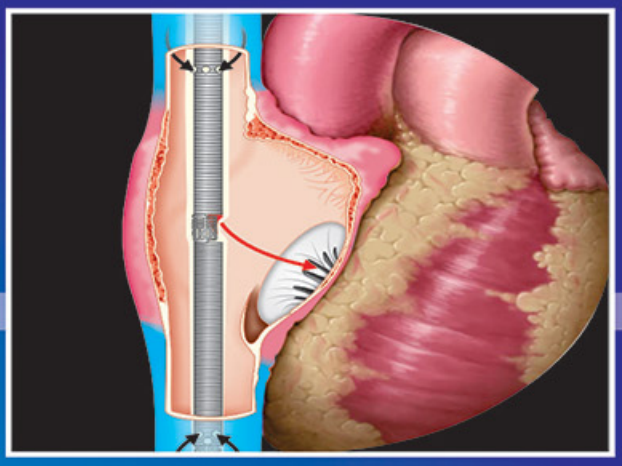

Manual of

Extracorporeal Membrane Oxygenation (ECMO) in the ICU

Forewords

Navin C Nanda, Naresh Trehan, Balram Airan, Steven A Conrad, Yatin Mehta

Editor
Poonam Malhotra Kapoor

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4 Evolution of Extracorporeal Membrane Oxygenation

Vijay Shankar, Poonam Malhotra Kapoor, Sameer Goel

CHAPTER OUTLINE

- *History of ECLS on a Patient of Pulmonary Embolism*
- *Bartlett—The Father of ECMO*
- *First Newborn: Population for ECMO*
- *Contribution of Bartlett*
- *Basis of ECMO*
- *History and Evolution of Mechanical Support*
- *Decade of 1960 and 1970*
- *First Attempt at Respiratory Mechanical Support on ECMO in Infants*
- *Clinical Trials on ECMO*
- *History of ECMO in India*

In May 1953, Gibbon used artificial oxygenation and perfusion support for the first successful open heart operation.[1,2] In 1954, Lillehei developed the cross-circulation technique by using slightly anesthetized adult volunteers as live cardiopulmonary bypass apparatuses during the repair of certain congenital cardiac disorders.[3] In 1955, at the Mayo Clinic, Kirklin et al improved on Gibbon's device and successfully repaired an atrial septal defect[4] in a baby who was suffering from meconium aspiration.

HISTORY OF ECLS ON A PATIENT OF PULMONARY EMBOLISM

Between the years of 1935 and 1954 John Gibbon, Clarence Dennis, and others pursued the development of a mechanical device to take over the function of the heart and lungs to permit surgical operations on the heart and great vessels. The entire project was stimulated by a patient with a lethal pulmonary embolism. Obviously a machine that could be used to permit cardiopulmonary bypass for this problem could be used for cardiac surgery and a variety of other applications. To substitute for the heart Gibbon used a roller pump which remains in general practice today.

To substitute for the lung, he devised a system in which anticoagulated blood was directly exposed to oxygen, dripping along the wires of a vertically-mounted metal screen. The approach of direct exposure of blood to oxygen was successful, and subsequently modified by Dennis, Morrow, Cross, DeWall, Rygg, and many others, leading to the single-use, disposable, direct gas interface oxygenators which are widely used today. Lillehei was the first to use extracorporeal circulation for cardiac surgery, establishing cross circulation between a parent and a child with congenital heart disease, using the parent as the heart/lung machine.

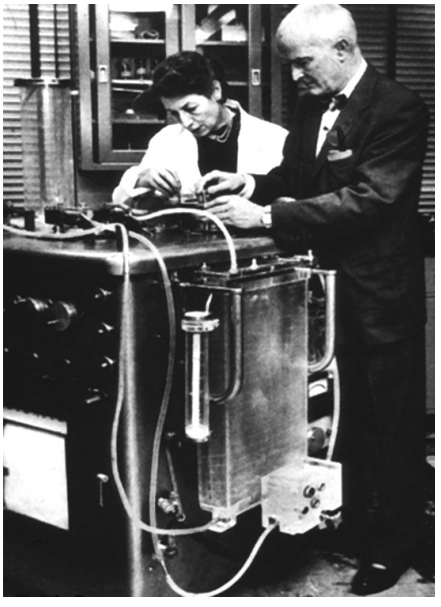

Fig. 1: ELCS—The beginnings

Gibbon was the first to use the prosthetic heart/lung machine for a cardiac operation, opening the door to the

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Table 1: ECLS History and Techniques

Respiratory support	*ECLS management*
• Venoarterial via neck	• Dedicated ECLS specialists
• Venovenous access via neck or groin	• ECLS-trained bedside nurses
• Arteriovenous access for CO_2 removal ($AVCO_2R$)	• Routine ICU procedure

routine application and success of extracorporeal circulation for cardiac surgery.

As experience with extracorporeal circulation developed during the 1950s, it was obvious that the life-supporting technique itself became lethal when used for more than a few hours. Thrombocytopenia, coagulopathy, hemolysis, generalized edema, and deterioration of organ function all occurred, in proportion to the amount of time on cardiopulmonary bypass. The experiments of Lee, Dobelle, and others indicated that the direct exposure of blood to oxygen gas was responsible for this apparent toxicity. These observations prompted the development of an artificial lung in which a gas-permeable membrane was interposed between the blood and the gas phase. Observation of blood in the Kolff artificial kidney, in which the blood was separated from the environment by a cellophane membrane, indicated that venous blood could become oxygenated if a suitable gas permeable membrane were developed. The first successful membrane oxygenator was built by Clowes et al. They used sheets of polyethylene membrane which had a low but definite permeability to oxygen and CO_2. By using a very large surface area, a device was built which allowed gas exchange without a direct gas interface, and this hand-made device was used for cardiac surgery in patients in 1956.

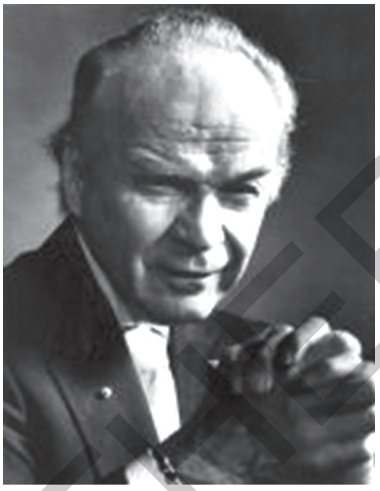
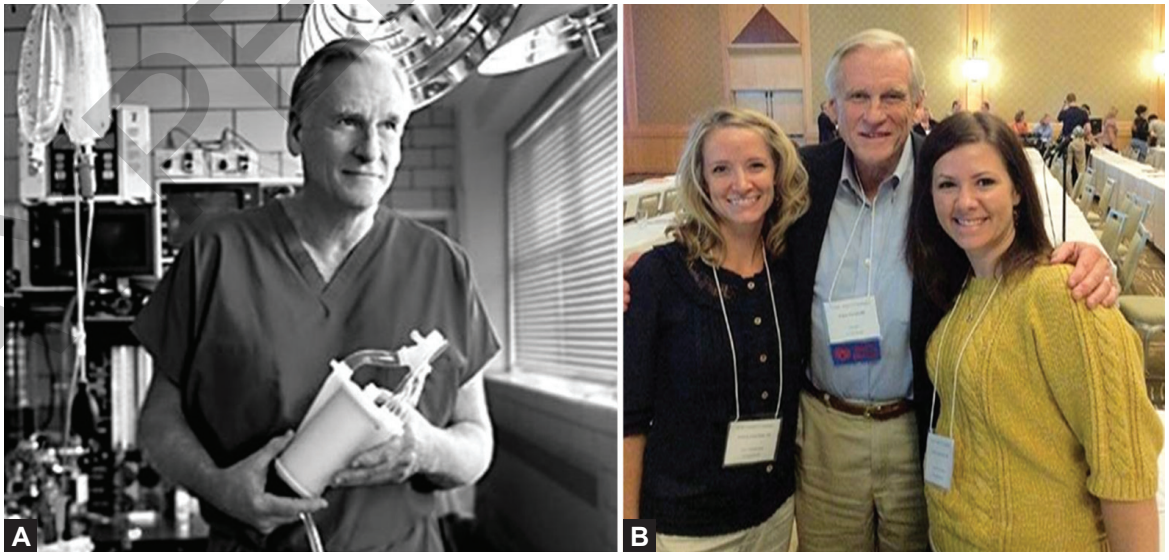


Fig. 2: Kolobow T—first attempt at ECMO

The development of dimethylpolysiloxane membranes by Kammermeyer in 1957 was a major advance. This unique material allows for the transfer of carbon dioxide and oxygen at rates that were more than ten times faster than those through other plastics. Using this new plastic (called 'silicone rubber') Kolobow, Lande, Pierce, and others constructed blood oxygenators which were quite efficient and successful.

BARTLETT— THE FATHER OF ECMO

In 1975 to 1976, Bartlett et al successfully applied bedside CPB to treat a newborn with meconium aspiration, marking the beginning of extracorporeal membrane oxygenation (ECMO) in critical care. ICU units forming, HD becoming more widely used, positive pressure ventilation better understood: infants, children, and adults all surviving initial cardiac/pulmonary



Figs 3A and B: Robert Bartlett

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insults. Acute respiratory distress syndrome (ARDS) emerging as the major problem ailing ICU population. Several clinical trials published demonstrating clear survival benefit in infants suffering from severe respiratory failure randomized controlled studies in adults with ARDS demonstrated no such benefit, but smaller studies and case reports emerged with reports of >50 percent survival in those treated with ECMO in addition to maximal ventilatory management 1989 ELSO and ELSO registry database formed 1991 NIH conference on diffusion of ECMO technology.

ECLS the evolution – 1975 to 1976, Bartlett et al successfully apply beside CPB to treat a newborn with meconium aspiration, making the beginning of ECMO in critical care.

FIRST NEWBORN: POPULATION FOR ECMO

The first newborn population chosen for ECMO was the premature infant with hyaline membrane disease. These infants suffered an unacceptably high risk of intracranial hemorrhage. The combination of hypoxia, hypothermia, acidosis, systemic heparinization, and alterations of cerebral circulation resulted in a prohibitively high mortality. ECMO was highly successful when Bartlett and associates pioneered the treatment of term or near term infants in acute, reversible respiratory failure.

The development of these early membrane oxygenators demonstrated: (1) that it would be possible to conduct prolonged extracorporeal circulation free of gas interfaces, (2) that diffusion of oxygen through blood would be the limiting factor in oxygenator design rather than the materials, and, (3) that blood flow patterns, headers and manifolds, and stagnant areas leading to thrombogenesis would be important considerations in the design of membrane—lungs. In the mid 1960s laboratory research began on prolonged extracorporeal circulation in the laboratories of teams that were studying function and improvement of membrane lungs, particularly Kolobow, Pierce, Galletti, Bramson and Hill, Lande and Lillehei, and Drinker and Bartlett.



Fig. 4: First successful ELCS patient, 1971—J Donald Hill MD and Maury Bramson BME, Santa Barbara, CA, 1971
(*Courtesy:* Robert Bartlett, MD)

CONTRIBUTION OF BARTLETT

Because of the pioneering efforts of Dr Bartlett and his associates, we are able to offer ECMO to this population successfully. There are currently over eighty-five centers, internationally, offering ECMO with over 20,000 infants treated to date. The average survival rate is 83 percent for newborns, whom previously had a predicted survival of 20 percent without ECMO.

Circuit flow may be achieved using a pump (centrifugal or roller) or by the patients arteriovenous pressure gradient (pumpless). At The Royal Adelaide Hospital ECMO involves a centrifugal pump to drive circuit flow.

BASIS OF ECMO

It is indicated when the patient has an acute, potentially reversible, life potentially reversible, life-threatening form of respiratory threatening form of respiratory failure which is unresponsive to conventional therapy.

Extracorporeal membrane oxygenation is the use of extracorporeal circulation and gas exchange to provide temporary life support to patients with cardiac or pulmonary failure. One key component of ECMO is the transport of oxygen into blood across a semi-permeable membrane. This phenomenon was first recognized in 1944 when Kolff and Berk noted that blood became oxygenated as it passed through the cellophane chambers of their artificial kidney.

HISTORY AND EVOLUTION OF MECHANICAL SUPPORT

The history and evolution of mechanical support is integral to the history of cardiopulmonary bypass. In the 1960s, it has been demonstrated that extracorporeal devices could be used to support patients for several days outside the operating theater. In 1972, Hill's group reported the first adult extracoporeal membrane oxygenation survivor. In 1976, Bartlett et al. reported the first neonatal ECMO survivor, who was appropriately named Esperanza ("Hope"). Following this, there was a proliferation of the use of ECMO for a variety of conditions leading to refractory cardiorespiratory failure.
In 1989, over one hundred ECMO centers from around the world established the Extracorporeal Life Support Organization (ELSO) as a platform for communication and research in extracorporeal support. Today, there are over 30,000 patients on the registry with an overall survival to hospital discharge rate of 65 percent (ECMO registry 2006).

The concept of cardiopulmonary bypass was developed in the early 1950s. Devices used at that time were bubble or disk oxygenators with a direct oxygen-blood interface. Hemolysis

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occurred after a few hours of bypass. This precluded its use for long-term support. The development of the first membrane oxygenator, by Clowes in 1956, enabled prolonged cardiopulmonary bypass to become feasible.

DECADE OF 1960 AND 1970

The 1960s and 1970s were noted for advances in techniques and research, for prolonged pulmonary support. A nine hospital collaborative study was organized by the National Heart, Lung, and Blood Institute to study ECMO therapy, in adults with pulmonary insufficiency. Unfortunately, survival was not improved. The study had several problems: (1) the patients varied greatly as to the type and complexity of their disease process; (2) patients were often entered when lung damage was predicted as irreversible; (3) intensive ventilatory support was continued, which perpetuated lung damage.

In 1965, Rashkind and coworkers were the first to use a bubble oxygenator as support in a neonate dying of respiratory failure.[6] In 1969, Dorson and colleagues reported the use of a membrane oxygenator for cardiopulmonary bypass in infants.[7]

- ICU units performing
- HD becoming more widely used
- Positive pressure ventilation better understood: Infants, children, and adults all surviving initial cardiac/pulmonary insults.

FIRST ATTEMPT AT RESPIRATORY MECHANICAL SUPPORT ON ECMO IN INFANTS

The first attempts at respiratory support in infants were reported by Rashkind, Dorson, and White. The first successful human case was reported by Hill, O'Brien, and others in 1972. The patient was a young man who sustained a ruptured aorta and other injuries in a motorcycle accident in Santa Barbara, California. Don Hill and his team from San Francisco brought the equipment to Santa Barbara, and managed the patient on venoarterial extracorporeal support for 3 days. The timing of Hill's success was important, because it was in the early 1970s that the full concept of intensive care units developed, acute renal failure was being treated with hemodialysis, and acute respiratory failure (ARDS) was the major problem in critically ill patients. It was hoped that a temporary period of life support with extracorporeal circulation would allow the damaged lung to recover, giving great impetus to both laboratory and clinical research on prolonged ECC. Reports of several other successful cases soon followed. In 1974 the Lung Division of the National Heart and Lung Institute proposed a multicenter prospective randomized study of ECMO in adult respiratory failure. This study began in 1975, which was a pivotal year for extracorporeal support.

In 1975 a meeting was held outside of Copenhagen which included most of the researchers on prolonged extracorporeal support. This meeting was hosted by Zapol and Qvist, and the proceedings were reported in a benchmark publication. The plans for the NIH ECMO study were reported and reviewed at that meeting. Four different membrane oxygenators were manufactured and used in 1975, the Kolobow Sci-Med, the LandÈ-Edwards, the Pierce-GE, and the Bramson (The Food and Drug Administration did not become involved with devices until 1976). And the first successful treatment of a newborn infant with ECMO was done in May 1975 and reported at the Copenhagen meeting.

It was in 1970, when Baffes et al. reported the successful use of extracorporeal membrane oxygenation as support in infants with congenital heart defects who were undergoing cardiac surgery.[8] In 1975, Bartlett et al. were the first to



Fig. 5: First cardiac ECMO survivor, 1972



Fig. 6: First neonatal ECMO survivor, 1975—Esperanze, age 1 day, 1972 (*Courtesy:* Robert Bartlett, MD)

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successfully use ECMO in neonates with severe respiratory distress.[9]

The early ECMO experience in children was similar to that in the adult. However, these studies suggested that in appropriate patients who were treated early and did not have irreversible lung damage, ECMO was technically feasible with the potential to reverse pulmonary failure.

CLINICAL TRIALS ON ECMO

The diffusion limitation of oxygen through the blood film, and the use of secondary flows to address this problem were studied by Weissman and Mockros, Bartlett and Drinker, and others. With the collaboration of medical industry a series of membrane lungs became available for clinical trials and general usage. Kolobow and Zapol, Bartlett and Drinker and others, demonstrated that extracorporeal circulation of the blood could be carried out for days or weeks without toxicity or hemolysis as long as the direct blood gas contact was avoided. Beginning with Gibbon, all the studies on extracorporeal circulation have been conducted with the use of heparin anticoagulation, using a dose sufficient to produce an infinitely long clotting time. Bartlett and Drinker demonstrated that much lower doses of heparin could be used, producing prolonged but measurable clotting time which minimized bleeding complications. Several groups studied the management and physiology of prolonged extracorporeal circulation in a variety of animal models.

- Several clinical trials published demonstrating clear survival benefit in infants suffering from severe respiratory failure.
- Randomized controlled studies in adults with ARDS demonstrated no such benefit, but smaller studies and case reports emerged with reports of >50 percent survival in those treated with ECMO in addition to maximal ventilator management.

With these modifications in the equipment and technology of cardiopulmonary bypass, it was possible to characterize physiologic and hematologic responses of the normal animal during prolonged extracorporeal circulation. Several investigators demonstrated that extracorporeal circulation for days was possible without causing significant injury to normal animals. Hemodynamics were easy to regulate. Acidosis, capillary permeability, and organ deterioration which often plagued cardiopulmonary bypass in the operating room did not occur. Bleeding was minimal with adequate control of heparin. Hemolysis was negligible. Thrombocytopenia inevitably occurred but was manageable. All of these studies in the animal laboratory showed that the technique was feasible, and provided the background for early clinical trials.

HISTORY OF ECMO IN INDIA

Extracorporeal membrane oxygenation was used for postoperative cardiac cases especially in pediatrics in cardiac surgical centers across country since 2000. The first being at AIIMS, Cardiac Neuro Center, New Delhi in cardiac surgery few anecodotal cases have been reported of using ECMO other than cardiac surgical cases. For a long time till 2008, ECMO was like a step son of major cardiothoracic surgical centers and its application remained limited as an extended cardiopulmonary bypass or in post cardiotomy cardiogenic shock especially after the surgical correction of complex congenital heart disease. Unlike the west, where ECMO was designed, developed and perfected on respiratory cases, our country could not use this non-cardiac intensive care centers could not use this power of science due to lack of logistics and technical back-up.

The ECMO year 2010 and 2011 has been an ECMO awareness drive in India and ECMO was also started as ECMO Society of India in 2010 in Mumbai. The ECMO India 2013 summit at New Delhi, brings together for the first time, members from India [AIIMS, Medanta, Narayana Hrudayalaya, RVCC (Mumbai) and Apollo (Delhi and

Table 2: History of ECLS: Clinical trials

Adult respiratory	*Neonatal respiratory*
• 1979 NIH-ARDS randomized trial	• 1985 Bartlett randomized trial
• 1986 Gattinoni $ECCO_2R$ cohort trial	• 1989 O'Rourke randomized trial
• 1994 Morris $ECCO_2R$ randomized trial	• 1996 UK Collaborative trial
• 2007 PEEK CESAR randomized trial	

Table 3: ECLS history: Devices and technology

Vascular access	*Anticoagulation*	*Membrane lungs*	*Servoregulated pumps*
• Direct cut-down – Chest tubes – Vascular cannulae • Seldinger technique – Thin walled cannulae – High flow double lumen cannulae	• Heparin titration to whole blood ACT • Nonthrombogenic surfaces – Passive – Active	• Solid silicone rubber-Kolobow Scimed/Medtronic • Microporous hollow fiber - Bentley/Terumo/Medtronic • Solid hollow fiber-Jostra/ Maquet/Novalung	• Roller pump with negative pressure control • Centrifugal pumps with bearing supported rotors–Biomedicus/ Medtronics • Centrifugal pumps with floating rotors- Jostra/Maquet/Levatronics

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Fig. 7: ECMO centers in India

Table 4: Summary of history of ECMO

- 1953—Gibbon 1st successful use of CPB
- 1967—Kolobow developed spiral coil membrane
- 1972—Hill 1st successful adult ECMO
- 1976—Bartlett 1st successful neonatal ECMO
- 1979—NIH Study
- 1989—ELSO established
- 2001—ECMO established in India, at AIIMS, New Delhi.

Chennai), BL Kapoor Hospital (Delhi)], and ELSO (USA) and Glenfield (UK) leave come together to enhance learning, academics and research in this field. ECMO has evolved and will flourish with newer technologies and advancements.

REFERENCES

1. Lowry AW, Morales DL, Graves DE, Knudson JD, Shamszad P, Mott AR, et al. Characterization of Extracorporeal Membrane Oxygenation for Pediatric Cardiac Arrest in the United States: Analysis of the Kids' Inpatient Database. Pediatr Cardiol. Mar 16, 2013;[Medline].
2. Gibbon JH Jr. Application of a mechanical heart and lung apparatus to cardiac surgery. Minn Med. 1954;37:180-5.
3. Lillehei CW. A personalized history of extracorporeal circulation. Trans Am Soc Artif Intern Organs. 1982;28:5-16.
4. Kirklin JW, Donald DE, Harshbarger HG, Hetzel PS, Patrick RT, Swan HJ. Studies in extracorporeal circulation. I. Applicability of Gibbon-type pump-oxygenator to human intracardiac surgery: 40 cases. Ann Surg. 1956;144(1):2-8. [Medline].
5. Trans Am Soc Artif. Intern Organs. 1971;17:350-4.
6. Rashkind WJ, Freeman A, Klein D, Toft RW. Evaluation of a disposable plastic, low volume, pumpless oxygenator as a lung substitute. J Pediatr Jan. 1965;66:94-102. [Medline].
7. Dorson W Jr, Baker E, Cohen ML, Meyer B, Molthan M, Trump D. A perfusion system for infants. Trans Am Soc Artif Intern Organs. 1969;15:155-60. [Medline].
8. Baffes TG, Fridman JL, Bicoff JP, Whitehill JL. Extracorporeal circulation for support of palliative cardiac surgery in infants. Ann Thorac Surg. Oct. 1970;10(4):354-63. [Medline].
9. Bartlett RH, Gazzaniga AB, Jefferies MR, et al. Extracorporeal membrane oxygenation (ECMO) cardiopulmonary support in infancy. Trans Am Soc Artif Intern Organs. 1976;22:80-93.

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