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

The following is draft supplementary guidance written by the UK adult ECMO audit / review group and with the support of Stephen Webb, co-chair of the FICM / ICS Standards Committee, and Dale Gardiner on behalf of NHSBT.

The criteria for the diagnosis of death using neurological criteria is as per the Academy of Medical Royal Colleges Code of Practice (2008). This supplementary guidance outlines how the criteria can be satisfied when the patient is on ECMO.

It is hoped for the following:
1) This document will be approved by the FICM / ICS Standards Committee at their next meeting.
2) The National Organ Donation Committee will endorse this supplementary guidance such that if death is confirmed using this guidance we would support donation after brainstem death proceeding.
3) The forms will be hosted on the FICM website, next to the current testing forms.
4) It is intended anyone using this supplementary guidance does so in conjunction with the established testing forms.
5) That as more experience is gained this supplementary guidance might be applied to paediatric patients but that this will require involvement of RCPCH and paediatric NODC.

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That we endorse in principle, that if the FICM/ICS Standards Committee endorse this supplementary guidance, we would support donation after brainstem death proceeding where this supplementary guidance has been used to diagnose Death using Neurological Criteria when the patient is on extracorporeal membrane oxygenation.

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

This supplementary guidance is endorsed by the Faculty of Intensive Care Medicine and Intensive Care Society Standards Committee and [ECMO Group] for adults and children of 16 years and above. The supplementary guidance 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 and Intensive Care Society.

Forms available: https://www.ficm.ac.uk/standards-and-guidelines/access-standards-and-guidelines

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 drugs, including sedatives and potentially paralytics, may wash out of the membrane into the patient membrane after cessation of administration, extending the effective half-life of the drug. This might make it difficult to exclude reversible causes of coma and apnoea. Where there is a concern that a drug might be contributing to the unconsciousness, apnoea and loss of brainstem reflexes, specific drug levels should be carried out, a reversal agent administered or a train of four count performed as deemed appropriate. Alternatively consider ancillary investigations. If doubt persists, do not proceed with diagnosing death using neurological criteria.

Apnoea Testing

Although extracorporeal clearance of CO_2 must be taken into account, apnoea testing is technically possible in the vast majority of patients on veno venous (VV) ECMO where the PCO_2 in the brain is the same as the PCO_2 in the peripheral arterial blood gas. On peripheral venoarterial (VA) ECMO, the pH/PCO_2 in the brain can be difficult to assess accurately depending on native cardiac ejection due to mixing of the native pulmonary-cardiac blood flow in the aorta, hence multiple sites (eg post-membrane and clinically relevant systemic arterial) may need to be sampled to demonstrate pH/PCO_2 changes in accordance with criteria. The highest pH and lowest PCO_2 must be used.

The guidance below sets out a protocol for apnoea testing in patients on VV and VA-ECMO. Where death is suspected in patients and the steps to diagnose death using neurological criteria on ECMO cannot be completed, ancillary testing would be required to confirm the diagnosis. In this circumstance it is recommended to seek consultant neurology and/or neurointensive care advice. 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 brain-stem 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 $PaCO_2 \geq 6.0$ kPa and starting pH <7.4 or [H+] >40 nmol/L.**
   In patients with chronic CO_2 retention, or those who have received intravenous bicarbonate, confirmation that the starting $PaCO_2 > 6.5$ kPa and the pH < 7.4 / $[H^+] > 40$ nmoles/L.
2. **There should be no spontaneous respiration within a minimum of 5 (five) minutes following disconnection from the ventilator.**
3. **Confirmation that the $PaCO_2$ 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 no native pulmonary function and complete consolidation as end-tidal CO_2 is not measurable and only respiratory effort may be visualised.

Apnoea testing on ECMO requires maintenance of the blood flow with a sweep gas inspired O_2 of 100% in order to preserve systemic oxygenation. The sweep gas flow rate can then be manipulated to achieve the initial PCO_2 and pH requirements. It is important to titrate down the sweep gas flow slowly to prevent rapid changes in PCO_2 as this can precipitate further neurological injury if the patient is not diagnosed deceased using neurological criteria.

Steps in apnoea testing on ECMO

Testing can occur on any form of ECMO (VV, VA or hybrid VAV). For VV ECMO, systemic arterial blood gases measured at any site will be the same. For VA or hybrid VAV ECMO post-membrane and systemic arterial blood sample most distal to the pump need to be performed in order to ensure that the pH and PCO_2 to which the brainstem is exposed is characterised.

The following steps should be undertaken:

1. Ensure sweep gas FiO_2 is 100%.
2. Sigh the membrane.
3. Adjust ECMO blood flow aiming to achieve $PaO_2 > 7$ kPa at all times at all sampling sites, note that the blood flow may need to increase above baseline rates.
4. Reduce sweep gas flow rate by 0.5 L/minute every 5 minutes. Perform an arterial blood gas at each point until the PCO_2 is ≥ 6.0 kPa and starting pH <7.4 or [H+] >40 nmol/L. For patients with an elevated bicarbonate, the PCO_2 will need to be higher to achieve the pH criteria.
   Do not reduce the sweep gas flow rate below 0.5 L/min.
5. Suction patient's airway to ensure the airway is clear of obstruction/secretions/soiling.
6. Consider undertaking a recruitment manoeuvre to optimise lung recruitment.
7. Disconnect patient from ventilator and attach to a Mapleson C circuit with valve adjusted to give approximately 10 cmH_2O CPAP and apply inline $ETCO_2$ monitoring.
8. Reduce sweep gas flow rate to no less than 0.5L/minute and perform an arterial blood gas at 5 minutes to demonstrate that the PCO_2 has risen by at least 0.5kPa above the starting level achieved above. If the criteria are not met the sweep gas flow rate should be reduced again and arterial gases reassessed. For VA or VAV ECMO the arterial blood gas sample with the lowest rise in PCO_2, whether post-membrane or distal systemic be at least 0.5kPa above the starting level.
9. During the period of disconnection, observe for evidence of respiratory effort – $ETCO_2$, chest/abdominal movement and movement of a Mapleson C circuit reservoir bag. This must be for a minimum of 5 (five) minutes.
10. Abandon test if there is significant oxygenation or cardiovascular instability, if respiratory effort is observed or if adequate rise in PCO_2 is not achievable.

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Bibliography

Saucha W, Sołek-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. Accessed November 21, 2017.

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