Chapter 1

A brief history of ECMO

Starting point

Extracorporeal membrane oxygenation (ECMO) support is a form of extracorporeal life support. ECMO is not a treatment and does not correct the underlying pathological insult. The technology is a direct extension from cardiopulmonary bypass and the heart–lung machine used in cardiac surgery.

Extracorporeal life support technologies include other devices, such as dialysis, continuous haemofiltration and ventricular assist devices

Table 1.1 lists the main events that contributed to the development of ECMO. Early attempts at mixing gas and blood were hindered by thrombus (blood clot) formation. The discovery of heparin at the start of the 20th century circumvented this obstacle. Various devices to allow mixing of gas and blood were developed, with the bubble oxygenator probably the most recognized. In this system, the gas literally bubbled up in the blood. Great attention to the size of the bubbles and the circuit design with traps allowed this to happen without the air bubbles being entrained into the patient's bloodstream and causing an air embolism. The mixing of gas and blood caused multiple disruptions to the blood homeostasis and

Table 1.1 Milestones in the history of ECMO support

Year	Event
1635–1703	Robert Hooke conceptualizes the notion of an oxygenator.
1869	Ludwig and Schmidt attempt to oxygenate blood by shaking together defibrinated blood with air in a balloon.
1882	von Schröder of Strasburg uses a bubble oxygenator to oxygenate an isolated kidney.
1882	Frey and Gruber describe the first 'two-dimensional', direct-contact extracorporeal oxygenator, which exposed a thin film of blood to air in an inclined cylinder, which was rotated by an electric motor.
1916	Discovery of heparin when Jay Maclean demonstrates that a phosphatide extracted from canine heart muscle prevents coagulation of the blood.
1929	First whole-body extracorporeal perfusion of a dog by Brukhonenko and Tchetchuline.
1930s	Gibbon and Kirkland further develop the concept of the oxygenator.
1948	Bjork describes the rotating disc oxygenator.
1952	All-glass bubble oxygenator by Clarke, Gollan and Gupta.
1953	First successful human intracardiac operation under direct vision using a mechanical extracorporeal pump oxygenator.
1955	Kirklin and colleagues at the Mayo Clinic further developed the Gibbon-type stationary screen oxygenator into the Mayo–Gibbon pump oxygenator apparatus, and made it available for commercial use.
1955	Lillehei and colleagues then begin to use the DeWall bubble oxygenator clinically.
1958	Clowes, Hopkins and Neville use 25 m^2 of permeable ethylcellulose (soon replaced by the mechanically stronger polytetrafluoroethylene or Teflon) in multiple sandwiched layers to form the first clinical membrane oxygenator.
1972	Hill reports the first adult survivor on ECMO.
1972	Editorial in the *New England Journal of Medicine* by Zapol: 'Buying time with artificial lungs'.

Table 1.1 (cont.)

Year	Event
1976	Bartlett reports the successful use of ECMO on an abandoned newborn nicknamed Esperanza by the nursing staff.
1978	Kolobow and Gattinoni describe using extracorporeal circulation to remove carbon dioxide, allowing a potential decrease in ventilation harm.
1979	Publication of a randomized controlled trial in adult patients with acute respiratory distress syndrome (ARDS) by the National Heart, Lung and Blood Institute: disappointing results with 10% survival in either group.
1989	Founding of the Extracorporeal Life Support Organization (ELSO).
2009	H1N1 influenza pandemic and data relating to clinical success with ECMO are widely disseminated, including in the lay press.
2009	'Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomized controlled trial', published in *The Lancet*.
2011	The National Health Service (England) commission a national respiratory ECMO service.
2014	Publication of 'Position paper for the organization of extracorporeal membrane oxygenation programs for acute respiratory failure in adult patients' in the *American Journal of Respiratory and Critical Care Medicine*.

limited the duration of exchange. Interposing a semi-permeable membrane between the air and the blood was a key development that allowed longer periods of support.

The birth of ECMO can be traced back to 1929 in Russia with the first successful reported extracorporeal perfusion of a dog. In humans, the first successful cardiopulmonary bypass was performed in 1953 by Gibbon.

In 1971, a trauma patient survived after being supported for 3 days with ECMO. He is considered to be the first patient to benefit from the technology. A few years later, Robert Bartlett reported the first infant to benefit from ECMO support. Many clinicians were then enthused by the technology and offered it to their patients.

In the beginning

A first trial of extracorporeal support in patients with respiratory failure was initiated by the National Heart, Lung and Blood Institute in the USA. The results, published in 1979, were very disappointing with most patients (90%) dying and with no difference between the groups. The authors acknowledged that ECMO was able to support patients but suggested that it did not stop the lungs deteriorating progressively with no recovery.

As a result, most clinicians stopped offering ECMO.

A minority continued to improve the technique. Others worked on modifying other aspects of the support of respiratory failure patients. Clinicians understood that lungs were being damaged by mechanical ventilation with positive pressure. Methods to decrease this mechanical insult were developed. The so-called protective ventilation strategies are in fact the least-damaging lung ventilation techniques. One promising method was to combine therapies using ECMO to remove carbon dioxide (CO_2) to reduce the amount of ventilation required with mechanical ventilation. However, there was no evidence in comparative

studies that using ECMO led to better outcomes than conventional therapy.

Clinicians using ECMO to support infants were convinced that they were saving lives, and several trials and case series proved this to be correct. Paediatric ECMO developed and was embraced by many. Paediatric centres continued to accumulate expertise and experience. But this book is about the adult patient. . .

Enthusiast clinicians teamed together and founded the Extracorporeal Life Support Organization (ELSO) in 1989, justified mainly by the successes observed in paediatric support. This network understood the importance of sharing practice and collecting data from all participating centres. Data about paediatric and adult ECMO were progressively accumulated to inform practice around the world.

Moving forward

At the beginning of the 21st century, technology had advanced with the development and optimization of devices used in cardiopulmonary bypass. The bubble oxygenator had long been forgotten and the membrane oxygenator was being used by all (allowing separation of blood and gas by a semi-permeable membrane). This, combined with the advent of centrifugal pumps, improved the biocompatibility of the whole process. Although still not harmless, the technique was becoming simpler. Improved design removed many mechanical issues. The introduction of smaller, less-intrusive circuits allowed portability. The changes were such that this

era can be referred to as the start of the next generation of ECMO (informally called ECMO v2.0).

Specialist centres had started using ECMO in specific patients, such as after lung transplantation. Others were exploring ECMO to support the heart and lungs. The technique was confined to highly specialized centres and the occasional patient.

In 2009, when confronted with a new subtype of influenza virus (H1N1) that targeted mainly young people, the clinical community used ECMO with success to support many patients to full recovery. While it is questionable that ECMO made a difference in outcome (some are convinced it did, but the data have been the subject of many debates), this experience led to a widespread use of the practice. Noteworthy was the fact that ECMO was offered to a large number of very sick patients during the pandemic, without modern health services imploding, albeit stretching available resources.

Simultaneous to the pandemic, the results of a large prospective trial of the use of ECMO in patients with acute respiratory distress syndrome (ARDS) was published in *The Lancet* (the CESAR trial) and fuelled both the controversy about and the use of the technology. This trial showed that transferring patients with ARDS to a specialist centre that could offer ECMO if required led to a better outcome. It did not show that ECMO itself helped.

As a result of the pandemic, and supported by the published evidence, clinicians started to consider ECMO earlier and many providers started to offer it. Some countries set up

national networks (e.g. the specifications of the National Health Service (England) national respiratory ECMO service can be accessed online; see Chapter 2).

Parallel to the development of ECMO to support respiratory function, ECMO has been used to support patients with cardiopulmonary failure. In this setting, ECMO can be seen as a way to provide cardiopulmonary bypass either rapidly (such as in a cardiac arrest situation) or for several days (such as when continuing cardiopulmonary bypass after cardiac surgery). Case series (and numerous case reports) are supporting the development of veno-arterial ECMO as a way to supply most organs with a continuous oxygenated blood supply. This support is being used in an increasing number of patients, based on clinicians' belief that it helps on some occasions. However, scientific evidence is lacking.

Key points

- This is a book about adult patients.
- ECMO circuits are now simpler and safer.
- ECMO saved lives during the H1N1 influenza pandemic.
- ECMO is a support modality and not a treatment.

TO LEARN MORE

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Peek GJ, Mugford M, Tiruvoipati R, *et al.* (2009). Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet*, 374, 1351–63.