Review Article

HOW TO CONSIDER AND MANAGE BRAIN DEATH IN AN EMERGENCY SETTING

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INTRODUCTION

There is at present considerable confusion with respect to the ethical guidelines that should govern the behavior of society and the physician confronted by problems resulting from the recent discoveries of medicine and science. The documentation of the ending of life has religious, legal, and practical implications (1). The use of life supporting devices raises the problem of determining when death has occurred and what is proper ethical procedure in dealing with the deficient half life caused by "Brain Death" (BD). Some guidance is obtained from a consideration of the nature of life, the nature of death, the nature of man, and the essence lost in death of man (2). The clinical tests correspondingly shift from those implying loss of brain function to those implying thermodynamically supracritical microstructural damage diffusely throughout the body (3).

It is of the utmost importance for physicians that accurate, infallible criteria define death. Such criteria enable us to terminate expensive medical care to corpses and also allow us to ethically request vital organs. Organ scarcity must not lead us to allow the criteria for life and death to become blurred because of the irreparable harm this would cause to the patient-physician relationship and the impact it could have on organ transplantation (4).

Although often allowing the individual physician to function in a difficult area, the physician's religious beliefs, and personal prejudices may affect decision-making and make differences of opinion in this area more based on belief than science (1). It is a certainty, however, that when BD occurs the life of man ends. (2).

EMERGENCY MEDICINE APPROACH AND DETERMINATION OF BRAIN DEATH

Patients brought to an emergency department (ED) with serious brain damage can be determined to be unsalvageable but usually cannot be declared brain dead. Most such patients should be admitted for physiologic support and formal BD determination (5).

Announcement of death in a patient is common in the practice of emergency medicine, be it in the ED, or in the field. Commonly the patient who fails to respond to resuscitative procedures is subject to this kind of evaluation. The more difficult situation arises in determining those patients who harbor cerebral insult such that they will ultimately meet criteria for brain death, but have, by some means, adequate circulation of blood and oxygen. The determination of these patients is important in regard: 1. to depicting a realistic scheme of the patient's prognosis for the family, and to assist in the beginning of the grieving process; 2. to "push the button", usually through involvement of consultants, that will allow the official declaration of the patient as being "brain dead"; and 3. to start the procedures that would allow the patient to become a potential organ donor.

First of all, the patient records in the ED should include the cause and irreversibility of the condition, the absence of brain stem reflexes, the absence of motor response to pain, the apnea test results, and result of any confirmatory tests.

There is a historical agreement that a person is dead when they are not breathing and the heart is not beating, but there has often been disagreement as to whether these findings defined death, or whether they

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were just signs of death (1). Current law in some countries (e.g., United States) authorizes physicians to diagnose BD by applying generally accepted neurologic criteria for determining loss of function of the entire brain. These include the possibility of diagnostic error, conceptual disagreements that may limit the use of neurologic criteria to diagnose death, the conflation of BD and loss of consciousness (6).

With the ability to maintain certain functions necessary for life, we are faced with the differentiation between death of the individual as a biologic entity and death of the individual as a person (7). This problem is further complicated by organ transplantation, making disconnection of a potential organ donor from all means of life support an unacceptable test for death because the quality of the donated organs might then be compromised.

DEFINITION OF BRAIN DEATH AND CURRENT CONSENSUS CRITERIA

Prior to any attempt to define brain death, one should discern entites like persistent vegetative state (PVS) that could be confused with brain death. BD depends on death of the brainstem, while PVS implies permanent and total loss of forebrain function. While brainstem death can be diagnosed clinically, prognosis in PVS requires additional investigation. BD is equal to death, while PVS is not (8).

Physiological disturbances in the brain dead organ donor result in a diffuse vascular regulatory injury and a diffuse metabolic cellular injury. The net result of the changes is an inexorable deterioration of all organs and eventual "cardiovascular death" of the patient (9).

The 'heart-lung' defnition of death was no longer satisfying for all conditions and was fostered in 1968 by the Harvard criteria (Table I) for whole BD (10). Most discussions (11,12) centered on "whole brain" death, which means complete death of not only the neocortex of the brain but also the brain stem. In 1980, the United States Presidential Commission, developed the United States Uniform Determination of Death Act, describing BD as "the irreversible cessation of all functions of the entire brain, including the brainstem (13). This document provided guidelines of BD for patients 5 years of age or older (14).

There is ongoing debate and discussion concerning the definition of BD (15,16). First, a patient may fulfill the criteria based on diagnostic tests for brain death, yet portions of the brain (e.g., the hypothalamus) may continue to demonstrate function, and second, a patient may have cessation of all function,yet one or more confirmatory tests may 'rule out' BD.

Our understanding of the concept and definition of death has changed over time. The British diagnostic criteria (17) for the diagnosis of brain stem death was published by the Royal Medical Colleges (1976) Others (18) have proposed a higher-brain definition of death based on the permanent loss of cognition as the sole criterion for death.

A statement for operational guidelines is presented in a 1995 article "Practice parameters for determining BD in adults" (19). This guideline defines BD as the irreversible loss of function of the brain, including the brain stem.

Before establishing the diagnosis of BD in a patient, both cause and irreversibility must be determined. There must be either clear clinical evidence or neuroimaging evidence that there is an acute CNS injury compatible with the clinical diagnosis of BD. Any disease that could mask the clinical picture of the patient with BD must be ruled out. Hypothermia, drug intoxication, severe electrolyte disorder, severe acid-base problem, or endocrine crises are some of these entities (Table II). Tests for BD may be undertaken after these criteria have been fulfilled.

Table I. Brain death: The Harvard criteria (10).

Patient unresponsive with core temperature > 32.2°C
Systemic absence of depressant drugs
No spontaneous patient movements
Patient apneic when on respirator for 3 min
Absent reflexes, including:
No decerebrate or decorticate posturing
No pupillary response to light
No vocalization or swallowing
No pharyngeal or corneal reflexes
No deep tendon or stretch reflexes
Isoelectric electroencephalogram
All of the above at one point in time and again 24 hours later

Table II. Findings that must be present prior to evaluation for brain death (19).

Clinical or neuroimaging evidence of catastrophic CNS event compatible with the clinical diagnosis of brain death
Exclusion/correction of medical conditions that may confound clinical assessment
Acid-base disorders
Severe electrolyte disorders
Endocrinopathies
Absence of drug intoxication or poisoning
Patient core (rectal) temperature > 32°C

Another point in the evaluation of BD in a comatose patient regards the alertness of healthcare professionals in the case of a possible BD and organ donation. Some data indicate that healthcare providers as a group are somewhat ignorant of the criteria for BD (20).

TESTS TO ESTABLISH A DIAGNOSIS OF BRAIN DEATH

The prerequisites sine qua non in the diagnosis of BD are the clinical diagnosis of deep coma, loss of all brainstem reflexes, and apnea (Table III).

Coma is demonstrated by the absence of any cerebral motor response to pain, e.g., given by supraorbital ridge pressure. This test is definitely invalidated by the use of neuromuscular blocking agents.

The absence of brainstem reflexes can be demonstrated by testing all of the following and eliciting a negative response (Table III): pupillary response to light; ocular movement (oculacephalic reflex and calorics); facial sensation and facial motor response, and pharyngeal and tracheal reflexes. Pupillary response should be absent in both eyes (21). In most patients with brain death, pupils may either be large or midpoint(22). Ocular instillation of drugs, local trauma, or pre-existing anatomic deficits should be ruled out. Ocular movement should be absent following rapid twisting of the head from the neutral position to 90 degrees to each side (absent doll's eyes reflex). This testing cannot be performed in any patient in whom a cervical spine injury might be present. Calorics should be tested by instilling 50 mL of cold water into each ear canal, allowing 1 minute after injection to ascertain any response. Sedatives, tricyclic antidepressants, anticholinergic and antiepileptic agents might alleviate the caloric respose. Local trauma may also restrict eye movements. Absent facial sensation and absent facial motor response may be found by lack of corneal reflex (done by touching a cotton, tipped applicator to the cornea), lack of jaw reflex (done by tapping on the chin and observing the jaw to close), and absence of grimacing with supraorbital pressure. Absent pharyngeal and tracheal reflexes can be demonstrated by lack of a gag reflex when the posterior pharynx is stimulated and lack of a cough response to suctioning (1).

Table III. Testing for brain death (19).

1. Coma (unresponsiveness)
No cerebral motor response to pain
2. Absent brain stem reflexes (all of the below)
No pupillary response to light
No oculocephalic reflex (doll's eyes; No response to cold water calorics)
No corneal reflex
No jaw reflex
No grimacing to painful stimulus
No gag reflex
No cough response to tracheal-bronchial stimulation
3. Apnea over 8 minutes with PCO2 > 60 mm Hg

Before apnea is shown by formal testing, a number of prerequisites must be provided: core temperature greater than 36.5°C, systolic blood pressure greater than or equal to 90 mm Hg, euvolemia, arterial PCO2>40 mm Hg and preoxygenation to obtain arterial PO2>200 mm Hg. Then the patient should be placed on a pulse oximeter, removed from the ventilator and supplied with 100% O2 at 6 L/min. The patient should be observed for any respiratory movements for approximately 8 minutes. At this time an arterial blood sample should be obtained and sent for blood gas analysis. The patient should be returned to the ventilator. If significant respiratory movements are seen, the apnea test is negative (i.e. does not support the diagnosis of BD). If the arterial PCO2 is greater than or equal to 60 mm Hg (or>20 mm Hg increase over a baseline PCO2), the apnea test is positive and supports BD. If the arterial PCO2 is less than 60 mm Hg with no cardiac arrhythmias or hypotension, the test may be repeated with 10 minutes of apnea. If the test was ended due to arrhythmias or hypotension, and the PCO2 is less than 60 mm Hg (or<20 mm Hg increase over baseline), the apnea test is indeterminate. Some studies suggest that apnea testing in patients with lesion of the brain stem should be carried out only after an isoelectric EEG (23).

If the clinical criteria are met, after an arbitrary interval such as 6 hours, a repeat clinical evaluation needs to be performed (1). If the patient continues to fulfill these criteria, the diagnosis of BD can be made at that time. In most situations, confirmatory testing will not be necessary, although in Germany they are required by law, (24) whereas in Britain confirmatory tests are not necessarily done (11).

CONFIRMATORY TESTING

In many situations that may interfere with the clinical diagnosis of BD (i.e. facial trauma, previous pupillary diseases, toxic drugs and sleep apnea) confirmatory testing should be considered (19).

Neurophysiological tests are recommended by a number of national professional societies as confirmatory tests to verify the clinical diagnosis of BD

and shorten waiting periods of 6-12 h. Most BD codes allow the use of electroencephalography, (EEG) which must demonstrate electrocortical silence over a certain period. Evoked potentials can demonstrate the loss of activity of various afferent pathways and are accepted in some countries as a confirmatory test (25,26). Brain scintigraphy with technetium-99m hexamethylpropyleneamineoxime brain scan (27), can confirm the loss of isotope uptake. Transcranial Doppler (TCD) sonography also demonstrates cessation of brain perfusion. Cerebral panangiography (28) may also be used to demonstrate the loss of brain perfusion but is less desirable since it might endanger the patient (29). These tests are not absolute in their sensitivity or specificity.

The results of one study with TCD indicate that TCD is a very sensitive and safe method for diagnosing cerebral circulatory arrest (30). TCD could be incorporated into protocols as an alternative to EEG for confirmation of BD (31).

One study suggests that cerebral angiography and CBF studies are the most reliable investigations whereas the role of EEG and TCD remains to be determined because of the presence of false negatives and positives (32). Some studies show that continuous BAEP monitoring can be of use for BD and for the earlier decision of organ explantation (33). MRI also offer another method of verifying BD (34).

These studies assist the clinician expediting the establishment of the diagnosis of BD while in some cases, conflicting results may only delay the final determination.

PEDIATRIC CONSIDERATION ON BRAIN DEATH

BD criteria generally involves adult patients. The President's Commission expanded the age criteria but children younger than 5 year of age were still excluded (13). The discussions (35-37) on standard waiting time and tests for the diagnosis of BD in children continue. At present, studies suggest that the same criteria used for adults can be accepted for children and full-term infants over 7 days of age (35). Neonatal BD definition is not yet agreed on.

PATIENT RECEIVES THE DIAGNOSIS OF BRAIN DEATH: SO WHAT?

Before making an organ donation request, healthcare providers must inquire about and address common misunderstandings people have about BD. Healthcare teams should develop and be trained on a clear protocol for communicating with the families of patients who may be potential organ donors (38).

Once the patient receives the diagnosis of BD and while the patient remains on a ventilator the patient's family should be clearly informed that the patient has died. At that time, organ donation may be discussed (39,40). To approach the relatives about organ donation is an uncomfortable task for physicians. However, this is an extension of our duty to care for the patient, who may have desired to be considered an organ donor (41). It is interesting that only 61% of the donor and 53% of the nondonor respondents said they had received an explanation of BD (38).

Significant proportion of bereaved families felt that organ donation offered them some comfort (42) and was helpful in the grieving process (43). If the family does not give consent for organ harvesting, supportive therapy and mechanical ventilation should be ceased after a period for family visitation. If organ donation is agreed to, local policies should be followed (1).

In a study investigating organ donation rates the major causes of brain stem death were head injury and intracranial haemorrhage (44). Consent to organ donation was obtained for 24 potential donors. Twenty nine patients did not donate organs. The commonest reasons for failure to donate were medical unsuitability (45) and the coroner not releasing the body (46).

SOME CONTRADICTORY POINTS

Some forms of patient activity are known to confound the diagnosis of BD (Table IV). For example the Babinski sign is a spinal cord reflex and, could be present with absence of any brain function.

In some reports, movement occurred, despite angiographically confirmed absence of a cerebral

Table IV. Clinical observations that can be seen in patients with brain death (19).

Certain spontaneous movements of limbs
Respiratory-like movements without significant tidal volumes
Sweating, blushing, tachycardia
Normal blood pressure without pharmacologic support
Absence of diabetes insipidus
Reflexes: deep tendon, superficial abdominal, triple flexion, Babinski

circulation, delaying decision making and organ donation (47). There are also cases with BD having a complex spinal automatism resulting in head shaking and arm extension (48), cases with acute Guillain-Barré syndrome (49) and suspected rabies encephalitis (50) confused with BD.

CURRENT REGULATION IN TURKEY

In Turkey, current regulations make it necessary for BD to be pronounced by a team of four physicians i.e., cardiologist, neurologist, neurosurgeon and anesthesiologist. The decision of BD should be agreed on with a unanimous vote. The law also forbids the patient's regular doctors and surgeons directly involved in the transplantation process to take part in the team (51).

CARE OF THE POTENTIAL DONOR

Before accepting the responsibility of maintaining a donor for vital organ collection, we should review data supplied in the chart supporting the diagnosis of BD and seriously question inconsistencies and insufficient testing conditions. Knowledge of BD criteria and proper application of these criteria could have changed the course of each of the cases presented (4).

Once the diagnosis of BD has been established clinically, the goal of the care shifts from that of resuscitation to that of organ preservation (1). This is generally carried out in the intensive care units, but it should begin in the ED. The care of these patients may be cumbersome, as these patients have a very high rate of cardiac arrest regardless of the efficiency of the care (9,52).

Hypotension, need for multiple transfusions, diabetes insipidus, disseminated intravascular coagulation, arrhythmias, cardiac arrest, pulmonary edema, hypoxemia, acidemia, seizures, and hypothermia are some of the problems that might be encountered in the potential donor (45).

Hemorrhage, diabetes insipidus, osmotic diuresis (due to mannitol) neurogenic shock, decreased catecholamines, and left ventricular dysfunction are some of the possible causes of hypotension. Central venous catheter monitoring may help in differentiating among some of the causes. In cases where hemorrhage is controlled, if any, and adequate circulating volume has been established, inotropic treatment (dopamine, epinephrine and norepinephrine) may be required (53).

Hypertension is usually short-lived, and generally does not require treatment. Titratable agents such as sodium nitroprusside could be administered if treatment is necessary.

Hypothermia is due to loss of central temperature regulation, exposure, or large amounts of fluid infusion, and may result in coagulopathy, decreased oxygen delivery to the tissues, and cardiac irritability or instability. Heated, humidified oxygen provided via the ventilator circuit may successfully treat as well as prevent hypothermia. Warmed fluids should be the rule in these patients.

Treatment of endocrinopathies is an area involving substantial controversy. T3, cortisol, insulin, and vasopressin might be given if the patient is unstable (53,54).

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