

Hospital of the University of Pennsylvania POLICY MANUAL	Number: 1-6-03
SUBJECT: POLICY REGARDING DETERMINATION OF DEATH BY NEUROLOGIC CRITERIA	Page 1 of 8 Effective: 10/15/05

KEY WORDS:

Brain Death
Coma

1-6-11 “Procedures Following Patient Death”

1-6-13 “Organ Donation and Anatomical Donation and Pennsylvania’s Anatomical Gift Act”

#1-6-17 “Withholding and Withdrawing Life Sustaining Therapy”

#1-7-07 “Care of Patients with Chronic Impairments of Consciousness ...”

POLICY

In accordance with the Pennsylvania Uniform Determination of Death Act, an individual is dead after sustaining either: (1) irreversible cessation of circulatory and respiratory functions; or (2) irreversible cessation of all functions of the entire brain, including the brain stem. The determination of death must be made by two clinical examinations including an apnea test, in accordance with acceptable medical standards.

PURPOSE

An individual with irreversible cessation of all brain function, including the brain stem, is dead. The purpose of this policy is to define the medical criteria that are to be used in the determination of death of a patient due to irreversible cessation of functioning of the entire brain (death by neurologic criteria). It is not intended to replace the judgment of a physician regarding futility of care in an acute situation.

SCOPE

The policy applies to all patients of the Hospital of the University of Pennsylvania.

IMPLEMENTATION

Chairman of the Medical Board, chairmen of clinical departments, Attending Physicians and House Staff Physicians licensed in Pennsylvania are to implement this policy.

PROCEDURE

Determination of Irreversible Cessation of all Functions of the Entire Brain in Adults, Including the Brain Stem

DIAGNOSTIC CRITERIA

The clinical diagnostic criteria in sections A, B, and C below must be met to declare death by neurologic criteria. Where indicated, the clinical diagnosis may be confirmed by “confirmatory studies”.

A. Prerequisites: brain death is the complete absence of function of the whole brain when the proximate cause is known and demonstrably irreversible.

1. Clinical and/or neuroimaging evidence of an acute central nervous system catastrophe that is compatible with the clinical diagnosis of brain death. For coma of unknown cause, additional investigation is necessary (see Section D).
2. Exclusion of complicating medical conditions that may confound the clinical assessment (no severe electrolyte, acid-base, endocrine, or nutritional disturbance).

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3. Toxicological screening, when appropriate, and no evidence of drug intoxication or poisoning. Specific levels of central nervous system (CNS) depressants that might complicate the examination are left to clinical judgment.
4. Demonstrated absence of neuromuscular blockade if the patient had recent or prolonged use of neuromuscular blocking drugs.
5. Core body temperature > 32° C (90° F) and no circulatory shock (MAP (mean arterial pressure) > 55 mmHg) present.

B. The three cardinal features of brain death are coma or unresponsiveness; absence of brainstem reflexes; and apnea.

1. Coma or unresponsiveness as determined by the absence of any cerebrally mediated motor responses to pain in all extremities (nail-bed pressure) and supraorbitally.
2. Absence of brainstem reflexes:
 - a) Pupils
 - i. No response to bright light
 - ii. Size: from midposition (4 mm) to dilated (9 mm)
 - b) Ocular movement
 - i. No oculocephalic reflex (testing only when no fractures or instability of the cervical spine is apparent)
 - ii. No deviation of the eyes to irrigation in each ear with 50 ml of ice water (observe for 1 minute after each irrigation and at least 5 minutes between testing on each side)
 - c) Facial motor response to stimulation
 - i. No corneal response to touch
 - ii. No jaw reflex
 - iii. No facial grimacing to deep pressure on nail bed, supraorbital ridge, or temporomandibular joint
 - d) Pharyngeal and tracheal reflexes
 - i. No response to stimulation of the posterior pharynx
 - ii. No cough response to bronchial suctioning
3. Apnea – formal apnea testing must be performed (see Criteria Form for procedure)

C. Irreversibility is determined by two examinations that meet the clinical criteria for brain death that are performed at least 6 hours apart. This interval may be shortened to 3 hours if a confirmatory study is performed.

D. Coma of unknown cause:

Coma of unknown cause (e.g., no evidence of brain trauma, stroke, hypoxic/hypotensive injury) requires a diligent search for the cause of coma before brain death determination. Special care must be taken to perform toxicology studies. In addition;

1. The interval between examinations that are consistent with the clinical criteria for brain death must be at least 24 hours apart.
2. A confirmatory neuroimaging study that demonstrates the absence of cerebral blood flow must be performed

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E. Conditions that may interfere with the diagnosis of brain death:

The following conditions may interfere with the clinical diagnosis of brain death, so that the diagnosis cannot be made with certainty on clinical grounds alone. In such cases, confirmatory tests are recommended.

1. Severe facial trauma
2. Preexisting pupillary abnormalities
3. Toxic levels of any sedative drugs, aminoglycosides, tricyclic antidepressants, anticholinergics, antiepileptic drugs, or chemotherapeutic agents
4. States of chronic retention of carbon dioxide (PaCO₂)

DOCUMENTATION

1. The attached form "Certification of Death by Neurologic Criteria" (Criteria Form) must be completed prior to certification of death. All applicable items must be marked "Yes" in order for brain death to be declared. The completed Criteria Form is to remain part of the patient's Medical Record.

The cause and irreversibility of coma should be determined and documented as a first step in the process.

2. It is also standard to document the following:
 - a. absence of complicating conditions
 - b. absence of responsiveness to pain
 - c. absence of brainstem reflexes
 - d. absence of respiration with PCO₂ > 60 mmHg (or 20 mmHg rise from baseline)
 - e. result of confirmatory test (if performed)
 - f. repeat neurologic examination
3. When the patient meets all the criteria on the Criteria Form, the attending physician or the covering attending must be notified. The form should be signed by the physician who completes the second clinical exam. This physician may not be a member of the transplant team. The time when the Criteria Form is signed is the legal time of pronouncement of death.

EXAMINATION PROCEDURES

1. Two clinical examinations must be performed. The examinations may be by the same physician, or two different physicians. At least one of the exams must be performed by an attending neurologist or neurosurgeon. The other exam must be performed by an attending neurologist/neurosurgeon, or the chief resident in neurosurgery, or an intensivist whose non-core privileges include determination of brain death. When the second sequential exam is done by an attending neurologist/neurosurgeon, the first exam may be done by a PGY 2 or higher in neurology/neurosurgery.

2. Both exams must be performed while the patient is in the Hospital of the University of Pennsylvania.

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3. Interval between exams

- a. There must be **AT LEAST 6 HOURS** between the two clinical examinations unless a confirmatory laboratory test is done.
- b. If a confirmatory test shows evidence of death by neurologic criteria, the interval between the first and second clinical exam can be shortened to **THREE HOURS**. The confirmatory test should be done between the first and second exam. The second clinical examination must be completed and documented even if the confirmatory test results are consistent with brain death.

4. The clinical examination may be affected by the following complicating conditions: a) severe hypothermia (<32° C or 90° F); b) circulatory shock (MAP <55 mmHg); c) drug intoxication; d) severe endogenous metabolic intoxication; i.e., renal or hepatic failure; and e) prolonged effects of neuromuscular blocking agents. Prior to certification of death by neurological criteria, the complicating conditions of hypothermia, circulatory shock, metabolic intoxication, and prolonged effects of neuromuscular blocking agents must be excluded from being clinically significant.

5. Drug intoxication can mimic clinical signs of death by neurological criteria and may result in electrocerebral silence on an electroencephalogram. Examples of such drugs include barbiturates, benzodiazepines, methaqualone, meprobamate and trichlorethylene. If such drugs have been administered, their blood levels must not be clinically significant in the clinical judgment of all attending physicians involved prior to certification of death by neurological criteria.

CONFIRMATORY TESTS

1. Brain death is a clinical diagnosis. These ancillary tests are not required for the determination of death by neurologic criteria.
2. A confirmatory laboratory test is required:
 - a. In situations in which specific components of clinical testing cannot reliably be performed or evaluated. This includes patients with ocular/facial trauma, preexisting pupillary abnormalities or conditions associated with chronic retention of CO₂ - precluding full clinical assessment of brainstem function.
 - b. If the interval of observation between the two neurologic exams required for brain death determination is less than 6 hours.
3. The preferred confirmatory test is a nuclear isotope blood flow scan. Alternatively, conventional four vessel cerebral angiography or electroencephalography (EEG) can be used.

OTHER CONSIDERATIONS

1. Determination of death by neurologic criteria is, by law, a medical responsibility and, therefore, consent of the family is not needed nor should it be requested. However, the responsible physicians should inform the family regarding the patient's grave prognosis at least by the start of the certifying process, and continue to keep the family informed throughout the process. Early and clear communication, as well as sensitivity for the family, is important during this time to prepare the family for cessation of continued medical therapy; e.g., removal of the mechanical ventilator from the

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deceased, which event should occur after certification of death by neurologic criteria. This removal following determination of death does not require the permission of the family.

2. Medical Examiner cases undergo the identical processes for certification and cessation of medical therapy. (see policy # 1-6-11, "Procedures Following Patient Death.")

Determination of Irreversible Cessation of all Functions of the Entire Brain, Including the Brain Stem in Neonates

The neonate cannot be declared dead by neurologic criteria until after five (5) days of age. After that time and up to sixty (60) days of age, the interval between clinical examinations must be at least 48 hours, and a confirmatory test must be done at the beginning and end of the interval.

Organ Donation

In accordance with HUP policy "Organ Donation and Anatomical Donation and Pennsylvania's Anatomical Gift Act," the Organ Procurement Agency (Gift of Life) should be notified when the brain death protocol is initiated.

SOURCES AND REFERENCES:

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2. Guidelines for the Determination of Brain Death in Children. Pediatrics 1987; 80: 298-300.
3. Quality Standards Committee of the American Academy of Neurology. Practice Parameters for Determining Brain Death in Adults. Neurology 1995; 45:1012-1014.
4. Wijdicks EFM. Current Concepts: The Diagnosis of Brain Death. NEJM 2001; 344:1215-1221.
5. 35 P.S. Section 10201
6. Developed, reviewed, and approved by:
Ad Hoc Ethics Subcommittee
Ethics Committee
Office of Legal Affairs
Associate Chair of Protocol and Policy of the Medical Board
Executive Committee of the Medical Board: February 1994 and March 1994
Medical Board: 21 March 1994
Ad Hoc Policy Review Group: March 2005
Office of the General Counsel: March 2005
Medical Board: September 28, 2005

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Certification of Death by Neurologic Criteria (Criteria Form)

Two in-hospital clinical examinations by a physician from Neurology or Neurosurgery, or an Intensivist (See bottom of page 3 for clarification on who should perform these exams.) conducted at least 6 hours apart, must demonstrate no evidence of function of the entire brain. If clinically indicated, a cerebral blood flow study or other confirmatory laboratory test, can be done between the first and second exam. In this case, the interval between the first and second exam can be shortened to three hours. The second clinical exam must be completed and documented even if the confirmatory test results are consistent with brain death.

	First Exam	Second Exam
A. 1. Date	_____	_____
2. Time	_____	_____
3. Examiner's Name (Printed)	_____	_____

Give specific information as requested below and answer "Yes" or "No."

B. Is the cause of the coma known and sufficient to account for irreversible loss of brain function? _____

Note: Coma of unknown cause requires a diligent search for the cause of coma, at least 24 hours between the examinations, and a confirmatory test that demonstrates absence of cerebral blood flow.

C. Complicating Conditions Were Excluded

1. Hypothermia is not present		
a. core body temperature must be >32°C or 90°F	_____	_____
2. Drug intoxication has been excluded		
a. toxicology screening, if appropriate	_____	_____
b. specific levels of CNS depressants that might complicate the examination are left to clinical judgment	_____	_____
3. Circulatory shock is not present (MAP < 55 mmHg)	_____	_____
4. Severe endogenous metabolic (renal, hepatic, electrolyte, endocrine, acid-base, and vitamin) deficiency or intoxication has been excluded	_____	_____
5. Neuromuscular paralyzing drug effect has been excluded	_____	_____

D. Unresponsiveness Documented

1. Response to painful stimuli is absent		
2. Spontaneous movements are absent, aside from spinal reflexes		
<small>Note: Deep tendon reflexes, including stereotypical triple flexor responses in the legs, are compatible with brain death. Purposeful movement or posturing preclude the diagnosis of brain death.</small>		
3. Locked-in state is excluded (testing of vertical eye movements)	_____	_____

E. Loss of Brain Stem Function Documented

1. Pupils are unresponsive to bright light (usually 4-9 mm)		
2. Corneal reflexes are absent	_____	_____
3. Oculocephalic reflexes are absent (no eye movement to doll's eye maneuver)	_____	_____
2. Oculovestibular reflexes are absent (no eye deviation to 50 ml of ice water in each ear canal)	_____	_____
5. Gag response to tracheal stimulation is absent	_____	_____

Signature of First Examiner _____ Date _____



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F. The Apnea Test

Date _____ Time _____ Physician Examiner (Print) _____

- a. Initial PaCO₂ (must be 35-45 mmHg) _____
- b. Final PaCO₂ _____
- c. For patients with chronic CO₂ retention, pre-test and final pH _____

Comments:

- 1. Apnea test showed no respiratory movements with the necessary CO₂ rise and pH fall? _____
- 2. Apnea test results are documented on page 3? _____

Signature _____

For the examiner performing the second neurologic examination: Have one of the following four criteria (I, II, III, or IV) been established?

Mark **ONE** as "YES":

- _____ I. Items B to E have been confirmed by two examinations separated by at least six hours, and item F, the apnea test, validates the clinical diagnosis of brain death.
- _____ II. **In the event of a shortened interval between clinical exams**
 - 1. Items B to E have confirmed as YES, and
 - 2. A confirmatory study is consistent with brain death and it has been documented, and
 - 3. A second exam at least three hours after the first, confirms items A to E as YES, and the apnea test validates the clinical diagnosis of brain death.
- _____ III. **In the event that E or F cannot be fully determined** because the injury or condition precludes evaluation (e.g., facial injury precluding caloric testing; apnea test is indeterminate due to chronic CO₂ retention), then the following apply:
 - 1. ALL items that are assessable are YES, and
 - 2. No cerebral blood flow is present by nuclear medicine cerebral blood flow scan or 4 vessel angiography, and it has been documented, and
 - 3. A second examination at least 3 hours after the first, confirms all assessable items as YES, and
 - 4. The apnea test validates the clinical diagnosis of brain death (except for those individuals whose apnea test is indeterminate)
- _____ IV. **In the case of coma of unknown cause, and item B cannot be fully determined, then the following apply:**
 - 1. A thorough search for the cause of coma has been performed, including toxicological studies and neuroimaging of the brain, and
 - 2. Items C to E have been confirmed as YES, and
 - 3. No cerebral blood flow is present by nuclear medicine cerebral blood flow scan or 4 vessel angiography, and it has been documented on page 3, and
 - 4. A second examination at least 24 hours after the first, confirms all assessable items as YES, and the apnea test validates the clinical diagnosis of brain death.

CERTIFICATION of Brain Death by Second Examiner

On the basis of the finding recorded above, indicating irreversible loss of function of the entire brain as described in hospital policy, I certify that patient _____ is dead.

DATE _____ TIME _____ PHYSICIAN SIGNATURE* _____ M.D. NAME PRINTED _____ M.D.

*This record must be signed by the physician who has conducted the second clinical examination of the patient and certifies him/her to be dead.

Note: If organ donation is contemplated, the physician who certifies brain death cannot participate in the procedure for removing or transplanting the organ.



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Methodology for Performing Apnea Tests

(Record results on Page 2)

1. After 15 minutes of pre-oxygenation on 100% oxygen and confirmation by ABG that the PaCO₂ is between 35-45 torr, an apnea test on 100% oxygen is performed while the patient is disconnect from the ventilator. Ten (10) minutes is usually sufficient.
2. After 10 minutes, the patient is reconnected to the ventilator while awaiting blood gas results. If over the ten minutes off the respirator there are no respiratory movements, and the final PaCO₂ is \geq 60 torr (option: 20 torr rise over baseline PaCO₂), the apnea test is **positive** (i.e., it validates the clinical diagnosis of brain death).
3. If the patient becomes hemodynamically unstable or cardiac arrhythmias develop, an ABG should be obtained, if possible, and the test should be discontinued with the patient placed back on the ventilator.
4. If prior loss of CO₂ responsiveness is suspected, as in patients with chronic CO₂ retention, a final value of pH < 7.26 (from a patient with pre-test pH of >7.40) can be used as an adequate test.
5. If the final PaCO₂ is < 60 torr, or < a 20 torr rise in PaCO₂ from baseline (or in respiratory failure patients the final pH is > 7.26, then the test is indeterminate. If the patient becomes hemodynamically unstable or cardiac arrhythmias develop, the test should be discontinued and considered indeterminate. In the case of an **indeterminate** apnea test, a cerebral blood flow scan should be performed as a confirmatory test.

Confirmatory Laboratory Test Performed (if done)

Study Performed (Circle One):

1. Nuclear medicine cerebral blood flow scan
2. Four vessel angiogram
3. Electroencephalogram

Results of study:

Date: _____ Time _____

Interpreted by: _____ M.D.

BRAIN DEATH EXAMINATIONS CAN BE PERFORMED BY:

FIRST EXAM

Attending Neurologist/Neurosurgeon

Intensivist with "brain death: non-core privileges OR
Neurosurgery Chief Resident OR
PGY 2 or above in Neurology/Neurosurgery

SECOND EXAM

Attending Neurologist/Neurosurgeon OR
Intensivist with "brain death: non-core privileges OR
Neurosurgery Chief Resident

Attending Neurologist/Neurosurgeon

