

The use of extra-corporeal membrane oxygenation to support critically ill neonates and infants

Extra-corporeal membrane oxygenation (ECMO) is an evidence-based method of providing respiratory or cardiorespiratory support to patients with potentially reversible conditions who cannot be adequately or safely supported using more conventional and less invasive intensive care techniques. This article discusses the background to and evidence behind ECMO, how it works, its use with neonatal and infant patient groups and possible future uses.

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Clinical use of ECMO began in the USA during the 1970s¹. Since that time ECMO centres around the world have successfully supported thousands of neonatal, paediatric and adult patients through severe episodes of respiratory or cardiorespiratory failure. ECMO was introduced to the UK at Glenfield Hospital, Leicester in the late 1980s and there are now four supra-regional centres located in London, Leicester, Newcastle and Glasgow. Between them the centres offer a neonatal and paediatric ECMO service covering both the UK and Ireland². Leicester is currently the only UK centre offering an adult ECMO service, taking patients from throughout the country.

respiratory support are provided because pumping the blood back into the patient via the arterial circulation supplements cardiac output.

Blood drains from the patient into the ECMO circuit by gravity. It then moves through a pump into the oxygenator where it passes through hollow fibres. A flow of oxygen passed along the outside of the fibres causes absorption of oxygen into the blood. At the same time CO₂ moves from the blood into the oxygen flow. The function of the lungs is thus mimicked and supplemented. Patient oxygenation and CO₂ levels can be manipulated as required because a faster pump speed results in more oxygen uptake, and a faster gas flow into the oxygenator will result in greater CO₂ removal. The action of the pump propels blood through the circuit and back to the patient.

A neonatal ECMO circuit may contain twice the baby's normal circulating volume. This amount of blood outside of the body is prone to both clotting and rapid cooling. Heparin is infused to prolong clotting time and prevent formation of clots in the circuit. To counteract heat loss a water heater continually bathes the outside of the oxygenator with warm water. Heat is thus transferred to the blood so that it re-enters the body at an appropriate temperature. This temperature can be manipulated if required to safely provide controlled hypothermia, thought to be beneficial for babies who have suffered an episode of severe hypoxia prior to ECMO³. Safety mechanisms built into the circuit will stop the pump, and thus blood flow into the patient, if there is an interruption to blood

Keywords

ECMO; respiratory support

Key points

Cornick, P. (2006) The use of extra-corporeal membrane oxygenation to support critically ill neonates and infants *Infant* 2(1): 25-28.

1. ECMO is used to provide either respiratory or cardiorespiratory support to patients who have a reversible condition but cannot be maintained by conventional intensive care.
2. Blood passes from the patient into an ECMO circuit where an artificial oxygenator adds oxygen and removes carbon dioxide. After gas exchange has occurred blood is rewarmed and pumped back into the patient.
3. ECMO support for neonates is validated by a large randomised controlled UK based trial. Its use with other patient groups is supported by the National Institute for Clinical Excellence (NICE).

How does an ECMO circuit work?

Extra-corporeal means 'outside of the body' and membrane oxygenation refers to the use of a device that mimics the function of the lungs. An ECMO circuit (**FIGURE 1**) drains venous blood and pumps it through an oxygenator, where gas exchange takes place, before returning it to the body. Blood is returned either into the venous circulation (veno-venous ECMO) or into the arterial circulation (veno-arterial ECMO). Veno-venous ECMO provides oxygenation and also carbon dioxide (CO₂) removal, thus supporting the respiratory system. For neonates and small infants this is usually carried out using a double lumen cannula inserted into the right atrium via the right external jugular vein. With veno-arterial ECMO, blood is drained using a single venous cannula and returned via an arterial one, (usually entering the aorta via the right common carotid artery). Both cardiac and

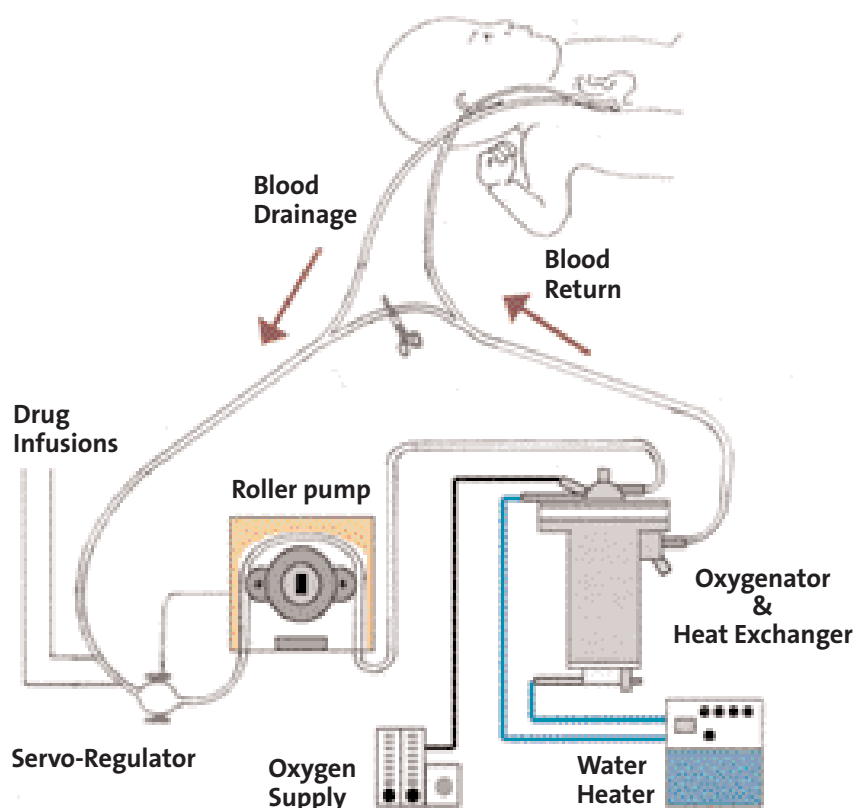


FIGURE 1 Diagrammatic view of neonatal veno-venous ECMO using a double-lumen cannula.

draining out of the patient. Use of bubble detectors can reduce the risk of air embolism by stopping the pump if air is detected in the circuit tubing.

Evidence base for ECMO

The use of ECMO to support neonatal patients with severe but potentially reversible respiratory failure was validated by the UK Collaborative ECMO Trial⁴. The four year follow-up for this trial⁵ confirmed that use of ECMO resulted in improved survival without increased morbidity. Lack of sufficient patient numbers and ethical problems have precluded large randomised controlled trials of ECMO with paediatric patients, either for respiratory support or for cardiac support post open heart surgery. Published case series and reviews⁶⁻⁹ do however reveal cardiac and respiratory ECMO to be appropriate and effective when used with these groups. The National Institute for Clinical Excellence supports such use and has published information related to the use of ECMO in post-neonatal patients¹⁰. ECMO for respiratory support in adult patients also appears very promising⁷ and is currently being studied in the UK with a large randomised controlled trial¹¹.

Criteria for using ECMO

ECMO should not be considered a 'rescue' device, it is an evidence-based option for patients with severe respiratory/cardio-respiratory failure. It is not an active treatment but a means of supporting a patient whilst the underlying disease process is managed/treated. For this reason it is only used if a patient's condition is considered reversible. Maximal use of other intensive care support, without significant improvement, is often an indicator of the need for ECMO, especially when considering that prolonged periods of high pressure ventilation may cause irreversible lung damage. Oxygenation index is a method of quantifying the severity of lung disease and risk of mortality in infants – an index of 40 or above is often used to help identify which infants should receive ECMO.

The use of heparin to prolong clotting times during ECMO increases the risk of bleeding and excludes very premature babies, at increased risk of intraventricular haemorrhage, from receiving ECMO. These babies may also be excluded by the technical difficulties of inserting large ECMO cannulae into very small vessels. For these reasons babies under 34 weeks gestation and 2.0kg in weight are often not

considered suitable for ECMO¹. Some centres quote a 1.8Kg limit² and a recent large review suggests that ECMO may be both safe and effective for some babies weighing as little as 1.6Kg¹².

Neonatal and infant patients

The most common use of ECMO is veno-venous support of term or near-term babies with severe respiratory failure. Typical patients (**FIGURE 2**) include babies with meconium aspiration syndrome, persistent pulmonary hypertension of the newborn, diaphragmatic hernia, respiratory distress syndrome and severe sepsis². Gas exchange is provided via the ECMO circuit oxygenator, allowing ventilation settings to be reduced to a level that maintains good inflation but avoids barotrauma. This allows the lungs to rest and recover. Whilst the introduction of therapies such as high frequency oscillation and inhaled nitric oxide have reduced the number of such babies requiring ECMO¹³, there continue to be significant numbers who do not respond to them and thus require ECMO support. Veno-arterial ECMO is used when babies require cardiovascular as well as respiratory support, for example babies with severe sepsis or with sub-optimal cardiac function whilst recovering from complicated open-heart surgery.

Infants requiring ECMO after the neonatal period often have severe respiratory failure as a result of bacterial or viral infections/pneumonias. Respiratory syncytial virus can lead to severe acute problems for small 'ex-premature' infants. ECMO may help reduce the risk of further lung damage in infants with severe acute respiratory problems over underlying chronic lung disease¹⁴.

Advantages and disadvantages

ECMO has an advantage over some other fairly recent approaches to severe neonatal respiratory failure, such as high frequency oscillation (HFO) or inhaled nitric oxide (iNO), in that it has been shown to reduce both mortality and morbidity⁴. It can support respiratory function, whilst recovery takes place, in severely compromised infants without causing barotrauma or other lung damage. Patients requiring significant inotropic support have been shown to require greatly reduced doses of inotropes within 24 hours even when receiving ECMO purely as respiratory support¹⁵. Use of ECMO for postoperative

cardiac support can allow surgeons to operate on infants whose heart may initially be unable to function adequately during the postoperative period.

ECMO is a very invasive procedure with inherent risks such as bleeding, infection and catastrophic equipment failure. Appropriate training and careful attention to detail are needed to minimise these risks. The relatively small number of patients, and the highly specialised nature of the work, have led to there being only four UK ECMO centres. This results in patients being transported considerable distances whilst acutely ill. Though there are obvious risks to such transfers the resulting morbidity and mortality appears to be very low^{4,16} and needs to be weighed against the risks of a patient not receiving ECMO. Parents may suffer both emotionally and financially from having a very sick baby in a hospital far from their home and may require a lot of support from ECMO centre staff. As mentioned above technical difficulties, and the risk of heparin-induced bleeding, can exclude very small or very premature infants from the benefits of ECMO.

Referral for ECMO

The need for long distance transfers to ECMO centres suggests that prompt referral of potential patients is prudent to ensure they are in as good a condition as possible for the journey. Advances in neonatal care have possibly made this both more important and more difficult. Therapies such as HFO and iNO are recognised as having reduced the use of ECMO^{13,17}. Whilst avoidance of such an invasive procedure may be desirable, there is the potential for use of these therapies to delay referral of patients when improvement is not achieved. More than 72 hours of ventilation prior to referral is associated with a need for longer times spent on ECMO¹⁸ and mortality has been directly related to duration of pre ECMO ventilation¹⁹. It is therefore vital to recognise treatment failure and refer promptly. It has been suggested that written guidelines for ECMO referral can help avoid delays, as can discussion of potential patients with an ECMO centre²⁰. Problems may arise with the use of HFO because whilst UK ECMO centres can transport patients receiving iNO, they do not currently have access to transport oscillators.

Safe provision of ECMO

It is widely believed that for ECMO to

achieve consistently good outcomes, an ECMO service requires a throughput of patients large enough to maintain skill levels and build up staff experience. A small number of centres providing ECMO frequently is therefore preferable to a larger number doing a small amount. ECMO is a highly specialised procedure that relies upon the skills of a large multidisciplinary team including surgeons, medical staff specialising in ECMO, ECMO co-ordinators, ECMO specialists, consultant intensivists, physiotherapists, perfusionists and pharmacists. This team must work together well to provide optimal care to their acutely ill patients. Adherence to well defined admission criteria and clinical protocols help ensure that the service is used in a manner that is safe, ethical and cost effective.

An ECMO patient will usually have two staff at the bedside at all times – a nurse and an ECMO specialist. The two work together to care for and observe the patient. The nurse is responsible for intensive care nursing of the patient whilst the specialist is responsible for care of the ECMO circuit and bedside management of the patient. Specialists are usually nurses who have undertaken further training. There is an ECMO co-ordinator (also usually a nursing role) either on-site or on-call at all times to oversee management of the patients and deal with referrals, problems and emergencies.

The ECMO specialist role and training

The main role of the ECMO specialist is to provide 'continuous surveillance of the extracorporeal life support system during clinical operation'²¹. The specialist works under the supervision of the co-ordinator and the ECMO medical team. This very extended role can be undertaken by staff from a variety of different disciplines² but in the UK, specialists are usually nurses. The role is utilised in a similar way in many centres worldwide²²⁻²⁴.

An ECMO specialist course is usually run over a very intensive week and involves a mixture of lectures and practical training. Theory is related to anatomy, physiology, respiratory and cardiovascular disease processes and the principles and practices of ECMO. Practical training is carried out using ECMO circuits filled with saline. Operation, fault finding and emergency procedures can thus be taught and practised in an environment that is realistic but away from real patients. After the course an exam must be passed and a period of supervised and assessed practice undertaken before a specialist can work independently.

An ECMO specialist shift begins with a handover covering all aspects of the patient's care and the condition of the ECMO circuit. A detailed examination of the circuit is carried out to ensure



FIGURE 2 Nicholas receiving veno-venous ECMO. (Photo used with kind permission of Benjamin and Fiona).

integrity. Written parameters are discussed and a plan of care worked out with the bedside nurse. The specialist is responsible for ensuring that the ECMO cannula, and the circuit as a whole, are kept patent and secure during patient handling. Ensuring that only the specialist handles the circuit tubing reduces the risks of circuit compromise or introduction of infection.

The ECMO circuit is examined and assessed regularly and blood gas values, clotting times and other laboratory values checked as required. Activated clotting time is checked at the bedside at least hourly. The specialist works within set parameters and guidelines to maintain the patient in optimum condition. Heparin, analgesic, inotrope and other infusions are titrated, blood products ordered and given, ECMO pump speed altered and oxygenator gas flow adjusted as required. Changes in patient condition are discussed with the ECMO co-ordinator or medical staff as necessary. Any deviation from set protocols or treatment is made only after such discussion. The use of tested protocols is an integral part of safe successful ECMO, as is effective teamwork²⁵. The specialist must be aware of potential emergencies that may arise and be able to organise immediate reaction whilst further help is summoned.

Future provision of ECMO services

There is an established worldwide pattern of reduced neonatal respiratory ECMO, but increased use with paediatric respiratory patients and after cardiac surgery. The results of the currently running adult ECMO trial¹¹ will have several implications for UK ECMO services. A positive trial outcome may lead to an increase in demand that requires the establishment of a second adult ECMO centre. Similarity between referral diagnoses of adults and older children may also result in increased paediatric referrals after the trial. Neonatal respiratory patients often have an uncomplicated clinical course whilst on ECMO, and their ECMO runs can be relatively short. These less complicated patients may increasingly be joined by cardiac, paediatric and adult patients who all tend to require more complicated management and have longer ECMO runs. Such changes to the use of ECMO may have major implications for the resources and staffing of ECMO services.

In some countries mobile ECMO systems are used to transport patients who require ECMO but are so unstable that transferring them presents major risks.

Such technology is not at present available in the UK but its introduction is being considered. Other newer uses of ECMO being introduced include 'rapid response ECMO'^{26, 27} to provide support in the event of extended resuscitation following cardiac arrest. Possible advances in circuit technology, such as physically smaller cannulae or new types of tubing that may reduce the need for anti-coagulation, have the potential to increase the availability of ECMO to small and premature babies.

Discussion

The UK neonatal ECMO trial⁴ showed that for every five neonates with severe respiratory failure put onto ECMO, an extra life is saved when compared to not using ECMO. This demonstrated the importance of ECMO in neonatal care and brings home the need for prompt referral. Great promise has also been shown with paediatric, cardiac and adult ECMO. Changes in the use of ECMO suggest that whilst neonatal respiratory use is falling, overall use has the potential to increase considerably. ECMO is highly specialised, expensive, invasive and not without risk. A well trained team frequently exposed to ECMO, backed by a skilled transport service, are able to minimise the risks and enable survival in patients whose prospects without ECMO are often very bleak.

References

1. Tulenko, D. An update on ECMO. *Neonatal Network* 2004; **23**(4): 11-18.
2. Liddell, M. Extracorporeal membrane oxygenation. *Scottish Nurse* 2003; **7**(10): 32-33.
3. Ichiba, S., Killer, H., Firmin, R., Kotecha, S., Edwards, A., Field, D. Pilot investigation of hypothermia in neonates receiving extracorporeal membrane oxygenation. *Arch Disease Child Fetal Neonatal Ed* 2003; **88**(2): F128-F133.
4. UK Collaborative ECMO Trial Group. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation. *Lancet* 1996; **348**: 75-82.
5. Bennett, C., Johnson, A., Field, D., Elbourne, D. UK collaborative randomised trial of neonatal extracorporeal oxygenation: Follow-up to age 4 years. *Lancet* 2001; **357**: 1094-96.
6. Chaturvedi, R., Macrae, D., Brown, K. et al. Cardiac ECMO for biventricular hearts after paediatric open heart surgery. *Heart* 2004; **90**: 545-51.
7. Bartlett, R., Roloff, D., Custer, J., Younger, J., Hirshl, R. Extracorporeal life support the university of Michigan experience. *JAMA* 2000; **283**(7): 904-08.
8. Peek, G., Sosnowski, A. Extra-corporeal membrane oxygenation for paediatric respiratory failure. *Br Med Bulletin* 1997; **53**(4): 745-56.
9. Lequier, L. Extracorporeal life support in neonatal and pediatric critical care: A review. *J Intensive Care Med* 2004; **19**(5): 243-58.
10. National Institute for Clinical Excellence. Extracorporeal membrane oxygenation in children. 2004. Published online at <http://www.nice.org.uk/pdf/ip/IPG038publicinfoenglish.pdf> (Accessed 25/10/05).
11. The CESAR Trial. Conventional ventilation or ECMO for severe adult respiratory failure. 2005. Published online at <http://www.cesar-trial.org> (Accessed 25/10/05).
12. Rozmiarek, A., Qureshi, F., Cassidy, L. et al. How low can you go? Effectiveness and safety of extracorporeal membrane oxygenation in low-birth-weight neonates. *Pediatric Surgery* 2004; **39**(6): 845-47.
13. Hui, T., Danielson, P., Anderson, K., Stein, J. The impact of changing neonatal respiratory management on extracorporeal membrane oxygenation utilization. *J Pediatric Surgery* 2002; **37**(5): 703-05.
14. Hibbs, A., Evans, J., Gerdes, M., Hunter, J., Cullen, J. Outcome of infants with bronchopulmonary dysplasia who receive extracorporeal membrane oxygenation. *J Pediatric Surgery* 2001; **36**(10): 1479-84.
15. Roberts, N., Westrope, C., Poobani, S. et al. Venovenous extracorporeal membrane oxygenation for respiratory failure in inotrope dependent neonates. *AAIO Journal* 2003; **49**(5): 568-71.
16. Westrope, C., Roberts, N., Nichani, Hunt, C., Peek, G., Firmin, R. Experience with mobile inhaled nitric oxide during transport of neonates and children with respiratory insufficiency to an extracorporeal membrane oxygenation center. *Pediatric Crit Care Med* 2004; **5**(6): 542-46.
17. Roy, B., Rycus, P., Conrad, S., Clark, R. The changing demographics of neonatal extracorporeal membrane oxygenation patients reported to the extracorporeal life support organisation (ELSO) registry. *Pediatrics* 2000; **106**(6): 1334-38.
18. Walker, G., Coutts, J., Skeoch, C., Davis, C. Paediatricians' perception of the use of extracorporeal membrane oxygenation to treat meconium aspiration syndrome. *Arch Disease Child Fetal Neonatal Ed* 2003; **88**: F70-F71.
19. Pranikoff, T., Hirschl, R., Steimle, C., Anderson, H., Bartlett, R. Mortality is directly related to the duration of mechanical ventilation before the initiation of extracorporeal life support for severe respiratory failure. *Crit Care Med* 1997; **25**: 28-32.
20. Carroll, W., Killer, H. Absence of written guidelines in neonatal units for ECMO referral may delay referral. *Arch Disease Child Fetal Neonatal Ed* 2000; **82**(3): F257.
21. Killer, H., Faulkner, G. Job profile-ECMO specialist. Unpublished Job Profile from Glenfield Hospital, Leicester, UK. 2000.
22. Vilardi, J. Defining a new expanded role for staff nurses: Role development and clinical practice issues for the ECMO specialist. *J Perinatal Neonatal Nursing* 1991; **5**(3): 51-60.
23. Fergusson, D., Copnell, B. ECMO: The expanded role of the nurse. *Paediatric Nursing* 1993; **5**(9): 12-15.
24. Pearson, J. Training for the role of ECMO specialist. *Paediatric Nursing* 1994; **6**(3): 22-24.
25. Firmin, R., Killer, H. Extracorporeal membrane oxygenation. *Perfusion* 1999; **14**: 291-97.
26. Schindler, M., Brown, K., Goldman, A. Outcome after cardiac arrest in a cardiac intensive care unit: Rapid response extracorporeal membrane oxygenation vs standard resuscitation. *Pediatric Crit Care Med* 2005; **6**(2): 238.
27. Vanderwal, P. New circuit developed for cardiopulmonary support – Children's Hospital of Wisconsin Internet Website. 2005. Published online at: <http://www.chw.org/display/router.asp?DocID=8335> (Accessed 25/10/05).