming that the AVO_2 differences is 5 cc/dl).

Table 3.1. Rated flow and gas exchange characteristics for different oxygenator sizes

Patient size (kg)	Avecor membrane lung surface area (m^2)	Rated flow (L/min)	Gas exchange (ml/min)
	0.4	0.5L	30
3-10	0.8	1L	60
	1.5	2L	120
10-30	2.5	3L	180
	3.5	4L	240
30+	4.5	5L	300

membrane lung may be rapid. Time is taken, however, for the oxygen to diffuse through the layer of blood. The challenge is for the oxygen to get through the layer in the limited amount of time.

b. The native lung is only able to contribute a small or negligible amount. In VA ECMO, cardiac support is also maintained by the

cardiopulmonary bypass circuit, with a variable contribution from the patient's native heart.

c. In VV ECMO, the arterial PaO_2 and SaO_2 will be identical to the values in the mixed right atrial blood. Therefore, the saturation will never be higher than 95%, and usually closer to 80% with a PaO_2 of about 40 torr. Systemic oxygen delivery is adequate as long as there is a compensatory increase in cardiac output.

d. Hemoglobin concentration
If the hemoglobin concentration is low or the venous blood saturation is high, the amount of oxygen that can be bound in the membrane lung is decreased. To compensate for decreased oxygen binding capacity, increase blood flow of the ECMO circuit or increase the hemoglobin concentration with a transfusion.

3. To increase the O_2 level:
   a. Increase the oxygen concentration in the sweep gas (inlet oxygen saturation),
   b. Increase pump flow rate, or
   c. Combination of both.

B. CO_2 Removal
1. CO_2 Production
   a. Affected by substrate oxidized. Ratio of CO_2 produced to O_2 consumption known as the respiratory quotient varies from 0.7 for fat to 0.8 for protein, to 1.0 for carbohydrates.
   b. Not affected by hemoglobin or cardiac output (unlike O_2 delivery).
   c. Affected by changes in ventilation. CO_2 is much easier to manage than O_2, as removal of CO_2 can be maintained at normal levels even during severe lung dysfunction.
2. Mechanical Factors for CO_2 Removal
   CO_2 removal on ECMO is usually less of a problem, as it is primarily dictated by the characteristics of the membrane oxygenator and the circuit.
      a. Membrane factors
         i. Membrane geometry
         CO_2 removal is independent of membrane thickness or blood path size
         ii. Surface material
         For any silicone rubber or microporous membrane oxygenator, CO_2 clearance will always be more efficient than oxygenation when the oxygenator is well ventilated and functioning properly.
         iii. Membrane oxygenator ventilating gas flow or "sweep flow." Usually the ventilating gas contains no CO_2 so that the gradient for CO_2 transfer is the difference between the blood $PaCO_2$ and zero.
      b. Circuit factors
         i. ECMO flow is of less importance in relationship to $PaCO_2$.

ii. Assuming there is no gas exchange across the native lung, the arterial PCO_2 will be the same as venous PCO_2, in VV ECMO. In VA ECMO, arterial $PaCO_2$ will be a function of mixing perfusate and pulmonary blood flow.

3. Modifying $PaCO_2$ on ECMO
   a. To manage excessive CO_2 removal and the resulting respiratory alkalosis: add CO_2 to the sweep gas in the form of carbogen (95% O_2, 5% CO_2), thus decreasing the gradient and decreasing the amount of CO_2 transfer to maintain an adequate arterial and postmembrane $PaCO_2$.
   b. To increase CO_2 removal, eliminate CO_2 in sweep gas and increase sweep gas flow rate
   c. Attempts in reducing CO_2 in physiologic range is of some importance, as attempts at pushing the CO_2 down (as in cases of pulmonary hypertension), may result in reductions in cerebral blood flow secondary to cerebral arteriolar vasoconstriction. The combination of decreased cerebral perfusion pressure, metabolic alkalosis, and systemic hypoxemia may impair cerebral oxygen delivery. Therefore, changes to alter $PaCO_2$ should be done slowly (over a period of 4-8 hrs) to prevent rapid reperfusion of the cerebrum with the risk of intracranial hemorrhage.

C. The Membrane Oxygenator
   1. Construction: The membrane lu involves a silastic membrane separating a column of air on one side and blood on the other (Fig. 3.4). The flow of gas and the flow of blood are traveling in opposite directions. The diffusion of gases across the membrane by this "counter-current" effect is the basis behind the functioning of the membrane oxygenator (Fig. 3.5).
   2. Function:
      a. CO_2 is much more diffusable than O_2. Compared to O_2 transfer, the movement of CO_2 is not as dependent on the characteristics of the membrane, thickness of blood phase, or rate of blood flow.
      b. The important issue is the relative tension of O_2 and CO_2 on each side of the membrane. When the difference between the blood and gas phase is great, diffusion of gases occurs. Diffusion stops when the concentration of O_2 and CO_2 in the gas phase equilibrates with that in the blood.
      c. Gas flow rate is also important. CO_2 excretion is limited by the speed at which the sweep gas equilibrates with the blood phase. Because of the smaller amount of CO_2 produced and the efficiency of diffusion, it is rare for the elimination of CO_2 to be a problem except with membrane damage.

III. Oxygen Consumption and Delivery

A. Oxygen Consumption (VO_2)

1. Defined as the amount of oxygen used by all tissue of the body in aerobic metabolism.
2. VO_2 is decreased by rest, paralysis, and hypothermia and increased by muscular activity, infection, hyperthermia, and increased levels of catecholamine and thyroid hormones. The metabolic rate (VO_2) in normal resting humans is 5-8 ml/kg/min in newborn infants, 4-6 ml/kg/min in children, and 3-5 ml/kg/min in adults.

B. Oxygen Delivery (DO_2)
1. Defined as the amount of oxygen delivered to peripheral tissues. DO_2 is usually 4-5 times the VO_2
2. Conditions that change VO_2 are usually matched by corresponding changes in DO_2
3. In disease states, the DO_2 may be insufficient for VO_2 requirements, leading to anaerobic metabolism, acidosis, etc. **The goals of ECMO are to increase DO_2 until resolution of the underlying pathologic process occurs.**

C. Calculations
1. VO_2 is measured as the product of tissue blood flow (cardiac output) and the extraction of oxygen by the tissue (the arterial—venous oxygen content difference).
2. Oxygen Content (CaO_2):
   [Hgb x O_2 sat x 1.36] + .00031 x pO_2
   oxygen bound to Hgb dissolved oxygen
   The dissolved oxygen component is usually very small compared to the oxygen bound to hemoglobin.
3. Oxygen consumption (VO_2) then, is measured as:
   $\underline{\text{C.O. x } (CaO_2 - CvO_2)}$,
   the cardiac output (C.O.) multiplied by the arteriovenous oxygen content difference. This fundamental equation gives rise to several useful facts.
   a. If C.O. stays constant, then conditions that give rise to increased VO_2 will manifest as a widening of the A-V O_2 difference. Usually, the arterial content is fixed as Hgb is maximally saturated. Under these conditions, more O_2 will be extracted by the tissues and the venous O_2 content (CvO_2) will fall. Devices that measure mixed venous saturation (SVO_2) are therefore useful as an index of VO_2 and tissue perfusion.
   b. If VO_2 increases, the body will attempt to compensate by delivering more O_2 to the tissues. This can be done by increasing C.O. or increasing CaO_2. **When C.O. cannot be increased further or the arterial blood cannot be adequately oxygenated (as in respiratory failure), ECMO support may be required.**
4. Oxygen Delivery (DO_2)
   a. ECMO support is valuable because of its ability to increase DO_2. It

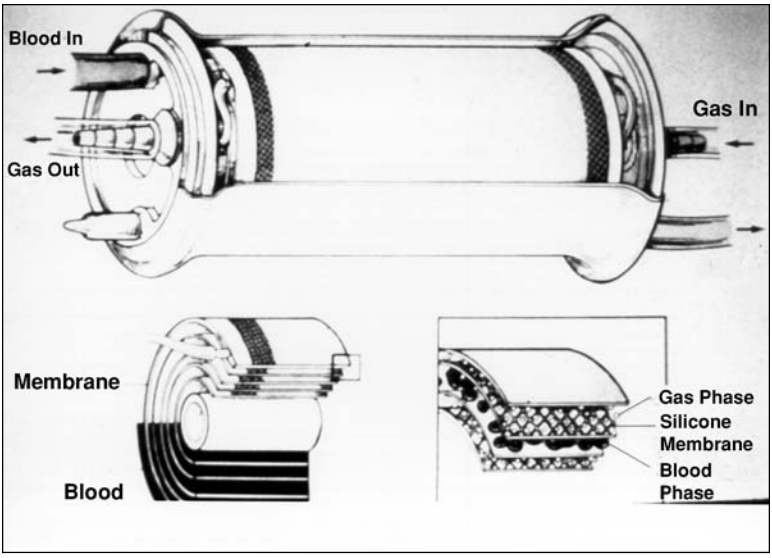

Fig. 3.4. Silastic membrane oxygenator

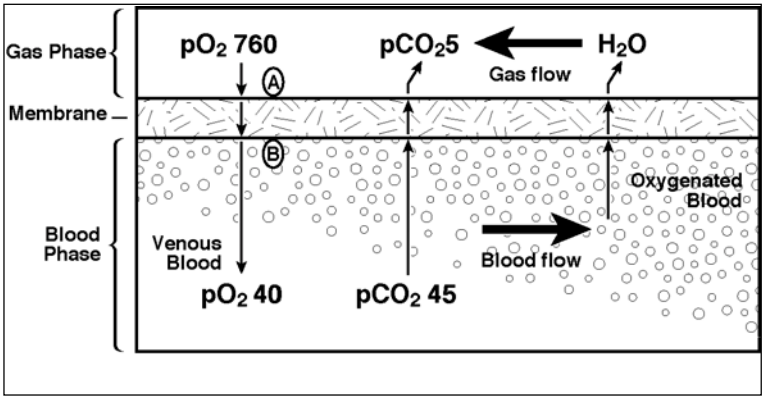

Fig. 3.5. Schematic of the counter-current effect

does this by providing increased flow and increased CaO_2. It is the only therapy that can support both components of oxygen delivery ($DO_2 = CaO_2 \times C.O.$).

b. Without resorting to ECMO, DO_2 can be increased by:
   i. increasing C.O. (for example, with inotropes)

ii. increasing CaO_2 by increasing Hgb levels (by transfusion of red blood cells)
iii. increasing O_2 levels in the arterial system (usually by increasing FiO_2 or modifying ventilation parameters)

c. ECMO support should be considered when these measures have failed and DO_2 is inadequate for the VO_2.
d. This failure will manifest as a fall in CvO_2 and can be measured as a fall in SVO_2.

5. Mixed Venous Oxygen Saturation (SVO_2)
   a. SVO_2 is normally about 75%, implying that only 25% of oxygen delivered is used by the tissues.
   b. If SVO_2 falls, this implies that the tissue oxygen supply is deficient.
   c. If SVO_2 is increased, this may mean that oxygen delivery has improved, or that oxygen demand has decreased. In extreme circumstances, it can also mean that perfusion is so poor and that the tissues are so damaged that there is an abnormally decreased tissue oxygen consumption.
6. Measuring SVO_2 on ECMO
   a. SVO_2 is a measurement of "mixed-venous" oxygen saturation, which reflects an average of oxygen content from all venous blood returning to the heart.
   b. Because blood returning to the heart via the IVC normally has a higher O_2 content than that returning via the SVC, obtaining a true value for SVO_2 is difficult.
   c. This is further complicated if left to right shunting occurs across a patent foreman ovale
   d. In patients not on ECMO, SVO_2 is usually measured from a pulmonary artery catheter. In patients on VA ECMO, pulmonary blood flow is decreased and may not accurately reflect SVO_2. It is generally recommended that SVO_2 be measured from the right atrium.
   e. However, because cannula position may affect SVO_2 readings, many clinicians rely more on changes or trends in SVO_2 as indicators of effectiveness of therapy.
7. Evidence of Improvement on ECMO
   a. VV ECMO
      As all blood delivered to the systemic circulation passes through the lungs, improvement in native lung function will manifest as a rise in arterial oxygen saturation, and a step up from venous to arterial saturation.
   b. VA ECMO
      In this mode, blood delivered to the systemic arteries comes from the ECMO circuit (which is fully oxygenated) and from ejection from the left ventricle (which has poorly oxygenated blood in respiratory failure). Therefore, the systemic PaO_2 may rise if lung function improves at constant ECMO flows. However, PaO_2 may also

improve without lung recovery if there is a relative increase in ECMO flow or a relative decrease in native cardiac output.

IV. Modes of ECMO

A. Venoarterial (VA) ECMO
   1. Background
      Although first used in adults in 1971, more widespread clinical applications for neonatal respiratory failure were reported in 1976 by Bartlett and associates. Since that time this technique has been performed in 15,000 neonates with survival rates approaching 80%.
   2. Advantages
      a. Full cardiorespiratory support allowing maximum rest for pulmonary and cardiac systems. Ability to offer support in situations of full cardiovascular collapse
      b. Maximize perfusion pressure to end organs
   3. Disadvantages
      a. Need to sacrifice carotid artery in neonates
      b. Potential for neurologic injury from vessel ligation or systemic embolization

B. Venovenous (VV) ECMO
   1. Background
      Since inception of the Extracorporeal Life Support Organization (ELSO) Registry to present, 2606 (18%) of the neonatal cases of ECMO utilized the venovenous approach. In recent years, use of VV ECMO has increased. The technique was studied by Kolobow and colleagues[1] in 1969, it was first used for neonatal respiratory failure in 1982.[2] Recent survival rates have been between 70-88%.
   2. Advantages
      a. Safety: avoids cannulation and ligation of carotid artery
      b. Using double lumen venous cannula reduces number of vessels required
      c. Less risk of systemic embolization
      d. Maintenance of adequate blood flow to lungs, may decrease risk of ischemic injury
   3. Disadvantages
      a. Does not provide circulatory support
      b. Lower oxygen level achievable, may not be adequate oxygen delivery in larger patients
      c. Two sites of cannulation sometimes necessary for adequate flow
      d. Potential for volume overload, as decreased renal function common during initial 48 hours of starting VV ECMO
      e. Recirculation: major disadvantage of VV ECMO
         i. Definition: recirculation fraction is the portion of oxygenated blood returning to the ECMO circuit immediately after being

infused into the patient. Recirculation fraction is calculated by:

$$R = \frac{SpreOx - SVO_2}{SpostOx - SVO_2}$$

where SpreOx is the oxygen saturation of blood entering the oxygenator, SpostOx is the oxygen saturation of the blood exiting the oxygenator, and SVO_2 is the true mixed venous oxygen saturation in the patient. The average recirculation fraction is around 30%.

ii. Incidence: Recirculation occurs to some degree in all VV ECMO patients (Fig. 3.6). Detected by observation of decreasing patient arterial saturation and increasing premembrane saturation. The blood draining from the right atrium will be nearly the same color as the blood returning from the pump. Factors affecting the degree of recirculation include catheter position, pump flow, cardiac output, and right atrial size (intravascular volume)

iii. Etiologies and solutions

a) Catheter position

1) Positioning of the double lumen catheter (DLC) is critical. With the patient's head in the midline, the arterial reinfusion port should be flat against the patient's neck behind the ear.

If a jugular and femoral vein approach is used (two-site VV ECMO), care must be taken to insure that the catheter tips are not in close approximation, otherwise recirculation will be high.

2) Management: catheter position should be checked with CXR as a first diagnostic step. Repositioning of the catheter with changing neck position or adding tension to the cannula may be of aid. If this is not successful, surgical repositioning may be warranted. Use of a cephalad cannula can help limit recirculation.

3) Cephalad catheter

The catheter placed into the right internal jugular vein towards the head, and advanced into the jugular venous bulb. This cannula decreases cerebral venous pressure, and may decrease intra-cranial pathology. Moreover, it adds to the venous drainage, contributing 35-50% of the total ECMO flow.

b) Pump flow

1) Directly related to the amount of recirculation: the higher the flow, the greater degree recirculation. The increased suction pressure causes streaming of oxygenated blood from the oxygen delivery port of the catheter to the venous drainage port.

2) Effective flow = total flow (1–recirculation fraction). As pump flow increases, the effective flow first increases, stabilizes, and then decreases. Optimally, pump flow would be the lowest level that produces the peak effective flow.
3) Management: monitor and adjust pump flow. If recirculation is high, (patient SaO_2 = 85%, premembrane SaO_2 = 86%), wean flow. If patient's saturations improve or stay the same, wean again. If they decrease, increase flow and look for other causes of recirculation.

c) Cardiac output
High cardiac output state decreases recirculation. If oxygenated blood delivered to the right atrium is rapidly moved into the right ventricle, it is less likely to be removed by the DLC. Efforts to modify cardiac output are sometimes needed, such as increasing heart rate or optimizing stroke volume using inotropic agents.

d) Right atrial size
A small atrial volume favors recirculation, as there is less room for the oxygenated blood to mix within the right atrium. Hypovolemia is treated by volume expansion as needed.

4. Types of VV ECMO
   a. One-site VV ECMO
   Commonly used for neonates. DLC available in sizes 12F-18F. If infant too small to accommodate a DLC, or too large to obtain adequate flows from the cannula, VA ECMO is used. Soon, larger DLC will be available for the pediatric and adult populations.
   b. Two-site VV ECMO
   Blood drawn from jugular system/replaced via femoral vein. For use in pediatric or adult population (>8 kg) due to the venous congestion associated with femoral cannulation in small patients. Some clinicians have advocated reinfusion of the oxygenated blood via the jugular vein, instead of the femoral vein, claiming improved oxygenation.
5. Patient selection
   a. Any hemodynamically stable neonate or child with acute respiratory failure is a candidate for VV ECMO
   b. Not recommended for patients with primary cardiac dysfunction. Patient must not require significant circulatory support such as after:
      i. Recent cardiac surgery
      ii. Recent cardiac arrest
      iii. Refractory dysrhythmias associated with hypotension
   c. Some hypotensive patients with biventricular failure may become hemodynamically stable after oxygenation improves on VV ECMO,

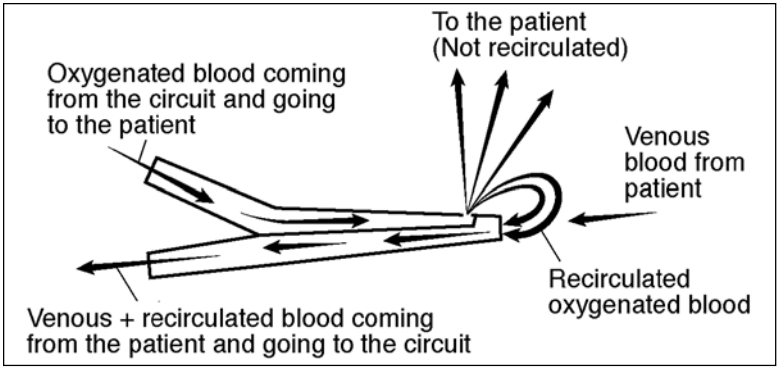

Fig. 3.6. The recirculation effect with a double lumen catheter.

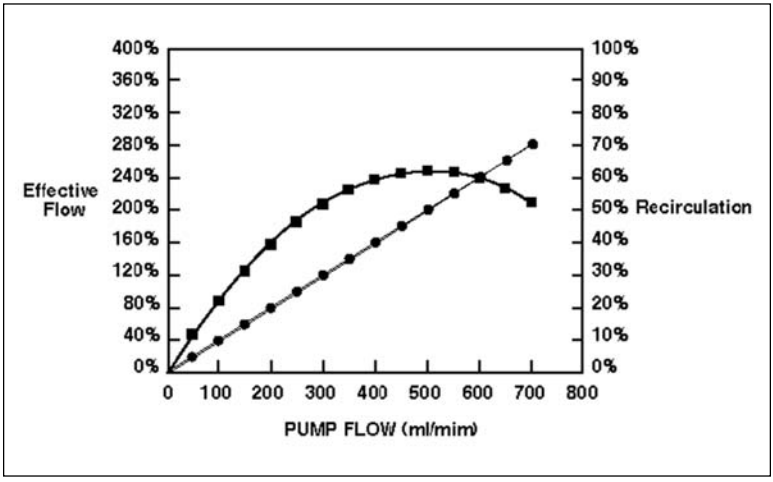

Fig. 3.7. Recirculation fraction (circles) increased almost linearly with increasing pump flow (squares). The amount of oxygen provided to the patient initially increases and subsequently decreases as pump flow increases beyond optimal rate. This decrease in effective oxygen delivery occurs when flow increases to greater than 500 ml/min.

allowing weaning cardiovascular drugs

d. If the primary goal is CO_2 removal ($ECCO_2R$), VV ECMO with relatively low flows may suffice.

6. Management
   a. Flow initiated at 20 ml/kg/min and increased slowly over a period of 15-20 minutes to a maximum of 150 ml/kg/min.
   b. Flow is then adjusted to meet the optimal oxygenation level. Typical flows are 110-140 ml/kg/min.

7. Measurement of oxygenation during VV ECMO
   In general, there is no reliable method to measure mixed venous oxygen saturation. Preoxygenator SaO_2 increases with increases in SVO_2 but also with increases in recirculation.
8. Most clinicians follow trends in:
   a. Preoxygenator saturation
   b. Pulse oximetry or arterial blood gas analysis
   c. Cephalad cannula saturations. These are also influenced by $PaCO_2$, as a fall in $PaCO_2$ will decrease the rate of blood flow measured in the cephalad cannula.

V. Cardiac

A. Cardiac Function on ECMO
   1. Hemodynamic changes
      a. Systemic blood pressure
         Blood pressure on ECMO is best expressed as mean arterial pressure (MAP) and typically the only means of expression in VA ECMO.
         i. Initiation of ECMO
            Causes a transient fall in systemic blood pressure due primarily to vasodilatation related to the inflammatory response to extracorporeal circulation. The degree and duration of this fall is partially related to the initial status of the patient.
         ii. During ECMO
            1) Increased afterload
               Once stabilized, patients on ECMO usually exhibit increased afterload. This may result from changes in the renin-angiotensin system.[10] Vasodilators, such as hydralazine, may be required to reduce the afterload. Inadequate sedation and hypervolemia may also contribute to the hypertension. Regardless of the cause, management of the hypertension is imperative, as the incidence of intracranial hemorrhage (ICH) is significant in this setting.
            2) Decreased afterload
               As ECMO is a closed system, any fall in systemic pressure in the setting of stable preload and cardiac output (native cardiac output plus pump flow) is due to a fall in systemic vascular resistance. This loss of vascular tone may result from pharmacologic manipulations or sepsis.
         iii. Afterload differences: VV vs. VA ECMO
            Increase in afterload is less frequently seen in VV ECMO than in VA ECMO. Fall in pulmonary vascular resistance is seen with VV ECMO, thought to be secondary to pulmonary vasodilatation from highly oxygenated blood being delivered to the pulmonary circulation.
      b. Heart rate
         Heart rate tends to be lower on ECMO. This may relate to the

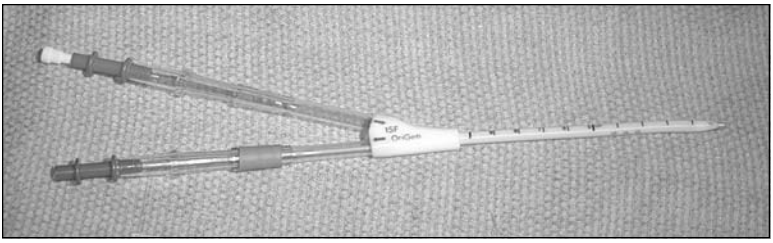

Fig. 3.8. DLVV ECMO cannula.

Table 3.2. VA vs. VV ECMO

	VA ECMO	**VV ECMO**
Cannulation site used	R IJV/RA or CFV Plus RCCA, axillary, CFA, or Aorta (direct)	RIJV +/- CFV Saphenous vein, or RA directly
Usual goal PaO_2	80-150 torr	45-80 torr
Indicators of Oxygenation	SVO_2 or PaO_2	SaO_2 or PaO_2 Cerebral SvO_2 Premembrane O_2 trend
Cardiac effects	Decreased preload Increased afterload Variable CVP Coronary oxygenation by LV Cardiac stun syndrome	Minimal effects on CVP, pulse pressure unaffected, Coronary O_2 improved may decrease RV afterload
Pulmonary circulation	Diminished	Unchanged
Circulatory support	Partial to complete	No direct effect but cardiac function may improve with improved oxygenation

RIJV—right internal jugular vein; CFV—common femoral vein; RCCA—right common carotid artery; CFA—common femoral artery

normal baroreflex response — a fall in heart rate with increased blood pressure.[4] In VV ECMO, lower heart rates may result from improvement in the oxygenation, correction of acidosis, and reduction of endogenous and exogenous catecholamines.

c. Cardiac contractility
Contractility is often described as decreased while on ECMO as

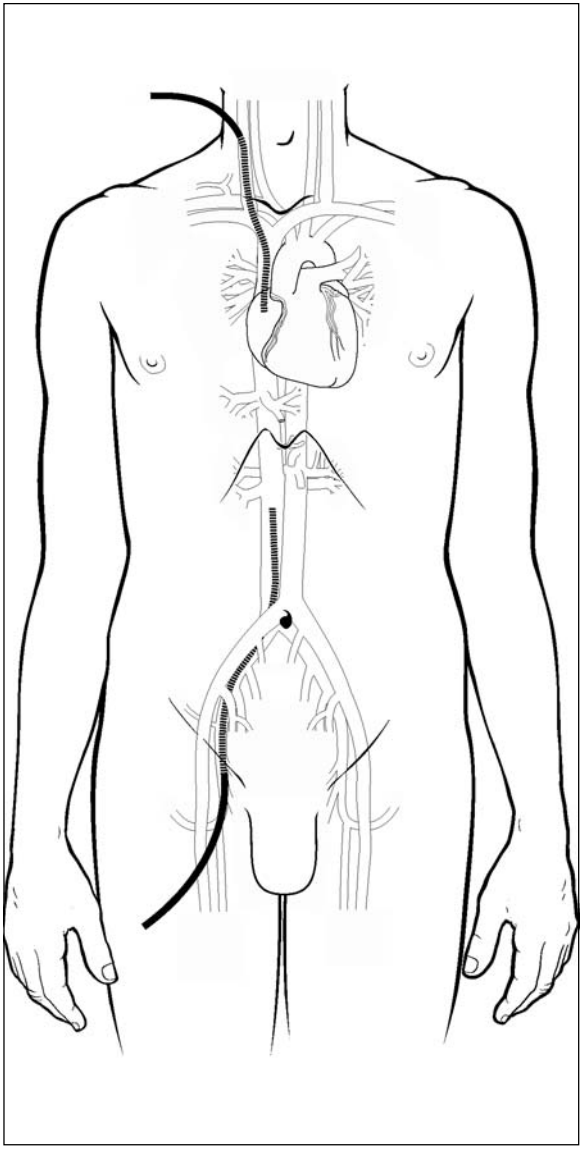

Fig. 3.9. Two-site VV ECMO

there is a decrease in left ventricular ejection phase indices and a fall in shortening fraction. However, studies using load-independent measures of systolic performance have shown that contractility is preserved during bypass when normalized for afterload.[5]

d. Summary

As demonstrated in Table 3.4, both right and left sided systolic pressures are damped with full VA ECMO support and conventional pressure indices of cardiac filling are rendered inaccurate.

2. Cardiac dysfunction

a. Changes in cardiac performance including left ventricle (LV) distension can occur on ECMO and may be due, in part, to loading conditions. Increasing ECMO flows may decrease left ventricular preload, but also increase LV afterload. If the afterload increase is the dominant effect, the LV may dilate further. Decreasing ECMO flow may actually reduce afterload and allow the patient to eject, thereby decreasing LV volume and relieving distension. However, flow must remain sufficient for adequate tissue perfusion.[6,7]

b. VA ECMO

A syndrome of cardiac stunning may occur with the initiation of ECMO. The etiology of myocardial stun is not fully elucidated but may be related to a reperfusion abnormality resulting in the release of oxygen-free radicals and the associated tissue damage after the initiation of ECMO. The presence of mismatch between afterload and myocardial contractility after starting ECMO may also play a role.[7] LV stunning typically resolves over a 48-hour period. Failure to see improvement after 4-5 days of ECMO support is worrisome and may suggest myocarditis or myocardial infarction.

c. VV ECMO

Any decrease in cardiac function is usually secondary to hypoxemia and acidosis and not to a primary cardiac cause. Cardiac function may improve with the improvement in oxygenation from ECMO. Perfusion of the pulmonary arteries more highly oxygenated blood may decrease pulmonary vascular resistance and right ventricular afterload. Rarely, cardiac dysfunction may be due to right ventricular stun. As the RV dilates, the interventricular septum encroaches on the LV chamber, compromising filling and cardiac output. Efforts at reducing RV afterload can be of use in management of these patients.

B. Changes in Blood Volume Distribution on ECMO

1. Vasodilatation

a. As ECMO is a closed circuit, any decrease in preload results from vasodilatation at the initiation of ECMO. This, in turn, results from an inflammatory reaction as the blood contacts the artificial surfaces of the tubing and especially the oxygenator. Inflammatory mediators activated include complement, cytokines, kinins, interleukins, oxygen-derived free radicals, and prostaglandins.[8]

Table 3.3. Chart of suggested blood pressures and heart rate by patient age.

Age	Blood pressure		Heart rate (bpm)	
	Systolic	Diastolic	Awake	Sleeping
Neonate (1 mo)	85-100	51-65	120-160	80-180
Infant (6 mo)	87-105	53-66	90-140	70-120
Toddler (2 yr)	95-105	53-66	80-110	60-90
School age (7 yr)	97-112	57-71	75-100	60-90
Adolescent (15 yr)	112-128	66-80	60-90	50-90

(Levin and Morris. Pediatric Critical Care. 1999, with permission)

b. Vasodilatation later in the ECMO course may be secondary to sepsis or acidosis

2. Fluid requirements
   a. Initial fluid requirements may be significant, but after stabilization, increased requirements may indicate sepsis, bleeding, or an intraabdominal process such as pancreatitis.
   b. Capillary leak syndrome often accompanies the onset of ECMO and is again related to the inflammatory response. Pulmonary capillary leak can result in a chest x-ray appearance of near total opacification. Blood volume distribution initially expands to the periphery, but equilibrates over time, unless capillary leak persists. The capillary leak syndrome typically resolves over 48-72 hours.

C. Peripheral Tissue and Organ Perfusion on ECMO
   1. With satisfactory ECMO support, peripheral perfusion should be adequate, with warm extremities and acceptable urine output.
   2. Microsphere studies[9] in an animal model demonstrated that ECMO did not significantly change overall blood flow to different regions of the body. In VA ECMO, tissue perfusion can arise from ECMO circuit flow or ejection from the native left ventricle. Studies have demonstrated that blood from the VA ECMO circuit flows preferentially into the arch vessels, while coronary and abdominal visceral blood flow arises primarily from left ventricular ejection.

VI. Pulmonary

A. Pulmonary Blood Flow
   Pulmonary blood flow decreases as ECMO flow is increased on VA ECMO but is maintained on VV ECMO (Fig. 3.10). Extent of decrease is directly proportional to the amount of flow through the extracorporeal circulation.[10]

B. Gas Exchange on ECMO
   Primarily dependent on the functioning of the membrane lung. There is typically very little contribution of the native lung to oxygenation or to CO_2 elimination. Oxygen uptake through the native lung as well as cardiac output through the pulmonary circulation may contribute to gas exchange to a limited degree. As native pulmonary function improves, however, gas

Table 3.4. Hemodynamics on VA ECMO.

Monitored parameter Hemodynamics	Non-ECMO Hemodynamics	VA ECMO
Arterial waveform	Reflects systole and diastole	Useful to show degree of bypass support (waveform dampens or flattens with increasing support)
MAP	Calculated from SBP and DBP	Only pressure parameter available on full ECMO
Pulse pressure	SBP-DBP	Increases (or appears) as underlying cardiac contraction improves or ECMO support decreases
	Decreases as CO (SV) falls	Narrowing may indicate tamponade
CVP	Normal 2-6 mmHg Reflects RA pressure, RV preload, volume status	Unreliable on ECMO
PA pressure	PA systolic pressure equates to RV peak pressure	Decreased in proportion to ECMO flow
PCWP	Normal 4-12 mmHg May reflect LAP	Inaccurate on ECMO
LA pressure	Normal 4-12 mmHg May reflect LV filling	Inaccurate on ECMO because of decreased PBF

PBF—pulmonary blood flow; SBP—systolic blood pressure; DBP—diastolic blood pressure; SV–; PA–pulmonary artery; PCWP—pulmonary capillary wedge pressure

exchange will become more pronounced. Over time, consideration to weaning the patient from ECMO will then ensue.

VII. Gastrointestinal

A. Blood Flow Patterns

Mesenteric blood flow patterns during ECMO or CPB are controversial. One study[11]has shown a decreased flow through the hepatic artery, portal vein, and total liver while another[12] found an increased flow through the gastrointestinal tract, spleen, and mesentery. The distribution of hepatic blood flow may change, with a decrease in hepatic arterial flow, accompanied by an increase in portal vein flow. No consistent alteration of pancreatic perfusion has been documented.

B. Hepatic Function
Hepatic dysfunction may arise from hypotension and/or hypoxemia at the initiation of ECMO

C. Gastrointestinal Function
1. Importance of nutritional supplementation in ECMO patients
2. In the neonatal population, total parenteral nutrition (TPN) is usually the initial mode of nutrition while on ECMO. If hemodynamics are stable, enteral nutritional support may be used but this is typically reserved for the older infant and pediatric patient. If enteral feeds not possible, TPN should be initiated, with care taken to minimize volume infused.

VIII. Renal

A. Renal Blood Flow on ECMO
1. Most blood flow information originates from studies on short-term cardiopulmonary bypass. During CPB, glomerular filtration rate is transiently reduced due to renal perfusion at a pressure outside of the autoregulatory range.
2. Pulsatile blood flow may improve renal cortical blood flow and preserve renal tubular histology.
3. Plasma renin activity is increased in infants during cardiopulmonary bypass. This may contribute to the increased peripheral vascular resistance seen on ECMO.

B. Renal Function
1. Prior to initiation of ECMO, patients frequently have hypotension, hypoxemia, and acidosis. Renal blood flow is usually decreased. When ECMO restores adequate MAP, renal perfusion improves and function typically recovers.
2. If acute renal failure develops, treatment is similar to non-ECMO patients. If dialysis is required, the ECMO circuit can be adapted for this therapy (Fig. 3.11).

C. Fluid and Electrolyte Requirements
1. Requirements are similar to those for other critically ill patients, except that insensible water losses from the membrane oxygenator must be considered. Estimates of insensible loss should be increased by 10% on ECMO (Table 3.5).

IX. Neurologic

A. Cerebral Blood Flow (CBF)
1. Carotid artery and jugular vein ligation (in VA ECMO) raises concerns about adequate CBF. Animal studies modeling prolonged hypoxia and vessel ligation have not demonstrated alterations in CBF and metabolism.[13] Studies in neonates have generally corroborated these findings,[14] although ECMO flow rates may contribute. Placement on VA ECMO at flows of 150 ml/kg/min has not shown alterations in

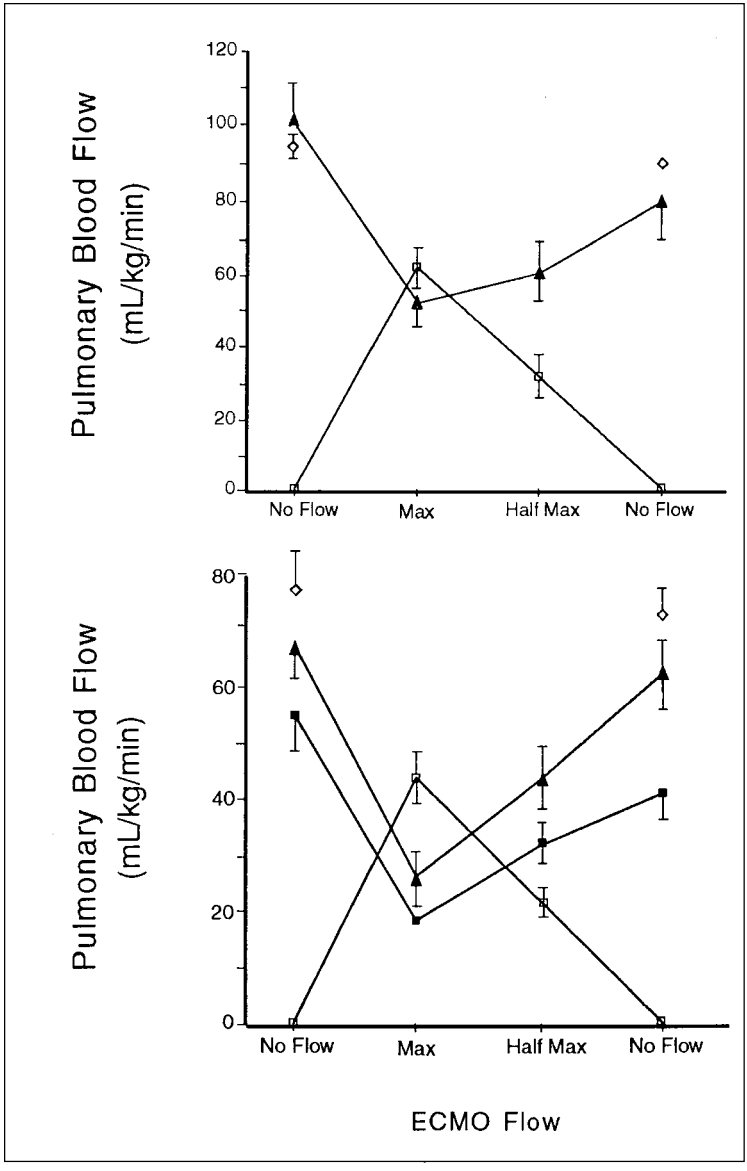

Fig. 3.10 Top: Effect of changing ECMO flow on PBF as measured in pigs using both rebreathing (solid triangles) and thermodilution (open diamonds) techniques for assessing flow. Open squares = ECMO. Bottom: Effect of changing ECMO flow on PBF as measured by rebreathing (solid triangles), flow probe [ECMO] (open squares), and thermodilution (open diamonds).

CBF, cerebral oxygen consumption, cerebral oxygen extraction, or oxygen transport.[15] With flows decreased to less than 100 ml/kg/min, CBF decreases.[16]

2. Mode of ECMO may influence CBF. Diastolic flow velocities change during nonpulsatile flow on VA ECMO. These changes are not seen in VV ECMO, as the heart still serves as the pump.
3. Autoregulation
4. Prolonged hypoxia results in loss of cerebral autoregulation when blood oxygen levels are restored by ECMO.[17,18] The result is reduced CBF at a given cerebral perfusion pressure, increasing the brain's vulnerability to injury. Cerebral autoregulation is particularly impaired at a cerebral perfusion pressure of <25 mmHg.[18] Autoregulation effects are more pronounced with VA than VV ECMO.
5. The internal jugular vein must be ligated in both VA and VV ECMO. This has resulted in a high incidence of posterior-fossa hemorrhages in ECMO patients, likely due to venous congestion.

B. Neurologic Complications and Management
   1. Critical aspect related to the success of neonatal ECMO
   2. The hypoxic neonate may have injury during both the pre-ECMO and ECMO phases of therapy.
      a. Pre-ECMO
         Most CNS events are related to hypoxia, acidosis, and other problems that occurred before starting ECMO.
      b. During ECMO
         CBF can be affected by hypoxia, hemodynamic instability, nonpulsatile flow, and vessel ligation. Systemic heparinization may contribute to cerebral hemorrhage.
   3. Neurologic monitoring
      Frequent neurologic checks while on ECMO, focussing on level of alertness and interaction, fullness of the fontanels, reflexes, tone, spontaneous movements, eye findings, and any evidence of seizures.
   4. Intracranial hemorrhage is the worst problem complicating ECMO. Sudden changes in $PaCO_2$ can cause rapid changes in cerebral blood flow. Cranial ultrasound is obtained before and within 24 hours of initiation of ECMO. It is then obtained on a daily basis in high-risk patients (those with a risk of asphyxiation, gestational age <36 weeks). In lower risk patients, it is performed after procedures or major events.
   5. Respiratory Alkalosis
      Respiratory alkalosis may be induced to vasodilate the pulmonary bed to treat pulmonary hypertension. This therapy also causes vasoconstriction of the cerebral circulation and may reduce cerebral blood flow. After periods of induced respiratory alkalosis, $PaCO_2$ should be normalized slowly (over a 24 hour period), to reduce the risk for cerebral hyperemia.

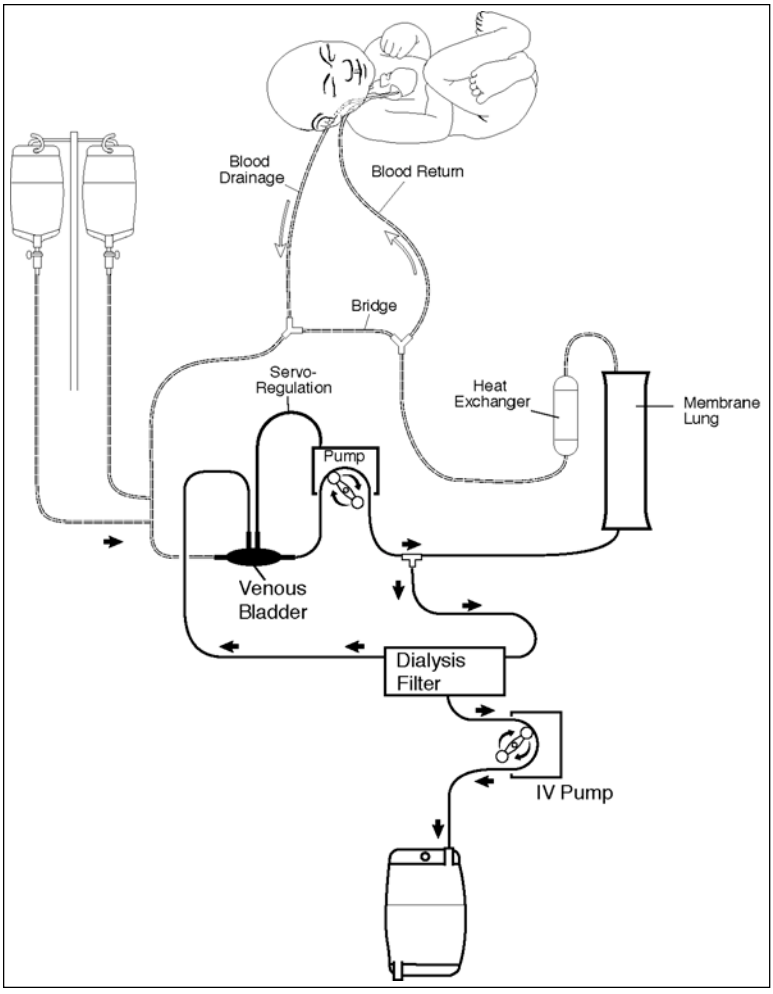

Fig. 3.11.Dialysis apparatus configured within ECMO circuit. Note pre-ECMO membrane placement of dialysis tubing.

X. Endocrine

Most available data is from the CPB literature, not specifically from ECMO.

A. Pancreatic Function

Some patients on ECMO may exhibit an increase in their pancreatic enzymes but this does not usually result in clinical pancreatitis. Data regarding specifics of endocrine or exocrine pancreatic function during ECMO is lacking.

Table 3.5. Estimated daily water loss and replacement requirements

Site of water loss	newborn-6 mo	6mo-5yr	5-10 yr	>10 yr
Insensible (mL/kg)	40.00	30.00	20.00	10.00
Urinary (mL/kg)	60.00	60.00	50.00	40.00
Fecal (mL/kg)	20.00	10.00	-------	-------
Total (mL/kg)*	120.00	100.00	70.00	50.00

* Does not include insensible losses that may occur from the ECMO membrane.

B. Adrenal Function
   1. CPB causes increases in epinephrine and norepinephrine levels.
   2. Adrenocortical hormones
      a. cortisol increases significantly during bypass. ACTH is also elevated.
      b. pulsatile perfusion fails to reduce these hormonal responses
      c. significance of elevated corticosteroid concentrations during bypass is uncertain.

C. Thyroid Function
   1. Free T3 and free T4 increase with heparin administration, as heparin or nonesterified fatty acids (released by heparin) displace hormones from binding proteins.
   2. T3 is an important regulator of cardiac rate, contractility, and oxygen consumption and also regulates the number and responses of β-adrenergic receptors on myocardial cell membranes. With initiation of bypass, total T3 concentrations drop significantly as a result of hemodilution.
   3. Thyrotropin (TSH) concentrations are unchanged during normothermic bypass. However, the TSH response to exogenous administration of thyrotropin-releasing hormone is blunted.

XI. Inflammatory Response

A. Blood Activation by ECMO Surfaces

The exposure of blood to the artificial surfaces of the ECMO circuits, especially the membrane oxygenator, invokes a systemic inflammatory response. Some studies have suggested that surface coatings may alter the inflammatory response. Clinical endpoints, such as survival, have not been shown to be affected by these coatings.

B. Host Defenses and the Systemic Inflammatory Responses in ECMO
   1. Humoral immunity
      a. Complement system

ECMO leads to activation of both the alternative and classical complement pathways, with the alternative pathway being the major component. Both CPB and ECMO have led to decreased total serum complement levels and increased C3a levels. Regardless of duration of ECMO, complement levels return to baseline within 24 hours.

b. Cytokines
Data on cytokine responses to ECMO are sometimes inconsistent,[19-21] but generally increases in interleukin (IL)-6 and IL-8 are seen without changes in IL-1 or tumor necrosis factor (TNF). The importance of these findings is not established.

2. Cellular immunity
   a. Neutrophils
   Absolute neutrophil counts consistently decreased in patients within 24 hours of initiation of ECMO and may remain low for 6 days.[22,23] Neutrophil chemotaxis is impaired by short-term CPB.[24] Neutrophils become activated and accumulate in the pulmonary perivascular and interstitial tissues. They may release oxygen-free radicals and contribute to increased capillary permeability, interstitial edema, and large alveolar-arterial oxygen differences during and after perfusion.
   b. Lymphocytes
   Total lymphocyte counts decrease within 24 hours after short-term bypass and may remain decreased for a week after surgery. Both B and T cell counts and function are decreased with CPB, as is the T helper/T suppressor cell ratio.[25,26] Limited data available regarding lymphocyte number and function during ECMO.
   c. Monocytes
   Absolute monocyte numbers do not change during short-term CPB. Their function, however, is activated during cardiopulmonary bypass, possibly by complement C3b. Phagocytic function of circulating monocytes is depressed during and after bypass.

XII. Hematology

A. Red Blood Cells (RBC)
Hemolysis occurs from shear forces generated by the roller or centrifugal pump (roller pumps more traumatic to RBCs)

B. Clotting Parameters
   1. Platelets
      a. Decreased in number during CPB. Most appear structurally normal, but platelet function is reduced.
      b. Thrombocytopenia related to dilution, platelet adhesion to circuit surfaces, and activation and removal of damaged platelets by the reticuloendothelial system. Thrombocytopenia during ECMO is a major cause of bleeding.
   2. Fibrinogen
      a. Required for the formation of clot
      Fibrinogen converted to fibrin by exposure to artificial surfaces in the ECMO circuit. Platelets in turn can bind to areas of fibrin clot.
      b. After the initial early drop in fibrinogen, levels usually return to normal as ECMO continues. Failure of levels to normalize may suggest disseminated intravascular coagulation (DIC) or sepsis.

c. Fibrin split products (FSP) or fibrin degradation products (FDP) formed from the breakdown of fibrin. An elevated level is indicative of DIC and the inability to form stable clot.

d. DIC

1) Definition

An intravascular release of thromboplastic substances resulting in diffuse intravascular thrombosis and thrombolysis. Consumption of clotting factors and platelets leads to clinical bleeding

2) Diagnosis

- Decreased platelet count, unresponsive to transfusion.
- visible clot formation throughout circuit
- increased ACTs , despite decreasing heparin
- clinical evidence of bleeding from surgical/other sites.

3. Antithrombin III (ATIII)

Interacts with heparin to promote heparin's anticoagulant activity. ATIII levels may become depleted after prolonged heparinization or in patients who have received multiple transfusions of packed red blood cells (PRBC) without fresh frozen plasma (FFP) administration.

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Mechanics of ECMO

I. General

A. Definition

A means of complete or near-complete pulmonary and cardiovascular support using mechanical devices.

B. Types of ECMO

1. VA ECMO
   a. Blood routed from the right atrium (usually via a right internal jugular catheter) into the ECMO circuit, oxygenated, and returned to the patient via the arterial system, usually through the right common carotid artery (in neonates).
   b. Mode of ECMO used in patients with respiratory failure combined with hemodynamic compromise
2. VV ECMO
   a. Technique provides respiratory support using only venous cannulation sites. A specially designed double-lumen cannula is placed through the right internal jugular vein with the tip resting in the right atrium.[1]
   b. In larger patients, or in those requiring greater flows, two venous cannulae may be used.
   c. Only used in hemodynamically stable patients with respiratory failure.
3. VV → VA-ECMO

   In select situations, conversion from VV ECMO to VA ECMO support is necessary, usually when hemodynamic compromise occurs while on VV ECMO.

C. Differences Between ECMO and CPB

1. In CPB, the heart is usually arrested during a portion of the procedure. During this time, blood may collect in the pulmonary circulation. Therefore, to prevent clot formation, a much larger dose of heparin is required.
2. No Venous Reservoir Used in ECMO.

   In CPB, as blood enters the operative field, suction catheters are used to drain the blood into a venous reservoir, another area of potential stagnation. Therefore, a greater level of anticoagulation is required. (Recommended ACT >500 for CPB, 160-220 for ECMO)
3. Hypothermia and Hemodilution

Various degrees of hypothermia used in CPB. To prevent complications from increased blood viscosity, hemodilution is used, keeping the hematocrit at 20%. This differs from ECMO, where the hematocrit should be >30% to optimize oxygen carrying capacity.

II. Components

A. Oxygenators

The first working oxygenator developed by Von Frey and Gruber (1888)

1. Types
   a. Microporous fiber membrane oxygenator
      i. Historically, the bubble oxygenator became the first oxygenator generally used for cardiopulmonary bypass, it was soon surpassed by the membrane oxygenator. The membrane oxygenator had the capacity to function longer and more efficiently than the bubble device.
      ii. Microporous materials have advantages over the solid silicone rubber membrane lung: gas exchange is more efficient, they are easier to prime, easier to produce, and have lower pressure drops. They have a great disadvantage for long-term use—plasma leakage can occur in an unpredictable manner.
      iii. New small-pore fiber oxygenators allow longer use, as the changes in the fiber characteristics have made them less susceptible to plasma breakthrough.
      iv. Microporous membranes can be treated with surface coatings for improved biocompatibility.
      v. Typical adult specifications—(Maxima Plus PRF Hollow Fiber Oxygenator with Improved Plasma Resistant Fiber (Medtronic) Fig. 4.1):

Recommended flow rate:	1-7 LPM
Membrane surface area:	2.3 m^2
Approx. number of fibers	4,600
Port sizes:	
Venous inlet	3/8″
Arterial outlet	3/8″
Recirculation	1/4″

   b. Silicone rubber membrane oxygenator
      i. For ECMO, Avecor developed a membrane oxygenator with the capacity for long-term use.
      ii. The Avecor membrane lung is a flat reinforced silicone rubber membrane envelope, wound in a spiral coil around a polycarbonate spool. It is then encased in a silicone rubber sleeve and a fiberglass outer shell. The interior of the envelope is the gas compartment containing a spacer screen permitting gas flow (Fig. 4.2).
      iii. Blood flows between turns of the envelope in a thin film. Oxy-

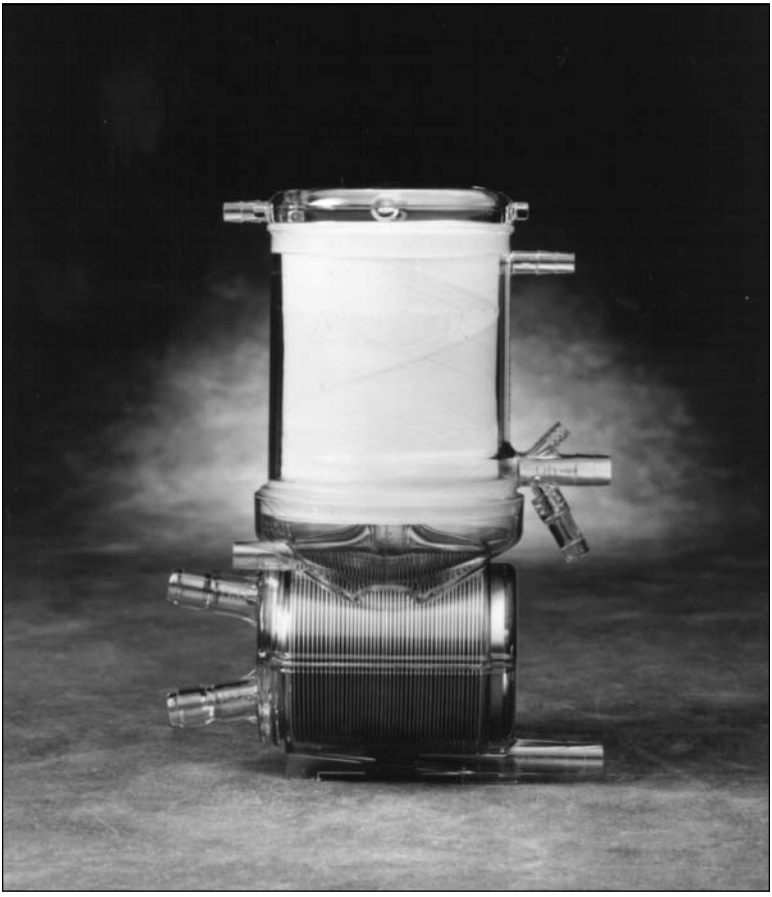

Fig. 4.1. Medtronic Affinity adult microporous hollow fiber membrane oxygenator. ©Medtronic

gen from the gas compartment diffuses through the membrane into the blood stream. Carbon dioxide diffuses through the membrane into the gas compartment and is flushed from the oxygenator by the gas flow.

iv. Specifications

The correct size oxygenator for the specific patient can be determined using the following data

AVECOR ECMO Membrane Oxygenators—Product Specifications

Fig. 4.2. ECMO extended capacity membrane oxygenators. ©Medtronic

©Medtronic

Model	**0400**	**0800**	**1500**	**1-2500**	**1-3500**	**1-4500**
Surface area (m^2)	0.4	0.8	1.5	2.5	3.5	4.5
Static priming volume (ml)	60	100	175	455	575	665
Maximum gas flow rate (l/min)	1.2	2.4	4.5	7.5	10.5	13.5
Maximum sizing by patient wt (kg)	4	11	19	70	95	≥ 96
Blood port dimensions	1/4″	1/4″	1/4″	3/8″	3/8″	3/8″
Maximum blood flow rate (l/min)	0.35	1.2	1.8	4.5	5.5	6.5
Maximum Blood Phase Pressure Drop (mmHg)	200	300	300	300	300	300
Maximum Blood Outflow Pressure (mmHg)	400	400	400	400	400	400
Maximum Transmembrane Pressure (mmHg)	750	750	750	750	750	750

c. Silicone ultrathin membrane oxygenator is currently in development

2. Management guidelines
    a. Flow
    ECMO flow should be maintained to provide adequate tissue perfusion, but should not exceed manufacturer's flow ratings.
    b. Pressure
    Inlet port pressure should always be greater than outlet port pressure, with a minimum gradient of 50 mmHg. Inlet pressure should be less than 750 mmHg, and outlet pressure should not exceed 400 mmHg. These pressures must be monitored closely during ECMO.
    c. Changing the oxygenator
        i. Secure necessary supplies
        ii. Do not discontinue ECMO until replacement oxygenator is ready and primed
        iii. Attach 3″ tubing with straight connectors to the blood inlet and outlet ports of new oxygenator and clamp both tubes
        iv. Attach 1/4″ stub to oxygen inlet port and clamp; attach vacuum line to gas exhaust port and clamp
        v. Place stopcock on recirculation port in OPEN position; attach stopcock on the venous side of luer in OFF position
        vi. Flush oxygenator with filtered 100% CO_2 through venous side luerlock port and exhaust through open stopcock on upper recirculation port for 2-3 minutes at 1-2 lpm gas flow
        vii. Discontinue 100% CO_2 flush and close both stopcocks
        viii. Release vacuum clamp and apply vacuum to oxygen exhaust port for 1-2 minutes
        ix. With vacuum working, plug IV into venous side stopcock. After vacuum is working for 1-2 minutes, open stopcock to prime oxygenator
        x. When oxygenator is primed to the top with fluid, close stopcock. Place mounted oxygenator into circuit
        xi. Discontinue bypass, double clamp near oxygenator on venous and arterial limbs, allowing enough room for the connectors to be placed. Open recirculation line to relieve pressure on the unit, reclamp, reattach the recirculation line to the new oxygenator
        xii. Cut tubes between clamps. Attach arterial and venous tubing, keeping it bubble-free. Continue the vacuum, and unclamp oxygenator inlet and recirculation line.
        xiii. Resume ECMO, recirculate through recirculation line until bubble-free, and then stop pump. Reclamp recirculation line. Discontinue vacuum, remove vacuum line from lower gas exhaust port, unclamp gas inlet line, unclamp oxygenator arterial outlet, and reinstitute bypass.
3. Caveats

a. Oxygen levels: postmembrane PaO_2 should not exceed 350-400, otherwise oxygen may come out of solution and form air bubbles or foam in the blood phase
b. Maintain a minimum sweep gas flow of 1 L/min in order to prevent water condensation or atelectasis
c. Once blood is present in the circuit, do not stop ECMO circulation for periods >5 minutes
d. Do not exceed 300 mmHg of vacuum during the priming procedure
e. Tie band all connections
f. Never obstruct gas or blood outlets

B. Pumps
1. Types
Pump selection is based on patient size, institutional preference, cost, and theoretical considerations
a. Centrifugal
i. mechanism of action: magnetically driven rotary cones generate the flow and pressure for the pump (Fig. 4.3). Other centrifugal pumps use impeller blades instead of rotating cones, and may create more turbulence than the cone systems (Bio-Medicus Bio-Pump®) (Fig. 4.4).
ii. significant amount of hemolysis and cavitation occurs at higher pump flows, especially with the impeller pump systems.
iii. risks of cavitation, gaseous emboli, and particle embolization may differ among pump products.
iv. Servoregulation devices have not been widely available for centrifugal pumps, therefore they are less commonly used for prolonged ECMO.
v. The console that regulates the speed and RPM levels of the centrifugal pump (Medtronic Bio-Medicus 550 Bio-Console®) also has an electromagnetic flow probe that enables an accurate determination of flow rate (Fig. 4.5).
b. Roller pump
i. Mechanism of action
The roller pump consists of two rollers positioned on a center rotating shaft. These rollers compress the circuit tubing which is positioned in a semicircular metal housing (a.k.a. raceway). The roller compresses the tubing against the raceway housing displacing the fluid within the tubing, pushing the blood out to the patient. There is an element of turbulence associated with this type of pump, specifically at the leading and trailing edges of the roller contact points with the tubing. Turbulence can potentially damage elements of the blood (Fig. 4.6). Sarns and Stockert/Sorin are commonly used manufacturers of these devices.
ii. Roller pumps are preferred over centrifugal pumps in neonatal

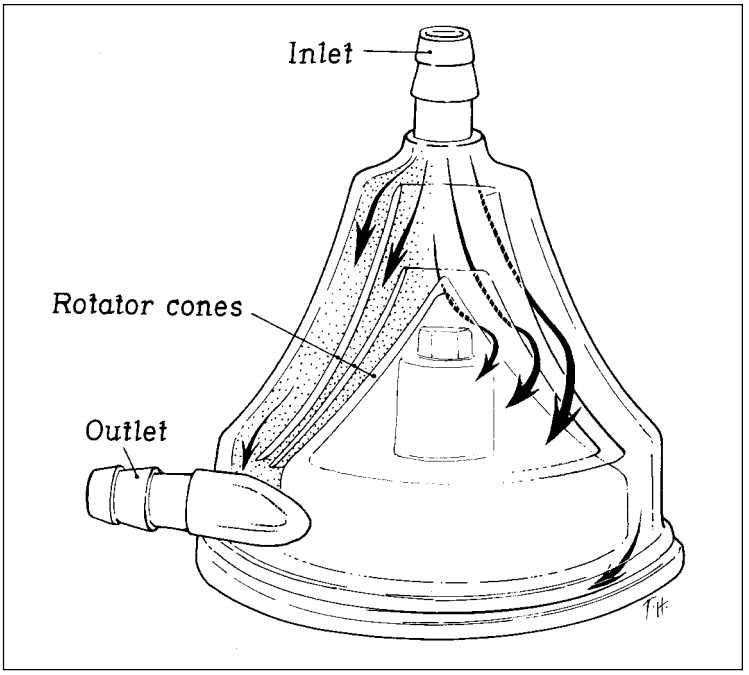

Fig. 4.3. Vortex created to propel blood in a magnetically driven cone system present in a centrifugal pump.

ECMO because of simplicity, durability, and the ability of the roller pump to function at the lower absolute flow rates required in neonates. The pump is filled passively via the venous line.

iii. The pump must be configured to insure that it does not generate inordinate amount of negative pressure on the venous line. This could cause increased cavitation and hemolysis. Poor venous drainage could also result as the catheter would cause collapse of the right atrial wall, and introduce the possibility of air entrapment and air embolism.

iv. In routine cardiac surgery with CPB, the venous line drains into a large venous reservoir, eliminating the problems listed above. However, in ECMO, a specially designed bladder is present and positioned at the lowest point in the venous line.

2. Pulsatile vs. nonpulsatile flow
   a. Long-standing debate in the field of circulatory support
   b. Full extracorporeal pump support results in an essentially nonpulsatile state. As long as blood flow is adequate for end-organ

Fig. 4.4. Bio-Medicus Bio-Pump® -80 centrifugal pump.

perfusion, there are no deleterious effects of nonpulsatile flow.

c. Possible advantages of pulsatile flow
   i. Renal
      Majority of studies have shown pulsatile flow improves urinary output. Some evidence that pulsatile flow preserves outer cortical blood flow and reduces renin release, both helping to preserve renal function. However, in patients with normal kidneys, the true clinical significance of pulsatile flow is uncertain.
   ii. Neurologic
      Clinical studies report no effect of pulsatile flow on cerebral blood flow or cerebral metabolic rate, suggesting no advantage for pulsatile perfusion. However, pulsatile CPB may cause a decrease in microcirculatory shunting, as well as a reduction in cerebral vascular resistance. Nonpulsatile flow is associated with increased sympathetic tone, however the impact in most conditions is negligible.
   iii. Rheologic
      No significant differences in plasma hemoglobin or platelet levels between the two modalities
   iv. No survival or morbidity advantages of pulsatile perfusion have been demonstrated

3. Specifications

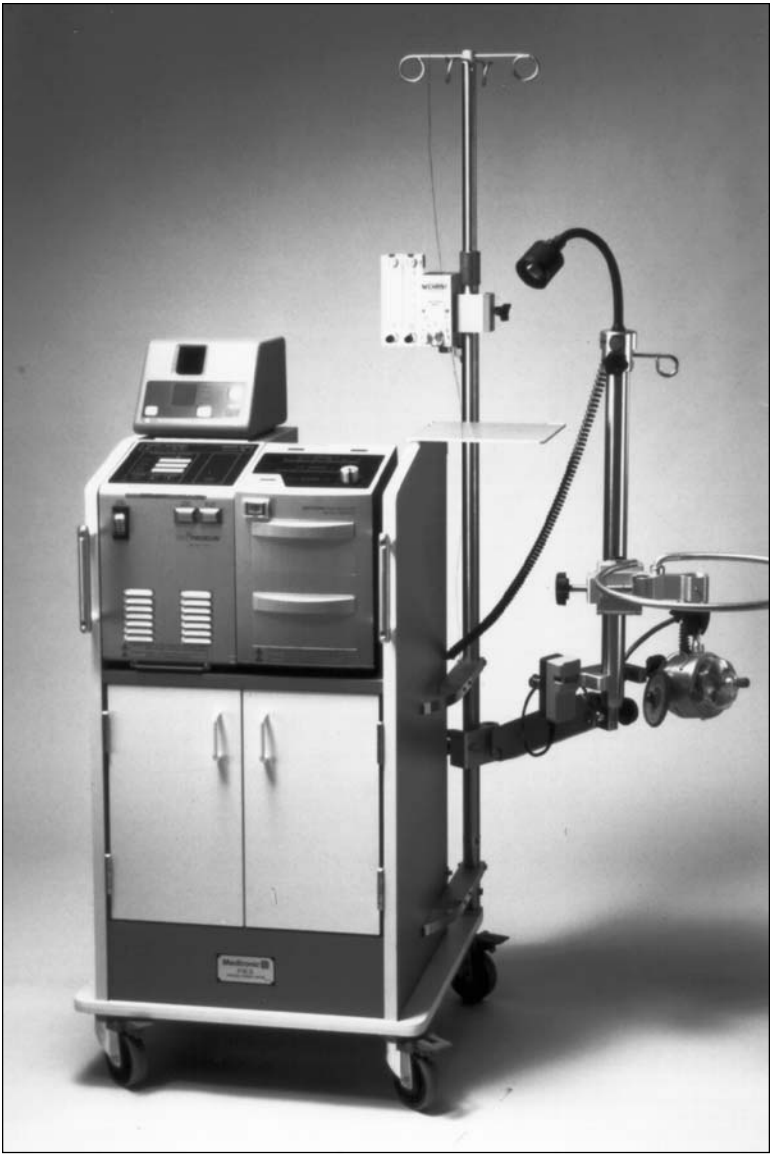

Fig. 4.5. Bio-Medicus 550 Bio-Console®.

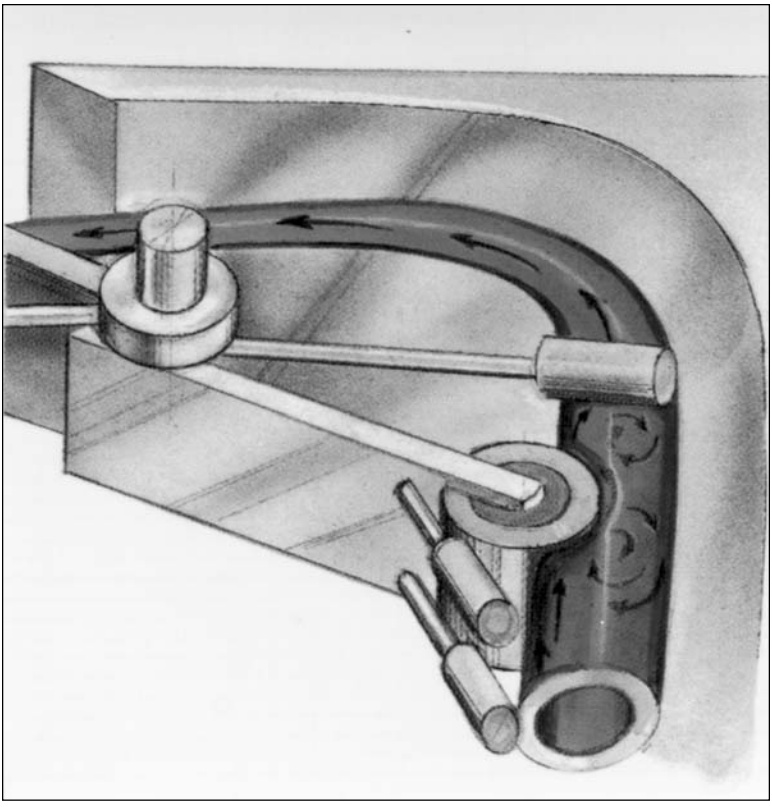

Fig. 4.6. Roller pump demonstrating displacement of blood forward within the raceway of the perfusion pump.

a. Centrifugal pump
   Medtronic Bio-Medicus 550® system
   Pediatric: Bio-Pump® -50 centrifugal pump
      1/4″ x 1/4″ in/out connector
      mL/min range: 0-10,000 ± 5%
   Adult: Bio-Pump® -80 centrifugal pump
      3/8″ x 3/8″ in/out connector
      L/min range: .15-15.00 ± 5%
b. Roller pump
   Sorin 3 Roller Pump
   RPM range 0 to 250 RPM
   L/min range 0 to 3.9 l/m for 1/4″ tubing
      0 to 6.8 l/m for 3/8″ tubing
      0 to 10.4 l/m for 1/2″ tubing

0 to 15.1 l/m for 5/8″ tubing

4. Management Guidelines
   a. Centrifugal pump
      i. With no servoregulation device available with these pumps, close monitoring of the system by the perfusionist or ECMO specialist required.
      ii. Unable to flow lower than approximately 300 ml/min, as accuracy of flow rate not reliable at these levels. Without a one-way check valve in place, low flow rates may also result in reversal of flow in the pump (depending upon aortic pressure).
   b. Roller pump
      i. To prevent problems with the generation of excessive negative pressure, a bladder device is positioned in line with the venous drainage tubing. The bladder is connected electrically to the pump, and drops or stops the roller pump whenever the pressure drops (i.e., negative pressure) and the bladder collapses. An alarm will sound at this point as well. It also restarts the pump immediately when the bladder refills.
      ii. Reasons for decreased filling of the bladder are many, including hypovolemia, kinking of the catheter, and tension pneumothorax. This servocontrol system allows for a degree of safety for prolonged use of ECMO.
5. Caveats
   a. Centrifugal pump
      Even at low flow, these very efficient pumps can generate significant negative pressure in situations where venous drainage is impaired or outflow is obstructed.
   b. Roller pump
      Raceway rupture identified by a visible crack in the raceway and manifested by (1) blood loss in the raceway, (2) air entry on the negative side of the raceway, or (3) clots in the patient bridge or oxygenator bridge

C. Bladder Reservoir
1. Function
   A disposable silicon reservoir used to hold a small volume of blood (Fig. 4.7). It is positioned in the venous limb of the circuit prepump. The pressure in the bladder is under servo control. With a drop in pressure, the bladder will collapse, the pressure limit will be triggered, causing the pump to stop. Currently used only with roller pumps (Fig. 4.8).
2. Types
   Medtronic R-14, R-38 assist reservoir (venous bladder)
   Gish VR-EMCO Silicone venous reservoir
3. Specifications

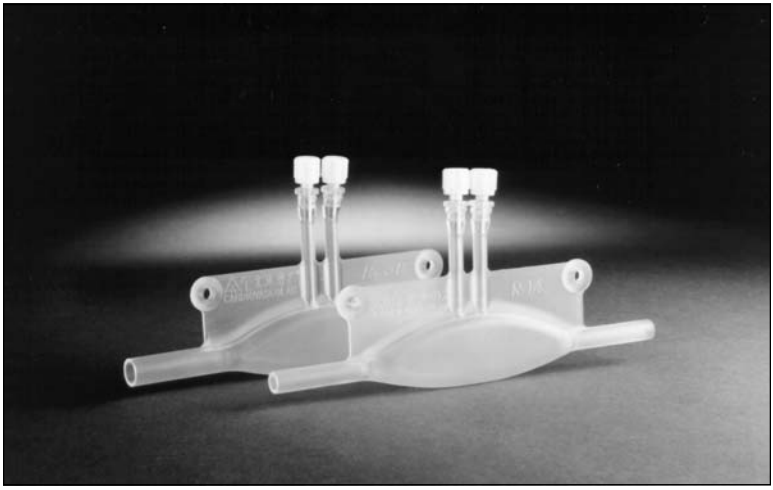

Fig. 4.7. Medtronic R-14, R-38 assist reservoirs (venous bladder). ©Medtronic

Model	Medtronic	R-14	R-38	Gish VR
Vent Tubing		1/8”	1/8”	1/8”
Inlet Tubing		1/4”	3/8”	1/4”
Outlet Tubing		1/4”	3/8”	1/4”
Priming volume (ml)		35	35	15
Min blood flow (ml/min)		50	50	—
Max blood flow (l/min)		0.50	4.00	—

4. Management Guidelines
   - Venous bladder change procedure:
   - Using sterile technique, assemble the new bladder device
   - Clean pre- and postbladder connections with betadine
   - Place bladder pressure monitor in standby mode
   - Come off ECMO
   - Place clamps on both sides of the bladder and cut out old bladder
   - Connect right side of bladder (double luer lock)
   - De-air bladder while connecting left side, infuse with saline, make an airless connection
   - Fill bladder before removing clamps
   - Remove clamps
   - Turn pump on slowly, recirculate
   - Survey for clamps, air
   - Resume bypass
   - Attach bladder transducer monitoring line
   - Zero bladder transducer, set alarm limits, test alarm function
   - Check ACT, Hematocrit

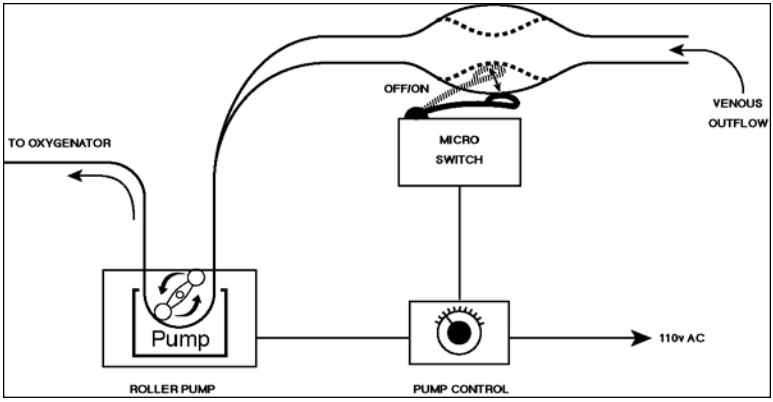

Fig. 4.8. Servo-controlled bladder box operation, for use with a roller pump.

- Document all actions on the ECMO flow sheet

5. Caveats (See Table 10.4).

D. Gas Control Module

Controls infusion of the standard gases used in ECMO, compressed air, oxygen, and carbogen (5% CO_2, 95% O_2).

1. Types

   Sechrist®–Standard model which allows connection of standard gas lines for use in mixing medical grade compressed air, oxygen, and carbogen.

2. Specifications

   Device reduces pressure of gases to 12 PSI to insure high pressures not transmitted to the membrane oxygenator. The gas control module houses four flow meters (which control the flow of air/O_2/and carbogen, independently), an oxygen analyzer (oximeter), pressure gauge, and indicator light for assessing the on or off status of the alarm.

3. Management guidelines
   a. Calibration

      Performs at the initiation of the ECMO interval; typically remains stable while patient on ECMO

   b. Maintenance
      i. Replacement of oxygen sensor
      ii. Battery replacement (important, as the oxygen analyzer is battery operated).

4. Caveats
   a. Pressure monitor is a critical component. An increased pressure in one of the gas lines could lead to membrane rupture and air embolus into the ECMO circuit.
   b. Low pressure may indicate that gas flow is decreased, gas source

tubing is disconnected or leaking, or gas source is low or depleted.

E. Heat Exchanger
   1. Function
      a. Heat loss via the membrane oxygenator is managed with the heat exchanger. Heat loss comes from the cool sweep gases, the ventilator, from exposed circuit tubing, and the water condensation from the oxygenator.
      b. Device functions to heat and circulate water through a column, which, using the countercurrent exchange principle, heats the blood in the ECMO circuit.
      c. Positioned downstream from the oxygenator and warms the blood just prior to returning it to the patient. Avecor heat exchanger is shown here (Fig. 4.9). The device position in the circuit, after the membrane lung, serves also to act as an air-bubble trap.
      d. As the last component of the circuit, helps insure blood returns to the patient at normothermia (36.5-37°C). The blood temperature is monitored continuously by an in-line thermister probe connected to the arterial filter. In larger patients and adults, the heat exchanger is a less important component.
      e. Water heater/pump is needed. The selected device may include a servo-controlled radiant warmer as an extra feature.
   2. Types
      • Avecor
      • Gish
   3. Specifications

	Medtronic ECMOtherm II Heat Exchanger Model A 19-38	OMNItherm (Adult)
Priming volume (ml)	50	135
Water phase pressure limits (psi)	65	45
Maximum blood flow rate (l/min)	2	6
Minimum blood flow rate (ml/min)	50	—
Blood port dimensions	1/4″	3/8″
Water port dimensions	1/2″	1/2″

GISH Heat Exchanger	HE-3	HE-4
Priming volume (ml)	20	60
Water phase pressure limits (psi)	65	65
Maximum blood flow rate (l/min)	2	2
Minimum blood flow rate (ml/min)	—	—
Blood port dimensions	1/4″	1/4″
Water port dimensions	1/2″	1/2
Integrated bubble trap (ml)	—	30

   4. Management Guidelines

Fig. 4.9. Medtronic heat exchanger.

a. Position heat exchanger on the positive pressure side of the pump
b. Heat exchanger blood outlet should be positioned lower than the blood inlet (orient vertically if possible, not <45° angle)
c. Consider monitoring both water and blood inlet and outlet temperatures to insure temperatures do not exceed maximum safe thermal gradients
d. Routinely examine the heat exchanger to monitor for air or thrombus formation

5. Caveats

a. Leaks can occur, requiring changing of device
   i. water to blood leak leads to:
      unexplained hemolysis
      decreased Hgb
      increased K+
      hypervolemia
   ii. blood to water leak leads to:
      blood in water hoses
      blood at vent sites of device
   iii. Management protocol is shown in Table 4.1.

F. Filtration Devices in ECMO
1. Function
An arterial filter (30-40 microns) is usually placed inline between the oxygenator and the reinfusion cannula to trap small emboli of air or debris within the arterial limb of the circuit. As the filter may capture significant volumes of gas, it should always be positioned at the highest point of the ECMO circuit (Fig. 4.10a, b).
2. Types
   a. Arterial line filter
   b. Arterial bubble trap
3. Specifications
Cobe/Sorin/Dideco/Terumo/Medtronic

	Neonatal	Pediatric	Adult
	1/4″	3/8″	3/8″
max flow rate	2.5 LPM	3 LPM	7 LPM
max pressure	300 mmHg	750 mmHg	750 mmHg
priming volume	40 ml	100 ml	212 ml
normal filter rating	32 microns	40 microns	38 microns

4. Management Guidelines
   a. If replacement required
      i. prime filter with PRBC and prime additives (heparin/albumin, THAM, NaHCO3, and calcium gluconate)
      ii. de-air filter with prime/place clamps/maintain sterility at tubing connection sites.
      iii. separate patient from bypass
      iv. double-clamp inlet and outlet portions of old filter
      v. using sterile technique, remove filter between clamps
      vi. replace with new device, and de-air
      vii. reinitiate ECMO, recirculating through bridge first
      viii. tighten all connections with tie bands
5. Caveats
   a. Arterial filter occlusion may manifest by elevated postmembrane pressure
   b. Clot formation may occur on the arterial side or outside of the

Table 4.1. Management protocol for changing heat exchanger

1. Turn heater off immediately and drain water hoses
2. Separate patient from ECMO
3. Double clamp heat exchanger
4. Using sterile technique, cut out heat exchanger
5. Place 1/4˝ x 1/4˝ connector/fill connection with sterile saline
6. Remove clamps, initiate ECMO flow through bridge
7. Place patient back on ECMO
8. Keep patient warm by external sources temporarily
9. Prime new heat exchanger
   a). In neonate, prime with 1 unit PRBC, heparin (100U), 25% albumin (40 ml), THAM(25ml), and Ca Gluconate (300mg)
   b). Place adequate PVC tubing on inlet and outlet ports
   c). Add blood prime to heat exchanger (de-air in the process)
   d). Clamp inlet and outlet tubing when de-airing complete
10. After priming complete, again separate from ECMO
11. Clamp on each side of the 1/4˝ x 1/4˝ connector, remove and replace with heat exchanger using sterile/airless technique
12. Remove clamps and place patient back on ECMO, first recirculating through bridge.
13. Tighten and tie-band all connections.

filter or bubble trap

G. Tubing
   1. Function
      Route blood to the oxygenator, the ECMO circuit, and back to the patient
   2. Types
      • Polyvinyl chloride (PVC)
      • Super Tygon—a more durable PVC preparation
   3. Specifications
      a. Material: PVC
      b. Dimensions
         3/8″ outer diameter; 3/32″ thickness
         May use smaller dimensions for circuit modifications (e.g., Arterial limb to lower extremity)
      c. Surface coatings: optional
         i. Carmeda™ bonded system (Medtronic)
         Heparin is covalently bound to component surfaces via "spacer arms" that are about 100 Angstroms long. Heparin bonded perfusion circuits selectively adsorb antithrombin, but an anticoagulant effect of surface bound heparin has not been demonstrated during clinical CPB or ECMO.
         ii. Siloxane-based surface modifying additives–(SMA) (Cobe)
         A microporous fiber coating consisting of polycaprolactone-polydimethylsiloxane block copolymers
         iii. Duraflow™ heparin bonded (Baxter)

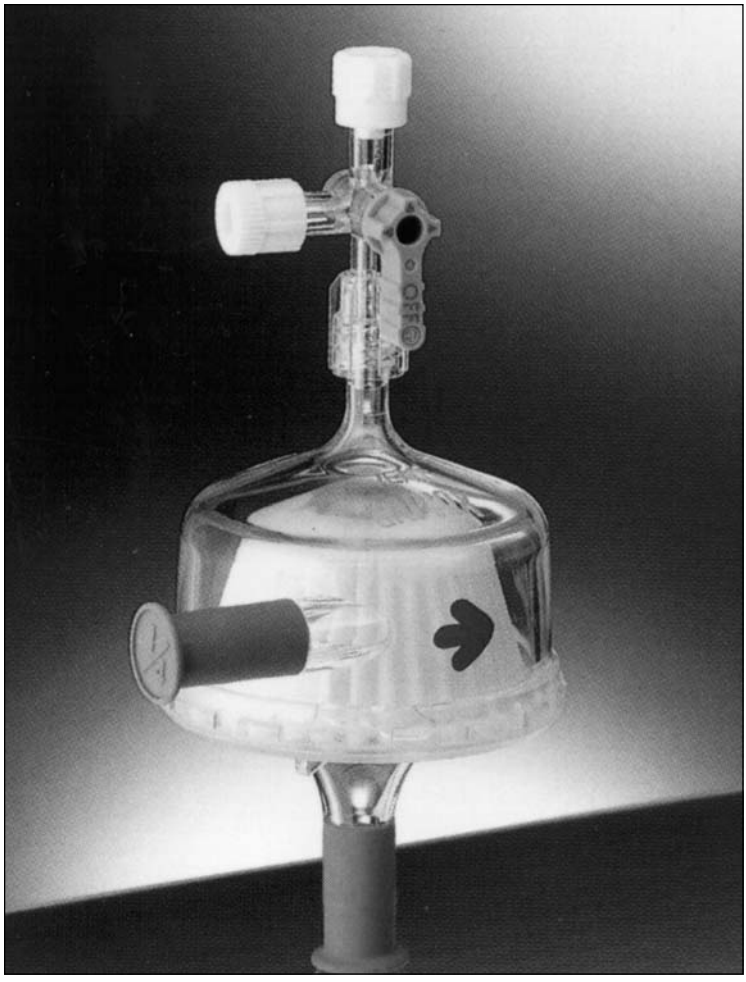

Fig. 4.10a. Arterial filter used for neonatal ECMO (Terumo®).

Ionically binds standard heparin using a proprietary process that retards heparin leaching into the circulation.

4. Management Guidelines
   a. General concepts
      i. Priming techniques may differ significantly between different ECMO centers based upon how the ECMO circuit is constructed, which may also vary
      ii. The basic steps of preparing a circuit are as follows

Fig. 4.10b. Arterial filter used for adult ECMO (Meditronic®).

a) Sterile set-up
b) CO_2 flush of the circuit
c) Displacement of CO_2 with crystalloid
d) Displacement of crystalloid with blood
e) Flow through bridge prior to passing lines to surgeon

b. Priming the circuit
   i. Minimize fluid volume. Use components which require low priming volumes (e.g., Medtronic heat exchanger volume -50 ml). However, components must be of sufficient dimensions to handle the required flow for the individual patient.
   ii. Priming the circuit—Roller Head Pump Circuit: Neonatal ECMO
      a) Circuit components selected
      b) Sterile assembly
         ECMO centers may either (1) prepare the entire circuits as needed, (2) have a circuit ready at all times, flushed with sterile CO_2, or (3) have the circuit flushed with crystalloid (maintains sterility up to 30 days).
      c) Circuit prime done first with CO_2, then with crystalloid, then frequently with blood.
      d) Flush system with 100% CO_2 (displaces nitrogen, which can come out of solution to form bubbles) for a minimum of 3 minutes at a rate of 1-2 l/min/M^2.
         1) Connect tubing from 100% CO_2 regulator to the venous reservoir ventilating port.
         2) Vent CO_2 from the luer-lock on the recirculation line.
         3) After flushing, turn the CO_2 off and immediately clamp the vent port on the venous reservoir and close the CO_2 exhaust site. The system should be totally closed to the atmosphere at this point
      b) Crystalloid prime
         1) Add clear saline prime (Normasol–2 liters, with 1000U of heparin (1:1000)) via priming reservoir to displace CO_2. Release the clamp from the blood outlet. When the oxygenator is primed on the top, place the pump tubing through the pump head and release the clamp on the recirculation line.
         2) Begin recirculation through the recirculation line. The vacuum must remain on during recirculation. Gradually increase the flow to 2.5 l/min to 4.5 l/min, depending on the membrane model to be used.
         3) After recirculating via the recirculation line to remove any remaining CO_2 bubbles in the oxygenator, fill and recirculate the arterio-venous (A-V) loop and expel gross air through the ventilating port on the

venous reservoir. Do not strike oxygenator or heat exchanger sharply on or near the sides of the end cap. De-air arterial bubble-trap and associated stopcock.

4) With flow rate at 1 l/min (0.5 l/min for model 0400-21), remove the gas line from the gas inlet port (upper green gas port) and draw room air through the gas phase of the oxygenator. Do this for 2 minutes or until all prime has made one pass through the oxygenator. This will remove excess CO_2 dissolved in the prime solution, and oxygenate the prime to a PO_2 of approximately 100 mmHg. Check the oxygenator for leakage during this aeration period.
5) Replace the unclamped gas line securely onto the upper green gas port. Disconnect vacuum, and allow the system to recirculate prior to bypass
6) Check pump occlusion. Vacuum should be off at this point.
7) Check and adjust the pH of the prime during recirculation after ventilating the prime
8) Stop the pump. Insure that the gas exhaust port is open and unobstructed. Clamp the recirculation line. Calibrate and place CDI sensors with pump off. Prime, place, and calibrate DLP lines. The system is ready to go.

c) Blood prime

If blood or blood components are used to replace any portion of the nonblood prime, add blood just before instituting bypass

1) If blood added, any further recirculation should be done prior to institution of bypass
2) Do not add blood in the presence of vacuum
3) Blood is recirculated and tested, normalizing electrolytes, ABGs. Temperature is maintained at 37°C

iii. Priming the circuit—Biomedicus BioPump Circuit (pediatric and adult ECMO)

As with priming the neonatal circuit, the specific steps in priming the pediatric and adult ECMO circuits will vary, often significantly, from center to center. The basic steps of preparing a circuit remains the same.

a) Open both stopcocks on priming fluid reservoir bag
   1) Clamp circuit below arterial bubble trap
   2) Clamp venous line of priming reservoir bag
   3) Clamp circuit tubing pre-BioPump
b) Flow CO_2 at 1 lpm through A-V loop for 1 minute
   1) Stop CO_2 and isolate A-V loop with clamps

2) Unclamp venous line of priming fluid reservoir bag and unclamp below arterial bubble trap
3) Restart CO_2 at 1 lpm and allow CO_2 to circulate in the system for 2-3 minutes
4) Turn off CO_2 and remove pre-BioPump tubing clamp

c) Clamp venous and arterial lines just below priming fluid reservoir bag, and place a clamp on the arterial side of priming fluid reservoir
1) Add Normasol (2 liters) and heparin (1000 U-1:1000) to priming fluid reservoir bag
2) Change position of arterial A-V loop clamp to bladder box side of Y connector
3) Remove arterial side A-V loop clamp and open arterial bubble trap stopcock
4) Release venous priming fluid reservoir clamp
5) Displace CO_2 with fluid, clamp venous side of priming fluid reservoir bag, and isolate fluid filled A-V loop with tubing clamps
6) Release the arterial and venous priming fluid reservoir bag clamps

d) Start pump at 300-500 ml/minute to displace remaining air from circuit, tapping circuit, releasing air via arterial bubble trap stopcock
1) Orient BioPump exit port inferiorly
2) Calibrate and place CDI sensors with pump off
3) Prime and place DLP lines
4) Isolate priming fluid reservoir and filter with clamps on arterial side of reservoir

e) Add blood prime to circuit
1) Recirculate blood prime through priming reservoir

f) Initiate gas flow to membrane oxgenator

g) Flow blood through bridge after isolating A-V loop

c. Connect to patient

d. Initiate ECMO

i. Replenish RBCs, platelets, maintain ionized calcium in normal range.

ii. Blood gas control
- Independent control of PO_2 and PCO_2
- Use a blender (an oxygen/air mixing device) to deliver specified F_IO_2

iii. Keep F_IO_2 at 100% with initiation of ECMO. Only F_IO_2, not PO_2 can be adjusted by changing the flow rate of oxygen or gas mixture

iv. PCO_2 controlled by the altering the sweep gas flow rate. Gas

flow limited by the specifications of the oxygenator

v. Pressure limitations
Blood compartment pressure must remain greater than the gas compartment pressure. Always start the pump before turning on the ventilating gas, and turn off the gas before turning off the pump.

vi. Limit transmembrane (blood to gas phase) pressure to 750 mmHg or less (alert ECMO team before reaching this level of pressure). Insure there are no restrictions to gas flow through the device. Limit the blood outflow pressure to 400 mm Hg or less.

vii. Problems that may occur if these recommendations are not followed include membrane or seal leaks, decrease of gas exchange, increase of resistance to blood flow, or deposition of platelets on the membrane.

e. Changing the ECMO circuit
   i. Performed in situations where:
      a) DIC with thrombus formed throughout the circuit
      b) Consumptive coagulopathy with elevated prothrombin time (PT) and activated clotting time (ACT), refractory thrombocytopenia, decreased fibrinogen level
      c) Blood culture confirmed sepsis
   ii. Arrange for adequate experienced assistance
   iii. Full sterile technique
   Prepare areas of disconnection and reconnection sterilely.
   iv. With new pump operational, take patient off ECMO. Double clamp venous outflow lines and arterial inflow close to patient. Connect sterile ends of new pump to the cut ends of the arterial and venous lines close to the patient, de-airing in the process.
   v. Resume ECMO

f. Raceway maintenance (present on roller pumps only)
   i. "Walking" the raceway
      a) Perform every 6 days (144 hours) to prevent extreme wear or stress on the tubing, leading to rupture
      b) The raceway tubing is of sufficient length to be walked at least twice.
      c) Procedure (two people required)
         1) Remain on ECMO to walk raceway (recommended for 1/4″ and 3/8″ raceways; for 1/2″ tubing, remove patient from ECMO)
         2) Mark inlet tubing with black marker
         3) Open inlet and outlet tubing gate clamps
         4) Hold securely, move the tubing forward, guiding the tubing through the pumphead
         5) When the black mark is all the way through the pump

Table 4.2. Blood prime (Childrens' Medical Center at Dallas)

Circuit	Dose	Priming volume
Neonatal		600 ml
THAM	75 ml	
Calcium gluconate	400 mg	
Albumin 5%	60 ml	
Beef lung heparin	500 U	
Packed RBCs	400-480 ml	
Pediatric		800 ml
THAM	85 ml	
Calcium gluconate	500 mg	
Albumin, 5%	80 ml	
Beef lung heparin	500 U	
Packed RBCs	600-650 ml	
Adult		1000 ml
THAM	100 ml	
Calcium gluconate	600 mg	
Albumin, 5%	100 ml	
Beef lung heparin	500 U	
Packed RBCs	750-800 ml	

head, secure the inlet tubing gate

6) Check the lay of the tubing in the raceway
7) Assess old tubing for evidence of damage, see if replacement of section is needed.

ii. Raceway replacement
   a) Perform if on ECMO longer than 12 days (288 hours)
   b) The section of tubing in the raceway should be replaced with a new portion of raceway tubing.
   c) Procedure
      1) Mark inlet tubing with black marker
      2) Remove patient from ECMO per protocol
      3) Turn off pump flow
      4) Replace raceway section of tubing, with careful de-airing
      5) Resume ECMO

iii. Management of raceway rupture
   a) Turn off pump immediately
      Separate from bypass
   b) Clamp inlet and outlet to pump head
   c) Open tubing gate clamps and remove raceway from pump head
   d) Double clamp each side of the raceway, sterilely remove

this segment by cutting between clamps, then place new segment.
1) Connect one end of the new tubing with connectors to the end of the circuit tubing closest to the bladder.
2) Release the clamp in this area and allow tubing to fill by gravity.
3) Clamp, de-air further, fill with saline and attach to the other end of the circuit tubing (premembrane).

e) Remove all clamps. Place tubing in the pumphead, secure gates. Set occlusion. Initiate pump head movement.
f) Administer volume as needed, turn pump on and recirculate through bridge.
g) Resume ECMO. Tighten and tie band all connections
h) Check fine occlusion with Transsonic flowmeter

iv. Caveats
a) Raceway rupture may be minimized by use of super tygon tubing
b) Avoid redundancy of tubing in the raceway to minimize buckling or kinking
c) Use only specialized tubing clamps to avoid damage to the tubing

H. Cannulas
1. Function
Serve as interface between ECMO circuit and patient vascular system
2. Types
a. Arterial
i. For placement in the common carotid artery, femoral artery, or ascending aorta
ii. Accessory femoral artery cannula may be used for distal limb perfusion
b. Venous
i. For placement jugular vein, femoral vein, or right atrium.
ii. Venous cannula size is typically the limiting factor affecting ECMO flow.
c. Double-lumen venous cannulas
i. Inserted via jugular vein with tip position in the right atrium.
ii. Used for venovenous ECMO, avoids need for carotid artery cannulation
3. Specifications
a. Sizing
Some authors advocate use of "M Number" to guide choice of cannula size. M Number is a dimensionless number which describes pressure-flow characteristics of vascular access catheters

(Figs. 4.4-4.11, Table 4.3).

i. Arterial cannulas
   a) Size according to the dimensions of the arterial inflow vessel
   b) ECMO flow limited by venous drainage and return, not by arterial flow
   c) Monitor line pressure, aiming for postpump pressure < 300 mmHg
   d) Pressure drop across the membrane oxygenator and reinfusion catheter (resistance) is monitored. Maintain goal pump flow as long as the resistance is acceptable (150 mmHg)

ii. Venous cannulas
   a) Venous drainage catheter is the limiting factor affecting blood flow through the ECMO circuit.
   b) Sizing important: attempt to use the catheter with the widest internal diameter, and shortest length.
   c) Drainage ultimately comes from the right atrium, usually via the superior vena cava. Resistance to blood flow varies directly with the length of the catheter and inversely with the fourth power of the radius of the catheter.
   d) Blood drains via the venous catheter and tubing are routed through a pump which in turn delivers the blood through the membrane oxygenator and then back to the patient.

iii. Double-lumen venous cannulas
   a) OriGen® Dual lumen polyurethane catheters, available in sizes 12F, 15F, and 18F OriGen (Biomedical, Inc. Austin, TX). Kendall® also offers some of these cannulae.
   b) Venous return lumen is more distal and is larger in diameter by an area ratio of 2:1 (Fig. 4.12).
   c) On insertion, position the tip in the mid-right atrium. This is usually 4-6 cm from the insertion site in the neonate. Orient the catheter with the arterial (red) line anteriorly.

4. Management Guidelines
   See section: Cannulation techniques
5. Caveats
   a. Dual-lumen cannulas
      Inlet obstruction
      i. One or more of the ports may have aspirated tissue
      ii. Management includes reposition of the patient, flushing catheter with sterile saline (if no resistance present), reposition the catheter including rotation and withdrawal, while observing the effect on flow
   b. Accidental decannulation
      i. Venous

Table 4.3. Selection of components for the ECMO patient

	2-5 kg	6-10 kg	10-16 kg	16-26 kg	>26 kg
Circuit	1/4"	1/4"	3/8"	3/8"	3/8"
Raceway	1/4"	3/8"	3/8"	1/2"	1/2"
Oxygenator (M^2)	0.4 / 0.8	0.8 / 1500	1500	1500 / 2500	2500
Cannulae-VA					
Arterial (F)	8-12	12-15	12-15	17-19	21+
Venous (F)	10-14	12-17	14-23	21-25	25+
Cannulae-VV					
Arterial return(F)	8-10	12-15	14-21	19-21	21+
Venous(F)	10-14	14-17	17-23	21-25	25+
Cannula-ceph	1 to 2 sizes <RIJ cannula				

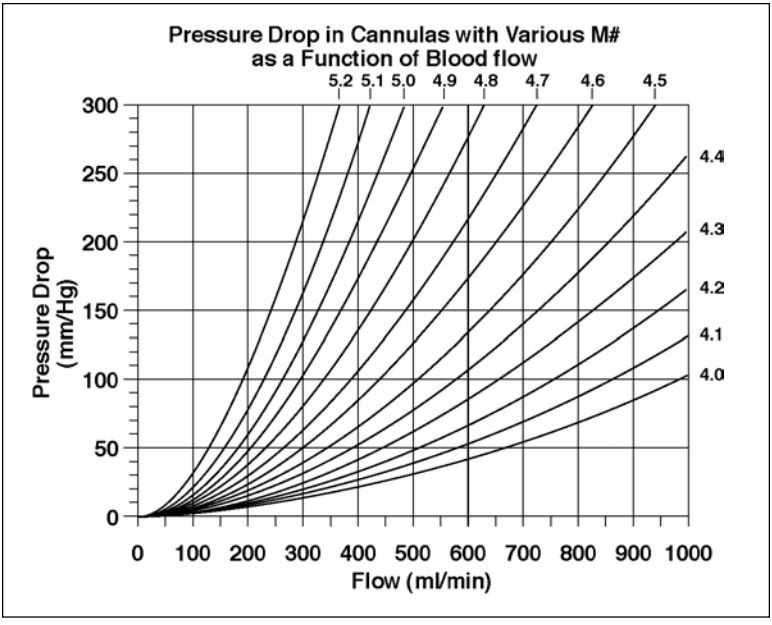

Fig. 4.11. M numbers for catheters used in neonatal and pediatric ECMO.

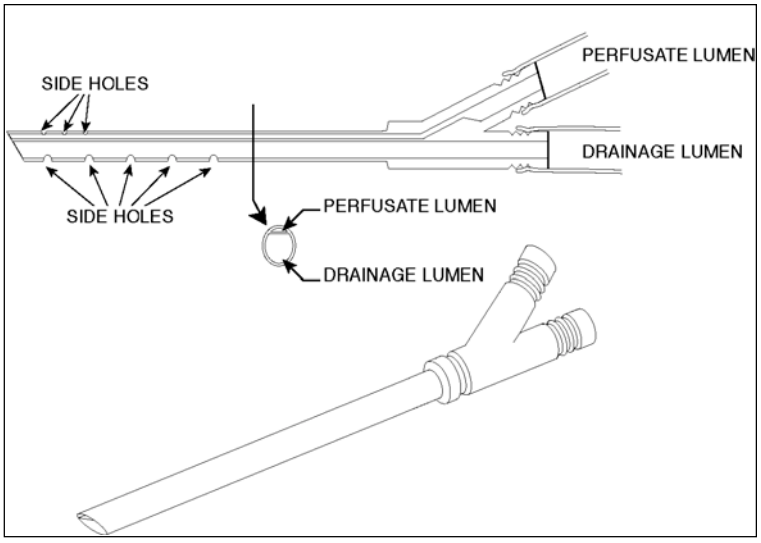

Fig. 4.12. Dual lumen venous cannula.

Diagnosis
a) air in the venous limb of the circuit
b) bladder alarm/pump stoppage
c) blood loss at cannulation site
d) cannula obviously out of incision

Management
a) Immediately turn off pump
b) Take patient off ECMO
c) Full ventilatory support as possible
d) Control bleeding at site
e) Volume resuscitate
f) Clamp bridge and unclamp arterial line/use for volume resuscitation. Recirculate via bridge every 5 minutes
g) Remove air from venous limb through bladder during recirculation

ii. Arterial decannulation

Diagnosis
a) Hemorrhage at cannulation site
b) Bladder alarm/pump stoppage
c) Cannula clearly out of patient
d) Lower pre- and postmembrane pressures

Management

a) Turn off pump immediately
b) Take patient off ECMO
c) Ventilator support as possible
d) Direct pressure to cannulation site
e) Volume resuscitate
f) Clamp bridge and unclamp venous line. Recirculate every 5 minutes for 30 seconds by clamping venous line and unclamping bridge.
g) Use venous pigtail on bridge as volume line
h) Preparation and support to replace cannula

References

1. 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 oxygenation. J Pediatr Surg 1991; 28:530-4.

Safety/Monitoring Devices

I. Anticoagulation

A. Virtually always anticoagulated with heparin
   1. Mechanism of Action
      Heparin acts in conjunction with ATIII by forming complexes with activated factors IX, X, XI. Its action is primarily on the intrinsic pathway. Heparin acts by blocking the conversion of prothrombin to thrombin, and to a lesser degree, by inhibiting the conversion of fibrinogen to fibrin.

B. Adequate anticoagulation does not prevent all thrombotic complications associated with ECMO

II. Anticoagulation Monitoring

A. ACT measured from whole blood. Patients vary in their response to heparin use. PT and partial prothrombin time (PTT) are not followed during ECMO.

B. ACT levels will remain stable if heparin infusion rate is constant. However, ACT can be affected by platelet count, fibrinogen level, clotting factors, heparin metabolism, and urine output. As urine output increases, ACT decreases. As platelet count increases, ACT decreases.

C. Types
   1. Hemochron® and Hemochron® Jr. coagulation systems (ITC (International Technidyne Corp., Edison, NJ))
   2. Medtronic® Systems (Automated Coagulation Timer II (ACT II) and HEPCON® HMS)

D. Specifications
   1. Hemochron®
      Instrument Model 801
      Portable and battery powered; easy to use
      Dual-well whole-blood coagulation monitoring system
      Components:

sample tubes	P214/P215
tube activator	glass particles
test tubes	plastic
sample size	0.4 ml

   2. Hemochron® Jr.
      a. Used in neonates
      b. Low blood requirement to perform ACT

c. Rapid, accurate system. Portable and battery operated
d. Monitoring can be done with either of two systems: kaolin and celite
e. Components:
1) Kaoli system:
a) Cuvettes – JACT+
b) Activator – Kaolin
c) Sample size – 0.015 ml (one drop)
2) Celite system:
a) Cuvettes – JACT-LR
b) Activator – Celite
c) Sample size – 0.015 ml (one drop)

3. Medtronic® Systems
a. Automated Coagulation Timer II (ACT II)
b. HEPCON® HMS
These 2 devices can also determine ACT, but have more complex features for use in surgery or complex coagulopathic situations. HEPCON HMS measures heparin needs of the individual patient by measuring actual heparin concentration

E. Management Guidelines
Initial heparin dose for cannulation (100 units/kg body weight), followed by continuous infusion of 25-100 units/kg/hour to maintain ACT 180-200 seconds. This range of ACT can be modified in situations of bleeding, at which time an ACT of 160 may be tolerated.

F. Caveats
1. Check manufacturer's data for fault codes. Fault codes display if no clot is detected after prolonged period, if early/premature clot is seen, or if calibration is needed. Under these conditions, ACT should be repeated to exclude operator error.
2. Maintenance
Keep device clean and dry, especially the test well and test tube drive collar

III. Arterial Blood Gases (ABG)

ABGs assessed periodically to evaluate adequacy of oxygenation, function of oxygenator, and acid-base status of the patient. Temperature corrections (alpha stat) are typically not required during ECMO, as normothermia is maintained.

IV. Mixed Venous Oxygen Saturation

This is an important parameter trend to follow in ECMO population drawn from venous return line. It is a fairly accurate representation of oxygen needs during VA ECMO. A value of 75% is optimal. This number will be even higher in VV ECMO, where recirculation is an issue.

V. ECMO Circuit Monitoring

A. Pressure Monitoring — Pre- and Postoxygenator

1. An increase in pressure gradient across the oxygenator may signal thrombus deposition in the oxygenator
2. An increase in the postoxygenator line pressure suggests catheter kinking or occlusion

B. Flow probes
   1. Function
      An ultrasonic transit time flow probe used to allow continuous monitoring of the extracorporeal blood flow during support
   2. Types
      a. Biomedicus Bio-Probe, flow transducer
      b. Transsonics bypass flowmeter
   3. Specifications
      a. Bio-Probe, flow transducer for use with centrifugal pump, placed in-line
      b. Transsonics flowmeter used with a roller head pump, positioned around the tubing (on-line).
   4. Management Guidelines
      a. Calibration
         Important to calibrate flowprobe at any new position or if displayed values are suspect
      b. Maintenance
         Keep sensor clean by use of alcohol. Do not immerse or autoclave this instrument
   5. Caveats
      Accuracy of flowmeter dependent on precise interface between probe and tubing.

VI. Other Monitors

A. Continuous Electrocardiogram (ECG)
B. Arterial Pressure Line
C. CVP Monitor
D. Foley Catheter
E. Transcutaneous Oximeter
F. End-Tidal CO_2 ($ETCO_2$) Monitoring
   Even with VV ECMO, $ETCO_2$ may be in the 5% range early in the ECMO course. As the patient's native lung function improves, ET CO_2 will slowly increase. As $ETCO_2$ approaches normal ($ETCO_2$ >35 torr) weaning of the ECMO circuit can be considered.

Peripheral Access for ECMO Support

I. Cannulation Sites

A. Venoarterial ECMO

1. Venous

   Right internal jugular vein is used for basically all venous cannulations in neonates. Largest internal diameter catheter with the shortest length is preferable. A smaller catheter is preferable if the M number is less than that dictated by the desired flow characteristics. In pediatric and adult patients, common femoral vein cannulation may be used. Again, however, the largest available cannula is preferred as the rate of venous drainage typically limits overall ECMO flow.

2. Arterial

   Right common carotid artery (CCA) used in neonates in veno-arterial ECMO. At some institutions, the right CCA is used in pediatric and adult populations as well. Advocates of this approach credit the lack of limb ischemia and preferential flow of oxygenated blood to the coronary and head vessels when using carotid arterial cannulation. The incidence of strokes is reportedly not increased by this technique. This may be a safe practice when there is sufficient time, as it is necessary to perform temporary occlusion to insure no evidence of left-sided motor and sensory function. However, a commonly used alternative site in the older patient is the common femoral artery. In the femoral artery, the use of a small percutaneous cannula will offer adequate flow and usually will not cause ischemia to the lower extremity. However, some clinicians advocate direct placement of a 10F arterial cannula aimed distally in the femoral artery (Fig. 6.1).

B. Venovenous ECMO Access

1. Neonatal

   Right internal jugular vein is used, dual lumen cannula is preferred, therefore only one site is required. Since 1989, a 14F double-lumen catheter (Kendall Infant ECMO Catheter, Kendall Healthcare Products Co., Mansfield MA) had been used. A percutaneous approach recently reported for neonates >3.0 kg in weight[1] using Jostra (Jostra GMBH, Hirrlingen, Germany) 12F and 15F double lumen venovenous (DLVV) ECMO cannula DLVV ECMO cannulae.

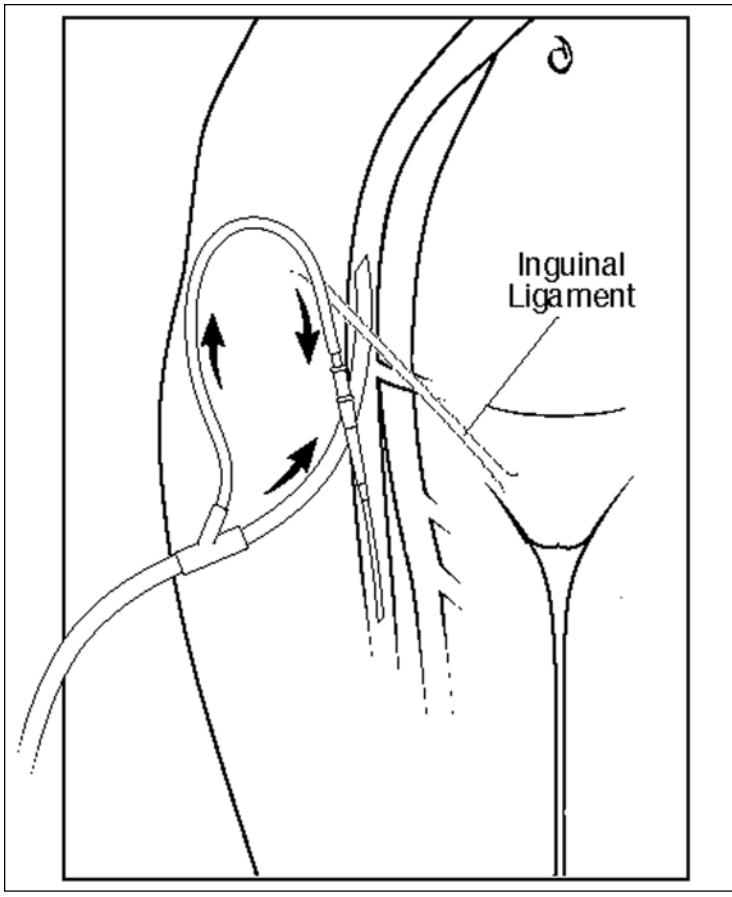

Fig. 6.1. Placement of accessory cannula distally in the superficial femoral artery should be strongly considered when femoral VA ECMO used.

2. Pediatric and Adult
   Right internal jugular vein is used for drainage, with reinfusion via a common femoral vein catheter positioned in the inferior vena cava. The delivery of oxygenated blood to the right atrium may influence lung recovery and improve right ventricular function

C. Cannulation for Cardiac Support
   Often an arterial cannula maintained in the original position (ascending aorta) is used during cardiac surgery. A venous cannula may also remain in position from the original operation or may be converted to the femoral vein or internal jugular vein.

II. Cannulation Techniques

A. Timing and Preparation
   1. Performed while the ECMO circuit is being setup
   2. Notify appropriate services (anesthesia/surgery/OR/respiratory therapy)
   3. Preparation
      All the conditions present in the operating room should be made available in the ICU including adequate lighting (including headlight), sterile field, operating room nurses, appropriate vascular instrument tray, and monitoring lines.

B. Patient Positioning
   1. Allow adequate space for the surgeon to be positioned at head of bed.
   2. Place roll transversely behind patient's shoulders. Bed with an air mattress should be place at this time. Turn head to left, while extending the neck (Fig. 6.2).

C. Medications
   1. For Procedure
      a. Vecuronium: 0.1-0.5 mg/kg IV (Neonates 0.1 mg/kg)
      b. Morphine Sulfate 0.05-0.3 mg/kg IV (Neonates .05 mg/kg)
      c. Midazolam 0.05-0.15 mg/kg IV
      d. Propafol 2-3 mg/kg IV
      e. Heparin sulfate 1000 U/ml
      f. Heparinized saline for infusion into catheters while preparing for connection to the ECMO circuit
      g. Lidocaine 1% without epinephrine
   2. Resuscitation Medications
      Advanced cardiac life support (ACLS) or pediatric advanced life support (PALS) drugs should be available.
   3. Antibiotic prophylaxis (in patients not already receiving antibiotics) 1st or 2nd generation cephalosporin is used.

D. Skin Preparation
   1. Standard betadine preparation of the right neck and chest.
   2. Drape patient to expose right neck, right ear, and chest.
   3. Maintain access to all monitoring equipment during cannulation.
   4. Maintain adequate intravenous access during procedure.

E. Surgical Procedure
   1. Venoarterial Cannulation in the Neonate
      a. 2 cm transverse incision made 1cm above the clavicle between the heads of the sternocleidomastoid muscle. Use electrocautery to minimize bleeding once heparinized. Identify right common carotid artery and internal jugular vein. Minimize dissection, as vasoconstriction can limit the size of cannula used. Place suture around the vessels proximally and distally, heparinize with 40U/kg IV. Repeat dose (with 1/2 of original bolus) if cannulation takes longer than 30 minutes. Topical lidocaine may limit the local vasoconstriction.

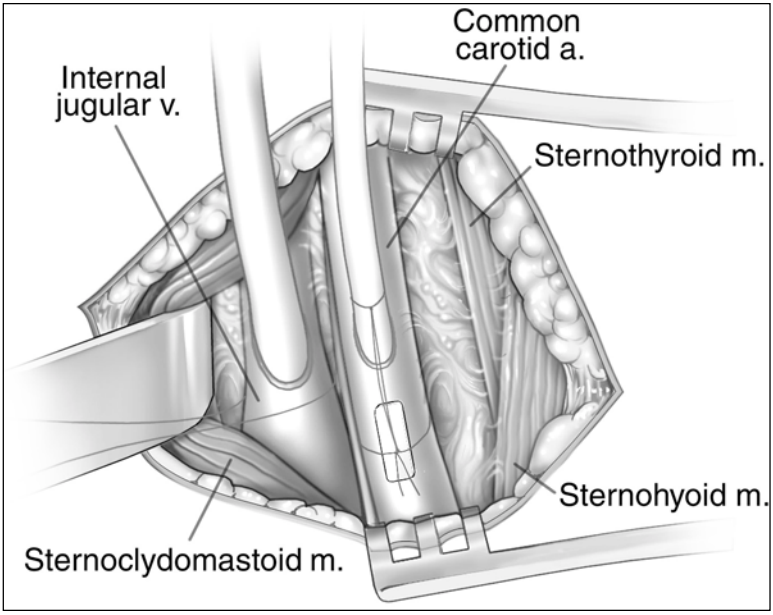

Fig. 6.2. Anatomical landmarks and cannulation method for VA ECMO utilizing the right common carotid artery and jugular vein.

b. Cannulate the artery first, using a 10F cannula for a neonate. After the transverse arteriotomy is made, a 6-0 prolene suture is often helpful to expose the lumen of the vessel and limit the chance of dissection. The tip position should be in the innominate artery. De-air, then attach the cannula to the arterial limb of the ECMO circuit.

c. Venous cannulation is usually more difficult, as a large cannula is critical for adequate ECMO flow. It may be difficult to place secondary to vein size and spasm. For neonates, a 14 Fr venous catheter is usually adequate. Prolene suture placement may also be helpful for exposure. Mineral oil or other sterile lubricant may help to advance the cannula. Cannula should be positioned so that the tip is about 6 cm from the venotomy site (in neonates), which corresponds to the mid-atrial position. De-air and connect the cannula to the venous limb of the circuit (Fig. 6.3).

d. Initiate ECMO.

e. Close wound

1. Prior to closure, carefully examine wound for evidence of bleeding.

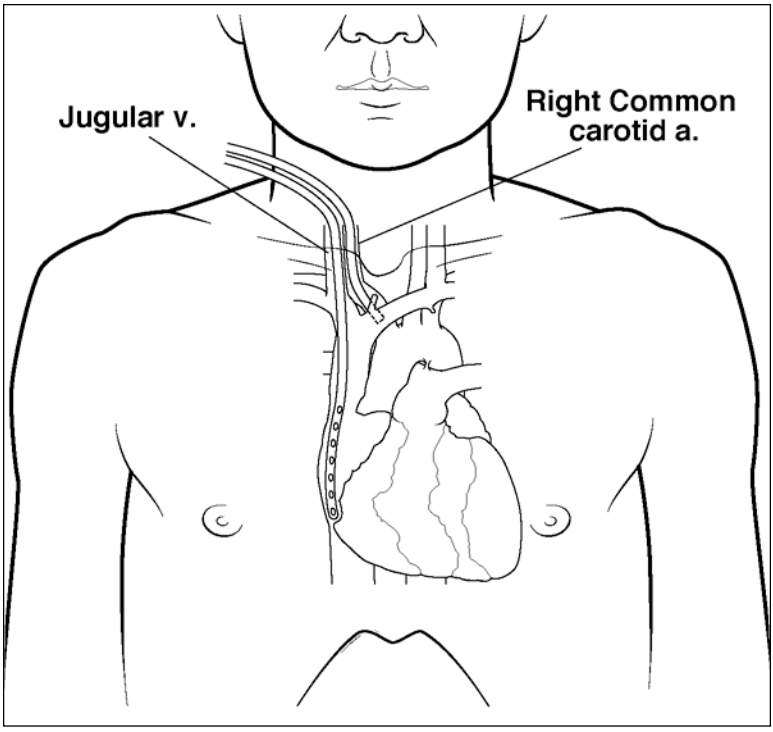

Fig. 6.3. Optimal positioning of VA ECMO cannulae.

2.) Fibrin glue (cryoprecipitate, $CaCl_2$, and thrombin) is often helpful and should be ordered prior to the procedure.

f. Stabilize cannulas

Secure cannulas to the skin of the neck and scalp (mastoid area behind the ear).

2. Veno-Venous ECMO Cannulation in the Neonate

The procedure is identical to that for VA ECMO cannulation with the exception that the common carotid artery is not utilized. The double lumen cannula, developed by Bartlett and associates, must be accurately positioned to allow adequate flow while limiting the amount of recirculation. The tip of the cannula should be in the mid-portion of the right atrium, and the arterial side of the catheter (outflow) is directed toward the ear. This is important so that the oxygenated blood is directed towards the tricuspid valve. If the catheter is too high in the right atrium, there will be arterialization (increased redness) of the venous drainage by the recirculation effect.

3. Cannulation in the Pediatric and Adult Patient
   a. While VA ECMO utilizes right internal jugular vein/right common carotid artery as the primary sites for cannulation, the femoral artery may be preferred in larger patients. Venous cannulation may then be performed via the femoral or internal jugular veins. To insure adequate blood supply to the lower extremity when femoral artery access is used, distal perfusion with a separate 10F arterial cannula is recommended.
      Technique: first prepare the circuit with a 3/8 x 3/8 x 1/4″ Y-connector on the arterial limb. Include a segment of clamped 1/4″ tubing on the side branch. Place the proximal arterial and venous cannulas, using a percutaneous technique. Place patient on ECMO. The distal cannula can then be placed in a more 'controlled fashion.' The skin can then be incised just distal to the main cannulation sites, to keep from entering the subcutaneous tissue planes thereby limiting the amount of bleeding. Expose the superficial femoral artery. Place a pursestring 4-0 or 5-0 prolene suture and cannulate the distal vessel using a 10F arterial cannula (Fig. 6.1).
   b. Another approach recently reported[2] uses central cannulation (ascending aorta and right atrium) for ECMO support of patients after lung transplantation. This technique may reduce the need for reexploration in this patient population, may improve ECMO support, and limit peripheral vascular complications.
   c. For veno-venous ECMO, both internal jugular and common femoral venous cannulation may be required. This can be accomplished at both sites using percutaneous techniques. If an open technique is selected, placement of the cannula through a pursestring suture at the sapheno-femoral junction obviates the need for a true vein repair at the time of decannulation. This technique may also reduce problems with venous obstruction. The tip of the venous cannula from the femoral vein should rest at the bifurcation of the vena cava (level of the umbilicus). Recent studies[3] have supported the use of the femoral venous cannula for drainage, with the oxygenated blood returning to the right atrial level (via the internal jugular vein). Using a femoro-atrial bypass circuit, they were able to obtain higher maximal ECMO flows, higher SVO_2 and required comparatively lower flow to maintain adequate circulatory support.
4. Cannulation for Cardiac ECMO
   In situations where the patient cannot be separated from cardiopulmonary bypass, the same cannulas that were used for the surgical procedure are kept in place. Occasionally, more long-term, conventional cannulation is adopted, to reduce risks of decannulation and bleeding. This subjects the patient to risks during the circuit exchange. Moreover, consideration

must be given to adequately decompressing the left ventricle to assist in cardiac recovery. A left atrial drain may be added, or, in neonatal and pediatric cases, a balloon atrial septostomy can be considered.[4]

III. Decannulation

A. Use sterile technique
B. Assemble formal operating team, securing adequate equipment including headlight
C. Position patient with shoulder roll (in Trendelenberg position)
D. Administer muscle relaxant to prevent inhalation of air into venous circulation during decannulation
E. Remove venous line first, as it is more dangerous because of the risk of air embolism
F. Do not repair vein or artery in neonates, simply ligate vessels
G. If femoral cannulation is selected, repair these vessels after decannulation.

References

1. Reickert CA, Schreiner RJ, Barlett RH et al. Percutaneous access for venovenous extracorporeal life support in neonates. J Pediatr Surg 1998; 33:365-369.
2. Meyers BF, Sundt TM III, Henry S et al. Selective use of extracorporeal membrane oxygenation is warranted after lung transplantation. J Thorac Cardiovasc Surg 2000; 120:20-26.
3. Rich PB, Awad SS, Crotti S et al. A prospective comparison of atria-femoral and femoro-atrial flow in adult venovenous extracorporeal life support. J Thorac Cardiovasc Surg 1998; 116:628-32.
4. Seib PM, Faulkner SC, Erickson CC et al. Blade and balloon atrial septostomy for left heart decompression in patients with severe ventricular dysfunction on extracorporeal membrane oxygenation. Cathet Cardiovasc Intervent 1999; 46:179-186.

Applications and Management of ECMO

I. Neonatal ECMO

A. General Indications

Respiratory failure secondary to

1. Meconium aspiration syndrome
2. Congenital diaphragmatic hernia
3. Sepsis
4. Hyaline membrane disease
5. Primary pulmonary hypertension
6. Persistent fetal circulation
7. Postcardiotomy cardiac failure

B. Pathophysiology

Respiratory failure of a transient or correctable etiology. Success of ECMO in the neonatal population is related to the potentially reversible nature of the pathologic process causing the respiratory failure

C. Neonatal ECMO Inclusion Criteria

1. Gestational age >34 weeks but less than 28 days
2. Evidence of severe, refractory respiratory failure as indicated by:
   a. Oxygenation index >40 on 3 of 5 blood gases drawn at least 30 minutes apart but not more than 60 minutes apart.
      (OI = mPaw x FiO_2 x 100/postductal PaO_2), or
   b. Severe, refractory respiratory failure with sudden decompensation (PaO_2 <40 torr) unresponsive to maximal medical management, or
   c. Failure to wean maximal ventilator settings, including persistent need for FIO_2 >0.9 after 4 days, or
   d. Inability to maintain a PaO_2 ≥45 with a pH <7.55, or
   e. Three or more decompensation episodes; defined as a decrease in baseline SaO_2 by 10%, requiring handbagging and/or other interventions, within a 12-hour time period
3. Severe primary and/or secondary cardiac dysfunction that is life threatening and unresponsive to other available measures as defined by but not limited to:
   a. Echocardiographic evidence of severe right ventricular dysfunction, or
   b. Inotropic support with
      i. Dopamine >20 mcg/kg/min; and/or
      ii. Epinephrine >0.2 mcg/kg/min; and/or

iii. Continued volume requirements

D. Neonatal ECMO Exclusion Criteria
   1. Gestational age <34 weeks
   2. Irreparable congenital heart defect
   3. Prolonged pre-ECMO ventilatory support (usually >10 days)
      Lung disease not likely to be reversible after 10-14 days
   4. Neurologic conditions
      a. Evidence of severe and irreversible brain damage
      b. Intraventricular hemorrhage of Grade II or greater
   5. Multiorgan system failure including pulmonary or cardiac failure and failure of two additional major organ systems
   6. Bleeding diathesis that would be uncontrollable on heparin
   7. Life threatening and untreatable nonpulmonary disease
      a. Positive HIV status (positive viral assay)
      b. Immunosuppression
   8. Lethal, untreatable metabolic diseases, malformations, or anatomic abnormalities or those with major chromosomal abnormalities (trisomy 13 or trisomy 18). Trisomy 21 not an absolute contraindication to ECMO.

E. Relative contraindications to ECMO
   1. Birthweight <2.0 kg
   2. History of recent invasive procedures
   3. Known or suspected bleeding diathesis
   4. Intraventricular hemorrhage (Grade I)
   5. Overwhelming sepsis with capillary leak
   6. More than 10 days of ventilatory support
   7. Severe oliguria or anuria
   8. Severe anasarca with poor perfusion secondary to sepsis and/or capillary leak syndrome
   9. Neonatal renal dysplasia
   10. Pre-ECMO CPR
      a. In situations with severe acidosis (pH <6.80) and prolonged CPR (>45 minutes), results of ECMO generally poor
      b. If pH >7.45, consider ECMO irregardless of duration of CPR, as prognosis is improved,
   11. Profound postductal hypoxemia
      a. postductal PaO_2 <20 torr for >3 hours or
      b. postductal PaO_2 <20 torr and pH <7.0 for >1 hour immediately postpartum, significant risk with ECMO because of the high incidence of intracranial hemorrhage (ICH).

II. Pediatric ECMO

A. General Indications
   1. Pneumonias (viral/bacteria/aspiration/pneumocystis)
   2. ARDS
   3. Acute respiratory failure, non-ARDS

B. Pathophysiology

   Disease processes differ than those of neonates, and the reversibility of pulmonary conditions in the pediatric group is more difficult to predict. Moreover, an extended ECMO course may be required before improvement is realized. This philosophy is similar in the adult ECMO population.

C. Pediatric ECMO Inclusion Criteria
   1. Patients >28 days and <18 years of age
   2. Patient must have a high risk of mortality without ECMO (>80%) with respiratory failure secondary to:
      a. Acute, life threatening, but potentially reversible, cardiovascular and/or respiratory decompensation which is unresponsive to pharmacologic support and amenable to ECMO.
      b. Acute hypoxemia unresponsive to medical management
   3. Oxygenation index(OI) >40 x 2 hours
   4. Hypercarbic respiratory failure defined as uncorrectable hypercarbia with a pH <7.0, and PIP >40
   5. Static lung compliance <0.5 cc/cm H_2O/kg
   6. Barotrauma as defined as a persistent air leak on maximal ventilator support

D. Pediatric ECMO Exclusion Criteria
   1. Life threatening or untreatable nonpulmonary disease
   2. Pulmonary and/or cardiac failure which is unlikely to be reversible in 10-14 days
   3. Diagnosis of a lethal condition in its terminal stages
   4. Multisystem failure consisting of pulmonary or cardiac failure and failure of two additional major organ systems
   5. Positive HIV status (positive viral assay)
   6. Fixed elevated pulmonary vascular resistance
   7. Evidence of severe or irreversible brain damage
   8. Ongoing hemorrhagic condition that may likely be uncontrollable on heparin

E. Relative contraindications
   1. Underlying high morbidity disease state
   2. Recent CNS hemorrhage
   3. Severe GI bleeding
   4. Recent invasive procedure or trauma
   5. Creatinine >3.0
   6. Profound shock refractory to medical management (>6 hours)
   7. Overwhelming sepsis with capillary leak
   8. Prolonged ventilatory therapy (10-14 days)

9. Need for prolonged pre-ECMO CPR
10. Immunosuppression

III. Adult ECMO

A. General Indications
   1. ARDS
   2. Pneumonia (bacterial, viral, aspiration)
   3. Postlung transplant graft dysfunction
   4. Postpneumonectomy pulmonary edema

B. Extreme judgement must be applied when ECMO is performed in this patient population. Adult ECMO is not proven in its efficacy[1] but is currently used in selected instances.[2] Selection criteria are therefore not well-defined. As with the pediatric population, ECMO has been used in patients with severe acute respiratory failure and acute ARDS from multiple etiologies.

C. Pathophysiology
   Etiology of respiratory or cardiac failure is critical to the success of this therapy, as a degree of reversibility is necessary to obtain benefit from ECMO.

D. Adult ECMO Inclusion Criteria
   1. Severe respiratory failure despite optimal treatment
      a. Shunt >30% with FiO_2 of >0.6
      b. Compliance <0.5 ml/cmH_20/kg
         1) Shunt calculation requires measurement of oxygen content in the arterial blood (CaO_2), mixed venous blood (CvO_2) and end-pulmonary capillary blood ($Cc'O_2$). The oxygen content of end-capillary blood is usually calculated from the alveolar and the oxygen dissociation curve.
         2) With this information, shunt fraction is calculated as
$$\frac{Qs}{Qt} = \frac{Cc'O_2 - CaO_2}{Cc'O_2 - CvO_2}$$
   2. Severe and life-threatening hypoxemia, unresponsive to conventional mechanical ventilation
   3. Hypercarbic respiratory failure defined as uncorrectable hypercarbia with: pH <7.0
      PIP >40 cm H_2O

E. Adult ECMO Exclusion Criteria
   1. Duration of respiratory failure and mechanical ventilation >7 days
   2. PaO_2/FiO_2 ratio <100 for >5 days
   3. Multiple organ dysfunction syndrome defined as >2 major organs systems failure
   4. Underlying severe chronic lung disease
   5. Terminal disease with short life expectancy
   6. Bleeding diathesis that would be uncontrollable on heparin
   7. Positive HIV status (positive viral assay)
   8. Uncontrolled metabolic acidosis

F. Relative contraindications
   1. Septic shock
   2. Severe fixed pulmonary hypertension mean pulmonary artery pressure (MPAP) >45 mmHg or 75% systemic)
   3. Acute or chronic irreversible myocardial dysfunction
   4. Immunosuppression
   5. Central nervous system injury or malfunction

IV. Cardiac ECMO

A. General Indications
   1. Postcardiotomy support
   2. Acute myocardial failure/Myocarditis
   3. Bridge to cardiac transplantation or left ventricular assist device (LVAD) support
   4. Neonatal or pediatric postoperative cardiac conditions:
      a. large L→R shunts
      b. persistent pulmonary hypertension
      c. postcardiotomy pulmonary vasoreactive crisis

B. Pathophysiology

   The underlying cause of cardiac dysfunction is important as success of ECMO depends on partial or complete reversibility of this process. In adults, conditions that lead to pure left or right ventricular dysfunction may be supported by ventricular assist devices (VADs), but VAD support assumes native lung function is adequate. ECMO can be used for support of any condition resulting in cardiac dysfunction, and is used most frequently in conditions associated with poor oxygenation and in small patients or children where cannulation for VADs may be difficult.

C. Cardiac ECMO Inclusion Criteria
   1. Cardiogenic shock unlikely to recover without a period of mechanical support as manifested by:
      a. Progressive hypotension
      b. Neonates <45 mmHg systolic
      c. Infants <55 mmHg systolic
      d. Children <65 mmHg systolic
      e. Poor peripheral perfusion
      f. Increasing filling pressures
      g. Decreasing renal function
      h. Decreased SVO_2
      i. Persistent acidosis
   2. Etiology of underlying heart disease and current decompensation known
   3. Known neurologic status (period of arrest known)

D. Exclusion Criteria
   1. Correct diagnosis uncertain.
   2. Unrepaired congenital cardiac defects

3. CNS damage
4. Malignancies
5. Irreversible end-organ damage (lungs, kidneys, liver)
6. Postoperative patient with uncontrolled hemorrhage

V. Assessment

A. Complete Review of Preoperative Evaluation
B. Complete Physical Examination
C. Chest and Abdominal Radiographs
D. Pre- and Postductal Arterial Blood Gases–Neonates
E. CBC, Differential, Platelets
F. Serum Electrolytes, BUN/Creatinine, Hepatic Profile
G. Lactate Level
H. PT/PTT, Fibrinogen
I. Renal Ultrasound, if Indicated
J. Neurological Examination
   1. Cranial ultrasound–neonates
   2. Head CT (pediatrics), if indicated
K. Cardiology Consultation
   1. Echocardiogram
   2. Right heart catheterization

VI. Management on ECMO

Goal of therapy: Maintain ECMO flow to supply adequate tissue perfusion, provide full oxygenation and ventilatory support, and facilitate lung rest.

A. Priming the Circuit
   Performed immediately before cannulation
B. Cannulation
   Make certain NO air present in circuit when connecting to ECMO
C. ECMO Flows
   1. After patient connected to ECMO circuit, slowly initiate bypass
   2. Initial pump flow rate should be 20 ml/kg/min
      a. Avoids too rapid of an increase in blood flow to the cerebral circulation
      b. Allows gradual mixing of patient blood with prime solution
   3. Increase flow to goal rate slowly over several minutes. The rate of flow increase relates to the length of time needed to get adequate mixing, as slow increases in the cerebral oxygen level may be better.
      a. VA ECMO
         i. Goal flow rates
            neonate: 120-150ml/kg/min
            pediatric: 100-120ml/kg/min
            adults: 70-80 ml/kg/min
         ii. Reach goal rate over 20-30 minutes

b. VV ECMO
    i. Goal rates of 150 ml/kg/min
    adjust accordingly to increase SaO_2, while decreasing recirculation affect
    ii. Reach goal rate over 10-15 minutes

4. Increasing flows
ECMO flows should be increased as needed to optimize oxygen delivery to the tissue. This is regulated not by changes in the oxygenator FiO_2 levels, but rather by increasing or decreasing ECMO flow rates. Poor functioning of the membrane oxygenator may be manifested by either a decrease in postmembrane PO_2 or an increase in $PaCO_2$ levels. Moreover, ECMO arterial line pressures will also be elevated, as will the transmembrane gradient (a pressure increase of >150 mmHg should trigger concern). During VA ECMO, SaO_2 should be >90%, while in VV ECMO, SaO_2 approximates 75-85%, with minimal recirculation.

5. Managing ECMO flows for cardiac ECMO
VA ECMO may impair coronary blood flow, as the majority of coronary blood flow during ECMO comes from left ventricular output. Hypoxic blood perfusing the coronaries may lead to increased left ventricular wall stress. Increasing ECMO flow in an attempt to decompress the LV may actually make matters worse. Left ventricular venting is not widely performed and increases the risk of the ECMO further because of the risk of air embolization.

D. Monitor SVO_2
1. ECMO flow selected to maximize oxygen delivery and CO_2 extraction, while supporting cardiac function as needed. The SVO_2 is the best indicator of oxygen delivery, with a target premembrane value of 65-75%. ECMO flows should be optimized to achieve the best possible SVO_2.
2. Decrease in SVO_2
    a. May indicate an increase in metabolic rate, which can often be treated by sedation or treatment of fever (if present)
    b. May indicate a decrease in O_2 delivery, managed by increasing the ECMO flow.
3. A major increase in SVO_2 with no other changes
    a. May indicate a return of native lung function
    b. May signal a decrease in metabolic rate
    c. May reflect recirculation during VV ECMO

E. Volume Requirements
1. Initiation of ECMO
Support volume requirements with 5% albumin (10 ml/kg), PRBCs, or FFP (5-10 ml/kg for neonates, larger amounts for larger patients).

Table 7.1. Blood component therapy

Agent	Dose
PRBCs	5-10 ml/kg
FFP	10 ml/kg
Platelets	3-4 U/M^2

2. Maintenance
   a. Use blood component therapy as much as possible to both maintain adequate indices and to minimize excessive volume infusion (Table 7.1).
   b. Insure this apparent hypovolemia not secondary to:
      i. Inadequate venous catheter diameter
      ii. Excessive catheter length
      iii. Improper catheter position
      iv. Improper calibration or set-up of the bladder transducer
      v. Improper occlusion setting (achieving more flow than the readout displays)
   c. Any sudden decrease in venous drainage should trigger surveillance as to the possible causes of this problem which may include hypovolemia, pneumothorax, cardiac tamponade, or catheter malposition or kinking.

F. Anticoagulation
   1. Check ACT early, as this may fall rapidly early in bypass
   2. Follow every 15 minutes until stable
   3. Start heparin infusion once ACT falls below 300 seconds, and maintain the level 200-220 in most situations. In cases of bleeding diathesis, ACT levels of 160-180 seconds are acceptable. For a fall in ACT, heparin boluses of 10-20 Units/kg is given, and infusion rate can be increased

G. Laboratory Data
   1. Platelets
      Keep platelet count >100K. Platelet transfusions usually required with initiation of ECMO because of the aggregation of platelets on the artificial surfaces of the circuit, especially the membrane oxygenator. When administering platelets, give postoxygenator
      a. Neonates: 1 single donor unit required
      b. Pediatrics/adults: 2 or more single donor units
   2. Hemoglobin
      Keep hemoglobin at 12-15 gm%

H. Sweep Gas Settings
   1. Composition: Sweep gas flow to the oxygenator consists of mixture of 100% oxygen, carbogen (95% oxygen and 5% carbon dioxide) to maintain $PaCO_2$ between 30 and 40 mmHg.

2. Starting settings
    a. Neonates: 1 lpm oxygen and 1 lpm carbogen at 100% delivered oxygen
    b. Pediatrics/Adults: 2 lpm oxygen and 2 lpm carbogen at 100% delivered oxygen
3. Modify as indicated by arterial blood gas determination
4. $PaCO_2$ maintained at 40 mmHg by manipulating flow rate and concentration of sweep gas

I. Medication Use

Dose adjustment not typically required on ECMO

1. Inotropic and pressor support should be slowly decreased and eliminated after stabilization on ECMO
    a. Milrinone (1mg/ml):
    load: 50 mcg/kg
    maintenance: 0.5 – 0.75 mcg/kg/min
    b. Norepinephrine (1 mg/ml): 0.05 – 1.0 mcg/kg/min
    c. Dobutamine (12.5 mg/ml): 5-15 mcg/kg/min
    d. Dopamine (40 mg/ml): 2-20 mcg/kg/min (2-5 mcg/kg/min dose used by some centers for renal perfusion)
    e. Epinephrine (1 mg/ml): 0.1 – 1 mcg/kg/min
2. Diuretics
    a. Furosemide (Lasix):
    Bolus: 0.5-1.0 mg/kg q 6-8 hours
    Continuous infusion:
    Load: 0.1 mg/kg
    Continuous: 0.1 mg/kg. Increase by 0.05 mg/kg/hour to maintain adequate urine output
3. Antihypertensive agents
    a. Sodium nitroprusside (50mg): 0.5-10.0 mg/kg/min IV
    b. Nitroglycerine (5mg/ml): 0.5 – 5.0 mg/kg/min IV
    c. Hydralazine (20mg/ml): 0.1 – 0.5 mg/kg/dose IV
    d. Esmolol (2.5 g/10ml): 500 mg/kg load; 50-150 mg/kg/min IV infusion
    e. Enalapril: 0.625 – 1.25 mg IV q6°
    f. Nifedipine (10 mg tablet): 0.25-0.50 mg/kg/dose, po
    g. Captopril: 0.5 – 1.0 mg/kg/24° divided in q8° doses, po
4. Sedatives/Analgesics/Anxiolytics
    a. Morphine sulfate: 0.02-0.1 mg/kg/hour
    b. Fentanyl citrate: 1-3 mcg/kg/hour
    c. Midazolam: 0.1-0.2 mg/kg/hr
    d. Lorazepam: 0.50 mg/kg/hr
5. Neuromuscular blocking agents
    a. Vecuronium: 0.06-0.1 mg/kg/hr
    b. Succinylcholine: 2 mg/kg IV
    c. Etomidate: 0.3-0.4 mg/kg IV

6. Prophylactic antibiotics (varies with center)
   Recommend gram positive and gram negative coverage
   a. Ampicillin (100mg/kg/dose q 12 hour)
   b. Cefotaxime (50 mg/kg/dose q 12 hour)
   c. Vancomycin (10-15 mg/kg q12°)
   d. Amikacin (7.5 mg/kg q 8-12°)
   e. Any 1st or 2nd generation cephalosporin acceptable
7. H_2 blocker or proton pump inhibitor (may be used in total parenteral nutrition (TPN))

J. Weaning/Cessation of ECMO Support
   1. Decision to initiate ECMO wean
      a. Dependent on assessment of many factors
         i. chest x-ray (CXR)
         ii. Arterial and mixed venous O_2 saturations
         iii. VA ECMO weaning also requires recovery of hemodynamic parameters
      b. Indicators of lung recovery
         i. Increasing PaO_2 without increases in ventilator settings
         ii. Increasing lung compliance
         iii. Improvement in CXR
      c. Indicators of cardiac recovery
         i. Increasing SVO_2
         ii. Improved contractility (on echocardiogram)
   2. Weaning
      a. When pulmonary or cardiac function deemed recovered, ECMO flow is slowly decreased
      b. Amount of flow weaned
         Neonates: 10-20 ml/min
         Larger pediatric patients: 100-200 ml/min
      c. Rate of weaning
         i. 15 minutes to several hours, depending on patient status
         ii. Resumption of full mechanical ventilatory support is initiated prior to beginning ECMO wean. When ECMO flow rates are reduced to 50 ml/kg/min, most of gas exchange is provided by the native lung. At this point, optimize ventilator and hemodynamic support and wean off ECMO.
         iii. VA ECMO
            a) Wean to idling flow of 10-20 ml/kg/min
            b) Continue circulating via bridge
            c) Maintain full anticoagulation
            d) Follow for stability of lung and cardiac function
            e) Decannulate
         iv. VV ECMO
            a) Wean to idling flow of 40-50 ml/kg/min
            b) Continue wean by decreasing gas flow to the oxygenator

c) Maintain full anticoagulation
d) If remains stable, stop ECMO support
e) Decannulate

v. Minimal recommended flow
a) Neonatal circuit:
Maintain a 500 ml/min flow for a 1/4″ circuit
b) Pediatric circuit
Maintain a 500 ml/min flow for a 3/8″ circuit

vi. 100% Oxygen challenge
a) For use with VA and VV ECMO
b) Flows usually at 30-50 ml/kg/min
c) Place ventilator FiO_2 on 100% for 15 minutes

K. Trial off–Final Step Prior to Decannulation

1. VA ECMO

a. For neonate, increase ventilator settings to full support levels: PIP 25-30 cmH_2O, PEEP 5 cm H_2O, respiratory rate 30 bpm, FiO_2 .50-1.00

b. For pediatrics, more variable settings depending on disease process

c. Change infusions to patient (instead of ECMO circuit)

d. Zero all monitors

e. Separate from ECMO
i. Clamp venous line near neck
ii. Open bridge, clamp arterial line
iii. Increase flow to 200 ml/min for neonatal circuit

f. Observe oxygenation and hemodynamic parameters
i. If patient does not tolerate the trial off, SaO_2, BP, and HR will change immediately. Resume ECMO
ii. If patient tolerates trial off, remain off, check ABG in 15 minutes
if ABG acceptable, decannulate
if ABG borderline, attempt ventilator changes, repeat ABG
iii. Flash cannula q 5-10 minutes during trial off, to prevent clot formation. To perform this, decrease flow to previous setting, place patient on ECMO for 3 seconds, remove from ECMO, return to recirculation flow.

g. Monitor circuit ACT q 15 minutes during trial off. After 30 minutes, check patient ACT as well

2. For VV ECMO

a. Increase ventilator settings to full support levels

b. Zero monitors

c. Gradually decrease FiO_2 of sweep gas to .21

d. Observe patient oxygenation

i. If not tolerating this trial off, SaO_2 will drop and $ETCO_2$ will increase. If patient decompensates resume gas flow to the membrane

ii. If patient tolerates procedure, check ABG after 15 minutes
If ABG acceptable, decannulate
If ABG borderline, attempt ventilator changes and repeat ABG in 15 minutes

L. Ventilator management

1. Goals of ventilator management

a. Lung rest to promote healing by minimizing effects of mechanical ventilation/barotrauma

b. Reduce risk of O_2 toxicity

c. Decrease further lung damage

2. When ECMO is used for primary respiratory support
VA or VV ECMO

a. Patients are initially on high ventilator settings. After ECMO initiated, these settings are reduced. With both VV and VA ECMO, small airways and alveoli tend to close as the distending airway pressure is decreased. Patient completely dependent on ECMO at this point. Backup ventilator settings in this situation would initially be FiO_2 1.0, peak airway pressure (PAWP) 30, PEEP 10, ventilator rate 20-30 bpm.

b. Lung rest settings (Table 7.2)

i. Prevent progressive lung injury by avoiding high ventilator settings

ii. Recruit new alveoli without further damaging the lung

iii. Maintain mean airway pressure 10-20 cm H_2O, FiO_2 <50%.

iv. Opacification of the lungs is often seen within the first 24 hours of ECMO, and chest radiograph worsens despite ventilator changes

v. Aim to avoid both atelectasis and lung hyperinflation. If atelectasis is a significant problem, increasing PEEP to 12-15 may be attempted. If more than 15 cm H_2O is needed, high-frequency oscillatory ventilation should be considered.

vi. Decrease PEEP as the lung inflation improves, usually after the first 24 hours. Although changing PEEP is done commonly, it is usually not necessary to change PIP. If increasing PEEP does not improve lung inflation, increase inspiratory time to 0.6. If this fails, increase PIP to 25-30 cm H_2O. Do not increase PIP greater than this.

M. Respiratory Therapy on ECMO

1. Pulmonary Toilet

a. Turn patient side to side for gentle percussion/postural drainage. Vibratory percussion preferable, as vigorous chest percussion may initiate bleeding

b. Avoid over-bagging

Table 7.2. Ventilator rest settings during ECMO

	Neonates[3]	Pediatrics	Adults	Cardiac
Peak inspiratory pressure (cm H_20)	20-30	30-35	30	20-30
Tidal volume (ml/kg) (if volume ventilator)	4-8	5-10	5	
PEEP (cmH_2O)	5-15 4-8 with airleak	10-15	10	5-15
Respiratory rate (bpm)	5-10	5-10	5-10	5-10
Inspiratory time	0.5 seconds	Alter to maintain Oxygenation/FRC	I:E ratio 2:1	
FiO_2	30%	40%	40%	40%
Other considerations		tolerate a higher $PaCO_2$ (55-65) pH >7.2		

c. Suction carefully, only with a soft catheter, and do not extend down further than a few mm below the end of the endotracheal tube to minimize suction trauma while heparinized

2. Bronchoalveolar Lavage
   a. Sometimes used in patients with severe meconium aspiration syndrome to mobilize secretions and meconium
   b. Try to avoid this procedure in neonates as it can deplete surfactant and cause pulmonary hemorrhage
   c. In pediatric patients, bronchoalveolar lavage used for:
      i. Removal of secretions
      ii. Treatment of mucous plugging
      iii. Obtaining cultures for optimal therapy
3. Aerosol treatment
   a. Beta agonists useful in treating bronchospasm
   b. May be helpful in mobilizing infected or large volume secretions
   c. Metered dose inhalers (MDI) may offer safety advantage
4. Bronchoscopy
   a. Used for both diagnosis (e.g., cultures) and therapy (e.g., management of mucus plugging)
   b. May be complicated by heparinized state

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Special Management Issues in Caring for Patients on ECMO

I. Renal Function

A. Standard Course
   1. Transient decline in renal function seen in patients with both VV and VA ECMO
   2. Urine output may decrease to .25-1 ml/kg/hr during the first 12-36 hours. No intervention is helpful during this period
   3. Normalization of urine output usually occurs after 36-48 hours
   4. Diuretic therapy (lasix, diuril) may be used to maintain urine output and achieve diuresis. Renal dose dopamine may also be considered.
   5. Adequate urine output
      Infant: 2 ml/kg/hour
      Child: 1 ml/kg/hour
      Adolescent: 0.5-1 ml/kg/hour

B. Renal Failure
   After 48 hours, if urine output does not increase and BUN/Cr does not decrease, closer assessment of renal function is warranted. In situations when renal function does not quickly return, hemofiltration or dialysis may be initiated through the ECMO circuit
   1. Hemofiltration
      Particularly attractive because of the ease with which it can be performed.
   2. Hemodialysis
      Also possible, using the same hemofilter and the addition of the dialysate which can be infused via a gemini pump through the remaining port on the hemofilter.
   3. Mechanics (see Fig. 3.11)
      a. Attach the hemofiltration coil to the arterial limb of the ECMO circuit.
      b. Arterial side of the hemofiltration circuit is connected to the premembrane pressure monitoring port (the point of highest pressure in the circuit).
      c. Venous side of the hemofiltration circuit is connected to an unused infusion port.
      d. Drainage of effluent
         i. Intravenous (IV) tubing is connected to the drainage port off the hemofilter.

ii. This tubing is in turn attached to a Gemini pump, then to a urine drainage bag.

e. In this way, blood is filtered from the high pressure premembrane region, to a low pressure prepump system. As a fraction of blood is shunted through the hemofiltration circuit, the net flow delivered to the patient is decreased. ECMO flow should be increased to compensate for this shunting.

4. Management considerations
   a. During initiation of dialysis or hemofiltration, increase the pump flow, as 180-200 ml/min of flow is routed through the filter. Increase the pump flow slowly until postmembrane pressure approaches prior levels.
   b. Use Transsonics® flow probe to accurately assess flow to the patient
   c Anticoagulation
   Check ACT q 30 minutes initially, as the heparin used to prime the hemofilter will affect the patient systemically. Target ACT levels are not changed with use of hemofiltration.
   d. Increasing volume requirements may indicate that the hemofiltration rate is too high
   e. Monitor electrolytes closely
5. Complications
   a. Clotting of the hemofiltration coil (most common problem)
   b. Hypovolemia, hypotension, electrolyte imbalance, and infection

C. Fluids and Electrolytes
1. Fluid gains
   a. IV fluid — maintenance (Table 8.1)
   b. Humidified ventilator gas
   c. Arterial line flushes
   d. Blood products (significant source of fluid gain)
2. Fluid losses
   a. Renal and GI losses
   b. Phlebotomy
   c. Losses from membrane oxygenator: 2 ml/M^2/hr
   d. Insensible losses secondary to
      i. mechanical ventilation
      ii. capillary leak
      iii. interstitial edema
3. Precise recording of intake/output critical
4. Electrolyte requirements
   a. Sodium: 2-3 mEq/kg/day
   b. Potassium: 2-4 mEq/kg/day
   c. Calcium gluconate: 100-500 mg/kg/day
   d. Magnesium: 6 mg/kg/day for neonates
   e. Phosphorus: 80 mg/kg/day
   f. Phosphorus levels often supplemented from citrate-phosphate-

Table 8.1. Maintenance fluid treatment in children

Weight (kg)	Hourly infusion rate
<10	4 ml/kg
20-20	40 ml + 2 ml/kg for every kg >10
>20	60 ml + 1 ml/kg for every kg >20

dextran (CPD A-1) or Optisol preservative present in blood products

II. Nutritional Support

A. Neonates
   1. Standard hyperalimentation initially
   2. Give lipids peripherally, as central administration into the ECMO circuit releases high concentrations of fat systemically
   3. Protein added to TPN after 2-3 days of ECMO
   4. Enteral feedings can be considered but limited data is available. Some small bowel permeability exists during ECMO. Some authors suggest that use of enteral feeds does not result in clinical deterioration.[1]

B. Pediatric Population
   1. Enteral feeds preferred over parenteral route[2]
   2. Provides nutrients for gut integrity, prevention of bacterial translocation
   3. Start enteral feedings with an age appropriate formula within several hours of stabilization on ECMO
   4. Increase feeding rate between 2-10 ml/hr every 2 hours until full maintenance is achieved
   5. Goal rate to be obtained within 24 hours of starting feedings
   6. Postpyloric feeding tube placement recommended. If not possible, close surveillance with gastric residual and/or pH monitoring critical
   7. If feedings not tolerated, consider use of a gastrointestinal prokinetic agents such as metoclopramide (Reglan)
   8. Use H_2 blockers (ranitidine/famotidine) often used for prophylaxis

III. Hematologic Management

Complications of bleeding often fatal while on ECMO

A. In Stable, Nonbleeding Patients, Maintain:
   1. Platelet count >100,000/mm^3
   2. Fibrinogen >100 mg/dl
   3. PT 13-15 seconds
   4. Hematocrit >40% / hemoglobin >13 g/dl. Maximize oxygen carrying capacity

B. In Bleeding Patients Maintain:
   1. Platelet count >150,000/mm^3
   2. Fibrinogen >150 mg/dl
      Transfuse FFP if fibrinogen is low (10 ml/kg/dose)

If not effective, give cryoprecipitate
Usual neonatal dose is 1-2 units (approximately 7-15 ml) postoxygenator

3. PT 13-15 seconds. Transfuse FFP if PT elevated. Give vitamin K if not already administered at birth.
4. Hematocrit >40% / hemoglobin >13 g/dl. Monitor Hematocrit q 6h, and PT and fibrinogen q 12h. Consider checking d-dimer, ATIII, heparin levels, FSP, heparin antibody assay (to exclude heparin induced thrombocytopenia)

C. Additional Recommendations Regarding Management of Bleeding on ECMO
   1. In extreme situations, heparin infusion rate may be reduced allowing ACT levels to decline. ACT should never fall below 160 seconds.
   2. Avoid invasive procedures if at all possible. This includes central lines, tube thoracostomies, nasogastric tubes, foley catheter changes, and intravenous lines. Moreover, procedures should be done by the most experienced person
   3. If invasive procedures are required, then is pre-emptive treatment important
      a. Optimize coagulation status
      b. Supplement with platelets, FFP, or cryoprecipitate as needed

D. Other Strategies for Management of Bleeding
   1. Pressure
      a. Pack sponges around cannula site, use pressure dressings for minor bleeds
      b. As an adjunct to packing, apply weights on bleeding wounds
      c. Direct pressure by dedicated individual is often helpful as it is more localized than above techniques
   2. Surgical Reexploration
      a. Used if pressure measures fail. Cannulation site is the most common culprit
      b. Occasionally, generalized oozing can be corrected with topical agents
         i. Fibrin glue (3 ml Ca+gluconate, 5ml thrombin, 10 U cryo-precipitate)/Tisseal
         ii. Avitene/gelfoam/surgical (with or without added thrombin)
   3. Pharmacological Resources
      a. Heparin
         i. May decrease rate to maintain ACT 180-200
         ii. If bleeding continues, maintain high ECMO flows while decreasing heparin for a target ACT of 160
      b. Amicar (Aminocaproic Acid)
         i. Used in cases of systemic hyperfibinolysis
         ii. Mechanism of action:
         Inhibits fibinolysis by blocking plasminogen activators and neutralizing plasmin

iii. Loading dose of 100 mg/kg
iv. Maintenance dose 20-30 mg/kg/hr for maximum of 96 hours. Risk of hypercoagulable state if used longer
v. Randomized study in ECMO using either Amicar or placebo failed to show a decrease in the overall incidence of hemorrhagic complications with Amicar[3]

c. Aprotinin
i. A serine protease inhibitor with anti-inflammatory and antifibrinolytic activity that has been shown to decrease bleeding during cardiopulmonary bypass.
ii. Dose: bolus 2 mil KIU, then 500,000 KIU/hour
iii. Risks: Anaphylaxis and immediate clotting have been reported.
iv. Procedure for use
a) Test dose is 1ml IV. Give >10 min. prior to scheduled surgery
b) Loading dose = 350 Units/ml of total blood volume (TBV). TBV = ECV (ECMO circuit volume) + Estimated blood volume (EBV) of patient
c) ECMO Circuit volumes
Infant (.8 m^2 oxygenator) = 530 ml
Infant (1.5 m^2 oxygenator) = 605 ml
Pediatric (1.5 m^2 oxygenator) = 555 ml
Adult oxygenators = 1,080-1,300 ml
d) EBV of patient: <2 months old = 80 ml/kg
>2 month old = 70 ml/kg
e) Loading dose in ml = ECV ml + EBV ml x 350 units/ml divided by 10,000 units/ml
f) Continuous infusion rate in ml/hr = pt weight (kg) divided by 1.4 mg/ml.

d. Vitamin K
i. Promotes formation of clotting factors II, VII, IX, and X.
ii. Administer if PT >15 seconds
iii. Dose 1 mg IV/subcutaneously

IV. Routine Laboratory/Diagnostic Studies During ECMO

A. ACT measured hourly and as needed
B. Hematocrit, platelet count measured every 6 hours and as needed; complete blood count with differential, serum electrolytes, pre- and postmembrane ABG, measured every 12 hours and as needed
C. Liver function tests, serum free hemoglobin, calcium, phosphorus, magnesium, PT/PTT, measured daily
D. Chest x-ray performed daily

V. General Care

A. Moving the ECMO Patient
1. Limit movement to avoid dislodgment of the ECMO cannulae; log

rolling may be useful
2. Risk of decubitus formation; air mattress/special beds should be in place prior to cannulation

B. Post-ECMO Management
1. Long-term pulmonary and neurologic care for these patients should be anticipated
2. Rehabilitation services should be established as early as possible in the post-ECMO course
3. Prolonged ECMO may lead to drug dependence of narcotics and/or sedatives

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Additional Management Issues

I. Transport of the ECMO Patient

A. Ground
   1. Feasible option for most patients, with current systems enabling safe transport without complications.
   2. ECMO should be instituted at the referring hospital, and a 1-2 hour stabilization period should precede transport.
   3. Mobile ECMO units are available, complete with roller pump, membrane oxygenator, oxygen supply, and water bath for the heat exchanger. All electrical parts of the mobile ECMO are supported by an independent power source.*
   4. During transport, continuous monitoring includes ECG, systemic arterial, pulmonary arterial and central venous pressures, SaO_2, and temperature. Hourly blood gas determinations are performed.

B. Air Transport
   1. Experience with air transport of ECMO patients limited to specialized centers such as Wilford Hall Medical Center, Lackland Air Force Base (San Antonio, Texas). All equipment must comply with aviation standards and by regulation cannot interfere with navigation systems.
   2. Fixed-wing aircraft should be pressurized. The effects of atmospheric pressure changes on oxygenation and on gas-filled spaces (e.g., pneumothoraces) must be considered. Helicopter transport is also used but has disadvantages of space limitations and ambient noise, making patient assessment difficult in cases of deterioration during flight.

II. Conduct of Procedures and Operations While on ECMO

A. Any procedure, regardless of the magnitude of the intervention, should be performed by the most experienced personnel available.

B. Sterile technique, operating room support in the ICU, adequate lighting including headlights, and an electrocautery device should be available.

C. Coagulation parameters should be optimized prior to the procedure
   1. ACT should be in lower range 160 – 180
   2. Transfuse platelets if <100K
   3. Keep hematocrit >30%

D. Have biologic glue material available

E. Make effort to limit any invasive procedures while on ECMO

III. Considerations for Discontinuing Support

A. A plan for duration of ECMO should be in place prior to or immediately after initiating support.
B. Frequent discussions with family members regarding prognosis are necessary throughout the support interval.
C. Consider discontinuing ECMO if no recovery of underlying organ dysfunction after predetermined time or if worsening of other organ systems occurs.
D. Development of sepsis while on ECMO portends a worse prognosis but does not eliminate the possibility of recovery.[1]
E. Development of neurologic insult (especially intracranial hemorrhage in neonates, seizures, deteriorating neurologic examination) should signal reassessment of continuation of ECMO.
F. If ECMO is planned as a bridge to transplantation, support may need to be continued for longer intervals.

References

1. Meyer DM, Jessen ME, Eberhart RC, and the Extracorporeal Life Support Organization. Neonatal extracorporeal membrane oxygenation complicated by sepsis. Ann Thorac Surg 1995; 59:975-80.

Trouble-Shooting

I. Air Embolism

A. Incidence

Rare complication. Thromboembolism is much more likely

B. Etiology/Sources of Air Embolism

1. High PaO_2 may force air out of solution
   Jarring the oxygenator or running it in a low pressure system (such as a nonpressurized cabin) or flowing at low rates such as during weaning may produce foam at the dependent (top) part of the oxygenator if the postmembrane PaO_2 is high.
2. Cavitation effect from obstruction in the venous side of the circuit may cause negative pressure to form in the blood path, drawing large amounts of air out of solution.
3. Air entering via a loosely secured venous cannula. Any loose connection near the patient may allow air to enter the circuit. An undetected disconnection or tubing rupture could cause this.
4. Membrane damage: if a tear occurs in the membrane it may allow blood to leak in the gas path of the oxygenator. If gas pressure exceeds blood pressure in the oxygenator, a massive air embolism is possible.

C. Management

1. The key to management of air embolism is prevention.
   Maneuvers used to help prevent this complication include:
   a. Use of gas trapping devices.
   b. Placement of bubble detector distal to the membrane before returning to the patient will stop the pump if air is detected.
   c. Maintenance of postmembrane PaO_2's below 500 torr, especially at low pump flows.
   d. Avoidance of any obstruction of venous return, especially between the bladder pressure port and the pump.
   e. Operation of the circuit with the bladder pressure alarm enabled at all times.
   f. Tie-band all connections.
   g. Strict raceway surveillance.
   h. Routine surveillance of the gas exhalation port of the membrane (No blood, just water, should be present).

2. Emergency maneuvers
    a. Air observed in the arterial line
        i. Stop pump, clamp arterial limb close to the patient, and place ventilator on emergency settings. Open bridge, clamp venous line. Increase flow to 100 ml/min. Remove arterial filter/bubble trap from holder and invert/de-air vigorously. Walk any bubbles down the arterial limb, tapping continuously. Walk air through the bridge. If patients needs to go back on bypass, do a complete circuit check then return patient to bypass. If amount of air is significant, it may require air removal from the bladder
        ii. If air is visible near a pigtail, attempt aspiration through the pigtail
        iii. If air is visible in patient bridge, manually work air to venous side and walk it down to the bladder for removal
        iv. Attempt to remove air if found at the top of the oxygenator, the top of the heat exchanger, or the top of the arterial filter.
        v. Best way to slow or stop air travel is by slowing or stopping the pump flow
        vi. Key issue: always identify the cause for the air, as it should not be there.
    b. If air has already entered patient, take patient off bypass as above, place in Trendelenberg position, de-air circuit, resume flow at high rate if possible. Correct etiology of air embolism. Consider hyperbaric oxygen treatment.

II. Acute Cardiorespiratory Arrest or Decompensation on ECMO

A. Etiologies (Table 10.1)
    1. Tamponade physiology (cardiac tamponade, tension pneumothorax, tension hemothorax)
    2. Hypovolemia
    3. Arrhythmia
B. Management (Table 10.2)
    1. Maintain pump flow
    2. Treat suspected problem (pneumothorax, fluid requirement, tamponade)
    3. Advanced life support protocol medications and interventions. Cardiopulmonary resuscitation (CPR) is rarely used with VA ECMO
    4. Management of cardiac stunning
    With VV ECMO, may not be possible to maintain pump flow. Start CPR immediately. Keep on pump. PALS protocols for medications. Continue CPR until condition is improved or when patient is converted to VA ECMO. In VV ECMO, the circuit may not lose venous return, but may simply be recirculating.

Table 10.1. Complications during ECMO

- **Mechanical complications**
  - Oxygenator failure
  - Tubing rupture
  - Pump malfunction
  - Cannula problems
  - Air/clots in circuit
- **Patient complications**
  - Hemorrhage
    - Surgical site/cannulation site
    - Intracranial
    - GI
- **Thrombotic complications**
  - Neurologic complications
    - Brain death
    - Seizures
    - Infarct
- **Infectious complications**
- **Renal complications**
  - ARF
- **Hemodynamic complications**
  - Hypotension
    - Hypovolemia
    - Hemodynamic instability
    - Pneumothorax/cardiac tamponade
    - Problems with cannula placement/vessel perforation
    - Poor blood return to patient
  - Hypertension
    - Increased volume status
    - Increased level of consciousness or anxiety
    - Improved overall function
  - Cardiac dysrhythmia
  - Myocardial stunning
  - PDA
- **Pulmonary complications**
  - Hypoxia
    - Shunt
    - Membrane failure
  - Hemorrhage
  - Pneumothorax
- **Metabolic complications**
  - Electrolyte abnormalities
  - Acidosis/alkalosis
  - Glucose abnormalities
  - Hyperbilirubinemia

Table 10.2. Management of mechanical complications

1. Low venous return/collapsed bladder **Diagnosis**	**Action**
Hypotension	Give volume
Flowing higher than rated cannula allows	Decrease flows
Cannula malposition	Check CXR, reposition cannula
Occlusion of flow	Check for venous tubing kinks or obstruction
Cannot flow high enough to support patient	Place additional venous cannula
2. Venous bladder damage or malfunction **Diagnosis**	**Action**
Clots in bladder or chimney which cannot be retrieved	Replace venous bladder
Perforation of bladder, rupture with loss of blood	
3. Oxygenator failure **Diagnosis**	**Action**
Leaks-blood dripping from the gas exhaust port	
If light, serosanguinous	Observe, measure
If more than a few drops/hour	Replace oxygenator
If fluid dripping constantly and frankly sanguinous	Replace oxygenator
If gas exhaust port with clotting or obstruction	Replace oxygenator
Borderline gas exchange	
Postoxygenator PaO_2 <350 torr	Replace oxygenator
Difference between pre- and postoxygenator $PaCO_2$ <10 torr	Replace oxygenator
Pressure changes	
If Pre-/ Postmember pressure >150 mm Hg or is <50 mmHg	Observe oxygenator closely (monitor hourly).
If the preoxygenator pressure >450 mmHg	Observe oxygenator closely (may cause a leak in the blood gas phase).
If the preoxygenator pressure >750 mmHg	Replace oxygenator
4. Failure of oxygen supply or blender	
Diagnosis	**Action**
Alarming of gas module Alarming of blender Fall in patient SaO_2	1. If high pressure alarm, disconnect gas line from oxygenator as first maneuver. Use portable O_2

continued

Table 10.2. Management of mechanical complications, continued

4. Failure of oxygen supply or blender	
Diagnosis	**Action**
Alarming of gas module Alarming of blender Fall in patient SaO_2	2. Troubleshoot system: a. Check all connections b. Look for disconnections, cracks, kinks in line from oxygenator to gas module as well as from the back of module to the wall c. Check for accidental change in sweep gas concentration d. Check for obstruction in the oxygenator (clots) e. Check wall connections 3. Replace gas module if necessary
5. High postmembrane pressure **Diagnosis**	**Action**
Cannula malposition	Check CXR, reposition cannula
Flowing too high for system (cannula/membrane)	Decrease flow
Outflow obstruction	Check for arterial tubing kinks
Limitations of arterial cannula	Consider change to larger arterial cannula
6. Hemolysis **Diagnosis**	**Action**
Red serum, Renal dysfunction High serum free Hgb	Check waterbath temperature, lower if too high Check roller occlusion, loosen if necessary Check pump speed, reduce RPM if too high Assess for DIC

5. Insure cannula position is not the problem. Check chest x-ray.
6. Assess for metabolic and acid-base abnormalities

III. Changes in PaO2 or PaCO2

A. In VA ECMO (Table 10.3)
B. In VV ECMO (Table 10.4)

IV. Renal Failure

See management guidelines above

Table 10.3. VA ECMO troubleshooting guidelines

Problem	Symptoms and signs	Possible causes
Changes in PaO_2		
Decreasing PaO_2	Cyanosis, lethargy Acidosis	Pneumothorax, atelectasis Ventilator malfunction/ETT problem Falling ECMO flow Unclamped bridge Gas line disconnected from membrane Oxygenator failure Decreased FIO_2 in sweep gas
	Patient appears stable	Improving pulmonary perfusion (increased shunt through pulmonary vasculature) Increased O_2 extraction Increased O_2 consumption Lab error
Increasing PaO_2	Patient appears stable	Improving pulmonary function ECMO flow rate high Decrease in contribution from native heart (with decrease in pulmonary blood flow
	Cyanosis, lethargy Acidosis, poor perfusion	Decreased O_2 consumption (including tissue death)
Changes in $PaCO_2$		
Decreasing $PaCO_2$	Patient apneic, alkalotic	Sweep gas flow too high Ventilator rate too high Improving lung compliance
	Patient tachypneic, alkalotic	Central respiratory stimulation from high postmembrane $PaCO_2$ Cerebral dysfunction
	Patient tachypneic, acidotic	Other organic acids in blood
Increasing $PaCO_2$	Patient tachypneic acidotic	Carbogen flow too high, Sweep gas flow too low Patient underventilated (pneumothorax, ETT problem, seizures impairing ventilation)
Changes in urine output		
Decreased urine output	Hypotensive	Hypovolemia Ischemic kidney damage
	Anasarca	Capillary leak syndrome
	Poor perfusion	Low CO and/or pump flow

continued

Table 10.3. VA ECMO troubleshooting guidelines, continued

Problem	Symptoms and signs	Possible causes
	PDA seen on ECHO	Steal syndrome
	Heme positive urine	Renal damage 2° to hemolysis
Increased urine output	Oliguric pre-ECMO	Response to improved flow
	Hypoxia, obstruction	Postinjury diuresis
	Improving pulmonary status	Recovery diuresis
Changes in bleeding or coagulation status		
Inconsistent ACTs	No change in patient	Recent platelet transfusion (low ACT)
		Decreased platelets (high ACT)
		ACT machine malfunction
		New heparin lot
		Increased urine output (low ACT)
	Patient coagulopathic	plt count low (high ACT)
		Vit K def, DIC, ATIII def
Patient bleeding	Hypotensive, low hematocrit	ACT too high, heparin dose too high
		Platelet count low, DIC, vitamin K not administered
		Invasive procedure before ECMO
		Cannulation problem

V. Patent Ductus Arteriosus (PDA)

A. Clinical Course

Development of renal failure may be the first indication that the neonate on ECMO has a PDA. The ductus may stay open in these patients secondary to the hypoxia of the underlying condition. VA ECMO changes pulmonary pressures and resistance. Any left to right shunt across a PDA will be exacerbated by the relatively greater systemic vascular resistance. These patients will not respond with the high oxygenation but rather will have a fall in peripheral O_2 saturation, a rise in $PaCO_2$, decreased peripheral perfusion, decreased urine output, acidosis, and increased ECMO flow and fluid requirements.

B. Diagnosis

Doppler echocardiography

C. Management options

1. IV indomethacin: poor choice secondary to the detrimental effects on platelets.

Table 10.4. VV ECMO troubleshooting guidelines

Arterial Saturation	Cephalad Saturation	Venous Saturation	Interpretation	Management
Increasing	Increasing or Stable	Increasing or Stable	Patient is improving Recovery of underlying process	Wean ECMO flow, plan for decannulation
Decreasing	Decreasing or stable	Decreasing or stable	Patient is deteriorating	Check catheter position and pump flow. Attempt to increase flow to improve perfusion.
Decreasing	Stable but with decreased flow	Increasing	Increased recirculation with loss of cephalad catheter flow	Evaluate catheter position, adjust head position, add or subtract shoulder roll, apply gentle traction to catheter; reassess
Decreasing	Decreasing or stable with good flow	Increasing	Increased recirculation from change in catheter position	Evaluate cardiac output and check catheter position, consider adding volume
Decreasing or stable	Increasing with increased flow	Stable	Under-ventilation ($PaCO_2$ is increased)	Check ABG. Adjust sweep gas flow or mix. If off ECMO adjust ventilator support
Stable	Decreasing with decreased flow	Increasing	Over-ventilation ($PaCO_2$ is decreased)	Check ABG. Adjust sweep gas flow or mix. If off ECMO adjust ventilator support.
Decreasing and decreased BP	Decreasing and decreased flow	Increasing	Worry about compromised cardiac output	Consider pericardial effusion if pulse pressure is decreased.

2. Surgical ligation: can be safely done on ECMO.
   Only attempt this if certain that PDA is the problem.
3. Conservative treatment: remain on bypass and wean flow as tolerated.
   This is often all that is required.

Results

I. Neonatal

A. Outcome

Clinical Experience

Since 1984, the Extracorporeal Life Support Organization (ELSO) Registry has collected data from 14,700 neonates placed on ECMO. The overall survival of this group has been 79%, a result that has been unchanged over the time period of the registry.[1]

B. Outcome by Diagnoses (Table 11.1)

C. Studies

1. Which is better? VA vs. VV ECMO. Gauger and associates[2]
   a. Study Design
      i. Retrospective matching of 643 VA and VV pairs
      ii. ELSO registry utilized
   b. Results:
      i. Survival advantage to VV ECMO when matching for respiratory failure (83.8% VA vs 91.5% VV, $p<0.001$) but not significant (in the context of multiple comparisons) when matching for hemodynamic failure (90.4% VA vs 94.5% VV, $p = 0.048$).
   c. Conclusions

      Overall, no survival advantage for VV ECMO when matched for degree of respiratory and hemodynamic failure. Hemolysis and catheter kinking more common in VV ECMO. No difference in incidence of intracranial hemorrhage.
2. UK collaborative randomized trial of neonatal ECMO[3]
   a. Study Design
      i. 185 newborn infants were randomized to either ECMO or conventional ventilator therapy after being diagnosed with severe respiratory failure
      ii. One year survival analyzed between groups
   b. Results
      i. 30 of 93 infants in the ECMO group died, while in the conventionally ventilated group, 54 of 92 infants died. ($p = 0.0005$)

Table 11.1. Cumulative data from ELSO

Primary Diagnosis	Total	Total survivors	Percent survived
Congenital diaphragmatic hernia	3132	1735	55
Meconium aspiration syndrome	5177	4860	94
Primary pulmonary hypertension/ persistent fetal circulation	2065	1659	80
Hyaline membrane disease/ RDS	1268	1093	84
Sepsis	2088	1589	76
Pneumonia	151	83	55
Air Leak syndrome	79	55	70
Other diagnosis	740	500	68
OVERALL	14,700	11,574	79

ii. The benefit of ECMO was also seen in the degree of severe disability at one year.

c. Conclusion
ECMO should be given to neonates with severe but potentially reversible respiratory failure.

3. Results of extracorporeal membrane oxygenation in neonates with sepsis.[4]
   a. Study Design
      i. ELSO registry data report
      ii. 6853 neonates (1060 with primary diagnosis of sepsis, 5793 with any other primary diagnosis)
   b. Results
      i. Survival is not different between the two groups
      ii. Morbidity greater in septic population (neurologic, renal, metabolic).
   c. Conclusions
      i. ECMO should not be withheld solely on the basis of sepsis.
      ii. Management strategies should focus on limiting the incidence or severity of common complications

II. Pediatric

A. Outcome
Clinical experience in the pediatric population, defined as ages greater than 14 days and less than 14 years, is much less extensive than the neonatal experience. The recent results from ECMO have improved slightly, but still do not approach the excellent results seen with neonatal ECMO. In 1998, 175 children were placed on ECMO and recorded in the Registry,

with a survival of 61%. In 1999, 32 patients were added to the ELSO registry, with a survival of 41%.

B. Outcome by diagnoses (Table 11.2)

C. Studies

1. Probability of survival after prolonged extracorporeal membrane oxygenation in pediatric patients with acute respiratory failure.[5]
   a. Study Design
      i. Retrospective review of 382 non-neonatal patients requiring ECMO for respiratory failure
      ii. Assessed the relationship between duration of ECMO support and outcome, focusing on patients requiring ECMO for >14 days.
   b. Results
      i. Overall, 48% survived
      ii. The survival rate in patients treated with ECMO courses >2 weeks was similar to the survival rate of patients treated for shorter periods of time.
   c. Conclusions
      i. Mortality was related to the severity of lung disease before ECMO, and to the occurrence of ECMO complications.
      ii. Duration of ECMO did not affect survival

III. Adult

A. Outcome

Results have remained poor in the US experience. The Registry data reflects an international population, although European centers may be under-represented. Because of the voluntary nature of the database, data may not necessarily reflect new methods and trends in adult ECMO support. In 1998, 71 adults were placed on ECMO, with a survival rate of 44%. In 1999, only seven patients were recorded with the ELSO registry, with a survival of 14%.

B. Outcome by diagnoses (Table 11.3)

C. Studies

1. Early experience with adult extracorporeal membrane oxygenation in the modern era.[6]
   a. Study Design
      i. A retrospective review from the University of Michigan on 10 patients placed on ECMO for respiratory failure.
      ii. The techniques of ECMO were varied, with half of the patients undergoing VV ECMO.
   b. Results
      i. The average ECMO time was 8.7 + 5.2 days for survivors, and 6.4 + 1.9 days for those that died.
      ii. The survivors tended to be younger (27.3 + 3.0 years vs 38.5 + 7.6 years), and were on mechanical ventilation a shorter

Table 11.2. Cumulative data from ELSO

Primary Diagnosis	Total	Total survivors	Percent survived
Bacterial pneumonia	175	92	53
Viral pneumonia	504	307	61
Acute respiratory failure, non-ARDS	524	259	49
Aspiration	141	92	65
Pneumocystis	15	6	40
ARDS, postop/trauma	27	15	56
ARDS, not postop/trauma	197	104	53
Other	140	77	55
OVERALL	1723	860	50

Table 11.3. Cumulative data from ELSO

Primary Diagnosis	Total	Total survivors	Percent survived
Bacterial pneumonia	96	42	44
Viral pneumonia	72	46	64
Pneumocystis pneumonia	2	0	0
Aspiration	22	13	59
ARDS, postop/trauma	50	19	38
ARDS, not postop/trauma	145	80	55
Acute respiratory failure, non-ARDS	19	8	42
Other	95	46	48
OVERALL	501	254	51

period of time before initiation of ECMO (1.8 days vs 6.3 days).

iii. Five patients recovered lung function and four were discharged to home. Causes of death were primarily due to progression of pulmonary injury.

c. Conclusions

The authors stressed early intervention as a key factor in survival in this patient population.

2. Extracorporeal life support for 100 adult patients with severe respiratory failure.[7]
    a. Study Design
        i. An update of the experience from the University of Michigan with 100 adult patients placed on ECMO for management of severe respiratory failure.
        ii. Venovenous percutaneous access was their preference (65% of patients) if cardiac function was adequate. Venous drainage was from the right atrium via the right internal jugular vein (R IJ), and arterialized blood returned via the femoral vein.
    b. Results
        i. Their results agreed with prior studies. Overall survival was 54%.
        ii. Duration of ECMO was 272 + 249 hours.
        iii. Predictors of outcome included duration of pre-ECMO ventilation, pre-ECMO PaO_2/FIO_2, and age.
    c. Conclusions
        i. The authors considered ECMO an option for this high risk group of patients
        ii. Improved results may be possible if patient selection is modified based on the outcome of predictors identified

IV. ECMO for Cardiac Support

A. Outcome

The requirement for ECMO support after cardiac surgery portends a poor outcome. Over the period of the Registry, no progress has been seen in the percent of patients surviving after using this technology in the cardiac patient population. In 1998, 338 patients were listed as requiring ECMO for a cardiac etiology, with 37% surviving. In 1999, 54 patients were added, with a 22% survival.

B. Outcome by Diagnoses (Table 11.4)

C. Studies

1. Determinants of success in pediatric cardiac patients undergoing extracorporeal membrane oxygenation.[8]
    a. Study Design
        i. Retrospective review of 31 children who required ECMO support for either postcardiotomy myocardial dysfunction (n = 25), or cardiomyopathy or myocarditis (n = 6).
    b. Results
        i. Patients with a residual defect after cardiac surgery did not survive.
        ii. If ECMO support for more than six days did not lead to recovery of the myocardium, results were uniformly fatal.
        iii. Four of the six patients with cardiomyopathy or myocarditis survived.

Table 11.4. Cumulative data from ELSO

Primary Diagnosis	Total	Total survivors	Percent survived
Congenital defect	2209	845	38
Cardiac arrest	71	15	21
Cardiogenic shock	81	29	36
Myocarditis	94	53	56
Cardiomyopathy	190	91	48
Other	406	162	40
OVERALL	3051	1195	39

c. Conclusions
   i. The authors concluded that the presence of a residual defect is a contraindication for ECMO.
   ii. If these patients are excluded, successful weaning from ECMO can be achieved in approximately 70%, with almost all recovery occurring in the first six days.

2. Mechanical circulatory support in children with cardiac disease.[9]
   a. Study Design
      i. These investigators reviewed their experience with both ECMO and ventricular assist devices (VAD) in children with cardiac disease that required mechanical support.
   b. Results
      i. Over a 10 year period, 67 patients requiring ECMO with a 40.3% survival
      ii. 29 patients supported with VADs had a 41.4% survival.
      iii. Failure of return of ventricular function was a negative predictor of survival.
   c. Conclusions
      i. Although no statistically significant improvement in survival was present, they did note that patients requiring ECMO after cardiac surgery had a 10% survival, but patients weaned from CPB with VAD placement had a 37% survival (7 of 19 patients).
      ii. The small number of patients and the complex anatomical differences involved makes comparisons of these technologies difficult.
      iii. In situations where elevated right sided pressures are present, ECMO or biventricular assist device (BIVAD) support may be preferred.

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Alternative Treatments

1. Inhaled Nitric Oxide

A. Neonatal Applications

1. Inhaled nitric oxide in full-term and nearly full-term infants with hypoxic respiratory failure. The Neonatal Inhaled Nitric Oxide Study Group.[1]
   a. Study Design
      A prospective, randomized trial comparing 121 infants with hypoxic respiratory failure requiring 100% oxygen managed with conventional ventilation, with 114 infants who also received inhaled nitric oxide (NO).
   b. Results
      i. 64% of the control group and 46% of the NO group died within 120 days of starting, or were treated with ECMO (p = 0.006).
      ii. 17% of the controls and 14% of the NO patients died (p = NS), and fewer of the NO patients required ECMO (39% vs 54%, p = 0.014).
   c. Conclusions
      NO use decreased the need for ECMO but did not effect the mortality in this group of critically ill children.
2. Inhaled nitric oxide and hypoxic respiratory failure in infants with congenital diaphragmatic hernia. The Neonatal Inhaled Nitric Oxide Study Group (NINOS)[2]
   a. Study Design
      i. Prospective, randomized, double-blind multicenter study).
      ii. Assessed the effect of NO in neonates with congenital diaphragmatic hernias (CDH) on mortality or the need for ECMO.
   b. Results
      i. In 28 control and 25 treated patients, death at <120 days of age or the need for ECMO occurred in 82% of control infants compared with 96% of NO infants (p = NS).
      ii. There were no differences in morbidity between the two groups as well.

c. Conclusions
    i. Short-term improvements in oxygenation seen in some NO infants may be helpful in stabilizing patients for transport and initiation of ECMO
    ii. NO did not reduce the need for ECMO or influence mortality in neonates with CDH and hypoxemic respiratory failure unresponsive to conventional therapy

3. Inhaled nitric oxide and persistent pulmonary hypertension of the newborn[3]
    a. Study Design
        i. An analysis of the effect of NO (80 ppm) on severe hypoxemia in infants with persistent pulmonary hypertension.
        ii. Prospective, randomized, multicenter study
    b. Results
        i. 58 infants randomized to either placebo or NO.
        ii. 16 of 30 (53%) patients receiving NO had an increase in systemic oxygenation, compared to only 2 of 28 (7%) control infants ($p = 0.002$).
        iii. ECMO was required in 71% of the control and 40% of the NO group ($p = 0.02$).
        iv. Mortality was similar between the two groups.
        v. NO did not cause systemic hypotension or increase methemoglobin levels.
    c. Conclusions
        Inhaled NO improves systemic oxygenation in infants with persistent pulmonary hypertension of the newborn (PPHN) and may reduce the need for ECMO.
4. Low-dose nitric oxide therapy for PPHN.[4]
    a. Study Design
        i. Prospective, randomized trial to determine whether low-dose iNO would reduce the need for ECMO in 248 neonates with pulmonary hypertension and hypoxemic respiratory failure.
        ii. Patients receiving iNO (n = 126) initially were given 20 ppm for 24 hours, then decreased by 5 ppm for no longer than 96 hours. Control group (n = 122) received conventional ventilatory support.
        iii. Primary endpoint was the need for ECMO.
    b. Results
        i. ECMO required in 78 neonates in control group (64%) and 48 neonates in the NO group (38%) ($p = 0.001$).
        ii. 30 day mortality was not different between groups (8% vs. 7%, control vs NO, respectively).
        iii. Incidence of chronic lung disease was less in the iNO group (7%) than in the control patients (20%) ($p = 0.02$).

c. Conclusions
NO reduces the need for ECMO support in neonates with respiratory failure and pulmonary hypertension.

B. Adult Applications
1. Inhaled nitric oxide versus conventional therapy. Effect on oxygenation in ARDS.[5]
   a. Study Design
      i. Randomized trial in patients with ARDS
      ii. Patients received either conventional therapy or conventional therapy plus NO for 72 hours.
   b. Results
      i. NO increased PaO_2/FiO_2 at one hour, 12 hours, and to a lesser extent at 24 hours. After 24 hours, both groups had an equivalent improvement in PaO_2/FiO_2.
      ii. Patients treated with NO were no more likely to tolerate a decrease in F_IO_2 >0.15 during the 72 hours following randomization (11 of 20 NO vs 9 of 20 with conventional therapy, p = 0.55).
   c. Conclusions
   In patients with severe ARDS, NO does not lead to a sustained improvement in oxygenation compared with conventional therapy.
2. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: Results of a randomized phase II trial.[6]
   a. Study Design
      i. 177 patients with ARDS were prospectively randomized to receive either placebo or NO at varying concentrations.
      ii. An acute response to treatment was defined as a >20% increase in PaO_2.
   b. Results
      i. An initial increase in oxygenation with a decrease in F_IO_2 was seen over the first 24 hours with NO
      ii. The intensity of mechanical ventilation over the first four days of treatment was also reduced.
      iii. No differences in mortality rate, the number of days alive off mechanical ventilation, or the number of days alive after meeting oxygenation criteria for extubation were seen.
      iv. No differences in the number and type of adverse events was observed between groups.
   c. Conclusions
      i. NO was well tolerated in the ARDS population and afforded a significant improvement in oxygenation early during treatment.
      ii. A larger phase III trial is suggested to assess clinical outcome.

II. High Frequency Ventilatory Modes

A. High Frequency Jet Ventilation (HFJV)
   1. Multicenter controlled clinical trial of HFJV in preterm infants with uncomplicated respiratory distress syndrome.[7]
      a. Study Design
         i. To test the hypothesis that HFJV reduces the incidence and/or severity of bronchopulmonary dysplasia (BPD) and acute airleak in premature infants who require mechanical ventilation for respiratory distress syndrome.
         ii. Randomized 130 patients to either HFJV or conventional ventilation (CV).
      b. Results
         i. Incidence of BPD was significantly lower in the HFJV group compared to CV patients (20.0% vs 40.4%).
         ii. Need for home O_2 also less in the HFJV group (5.5% vs 23.1%).
         iii. Survival, airleak, and other complications were similar between the groups.
         iv. A decrease in the exposure to hypocarbia was seen in the HFJV group
         v. A reduction in the risk of grade III-IV intraventricular hemorrhage (IVH) and/or periventricular leukomalacia (PLV) was also seen with HFJV.
      c. Conclusions
         HFJV, when used to optimize volume instead of airway pressures, led to an improvement in oxygenation and a reduction in long-term complications

B. High Frequency Oscillatory Ventilation (HFOV)
   1. The Provo Multicenter Early High-frequency Oscillatory Ventilation Trial: Improved Pulmonary and Clinical Outcome in Respiratory Distress Syndrome[8]
      a. Study Design
         i. Prospective, randomized trial of 125 neonates
         ii. Compared management of preterm infants with respiratory distress treated with surfactant and HFOV or conventional mechanical ventilation (CMV).
         iii. All received exogenous surfactant therapy.
      b. Results
         i. When used early, HFOV after surfactant therapy resulted in clinical outcomes consistent with a reduction in both acute and chronic lung injury.
         ii. Survival without chronic lung disease was greater in the HFOV group.
         iii. Overall hospital morbidity was less in the HFOV group.

c. Conclusions
HFOV plus surfactant therapy offers outcome advantages over conventional ventilation in premature infants with respiratory distress syndrome

2. A prospective, randomized multicenter trial of high-frequency oscillatory ventilation compared with conventional ventilation in preterm infants with respiratory distress syndrome receiving surfactant.[9]
   a. Study Design
      i. A prospective, randomized study comparing HFOV and intermittent positive pressure ventilation (IPPV) in preterm infants with respiratory distress syndrome.
      ii. 96 patients were included in the study, all of which received natural surfactant (Survanta).
   b. Results
      i. Five patients in the HFOV group died, and nine did not respond to HFOV and crossed over to an unassigned ventilatory mode.
      ii. Four patients in the IPPV group died, and nine crossed over to HFOV.
      iii. No differences were seen in gas exchange or ventilator support over the first 72 hours.
   c. Conclusions
   After surfactant therapy, HFOV, as a primary ventilation mode in this patient population is as safe and efficacious as conventional ventilation.

III. Liquid Ventilation

A. Theory
1. Total Liquid Ventilation (TLV)
Lungs are filled with perfluorocarbon to a volume equivalent to functional residual capacity (FRC, approx. 30ml/kg), and a liquid ventilator is used to obtain tidal breathing with perfluorocarbon. O_2 transfer facilitated by the high O_2 carrying capacity of perflourocarbons. Optimal CO_2 clearance possible even when ventilated at a rate of 4-5 breaths/min. Tidal volumes typically range from 15-20 ml/kg. This technique has advantages, in that the exudate in the airway may be more effectively lavaged in the setting of respiratory failure. Also, more uniform distribution of the perfluorocarbon is possible using TLV.
2. Partial Liquid Ventilation (PLV)
During PLV, gas ventilation of the perfluorocarbon-filled lungs is performed using a standard gas mechanical ventilator. No special equipment is required. The dose of perflourocarbon, which equates to the patient's FRC, is determined by visualizing the meniscus of perfluorocarbon within the endotracheal tube at end expiration.

B. Clinical Results in Neonates
   1. Partial liquid ventilation with perflubron in premature infants with severe respiratory distress syndrome.[10]
      a. Study Design
         i. Descriptive study of 13 premature infants with severe respiratory distress syndrome who failed conventional therapy including surfactant administration
         ii. PLV was initiated using perflubron.
         iii. Infants were considered to have completed the study if they received PLV for at least 24 hours.
      b. Results
         i. Three infants were switched to high-frequency ventilation, with the remaining 10 receiving PLV for 24-76 hours.
         ii. There was a 138% increase in arterial oxygen tension, and a 61% increase in compliance. Mean OI decreased from 49 + 60 to 17 + 16.
         iii. Infants were weaned from PLV to gas ventilation without complications.
         iv. Eight infants survived to 36 weeks corrected gestational age.
      c. Conclusions
         PLV offers clinical improvement and survival in some infants with severe respiratory failure who would otherwise not likely survive (Fig. 12.1).
   2. Partial liquid ventilation in newborn patients with congenital diaphragmatic hernia.[11]
      a. Study Design
         An examination of the safety and efficacy of liquid ventilation with perfluorocarbon in four newborns with CDH and severe respiratory failure.
      b. Results
         i. After 2-5 days on ECMO, PLV was initiated with perflubron.
         ii. A significant increase in PaO_2 and an improvement in static compliance was observed.
      c. Conclusions
         The use of perflubron can be performed safely in newborn patients with severe respiratory failure and a CDH, and may offer improvement in gas exchange and pulmonary compliance.
C. Clinical Results in Adults
   1. Initial experience with partial liquid ventilation in adult patients with the acute respiratory distress syndrome.[12]
      a. Study Design
         i. Another phase I study examining the safety and efficacy of PLV in patients with ARDS.
         ii. 10 adult patients, all of whom were on ECMO, underwent PLV with perflubron for 1-7 days.

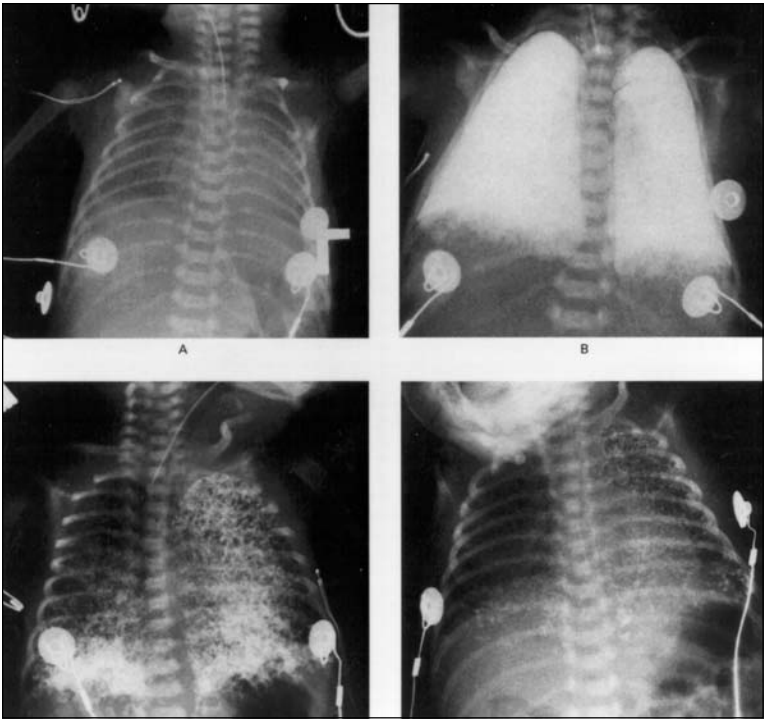

Fig. 12.1. Chest x-rays of an infant before (A), during (B), 48 hours after (C), and 3 weeks after (D), treatment with PLV.

b. Results
   i. A decrease in physiologic shunt from 0.72-0.46 was seen over a 72 hour period.
   ii. Static pulmonary compliance increased from 0.16 ml/cm H_20/kg to 0.27 ml/cm H_20/kg over the same time period.
   iii. Overall survival was 50%.

c. Conclusions
   Perflubron can be administered safely into the lungs of adult patients with severe respiratory failure receiving ECMO and may be associated with an improvement in gas exchange and pulmonary compliance.

2. Partial liquid ventilation in adult patients with ARDS. A multicenter phase I-II trial.[13]
   a. Study Design
      Safety and efficacy of PLV were studied in nine adult patients who were not on ECMO

b. Results
   i. A significant decrease in mean (A-a)DO_2 (baseline = 430 + 47, 48 hours = 229 + 17, p = 0.0127) and FIO_2 (baseline =0.82 + 0.08, 48 hours = 0.54 + 0.06, p = 0.025) was found
   ii. S_vO_2 also increased significantly over the study time period.
   iii. Seven of nine patients survived beyond 28 days after initiation of PLV, and five patients survived to discharge.
   iv. Three adverse events (hypoxia (2) and hyperbilirubinemia (1)) were labeled as severe.

c. Conclusions
   PLV may be performed safely with few side effects and leads to some improvement in gas exchange.

IV. Surfactant Therapy

A. Neonatal Studies

1. Survanta Multicenter Study[14]

a. Study Design
   i. Prospective randomized trial of 328 newborns with respiratory failure (due to MAS, sepsis, PPHN).
   ii. To test the efficacy of surfactant (beractant) to reduce the incidence of severe complications through 28 days of life and decrease the need for ECMO.

b. Results
   i. ECMO therapy was significantly less frequent in the surfactant group than in the placebo group (p = 0.038).
   ii. The advantage of surfactant use was more pronounced in the lowest oxygenation index range (15-22; p = 0.013).

c. Conclusions
   The use of surfactant, especially in the early stages of respiratory failure, significantly decreases the need for ECMO in the treatment of term newborns with respiratory failure, without increasing the risk of complications.

2. Surfactant replacement therapy for meconium aspiration syndrome[15]

a. Study Design
   i. A randomized controlled study to assess whether high-dose surfactant therapy (Survanta) improves pulmonary morbidity in patients with MAS.
   ii. Rationale: MAS is not only related to mechanical obstruction of the airways and chemical injury to the respiratory epithelium but also to surfactant inactivation by meconium.

b. Results
   i. One patient in the Survanta group (n = 20), and 6 in the placebo group (n = 20) required ECMO (p = .037).
   ii. The duration of mechanical ventilation, oxygen use, and hospitalization was longer in the control group (p<.05),

but mortality, need for home oxygen, and degree of chronic lung injury was similar between the two groups.

c. Conclusions

Surfactant replacement therapy, if started within six hours of birth, improves oxygenation and reduces the incidence of air leaks, severity of pulmonary morbidity, and hospitalization time of term infants with MAS.

B. Adult Studies

1. Aerosolized surfactant in adults with sepsis-induced acute respiratory distress syndrome.[16]
   a. Study Design
      i. Prospective, randomized study of 725 patients with sepsis-induced ARDS
      ii. Patients received aerosolized surfactant (Exosurf) or placebo for up to five days.
   b. Results
      i. Hemodynamic parameters, duration of mechanical ventilation, duration of ICU stay, and the incidence of significant complication did not change between groups.
      ii. Survival at 30 days was similar between groups (60%).
   c. Conclusions
      i. The administration of aerosolized surfactant had no effect on survival or other secondary endpoints in this patient population.
      ii. The dosage and type of surfactant preparation may have influenced the outcome of this trial.
2. Bovine surfactant therapy for patients with acute respiratory distress syndrome[17]
   a. Study Design
      i. A multicenter, prospective trial of 59 patients with ARDS
      ii. 43 were randomized to receive different doses of surfactant (Survanta,), and 16 patients served as controls.
   b. Results
      i. FiO_2 after 120 hours of treatment was significantly decreased in the group that received high dose surfactant as compared to the control ($p = 0.011$).
      ii. Mortality tended to be lower in the high dose surfactant group as compared with the control (18.8% vs 43.8%, $p = 0.075$).
   c. Conclusions

   This preliminary study indicates a potential benefit of surfactant for the treatment of patients with ARDS.

V. Future Therapies

A. Arteriovenous CO_2 removal

1. Significant reduction in minute ventilation and peak inspiratory pressure with arteriovenous CO_2 removal during severe respiratory failure[18]
    a. Study Design
        i. An animal study using a sheep smoke inhalation model of respiratory failure
        ii. The goal of this method of respiratory support is to provide adequate gas exchange without the multiple mechanical and pathophysiologic complications seen in ECMO.
        iii. The study evaluated the effect of arteriovenous gas exchange therapy on ventilatory requirements during acute respiratory failure.
    b. Results
        i. The device shunted approximately 25% of the animal's cardiac output, and removed 96% of the total CO_2 production.
        ii. Minute ventilation was reduced from 10.3 + 1.4 L/min to 0.5 + 0.0 L/min at six hours of treatment
        iii. Peak inspiratory pressure fell by 50%, and an adequate PaO_2 was maintained, with the animals remaining hemodynamically stable throughout.
    c. Conclusions
        Arteriovenous CO_2 removal may have a role in the management of severe respiratory failure
2. Percutaneous extracorporeal arteriovenous CO_2 removal for severe respiratory failure[19]
    a. Study Design
        i. A report of 5 patients with ARDS and CO_2 retention who underwent percutaneous extracorporeal arteriovenous CO_2 removal using femoral arterial and venous cannulas.
        ii. Patients were connected to a low-resistance, 2.5 m^2 hollow-fiber oxygenator for 72 hour trial period.
    b. Results
        i. There were no adverse hemodynamics events related to this intervention.
        ii. A decrease in minute ventilation from 7.2 + 2.3 L/min at baseline to 3.4 + 0.8 L/min at 24 hours was observed.
        iii. Approximately 70% CO_2 removal could be achieved using their system. Three of the five patients survived.
    c. Conclusions
        i. This technology may have a role in management of severe respiratory failure.
        ii. Improvements in the heparin dosing, cannulation sizing, and ventilator management should be investigated.
        iii. A prospective, randomized clinical trial is needed to accurately assess this technology.

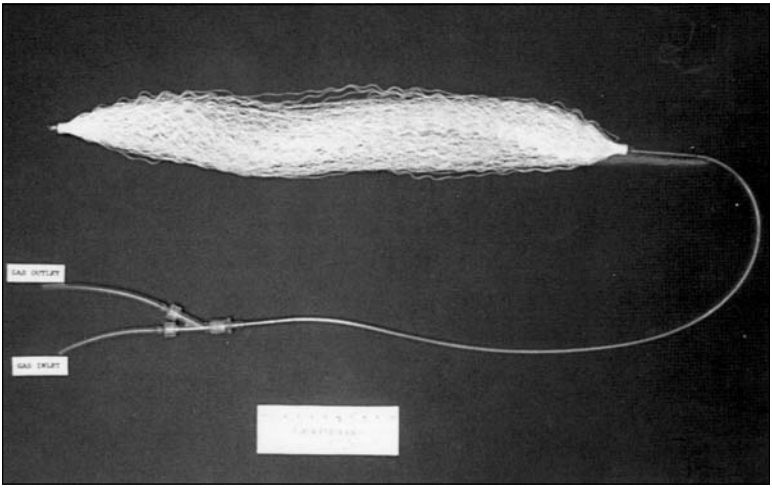

Fig. 12.2. The IVOX device, consisting of multiple hollow-fiber membranes connect to a double-lumen gas conduit, for intracaval placement via the common femoral vein.

B. IVOX

Intravascular Oxygenation and Carbon Dioxide Removal Device[20]

1. Background
   a. The device is a miniature membrane (hollow fiber, thin silicone coated) lung placed in the inferior vena cava for the purpose of blood oxygenation and CO_2 removal without the need for ECMO (Fig. 12.2).
   b. The fibers are engineered for maximal blood-membrane contact time.
2. Prior Study Results
   Multicenter trial reported in 1994 showed a 30% survival in the IVOX group. No control arm was included.
3. Device Modifications
   a. Design changes under investigation to improve the function of this device include increased fiber number, decreased fiber length, decreased fiber diameter, and increased crimping of the fiber to increase gas transfer.
   b. Techniques to actively increase the blood mixing within the device, newer ventilator strategies and alternative IVOX surface coatings are also under investigation
   c. With improvements, device may facilitate removal of up to 80% of CO_2 production (current device capacity of approximately 44-71%) during ARDS. O_2 transfer capability of the IVOX used in this trial was 40-72%.

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A

Activated clotting time (ACT) 45, 57, 67, 74, 75, 91, 94, 99, 101, 102, 104

Acute respiratory distress syndrome (ARDS) 4, 14, 15, 86, 87, 123, 126, 129

Acute respiratory failure 14, 15, 29, 86, 87, 116, 117, 130

Adult ECMO 14, 15, 63, 65, 86, 87, 116

Aerosol treatment 96

Air embolism 9, 51, 83, 106, 107

Air leak syndrome 13, 115

Amicar 101, 102

Anticoagulation 45, 74, 91, 93, 94, 99

Aprotinin 102

Arterial blood gas (ABG) 31, 75, 89, 92, 94, 95, 102, 113

Arterial cannula 70, 77, 78, 79, 82, 110

Arteriovenous CO_2 removal 129, 130

Ascending aorta 69, 78, 82

Aspiration 5, 13, 14, 84, 86, 87, 96, 107, 115, 117, 128

Assessment 89, 93, 98, 104

Assist control ventilation (AC) 1

Azygous flow principle 9

B

Bacterial pneumonia 87, 117

Beractant 128

Bladder reservoir 55

Bleeding 10, 35, 42, 43, 72, 75, 79, 80, 82, 85-87, 91, 95, 100-103, 112

Blood prime 60, 66, 68

Blood volume distribution 34, 35, 102

Bronchoalveolar lavage 96

Bronchoscopy 96

C

Cannulation 10, 20, 26, 27, 29, 32, 45, 70, 77, 79, 82

Cardiac arrest 29, 119

Cardiac ECMO 82, 88, 90

Cardiac recovery 83, 93

Cardiogenic shock 119

Cardiomyopathy 118, 119

Cardiopulmonary bypass 9, 10, 18, 22, 37, 42, 46, 82, 102

Central nervous system 88

Centrifugal pump 1, 42, 50, 51, 53, 54, 55, 76

CO_2 removal (carbon dioxide removal) 15, 22, 23, 30, 129-131

Common femoral artery 77

Common femoral vein 77, 78, 131

Complications 10, 39, 46, 74, 82, 99, 100, 102, 104, 108, 109, 115, 116, 124, 126, 128, 130

Congenital diaphragmatic hernia (CDH) 5, 10, 11, 13, 84, 115, 121, 122, 126, 132

Contractility 34, 41, 93

Counter-current effect 23, 25

Cross-circulation 9, 10

D

Decannulation 70, 72, 82, 83, 94, 113

Discontinuing support 105

Diuretics 92

Double lumen cannula 81

E

ECMO 10, 108, 111-113, 128, 130, 131

- adult 5, 6, 12, 14, 15, 82, 86, 87, 88, 116, 127, 128
- cardiac 5, 6, 32, 34, 45, 51, 82, 88, 90, 93, 107, 118, 119, 121
- components 18, 45, 60, 80, 89, 90
- neonatal 5, 10, 11, 13, 15, 20, 39, 77, 84, 85, 112, 114-116, 122, 123, 126, 128
- pediatric 14, 86, 87, 121

Electrolytes 65, 89, 99, 102

Endocrine 40

Exclusion criteria 85-88

Exosurf 129

Extracorporeal CO_2 removal ($ECCO_2R$) 15, 30

Extracorporeal Life Support Organization (ELSO) 27, 114, 115-117, 119

F

FFP 90, 101

Fibrinogen 42, 67, 74, 89, 100, 101

Filtration devices 60

Flow probe 38, 76

Fluids 99

Fresh frozen plasma (FFP) 43

G

Gas control module 57

Gas exchange 5, 15, 18, 21, 23, 35, 36, 46, 67, 93, 109, 125, 126, 127, 128, 130

Gastrointestinal 36, 37, 100

Goal flow rates 89

H

Heat exchanger 13, 58, 59, 60, 64, 65, 104, 107

Hemodialysis 98

Hemodynamic changes 31

Hemofiltration 98, 99

Hemoglobin 22, 24, 52, 91, 100-102, 122

Hemolysis 42, 50, 51, 60, 110, 112, 114

Heparin 15, 39, 41, 43, 45, 60, 61, 62, 64, 66, 68, 74, 75, 79, 85, 86, 87, 91, 96, 99, 101, 112, 130

High frequency jet ventilation (HFJV) 6, 124

High frequency oscillating ventilation (HFOV) 10, 124, 125

Hyaline membrane disease 13, 84, 115

Hypotension 29, 37, 88, 99, 108, 109, 122

I

Inclusion criteria 84, 86-88

Indications 84, 86-88

Inflammatory response 5, 31, 35, 41

Inhaled nitric oxide (NO) 10, 121, 122, 123, 132

Initial flow rates 89

Inotropic support 26, 84, 92

Internal jugular vein 28, 32, 39, 45, 77-79, 82, 118

Inverse ratio ventilation (IRV) 4, 15

IVOX 131

L

Laboratory 11, 91, 102

Liquid ventilation 125-127

Lung recovery 27, 78, 93

Lung rest settings 89, 95

M

M numbers 71

Management 5, 6, 11, 13-15, 30, 31, 34, 39, 49, 55-57, 59, 60, 62, 68, 70, 73, 75, 76, 84, 86, 89, 95, 96, 99-101, 103, 106, 107, 109, 110, 112, 113, 115, 118, 124, 130

Meconium aspiration syndrome (MAS) 5, 13, 84, 96, 115, 128, 129

Medications 79, 107

Mixed venous oxygen saturation (SVO_2) 24, 26, 28, 31, 32, 75

Myocarditis 34, 88, 118, 119

N

Neonatal ECMO 10, 15, 20, 27, 37, 39, 51, 62, 64, 84, 85, 114, 115

Neuromuscular blocking agents 92

Nonpulsatile flow 39, 51, 52

Nutrition 37, 93, 100

O

Outcome 114-116, 118, 123, 124, 125, 129

Oxygen consumption (VO_2) 24, 26, 39, 41

Oxygen delivery (DO_2) 18, 19, 22-27, 29, 31, 90

Oxygenation index (OI) 86, 126, 128

Oxygenators 46, 48, 49, 102

- bubble 10, 13, 46, 49, 50, 58, 65
- changing 49
- failure 108, 109, 111
- hollow-fiber membrane 12, 46
- screen 10, 13
- sheet 13
- silicone rubber membrane 15
- silicone rubber/silastic membrane 15, 22, 46

P

Partial liquid ventilation (PLV) 125, 126, 127, 128

Pathophysiology 5, 6, 84, 86-88

Pediatric ECMO 14, 71, 86

Perfluorocarbon 125, 126

Permissive hypercapnia 4

Persistent fetal circulation 5, 13, 84, 115

Platelets 42, 43, 66, 67, 74, 89-91, 100-102, 104, 112

Pneumonia 5, 13, 14, 86, 87, 115, 117

PRBC 43, 60, 90

Pressor support 92

Pressure control ventilation (PCV) 3, 4

Pressure support ventilation (PSV) 2

Primary pulmonary hypertension (PPHN) 13, 84, 115, 122, 128

Priming the circuit 64, 65, 89

Prophylactic antibiotics 93

Pulmonary blood flow 15, 18, 23, 26, 35, 111

Pulmonary toilet 95

Pulsatile flow 51, 52

R

Raceway maintenance 50, 55, 67-69, 71

Recirculation 18, 27-29, 31, 46, 49, 64, 65, 72, 75, 81, 90, 94, 113

Red blood cells 26, 42, 43

Renal 27, 37, 52, 85, 88, 89, 92, 98, 99, 108, 110, 112, 115

Renal failure 37, 98, 112

Respiratory distress syndrome (RDS) 4, 5, 10, 115, 123-126, 129

Right atrium 18, 26, 28, 29, 45, 69, 70, 78, 81, 82, 118

Right common carotid artery 45, 77, 79, 81, 82

Roller pump 42, 50, 51, 54-56, 67, 104

S

Sedatives/analgesics/anxiolytics 92

Sepsis 13, 31, 35, 42, 67, 84-86, 105, 115, 128, 129

Surfactant 2, 5, 10, 96, 124-126, 128, 129, 132

Survanta 125, 128, 129

Sweep gas settings 50, 58, 67, 91

Synchronized intermittent mandatory ventilation (S 2

T

Total liquid ventilation (TLV) 125

Transport operations 122

Troubleshooting 111, 112, 113

Tubing 34, 40, 49, 50, 54-56, 58, 60, 61, 64-70, 76, 82, 99, 106, 108, 109, 110

V

Venoarterial (VA) ECMO 18, 22, 23, 26, 27, 29, 31, 32, 34, 35, 36, 37, 39, 45, 75, 77, 79-82, 89, 90, 93-95, 98, 107, 110-112, 114

Venous cannula 27, 45, 69, 70, 72, 77, 78, 80, 82, 106, 130

Venovenous (VV) ECMO 15, 18, 22, 23, 26-35, 39, 45, 69, 75, 76, 77, 90, 94, 95, 107, 110, 113, 114, 116

Ventilation 1-6, 10, 14, 15, 22, 26, 87, 95, 99, 111, 113, 116, 118, 121, 123-130

Ventilator management 5, 6, 95, 130

Viral pneumonia 117

Vitamin K 101, 102, 112

Volume requirements 85, 90, 99

W

Weaning/cessation 2, 4, 30, 36, 76, 93, 106, 119

Dedication

To the brave patients that endured the technology which we thrust upon them, and the patients' families that had the courage to allow us to try.

Preface

It has been nearly 30 years since the pioneering studies from the laboratory of Dr. Robert H. Bartlett paved the way to clinical use of extracorporeal membrane oxygenation (ECMO) for neonates with respiratory failure. A 56% survival rate was initially reported, a monumental achievement in a disease process which, to that point in time, carried an 80-90% mortality. Subsequent to these early reports, the use of this technology has flourished, with the introduction of new techniques, equipment, and management schemes, each designed to improve the results of this lifesaving procedure. Over time the use of ECMO has expanded into other neonatal diseases and into pediatric and adult patient populations, albeit with less success. Through the continued research efforts of many investigators, ECMO has become the standard of care for a variety of processes causing neonatal respiratory failure, some of which now have survival rates approaching 95%.

The field of ECLS (extracorporeal life support) has now expanded beyond the use of ECMO alone, and many new adjunctive and complementary technologies have been developed. These include new sophisticated ventilator strategies, and novel medications such as surfactant, inhaled nitric oxide, and perfluorocarbons. In some instances these therapies have reduced the need for ECMO, although ECMO remains an important therapeutic option for a variety of pulmonary and cardiac conditions.

This handbook is directed at intensivists, surgeons, pediatricians, residents, perfusionists, nurses and ECMO technologists involved in the care of patients with respiratory or cardiac failure which may require extracorporeal support. It provides specific information on the mechanics of ECMO, the equipment required, the physiology of extracorporeal support, and the management of patients supported on ECMO. Current results of ECMO and alternative support options are also reviewed in the later Chapters of this book. A detailed description of each area is not attempted in this handbook. Instead, our goal is to present clinically useful information in a manner that enables the reader to rapidly assess clinical situations, troubleshoot problems, and understand the expected results of therapy.

Today, ECMO support has an important role in most major medical centers caring for critically-ill patients, whether for neonatal respiratory failure, cardiac failure, or for cardiopulmonary support after cardiac surgery or thoracic organ transplantation. No doubt new applications and refinements of this technology will appear in the future. Our hope is that this handbook is useful to the many health care professionals that give their time and efforts to treating these challenging patients.

Dan M. Meyer, M.D.
Michael E. Jessen, M.D.

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Extracorporeal Life Support Organization (ELSO) Registry and Publications

Medical Illustrations

S. Talmond Brown, MA

Abbreviations

ACLS	advanced cardiac life support
ACT	activated clotting time
ACTII	automated coagulation timer II
APRV	airway pressure release ventilation
ARDS	adult respiratory distress syndrome
ASD	atrial septal defect
ATIII	antithrombin III
A-V	arteriovenous
BIVAD	biventricular assist device
BPD	bronchopulmonary dysplasia
CBF	cerebral blood flow
CDH	congenital diaphragmatic hernia
CFA	common femoral artery
CFV	common femoral vein
CMV	control mode ventilation
CO	cardiac output
CPB	cardiopulmonary bypass
CPD	citrate-phosphate dextran
CPR	cardiopulmonary resuscitation
CV	conventional ventilation
CVP	central venous pressure
CXR	chest x-ray
DBP	diastolic blood pressure
DIC	disseminating intravascular coagulation
DLC	double lumen catheter
DLVV	double lumen venovenous ECMO cannula
DO_2	oxygen delivery
EBV	estimated blood volume
ECG	electrocardiogram
ECLS	extracorporeal life support
$ECCO_2R$	extracorporeal carbon dioxide removal
ECMO	extracorporeal membrane oxygenation
ECV	ECMO circuit volume
$ETCO_2$	end tidal CO_2
FDP	fibrin degradation products
FFP	fresh frozen plasma
FRC	functional residual capacity

continued

Abbreviations (continued)

FSP	fibrin split products
HFJV	high frequency jet ventilation
HFO	high frequency oscillatory
HFOV	high frequency oscillating ventilation
HFPPB	high frequency positive pressure ventilation
ICH	intracranial hemorrhage
IL	interleukin
IMV	intermittent mandatory ventilation
IPPV	intermittent positive pressure ventilation
IRV	inverse ratio pressure control ventilation
IV	intravenous
IVH	intraventricular hemorrhage
IVOX	intravascular oxygenation and CO_2 removal device
ITC	International Technidyne Corp.
LV	left ventricle
LVAD	left ventricular assist device
MAP	mean arterial pressure
MAS	meconium aspiration syndrome
MPAP	mean pulmonary artery pressure
NIH	National Institutes of Health
NINOS	neonatal inhaled nitric oxide study
NO	nitric oxide
OI	oxygenation index
PA	pulmonary artery
PALS	pediatric advanced life support
PAWP	peak airway pressure
PBF	pulmonary blood flow
PCV	pressure control ventilation
PCWP	pulmonary capillary wedge pressure
PDA	patent ductus arteriosus
PEEP	positive end expiratory pressure
PIE	pulmonary interstitial emphysema
PIP	peak inspiratory pressure
PLV	periventricular leukomalacia OR partial liquid ventilation
PPHN	persistent pulmonary hypertension of the newborn
PPT	partial prothrombin time
PRBC	packed red blood cells
PT	prothrombin time

Abbreviations (continued)

PSV	pressure support ventilation
PVC	polyvinyl chloride
RBC	red blood cells
RCCA	right common carotid artery
RDS	respiratory distress syndrome
RIJV/RA	right internal jugular vein/right atrium
RV	right ventricle
SBP	systolic blood pressure
SIMV	synchronized intermittent mandatory ventilation
SMA	surface modifying additives
SVO_2	mixed venous oxygen saturation
TBV	total blood volume
TNF	tumor necrosis factor
TLV	total liquid ventilation
TPN	total parenteral nutrition
VA	venoarterial
VAD	ventricular assist device
VO_2	oxygen consumption
VSD	ventricular septal defect
VV	venovenous