

## Supplementary Guidance for the Diagnosis of Death using Neurological Criteria when the patient is supported with extracorporeal membrane oxygenation (ECMO)

This supplementary guidance is endorsed by the Faculty of Intensive Care Medicine, the Intensive Care Society Standards Committee and the NHS England Severe Respiratory Failure Network for adults and children older than 16 years. It should be used in conjunction with the Academy of Medical Royal Colleges (AoMRC 2008) *A Code of Practice for the Diagnosis and Confirmation of Death* and the forms for the Diagnosis of Death using Neurological Criteria endorsed by the Faculty of Intensive Care Medicine, Intensive Care Society and the National Organ Donation Committee.

Forms available: <https://www.ficm.ac.uk/standards-and-guidelines/access-standards-and-guidelines> or <http://www.ics.ac.uk/ICS/GuidelinesAndStandards/GeneralGuidance.aspx>

### Challenges of diagnosing death using neurological criteria on ECMO

#### Pharmacokinetic

It is known that ECMO circuits sequester drugs, both by adsorption and absorption, leading to the potential for altered kinetics, particularly clearance. It is also possible that some drugs including sedatives and potentially muscle relaxants may wash out of the membrane into the patient after cessation of administration, extending their effective half-life. Measures to exclude reversible causes of coma and apnoea may therefore be unreliable. Where there is concern that drugs may be contributing to unconsciousness, apnoea and loss of brainstem reflexes, specific drug levels should be performed, a reversal agent administered and/or train of four performed as deemed appropriate. If doubt persists, diagnosing death using neurological criteria should be abandoned and consideration given to undertaking ancillary investigations.

#### Apnoea Testing

Extracorporeal clearance of CO<sub>2</sub> must be taken into account when performing apnoea testing on ECMO, and sweep gas flow titrated carefully to avoid large-scale, acute changes in cerebral PaCO<sub>2</sub>. In venovenous (VV) ECMO, the cerebral PaCO<sub>2</sub> is identical to the PaCO<sub>2</sub> at all peripheral arterial blood gas sampling sites. Modification of the PaCO<sub>2</sub> through sweep gas changes, and subsequent analysis of the peripheral PaCO<sub>2</sub> allows apnoea testing to proceed reliably. In peripheral venoarterial (VA) or hybrid VVA ECMO, the PaCO<sub>2</sub> in the cerebral circulation may differ from the PaCO<sub>2</sub> in some systemic arterial sampling sites due to the variable location of a mixing point between native pulmonary-cardiac blood flow and ECMO circuit blood flow in the aorta. Consequently, to provide absolute reassurance that blood gas measurements reflect the cerebral PaCO<sub>2</sub>, multiple sites (including post-membrane and systemic arterial sites furthest from the ECMO return flow) must be sampled and all PaCO<sub>2</sub> levels taken into account when assessing the absence of neurological responses. The highest pH and lowest PaCO<sub>2</sub> must be used.

The guidance below sets out a protocol for apnoea testing in patients on VV and VA-ECMO. Where brainstem death is suspected but the steps to diagnose using neurological criteria on ECMO cannot be reliably completed, ancillary testing is required to confirm the diagnosis. In this circumstance it is recommended that consultant neurology and/or neurointensive care advice is sought. It is important to appreciate that MRI cannot be undertaken on ECMO, however CT, CT angiography and electrophysiological tests (including somatosensory evoked potentials) are all possible.

**With the exception of the pharmacokinetic and apnoea testing challenges above, testing for absence of brainstem reflexes on ECMO is otherwise undertaken in accordance with standard practice.**

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## Apnoea testing on ECMO

AoMRC (2008) Code of Practice apnoea test requires:

1. **Starting apnoea test PaCO<sub>2</sub> ≥ 6.0 kPa and starting pH <7.4 or [H<sup>+</sup>] >40 nmol/L.**  
In patients with chronic CO<sub>2</sub> retention, or those who have received intravenous bicarbonate, confirmation that the starting PaCO<sub>2</sub> > 6.5 kPa and the pH < 7.4 / [H<sup>+</sup>] > 40 nmol/L.
2. **There should be no spontaneous respiration within a minimum of 5 (five) minutes following disconnection from the ventilator.**
3. **Confirmation that the PaCO<sub>2</sub> has increased from the starting level by more than 0.5 kPa.**
4. **Oxygenation and cardiovascular stability should be maintained through each apnoea test.**

These steps are possible on ECMO, although observation of spontaneous respiration may be challenging in a patient with absent native pulmonary function and total parenchymal consolidation. End-tidal CO<sub>2</sub> may not be measurable in these circumstances although respiratory effort may be visualised.

Apnoea testing on ECMO requires maintenance of the extracorporeal blood flow with a membrane sweep gas FiO<sub>2</sub> 100% in order to preserve systemic oxygenation. The sweep gas flow rate can then be manipulated to achieve the starting PaCO<sub>2</sub> and pH requirements. During testing, it is important to titrate the sweep gas flow downwards in small decrements to prevent rapid changes in PaCO<sub>2</sub> and potential precipitation of further neurological injury.

## Steps in apnoea testing on ECMO

Testing can occur in any ECMO circuit configuration (VV, VA or hybrid VVA). For VV ECMO, systemic arterial blood gases measurements at any site will be identical. For VA or hybrid VVA ECMO both right upper limb and femoral blood samples need to be performed in order to assess variability in the systemic blood gas measurements. All sites measured need to fulfil the criteria outlined below.

**The following steps should be undertaken:**

1. Ensure sweep gas FiO<sub>2</sub> is 100%.
2. Temporarily increase the sweep gas flow rate to maximum and then reduce again to 'sigh' the extracorporeal membrane and eliminate condensation.
3. Adjust ECMO blood flow to achieve PaO<sub>2</sub> > 10 kPa at all times at all sampling sites. Note that the blood flow may need to be increased above previously established baseline rates.
4. Reduce sweep gas flow rate by 0.5 L/minute every 5 minutes. Perform arterial blood gas analysis at each 5-minute point until the PaCO<sub>2</sub> is ≥ 6.0 kPa and starting pH <7.4 or [H<sup>+</sup>] >40 nmol/L. In patients with an elevated bicarbonate, the PaCO<sub>2</sub> may need to be further titrated to achieve the desired pH. **Do not reduce the sweep gas flow rate below 0.5 L/min.**
5. Suction the patient's airway to ensure it is clear of obstruction, secretions or soiling.
6. Undertake a ventilator recruitment manoeuvre to optimise pulmonary gas exchange.
7. Disconnect the ventilator circuit and attach a Water's (Mapleson C) circuit with inline ET/CO<sub>2</sub> monitoring and valve adjusted to give approximately 10 cmH<sub>2</sub>O CPAP to the lungs.
8. Reduce the sweep gas flow rate further by 0.5 L/minute every 5 minutes and perform an arterial blood gas at each 5-minute point until all measured PaCO<sub>2</sub> values have risen by at least 0.5kPa above the starting level. **Do not reduce the sweep gas flow rate below 0.5L/min.**
9. During the period of disconnection, observe for any respiratory effort – ET/CO<sub>2</sub>, chest excursion and/or movement of the circuit reservoir bag. This must be for a minimum of 5 (five) minutes.
10. Abandon test if there is significant deoxygenation or cardiovascular instability, if respiratory effort is observed or if adequate rise in PaCO<sub>2</sub> is not achieved.

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## Bibliography

Saucha W, Solek-Pastuszka J, Bohatyrewicz R, Knapik P. Apnea test in the determination of brain death in patients treated with extracorporeal membrane oxygenation (ECMO). *Anaesthesiol Intensive Ther.* 2015;47(4):368-71.

Smilevitch P, Lonjaret L, Fourcade O, Geeraerts T. Apnea test for brain death determination in a patient on extracorporeal membrane oxygenation. *Neurocrit Care.* 2013 Oct;19(2):215-7.

Talahma M, Degeorgia M. Apnea Testing for the Determination of Brain Death in Patients Supported by Extracorporeal Membrane Oxygenation. *J Neurol Res.* 2016;6(1):28-34.

Determination of brain death on ECMO: Australian experience in the development of a protocol for performing an apnoea test. <https://www.alfredicu.org.au/assets/Miscellaneous-Downloads/Abstract-Determination-of-brain-death-on-ECMO.pdf>. Accessed October 24, 2017.

Jarrah RJ, Ajizian SJ, Agarwal S, Copus SC, Nakagawa TA. Developing a standard method for apnea testing in the determination of brain death for patients on venoarterial extracorporeal membrane oxygenation: a pediatric case series. *Pediatr Crit Care Med.* 2014 Feb;15(2):e38-43.

Kreitler K, Cavarocchi N, Hirose H, West S, Hasz R, Ghobrial M, Bell R. Declaring a Patient Brain Dead on Extracorporeal Membrane Oxygenation (ECMO): Are There Guidelines or Misconceptions? [abstract]. *Am J Transplant.* 2015; 15 (suppl 3). <http://atcmeetingabstracts.com/abstract/declaring-a-patient-brain-dead-on-extracorporeal-membrane-oxygenation-ecmo-are-there-guidelines-or-misconceptions/>. Accessed October 24, 2017.

Muralidharan R, Mateen FJ, Shinohara RT, Schears GJ, Wijdicks EF. The challenges with brain death determination in adult patients on extracorporeal membrane oxygenation. *Neurocrit Care.* 2011 Jun; 14(3):423-6.

Academy of Medical Royal Colleges. A Code of Practice for the Diagnosis and Confirmation of Death. October 2008. [http://aomrc.org.uk/wp-content/uploads/2016/04/Code\\_Practice\\_Confirmation\\_Diagnosis\\_Death\\_1008-4.pdf](http://aomrc.org.uk/wp-content/uploads/2016/04/Code_Practice_Confirmation_Diagnosis_Death_1008-4.pdf). Accessed November 21, 2017.

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