HONG KONG SOCIETY OF CRITICAL CARE MEDICINE Ltd.

GUIDELINES ON CERTIFICATION OF DEATH FOLLOWING THE IRREVERSIBLE CESSATION OF BRAINSTEM FUNCTION

INTRODUCTION

The irreversible cessation of brainstem function ("brainstem death") is established by the documentation of irreversible coma and irreversible loss of brain stem reflex responses and respiratory center function or by the demonstration of the cessation of intracranial blood flow. Despite philosophical arguments, the concept that brainstem death is equivalent to death is accepted within the medical community and medical professional bodies in Hong Kong and legally in common law jurisdictions. Once brainstem death has occurred, artificial life support is inappropriate and should be withdrawn. It is a good medical practice to confirm brainstem death has occurred regardless of whether organ donation is being considered, in order to spare relatives from the further emotional trauma of futile interventions.

The purposes of this document are:

1. To provide recommendations for qualified medical practitioners (*vide infra*) in relation to certification of death following the irreversible cessation of brainstem function for patients who are 2 years of age or older; and
2. To provide a reference for the Hong Kong community in order to reassure them that certification of death following the irreversible cessation of brainstem function is performed with diligence, and in accordance with prevailing scientific evidence, ethical and clinical practice.

The diagnostic criteria presented for certification of death following the irreversible cessation of brainstem function are based on the following documents:

> Greer DM, Shemie SD, Lewis A, Torrance S, Varelas P, Goldenberg FD, Bernat JL, Souter M, Topcuoglu MA, Alexandrov AW, Baldisseri M, Bleck T, Citerio G, Dawson R, Hoppe A, Jacobe S, Manara A, Nakagawa TA, Pope TM,

Silvester W, Thomson D, Al Rahma H, Badenes R, Baker AJ, Cerny V, Chang C, Chang TR, Gnedovskaya E, Han MK, Honeybul S, Jimenez E, Kuroda Y, Liu G, Mallick UK, Marquevich V, Mejia-Mantilla J, Piradov M, Quayyum S, Shrestha GS, Su YY, Timmons SD, Teitelbaum J, Videtta W, Zirpe K, Sung G. Determination of Brain Death/Death by Neurologic Criteria: The World Brain Death Project. JAMA. 2020 Sep 15;324(11):1078-1097. doi: 10.1001/jama.2020.11586. PMID: 32761206.

A Code of Practice for the Diagnosis and Confirmation of Death. Academy of the Medical Royal Colleges, London, 2008. Available from https://www.aomrc.org.uk/wp-content/uploads/2016/04/Code_Practice_Confirmation_Diagnosis_Death_1008-4.pdf

Form for the Diagnosis of Death using Neurological Criteria
Written by Dr Dale Gardiner, Nottingham and Dr Alex Manara, Bristol
Endorsed for use by Intensive Care Society and the Faculty of Intensive Care Medicine, United Kingdom.
Available from https://www.ficm.ac.uk/diagnosing-death-using-neurological-criteria

Supplementary Guidance for the Diagnosis of Death using Neurological Criteria when the patient is supported with extracorporeal membrane oxygenation (ECMO)
Written by the NHS England "ECMO in adults with severe respiratory failure" commissioned service.
Endorsed for use by Intensive Care Society and the Faculty of Intensive Care Medicine, United Kingdom.

The ANZICS Statement on Death and Organ Donation. Edition 4.1. Australian and New Zealand Intensive Care Society, Melbourne, 2021. Available from https://www.anzics.com.au/death-and-organ-donation/

Sandroni C, Nolan JP, Andersen LW, Böttiger BW, Cariou A, Cronberg T, Friberg H, Genbrugge C, Lilja G, Morley PT, Nikolaou N, Olasveengen TM, Skrifvars MB, Taccone FS, Soar J. ERC-ESICM guidelines on temperature control after cardiac arrest in adults. Intensive Care Med. 2022 Mar;48(3):261-269. doi: 10.1007/s00134-022-06620-5. Epub 2022 Jan 28. PMID: 35089409.

They are accepted as sufficient to distinguish between those patients who retain the functional capacity to have a chance of even partial recovery from those in whom no such possibility exists.

DIAGNOSTIC CRITERIA

Preconditions and exclusions prior to considering certification of death following the observation of likely irreversible cessation of brainstem function

1. Diagnosis of severe brain injury or a disorder which is consistent with progression to brain death (the clinical diagnosis is usually confirmed by neuro-imaging)
   There should be no doubt that the patient's condition is due to irreversible structural brain damage.

   1.1 It may be obvious within hours of a primary intracranial event such as severe traumatic brain injury, spontaneous intracranial haemorrhage, or after neurosurgery that the condition is irreversible.

   1.2 However, when a patient has suffered primarily from cardiac arrest, hypoxia, or severe circulatory insufficiency with an indefinite period of cerebral anoxia or is suspected of having cerebral air or fat embolism, it may take longer to establish the diagnosis. Neuroimaging is encouraged to provide additional evidence of cerebral injury.

2. The patient must be apneic, and receiving mechanical ventilation
   If the patient is unresponsive and not breathing spontaneously, neuromuscular blocking agents and other drugs must be excluded as a cause of such findings (*vide infra*).

3. Exclusion of potentially reversible causes of coma

3.1 Depressant drugs or poisons

The confounding clinical effects of sedative drugs and/or muscle relaxants must be excluded before confirmation of brainstem death.

3.1.1 It is recommended that the drug history should be carefully reviewed and adequate intervals allowed for the persistence of drug effects to be excluded. This is of particular importance in patients whose primary cause of coma lies in the toxic effects of drugs resulting in anoxic cerebral damage. The period of observation depends on the pharmacokinetics of the sedative drugs, the doses used, the liver and renal function of the patient and the use of extracorporeal support or targeted temperature management particularly if body temperature of less than 34-degree has been maintained.

3.1.2 Blood and urine screening tests and measurement of relevant serum drug concentrations should be made when necessary. If serum drug concentrations cannot be measured accurately, and drug elimination is known to be prolonged, e.g. following the use of barbiturates, a confirmatory investigation is recommended (*vide infra*).

3.1.3 If there is doubt about the persisting effects of opioid or benzodiazepines, an appropriate drug antagonist may be given.

3.1.4 A peripheral nerve stimulator should always be used to confirm intact neuromuscular conduction.

3.2 Primary hypothermia

The observed body temperature may be low because of depression of central temperature regulation by drugs or brain stem damage. A low-reading thermometer should be used to measure the core temperature. It is recommended that the core temperature should be greater than 35-degree before diagnostic tests are carried out.

3.3 Metabolic and endocrine disturbances including marked derangement of glucose (<3mmol/L or >25mmol/L), sodium (<125mmol/L or > 160mmol/L), phosphate (<0.5mmol/L) or magnesium (<0.5mmol/L), urea >40mmol/L, untreated severe

hypothyroidism or hypoadrenalism and severe decompensated liver failure

3.4 Arterial hypotension with systolic blood pressure ≤ 90mmHg or mean arterial pressure (MAP) ≤ 60mmHg

CLINICAL TESTS OF BRAIN STEM RESPONSES

All brain stem reflexes must be absent. The testing of all the following is considered sufficient

1. Pupils are fixed, ≥ 4mm in diameter and do not respond to changes in the intensity of light.

2. The corneal reflex is absent.

3. The vestibulo-ocular reflex is absent.
   3.1 Elevate the head to 30°.
   3.2 Clear access to the tympanic membrane should be established by direct inspection prior to injection of Ice-cold water.
   3.3 This reflex is absent when no eye movement occurs in either eye during or after the slow injection of at least 50ml of ice-cold water into at least one external auditory meatus, or preferably into each external auditory meatus in turn. Hold eyelids open and observe for eye movement for a minimum of 60 seconds.
   This test may be contraindicated on one or other side by local trauma.

4. When testing the reflexes as described in 1, 2, 3 of this section above, testing of these reflexes may be prevented on one side by local injury or disease. Unilateral testing does not invalidate the diagnosis of brainstem death. In the case of bilateral injury or disease, a confirmatory investigation must be implemented.

5. No motor responses in cranial and somatic distribution can be elicited by adequate painful stimulation within trigeminal nerve distribution.

6. There is no gag reflex.

7. There is no cough reflex.

8. The apnoea test should be done last. No respiratory movements occur when the patient is disconnected from the mechanical ventilator for long enough to ensure that the arterial carbon dioxide tension rises above the threshold for stimulating respiration.
   8.1 The threshold for stimulating respiration is defined by the following: $PaCO_2$ must be greater than 8.0kPa (60mmHg) and arterial pH less than 7.30. Blood-gas analysis must be available for this test to be performed. If the test is not available the patient must be moved to a facility where this test is routinely available. In patients with pre-existing hypercapnia, it is recommended to wait for a $PaCO_2$ rise of >2.7 KPa (20 mmHg) above the baseline level, with a pH<7.30.
   8.2 These patients may be moderately hypothermic (35-degree – 37-degree), flaccid, and with a depressed metabolic rate, so that $PaCO_2$ rises only slowly in apnoea (about 0.27kPa/min or 2mmHg/min). The patient should be disconnected from the mechanical ventilator when their $PaCO_2$ is close to normal, and should remain apneic while the $PaCO_2$ rises to the threshold level.
   8.3 Hypoxaemia during disconnection should be prevented by preoxygenation and administration of oxygen during the test, e.g. by delivering oxygen through a catheter into the trachea or connecting a bag-valve resuscitator to the endotracheal tube with or without a PEEP valve .
   8.4 In patients receiving VA-ECMO, reduce the sweep gas flow on the ECMO circuit to 1 L/min to allow the $PaCO_2$ to rise and keep the same blood flow to maintain the haemodyanamic state. Hypoxaemia may develop before the required threshold level of hypercapnia is reached by the patient, and if this occurs, the apnoea test should be abandoned. An arterial blood gas should be taken from **Both** the circuit post-membrane site **and** the usual systemic arterial site. Both measurements should fulfilled the pH and $PaCO_2$ thresholds criteria of apnea test.

OTHER IMPORTANT CONSIDERATIONS

1. Period of observation and repetition of tests

   Clinical confirmation of the diagnosis of brainstem death requires that irreversibility of cessation of brainstem function is established after a period of observation. Two separate examinations should be performed, each by a different medical practitioner.

   1.1 The first formal examination should only be performed after

      1.1.1 All preconditions have been met throughout the observation period.

      1.1.2 A minimum of four hours observation is required, during which the patient has been comatose (Glasgow Coma Score 3, with painful stimulus applied to areas supplied by the trigeminal nerve), had non-reacting pupils, absent cough reflex, and no spontaneous breathing effort.

   1.2 The second examination can be performed any time after the first examination, so that the total period of observation is a minimum of four hours. However, the minimum period of observation needs to be extended to a total of 24 hours in case of hypoxic-ischaemic encephalopathy after cardiorespiratory arrest. (See item 1.2 in the section on Preconditions and exclusions prior to considering diagnosis of brainstem death.)

   1.3 Targeted temperature management (TTM) with prolonged hypothermia (temperature less than 35-degree for more than 6 hours) or accidental hypothermia of a similar magnitude, may modify outcome prediction after cardiac arrest. There is published evidence suggesting that determination of brain death might be confounded either by TTM or accidental hypothermia itself, or by impaired clearance of medications at lower body temperature. If TTM (less than 35-degree but equal or more than 34-degree) has been applied after resuscitation from cardiorespiratory arrest, clinical testing for brain death should be delayed to 24 hours after rewarming to normothemia (≥36-degree). If body temperature has been lowered to less than 34-degree, further delay for more than 24 hours in brainstem testing should be considered, especially if large doses or prolonged infusion of

sedative agents have been used. Brain death may however be determined by demonstration of absent intracranial blood flow without any delay for different extents of hypothermia (*vide infra*).

2. The following observations are compatible with the diagnosis of brainstem death
   - 2.1 Movements of limbs in response to a stimulus outside the distribution of cranial nerves.
   - 2.2 Presence of deep tendon reflexes.
   - 2.3 Presence of extensor plantar reflex
   - 2.4 Sweating, blushing, tachycardia.
   - 2.5 Normal blood pressure without pharmacological support.
   - 2.6 Absence of diabetes insipidus (normal osmolar control mechanism)

3. The following observations are incompatible with the diagnosis of brainstem death
   - 3.1 Decerebrate or decorticate posturing
   - 3.2 Seizures

4. Confirmatory investigations

   If the preconditions for clinical diagnosis of cessation of brainstem function cannot be satisfied, or clinical testing of brainstem responses is incomplete, objective demonstration of absence of intracranial blood flow is required.

   - 4.1 Such situations will include:
     - 4.1.1 No clear cause of coma
     - 4.1.2 Possible metabolic or drug effect
     - 4.1.3 Cranial nerves cannot be adequately tested
     - 4.1.4 Suspected or confirmed cervical cord injury
     - 4.1.5 Cardiovascular instability precluding apnoea test
     - 4.1.6 Severe hypoxaemic respiratory failure precluding apnoea test

   - 4.2 Confirmatory investigations which may be used include:
     - 4.2.1 Four vessel radio-contrast angiography by digital subtraction, can be used to demonstrate absent intracranial blood flow. Blood flow should be absent

from both vertebro-basilar and supratentorial circulation

4.2.2 Radionuclide examination which reliably demonstrates absent brain perfusion can also be used for this purpose. A radiopharmaceutical which can cross the blood-brain barrier and be retained by brain parenchyma, either technetium-99m hexamethylproylene amine oxime (^{99m}Tc-HMPAO) or technetium-99m ethyl cysteinate dimer (^{99m}Tc-ECD), should be used. The technique of single-photon emission computed tomography (SPECT) is employed in determining the perfusion of brain stem, cerebrum and cerebellum.

4.3 The four hour period of observation of coma and of absent brain stem responses, where these can be tested, should also apply and should precede the confirmatory investigation.

4.4 Written certification of brain death should be made by the two medical practitioners (not including the medical practitioner who performed the confirmatory investigation) who, having performed the clinical test of brain stem function and with the knowledge of the circumstances of the aetiology of the coma, are further assisted in making the diagnosis of brain death by evidence of absent intracranial blood flow. At least one set of the two required clinical tests should be performed before the confirmatory test. If there is any brain stem response elicited during the clinical tests, the confirmatory investigation should not proceed.

5. Time of death

5.1 If no confirmatory investigation is performed, the time of death should be recorded as the time when certification of brain death has been completed, that is, following the second clinical examination of brain stem responses.

5.2 If a confirmatory investigation confirms absent intracranial blood flow, then the time of death should be made after the completion of the second clinical examination of brain stem function. If both sets of clinical tests were performed

before the confirmatory test, then either one of the clinicians who performed the clinical testing needs to check and interpret the imaging result, and complete the certification process. The time of death will be the time that the examining clinician confirms the absence of intracranial blood flow after interpreting the imaging result.

GENERAL RECOMMENDATIONS

It is recommended that hospitals establish a policy and set of procedures incorporating these guidelines that will govern the confirmation of brainstem death. These would include:

1. A description of the procedures for certification of death following irreversible cessation of brainstem function within the hospital including:
   - 1.1 Certification of brainstem death based upon this document;
   - 1.2 The duties and responsibilities of designated officers;
   - 1.3 The location of all necessary documents;
   - 1.4 The location of contact numbers for police, forensic pathologists and coroner;
   - 1.5 Details of support services available to staff and families.

2. Recommendations for the status of the two medical practitioners certifying death following irreversible cessation of brainstem function and a registry of suitably qualified practitioners accredited to perform such procedures in the hospital.
   - 2.1 One of the medical practitioners must be a specialist recognized and designated by the appropriate College as having demonstrated skill and knowledge in the certification of death following irreversible cessation of brainstem function. This should usually be an intensivist, critical care physician, neurologist or neurosurgeon.
   - 2.2 The other medical practitioner should preferably be of the same qualification as described in 2.1 but should be at least 6 years after registration and possess the skill and knowledge in the certification of death following irreversible cessation of brainstem function.

2.3 The person authorizing removal of tissues and the person removing tissues MUST NOT be responsible for determining brainstem death.

2.4 The intensivist caring for an intensive care patient (e.g. with acute liver failure who is listed for urgent transplantation) who is a potential recipient of organs from the potential donor, should not discuss organ donation with the family of the potential donor.

2.5 The other medical practitioner should preferably be of the same qualification as described in 2.1 but should be at least 6 years after registration and possess the skill and knowledge in the certification of death following irreversible cessation of brainstem function.

2.6 The person authorizing removal of tissues and the person removing tissues MUST NOT be responsible for determining brainstem death.

2.7 The intensivist caring for an intensive care patient (e.g. with acute liver failure who is listed for urgent transplantation) who is a potential recipient of organs from the potential donor, should not discuss organ donation with the family of the potential donor.

3. A registry of suitably qualified practitioners accredited to perform confirmatory investigations in the hospital should be kept. Recommendations of the appropriate College should be followed where applicable.

4. Suitable forms to certify death following irreversible cessation of brainstem function should be available.

5. Access to information about brainstem death and organ donation must be ensured. This information should be suitable for doctors, nurses and allied health practitioners as well as lay people, and should be available for the relatives of patients who are confirmed dead following irreversible cessation of brainstem function.

August 2023