Determining Brain Death

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As technological complexity and advancements in critical care continued to explode during the past several decades, the concept of death as defined by neurological criteria, that is, "brain death," emerged and evolved as a necessary measure for determining death. Before the development of these neurological criteria, death was classically described as the cessation of circulation and respiration. However, the advent of mechanical ventilation and of methods for cardiovascular support presented new challenges for determining the end of life for patients with catastrophic cerebral injuries whose lives could be preserved by using these complex technological devices.¹²

Initial efforts to define death in this age of technological advancement included development of the Harvard criteria in 1968 by an ad hoc committee on brain death at Harvard Medical School.² These criteria described determination of a condition known as "irreversible coma," "cerebral death," or brain death.² Since the initial introduction of these criteria, the Uniform Determination of Death Act, promulgated in 1980 and supported by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, has served as a model statute for the adoption of state legislation that defines death.³ The act asserts: "An individual, who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brainstem, is dead. A determination of death must be made in accordance with accepted medical standards."
The concept of brain death continues to be a topic of international debate among medical clinicians, anthropologists, philosophers, and ethicists. Much of this discussion is the result of the awareness of continuing technological advances, neurodiagnostic developments, and clinical insight. Thus, this ongoing dialogue can be viewed as a dynamically developing process of achieving a multidisciplinary consensus that is responsive to a continually changing technological environment.4-12

Although the concept of death determination continues to evolve, clinical and scientific experts have generated clinical practice parameters for the diagnosis of brain death that are grounded in empirical knowledge, supported by sufficiently rigorous research, and substantiated by moderate to high degrees of clinical certainty.2,13 Neuroscience experts continue to define brain death as irreversible cessation of all functions of the entire brain, including the brain stem. This definition remains consistent with the definition of brain death initially presented by the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.1,13

In this article, we summarize the most recent evidence-based guidelines for determining brain death. Although these guidelines reflect generic, scientifically based recommendations, adaptation of certain details may vary across practice settings and states according to variations in institutional policy and local legislation.

Criteria for Clinical Determination of Brain Death
Initial requirements for clinical determination of brain death include the elements in Table 1. Cardinal findings in brain death include coma or unresponsiveness, absence of cerebral motor responses to pain in all extremities, absence of brain stem reflexes, and apnea.13

| Table 1 Initial requirements for: Clinical determination of brain death
| Clinical or neuroimaging evidence of an acute catastrophic cerebral event consistent with the clinical diagnosis of brain death
| Exclusion of conditions that may confound clinical assessment of brain death (e.g., acute metabolic or endocrine disturbances)
| Confirmation of the absence of drug intoxication or poisoning
| Core body temperature ≥32°C (95°F)

X

Coma
In most patients with brain death, neuroimaging studies show abnormalities consistent with loss of brain and brain stem function. Although clinical diagnosis of brain death is rare when findings on neuroimaging studies are normal, occasionally patients with ischemic-anoxic cerebral injury and resultant brain death have normal neuroimaging findings. Determining brain death in patients with coma of undetermined origin remains difficult but can be accomplished through prolonged observation and confirmation that the patient’s condition fits clinical and diagnostic criteria.

Cerebral Motor Responses to Pain
Cerebrally modulated motor responses of all extremities are absent in brain death. These motor responses should be absent after painful stimulation with pressure to
the supraorbital ridge and the nail beds. However, motor responses may occur spontaneously during apnea testing in the presence of hypoxia or hypotension and are considered due to spinal cord reflexes. Respiratory acidosis and brisk neck flexion may also generate spinal cord reflexes. Spinal reflex responses occur more often in young adults than in the elderly and include rapid spontaneous flexion and muscle stretch reflexes in arms and legs, resulting in movements that resemble grasping or walking. In addition, use of neuromuscular blocking agents may confound motor testing in patients with brain death because of pharmacologically induced motor weakness. If neuromuscular blockade has been used, assessment with a bedside peripheral nerve stimulator is required.

**Brain Stem Reflexes**

**Pupillary Signs.** Round, oval, or irregularly shaped pupils are compatible with brain death, and most pupils are midsize (4-6 mm). However, dilated pupils may occur even in the presence of brain death, because sympathetic cervical pathways to the pupillary dilator muscle may still be intact. The pupillary light reflex must be absent in brain death. Although many drugs can influence pupillary size, the pupillary light reflex remains intact only in the absence of brain death. Standard doses of atropine administered intravenously do not markedly affect pupillary response; similarly, neuromuscular blocking agents do not markedly influence pupillary size. However, topical administration of drugs and ocular trauma may influence pupillary size and reactivity. Preexisting ocular anatomic abnormalities may also confound pupillary assessment in brain death.

**Ocular Movements.** Both oculocephalic ("doll's eye"; Figure 1) and vestibulo-ocular (caloric test; Figure 2) reflexes are absent in brain death. Contraindications to testing for oculocephalic reflexes include suspected fracture or instability of the cervical spine. Likewise, contraindications to testing of vestibulo-ocular reflexes include impaired integrity of tympanic membranes.
The oculocephalic reflex is elicited by rapidly and vigorously turning the head to 90° laterally on both sides. The normal response is deviation of the eyes to the opposite side of head turning. In brain death, oculocephalic reflexes are absent, and no eye movements occur in response to head movements.

The vestibulo-ocular reflex is elicited by elevating the head 30° and irrigating both tympanic membranes with 50 mL of iced saline or water. In brain death, vestibulo-ocular reflexes are absent, and no deviation of the eyes occurs in response to ear irrigations. The patient should be observed for up to 1 minute after each ear irrigation, with a 5-minute wait between testing of each ear. Several classes of
drugs can diminish vestibulo-ocular reflexes, including sedatives, aminoglycosides, tricyclic antidepressants, anticholinergics, and antiseizure agents. Facial trauma involving the auditory canal and petrous bone can also inhibit these reflexes.

**Facial Sensory and Motor Responses.** Corneal and jaw reflexes are absent in brain death. Corneal reflexes should be tested by using a cotton-tipped swab. Grimacing in response to pain can be tested by applying deep pressure to the nail beds, supraorbital ridge, or temporomandibular joint. Severe facial trauma can inhibit interpretation of facial brain stem reflexes.

**Pharyngeal and Tracheal Reflexes.** Both gag and cough reflexes are absent in patients with brain death. The gag reflex can be evaluated by stimulating the posterior part of the pharynx with a tongue blade, but the results can be difficult to evaluate in orally intubated patients. The cough reflex can be tested by using bronchial suctioning.

**Apnea**

An essential component in clinical determination of brain death is detection of apnea. Loss of brain stem function definitively results in loss of centrally controlled breathing, with resultant apnea. Respiratory neurons are controlled by central chemoreceptors that sense changes in \( \text{Pco}_2 \) and pH of the cerebrospinal fluid, which in turn accurately reflects changes in plasma \( \text{Pco}_2 \). A variety of complex mechanical and chemical stimuli influence these respiratory neurons of the brain stem.

The exact level of \( \text{Pco}_2 \) necessary to maximally stimulate the chemoreceptors of central respiratory centers remains unknown in conditions consistent with hyperoxegenation and brain stem destruction. Target \( \text{Pco}_2 \) levels have been derived on the basis of both clinical observations and research involving apnea testing in brain death. Advisory guidelines for determination of death based on these clinical and research data recommend achieving \( \text{Paco}_2 \) levels greater than 60 mm Hg for maximal stimulation of brain stem respiratory centers.\(^1\) Target \( \text{Paco}_2 \) levels for apnea tests in the determination of brain death may be higher in patients with chronic hypercapnia. If the results of initial arterial blood gas analysis confirm chronic hypercapnia, additional noninvasive confirmatory testing is recommended.

Hypocarbia can also occur in patients with acute catastrophic cerebral injuries and can be caused by therapeutic hyperventilation or hypothermia. Although correction of hypocarbia should precede apnea testing, use of carbon dioxide admixtures should probably be avoided because of associated consequences, including severe hypercapnia and respiratory acidosis.

Cardiac dysrhythmias and systemic hypotension can occur during apnea testing. Cardiac dysrhythmias are usually due to hypercarbia and respiratory acidosis and occur most often in patients with hypoxia. Severe hypotension can occur in well-oxygenated patients whose \( \text{Paco}_2 \) increases to high levels with acidosis.

Hemodynamic disturbances can be avoided during apnea testing if respiratory acidosis is limited to a pH of 7.17 (±0.02) and the \( \text{Paco}_2 \) is 60 to 80 mm Hg.\(^{15}\) Hyperoxegenation beforehand and administration of oxygen during the test procedure also can prevent marked hypoxemia during apnea testing.

Investigators have experimented with a variety of derivations in apnea testing.
including use of carbon dioxide insufflation and bulk diffusion techniques.\textsuperscript{16-19} Other researchers\textsuperscript{20} have reported that a streamlined approach to apnea testing may include establishing baseline Paco\textsubscript{2} levels of 40 mm Hg before the test is done, thereby facilitating achievement of the target Paco\textsubscript{2} level of 60 mm Hg in less time and with fewer episodes of cardiovascular instability or hypoxia. The current recommendations for apnea testing in brain death are based on review of empirical, research, and clinical evidence.\textsuperscript{13}

The procedure for apnea testing is given in Table 2. To avoid the cardiac dysrhythmias and systemic hypotension that may occur during the test, clinicians should follow the recommendations given in Table 3. The results of apnea tests are interpreted as (1) positive, (2) negative, (3) occurrence of cardiovascular or pulmonary instability, and (4) inconclusive (Table 4).

<table>
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<th>Table 2: Apnea testing</th>
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<tr>
<td>1. Disconnect the ventilator.</td>
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<td>2. Deliver 100% oxygen at a rate of 6 L/min. The oxygen cannula can be placed at the level of the carina.</td>
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<tr>
<td>3. Observe the patient closely for respiratory movements (ie, abdominal or chest excursions that produce adequate tidal volumes).</td>
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<tr>
<td>4. Measure Paco\textsubscript{2}, Paco\textsubscript{2}CO\textsubscript{2}, and pH after approximately 8 minutes and reconnect the ventilator.</td>
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<th>Table 3: Precautions for apnea testing</th>
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<tr>
<td>Maintain patient’s core body temperature at ( \geq 36.5^\circ\text{C} ).</td>
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<tr>
<td>Maintain patient’s systolic blood pressure at 90 mm Hg.</td>
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<tr>
<td>Establish euolemia (normal volumes) in the patient.</td>
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<tr>
<td>Establish euolemia (Paco\textsubscript{2} ( \geq 40 ) mm Hg) in the patient.</td>
</tr>
<tr>
<td>Maintain or achieve normoxemia (Option: Paco\textsubscript{2} ( \leq 200 ) mm Hg) in the patient.</td>
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Clinical Observation Intervals

In clinical determination of brain death, persistent observation further confirms the irreversibility of the patient's condition. A repeat clinical evaluation of cardinal findings in brain death is recommended. Most experts recommend an arbitrary interval of 6 hours between initial and repeat observations for clinical determination of brain death in adults; however, a firm recommendation based on scientific literature cannot be given.13,21 All clinical tests of cardinal findings are equally essential in declaring brain death.

**Confirmatory Tests for Determination of Brain Death**

Although confirmatory tests are not mandatory in most situations, additional testing (Table 5) may be necessary for declaring brain death in patients in whom the results of specific components of clinical testing cannot be reliably evaluated.13 Clinical experience with confirmatory tests other than conventional angiography, electroencephalography, and transcranial Doppler sonography is limited. Research involving use of confirmatory tests for determination of brain death is constrained by lack of blinded evaluation, absence of interobserver reliability data, and sparse use of control groups.
Conventional Cerebral Angiography
Selectie 4-vessel angiography may be performed in the neuroradiology department. In patients with brain death, intracerebral filling is absent at the level of the carotid bifurcation or circle of Willis, whereas the external carotid circulation is patent\textsuperscript{13} (Figure 3).

Electroencephalography
A 16- or 18-channel instrument and guidelines developed by the American Electroencephalographic Society are used to determine brain death.\textsuperscript{22,23} In patients with brain death, no electrical activity occurs during a period of at least 30 minutes of electroencephalographic recording.\textsuperscript{13}

Transcranial Doppler Sonography
In transcranial Doppler sonography, intracranial arteries are insonated bilaterally (ie, middle cerebral artery through the temporal bone above the zygomatic arch). Ten percent of patients may not have temporal insonation windows. Therefore, initial absence of Doppler signals cannot be interpreted as consistent with brain death. Findings consistent with brain death indicate high vascular resistance associated with greatly increased intracranial pressure and include (1) absent diastolic or reverberating flow, (2) systolic-only flow or retrograde diastolic flow, and (3) small systolic peaks in early systole. Blood flow velocities may be influenced by marked changes in \textit{Paco}_2, hematocrit, and cardiac output.\textsuperscript{12,13,24-27}

Somatosensory and Brain Stem Auditory Evoked Potentials
Testing for somatosensory evoked potentials is done at the bedside with a portable instrument that provides bilateral stimulation of median nerves. In studies\textsuperscript{13,28-31} of patients with brain death, most patients had no responses to tests for somatosensory and brain stem auditory evoked potentials. Both types of tests are less sensitive than previously mentioned confirmatory tests.

Cerebral Blood Flow and Magnetic Resonance Imaging Studies
In one investigation, patients who met clinical criteria for brain death had no responses to tests for brain stem auditory evoked potentials and no cerebral perfusion as measured by radionuclide cerebral angiography and brain perfusion studies. Cerebral blood flow studies with xenon 133 have also been used to confirm brain death, and magnetic resonance imaging has been explored as a noninvasive method for determining the nonfilling phenomenon that occurs in brain death. In patients with brain death, technetium Tc 99m brain scans show no uptake of the radionuclide in brain parenchyma ("hollow skull phenomenon").

Neurophysiological technology and neurodiagnostic testing have great promise for becoming the gold standards for confirmatory tests of brain death. However, current investigations of technology-driven confirmatory tests still require further replication and clinical application.

**Misconceptions About Brain Death**

Having a clear understanding of how brain death is determined and being able to recognize that the criteria for brain death differ from the cardiopulmonary criteria used to determine death are the first steps in eliminating the confusion and misconceptions often associated with brain death. Family members of patients with brain death need reassurance and accurate information. They may think that their loved one has a heartbeat and is therefore being "kept alive" by mechanical ventilation. They may also think that their loved one will get better through treatment or intensive rehabilitation.

First and foremost, brain death is irreversible. Patients who are brain dead have permanently lost the capacity to think, be aware of self or surroundings, experience, or communicate with others. As stated by Bernat:

> The common pathological processes leading to brain death include massive head trauma, intracranial hemorrhage, and hypoxic ischemic damage suffered during cardiopulmonary arrest. These conditions rapidly produce marked brain edema, which increases brain volume. Because of the skull's fixed capacity, the increase in brain volume produces an inevitable increase in intracranial pressure causing two morbid events to occur: (1) herniation and infarction of the brain stem as it is forcibly displaced from its original location; and (2) loss of cerebral perfusion pressure as intracranial pressure exceeds mean arterial blood pressure.

Both healthcare professionals and the lay public remain confused about the meaning and implication of brain death. In one study of 195 physicians and nurses likely to be involved in the care of patients with catastrophic brain injury, only 35% of respondents correctly recognized the legal and medical criteria for determining brain death. Furthermore, 58% of respondents did not use a coherent concept of death consistently. In another study, the next of kin of 164 brain-dead patients who were medically suitable for organ donation were interviewed to determine the next of kin's understanding of brain death. Only 61% of the families who agreed to donation and 53% of the families who did not agree to donation stated that they were provided an explanation of brain death. All respondents also were queried about their understanding of brain death.

An overwhelming majority said that their family member was brain dead. Respondents were further queried to substantiate their understanding of brain death by asking them to distinguish whether a person with a diagnosis of brain dead is dead or in a coma. Twenty-eight percent of the respondents stated that brain death was the same as coma, and 9% did not know. It is difficult for some families to understand that a person who has a heartbeat can be brain dead,
because historically the presence of a heartbeat indicated life.

**Talking to the Family**
Critical care nurses should become familiar with the concept of brain death and its medical and legal criteria, because they may need to explain brain death to family members who are confused and in crisis. Sometimes the use of certain terminology appears to conflict with reality when the terminology is applied to cases in which patients are pronounced dead on the basis of neurological criteria. One source of confusion in the determination of death may be the use of the actual words "brain death" to describe human death as determined by neurological criteria. The term can be misleading because it implies that only the brain is dead and that everything else is alive. It also implies that more than one type of death exists.36

Thus, in order to avoid confusion, it is more helpful to tell a family that their loved one is "dead," because use of this word can help the family understand that death has occurred. A clear definition of brain death must be given and reinforced.

Sometimes the use of familiar nursing terms can also be confusing to family members. Telling the family that the patient is being maintained on "life support" more than implies that the patient is not truly dead. Terms such as "mechanical ventilation" or "artificial respiration" may be a less confusing and more accurate description of the condition, because such terms do not imply that life is present.39

Sometimes confusion exists as to when death should be recorded in the patient's chart. Nurses may think that a brain-dead patient is "allowed to die" once the ventilator is removed and that a certain time will lapse between the removal of mechanical ventilation and death. When death is pronounced on the basis of neurological criteria, the time of death is recorded as the time at which the patient met the criteria of brain death. Death is not recorded as the time at which the patient is removed from ventilatory support in the critical care unit or the operating room or when cardiopulmonary function ceases. Stating that a patient was "kept alive" through mechanical ventilation for the purpose of recovering organs for donation and then "allowed to die" sends an inappropriate message to the patient's family members that their love one is really alive and not dead.

**Talking to the Patient**
As a way to express compassion and respect for a patient who is pronounced brain dead, or to deal with their own sense of loss, some critical care nurses may find comfort in talking to the patient. Talking to a brain-dead patient can be confused with talking to or stimulating a comatose patient. This "caring" behavior may be perceived by the family as an underlying belief on the part of the nurse that the patient has some remaining sensory capacity. Because the behavior of the nurse seems to indicate that the patient is alive, family members may have great difficulty accepting the death of their loved one.

**Brain Death and Organ Donation**
Brain-dead patients, barring other influencing factors, may be medically suitable for organ donation. Understanding the concept of brain death is an important factor that influences a family's decision to donate organs and tissues for transplantation. Families who are approached for donation without having all their questions about brain death answered may refuse to consent to donation.37

In order to facilitate the offer of donation, the organ procurement organization should be contacted a reasonable time before pronouncement of death to determine the patient's suitability for donation. Once a patient is pronounced dead and the family has been given time to accept the death, the option of donation...
should be offered to the family. In many cases, the critical care nurse has an established relationship with the family and is encouraged to work collaboratively with the organ recovery coordinator or the designated hospital requestor to make the request for donation.39,40

If the patient will be an organ donor, mechanical ventilation is continued to maintain organ viability. If the family does not give consent for donation, mechanical ventilation should be stopped and the patient should be given post mortem care according to hospital protocol. Every patient’s family has the right to be offered an opportunity for organ donation when its loved one meets accepted criteria. Regardless of the decision, the critical care nurse can best help families as they grieve the loss of their loved one by supporting them in their choice.

Conclusion
A clear understanding of the criteria for brain death and the misconceptions associated with pronouncement of brain death is the first step a nurse can take to better participate in the care of brain-injured and brain-dead patients. Assisting with diagnostic testing and close observation will aid in the timely determination of death. Accurate information can provide a sound basis for talking to families about brain death and can assist them in coping with the devastating loss of a brain-dead loved one.

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