Brain Death*

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Until recently determination of death was simple. The heart stopped. There was no pulse, no recordable blood pressure, and no heart sounds. There was no breathing. Now, methods of cardiopulmonary resuscitation are common knowledge, both to the layman and to the physician.[1] Hospitals have special "Code Blue" teams; emergency rooms and intensive care units are superbly equipped for life support; hearts that stop are started again.[2] Machines do an excellent job of respiration. Nevertheless, the patient's brain may be dead and damaged beyond recovery, either in whole or in part. When the whole brain is seriously damaged, including the cerebral cortex and brain stem, there is no possibility of return to an independent existence and even machines cannot keep the person alive longer than a week or two. When the brain is partially damaged, particularly with destruction of portions or layers of the cortex, or connections to the cerebral cortex, the patient may indeed survive with brain stem function alone in a so-called "vegetative state."[3] In this condition spontaneous respiration will occur and if the patient is fed and carefully nursed he may survive for months or years.

In addition to the common occurrence of cardiopulmonary resuscitation, the practice of transplantation of human organs has added another dimension to the necessity for determination of "brain death." Organs such as kidneys can be maintained for a while outside the body, but for best results they should be removed from the body while still in a healthy state. As a result, extensive studies have been carried out in an attempt to devise proper and foolproof criteria for the determination of brain death.

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Though the requests for determination of brain death are greater in the larger medical centers, the matter must often be faced in smaller hospitals. For this reason, knowledge of the possible outcome of the patient in deep coma is useful to the primary attending physician in advising the family as to the value of transfer to a larger medical center, or that brain death has occurred and donation of organs for transplantation would be reasonable.

The first widely accepted criteria for determination of brain death were prepared by a committee at the Massachusetts General Hospital and the Harvard Medical School.[4] Following the publication of this article in 1968, the so-called "Harvard criteria" were widely used in determination of brain death. Essential elements of these criteria include a complete lack of response on the part of the patient to painful or other stimuli; the complete absence of both cranial and spinal reflexes; the complete absence of spontaneous respiration; and the recording of an electroencephalogram (EEG) showing no evidence of brain activity (a so-called isoelectric EEG or EEG showing electrocerebral silence). The criteria further stated that these conditions should be met over a twenty-four-hour period, or that the findings exist on two examinations at least twenty-four hours apart. In addition, there should be no history of drug overdose and no severe hypothermia.

Since the use of the electroencephalogram to measure brain activity was a part of the Harvard criteria, it rapidly became evident that the electroencephalographic records must be made with the most exacting techniques. Cases were reported that showed isoelectric EEGs on two occasions, twenty-four hours apart, and the patient still survived. Studies of these cases carried out by a committee of the American Electroencephalographic Society showed that in most instances there were technical problems in the EEG

recording. A lack of use of proper distance between electrode placement and lack of use of the highest possible amplification were the most common errors. In addition, a number of cases occurred where the patients were reported to show brain activity in the EEG recording, but a review of the EEG records demonstrated this to be an artifact. The criteria for EEG recording in cerebral death have recently been published by the American EEG Society[5] and include:

1. A minimum of eight scalp electrodes and ear lobe reference electrodes.
2. Interelectrode impedances under 10,000 ohm but over 100 ohm.
3. Testing the integrity of the entire recording system.
4. Interelectrode distances of at least 10 centimeters.
5. Sensitivity increase from 7 (7.5) μV/mm to 2 μV/mm during most of the recording with inclusion of appropriate calibrations.
6. Use of time constants of 0.3 to 0.4 seconds during part of the recording.
7. Use of monitoring techniques.
8. Tests of EEG reactivity to intense stimuli such as pain (for example, pinch), loud sound, and (optionally) strong light (stroboscopic if available).
9. Recording time of at least 30 minutes.
10. Recordings to be made only by a qualified technologist.
11. Repeating EEG if there is doubt about electrocerebral silence.
12. Telephone transmission of EEG not to be used for determination of electrocerebral silence.

In addition, as a result of the National Institutes of Health (NIH) study on cerebral survival, an atlas of the EEG in coma and death has been published,[6] setting forth the proper criteria for recording and also demonstrating the great variety of artifacts which may hamper the demonstration of electrocerebral silence.

Over a period of time it became evident to a number of physicians in the neurosciences that the Harvard criteria were perhaps over-demanding. In an attempt to establish a wider experience and a broader-based study the National Institute of Neurological Diseases and Stroke supported a study on cerebral survival from 1970 to 1973. This was carried out in eight centers throughout the country, one of which was the Medical College of Virginia. A total of 503 patients were included in the major portion of this study, of which 87 came from MCV. Actually, many other patients were studied before, and an even larger number of patients have been studied since, at MCV.

This experience has led to criteria for brain death somewhat different from those of the Harvard criteria. It was quickly demonstrated that the presence of spinal reflexes such as deep tendon or muscle stretch reflexes was not a criterion for brain death. It was further demonstrated that the absence of cranial or cephalic reflexes was of major importance. This included, particularly, dilated fixed pupils, absence of oculocephalic reflexes, and the absence of spontaneous respiration. If these clinical findings existed and the patient's coma was not the result of an overdose of medication, or in rare cases due to hypothermia, then the electroencephalogram was almost invariably isoelectric and the outcome was always death. These criteria applied in patients examined six hours or more after the onset of their coma and lack of respiration. Studies at MCV, particularly, also demonstrated the usefulness of succinylcholine chloride injections or some similar muscle relaxant, such as pancuronium bromide (Pavulon), to remove muscle artifact in the EEG records, thereby making a more exact determination of electrocerebral silence.[7]

If any additional proofs of brain death might be needed, it had previously been demonstrated, especially in Europe,[8,9] that the dead brain did not show evidence of cerebral circulation. Cerebral arteriograms carried out in some patients showed little or no evidence of contrast in the vessels in the brain. A radioisotope method of studying cerebral circulation by injection of a bolus of radioactive material also demonstrated that patients meeting the other criteria for brain death showed no evidence of cerebral blood flow.[10]

Partly because of the interest in organ transplantation at MCV, the State of Virginia was one of the first states to pass a law concerning "brain death." The Virginia statute is printed at the end of this article.

In view of the Virginia law, and in view of our experience at MCV, the following constitutes our present criteria for determination of brain death. This is a personal evaluation used in our practice in the Department of Neurology and not an official document, either of MCV or of any other body. It con-

forms essentially, however, to the conclusions recently published in the final report of the NIH study of cerebral death.[11]

Criteria for Establishment of Brain Death (Cary Suter, M.D., Medical College of Virginia, 1977)

Where, from the history and medical record, it is clear that the patient has suffered a sudden and definable episode of brain damage, either from cerebral anoxia, severe head trauma or wounds, or sudden stoppage of respiratory function in the course of illness such as brain tumor, or cerebral hemorrhage, then the following conditions, if they are found six hours or more following such an insult and exist for a period of thirty minutes, shall be considered sufficient criteria for declaring brain death. These criteria shall include the absence of severe hypothermia and the absence of drug overdose; the presence for thirty minutes or more of electrocerebral silence recorded according to the standards set forth by the ad hoc committee of the American EEG Society and interpreted by a duly licensed physician who regularly functions as a specialist in electroencephalography; the absence for a period of thirty minutes of any evidence of cerebral responsivity to any stimuli; the absence of all cranial nerve reflexes; the presence of dilated fixed pupils; evidence that there is no spontaneous respiration. These findings must be confirmed by a consultant in Neurology or Neurosurgery and be reviewed and concurred in by the attending physician.

In the absence of a clear time of onset of the cerebral insult, then the above conditions must be met for a period of thirty minutes and recorded again six hours later for another period of thirty minutes. If, at this point, the attending physician, the consulting Neurologist or Neurosurgeon or the Electroencephalographer have any doubts that brain death has occurred then other tests (such as tests of cerebral blood flow) should be done and an additional period of time shall be allowed to elapse until the consultants and the attending physician agree that the criteria for brain death have been completely met.

It should be clearly understood by the physicians, nurses, and other paramedical personnel as well as by the patient's family that in the presence of brain death, regular cardiac function may remain quite a long time and also that spinal reflexes resulting in the reflex movements of the body below the neck may occur. It should also be understood that these criteria have not yet been established for infants or newborns.

It is easy to see that the conclusions quoted from the cerebral death study are very much like the above.[11] That study concluded that:

> Based on the findings in a collaborative study of 503 comatose and apneic patients, the establishment of cerebral death requires (1) that all appropriate examinations and the therapeutic procedures have been performed, (2) that cerebral unresponsivity, apnea, dilated pupils, absent cephalic reflexes, and electrocerebral silence be present for 30 minutes at least six hours after the ictus, and (3) that if one of these standards is met imprecisely or cannot be tested, a confirmatory test be made to demonstrate the absence of cerebral blood flow. This would allow the diagnosis of a dead brain to be made in patients with small amounts of sedative drugs in the blood, in patients undergoing therapeutic procedures that make examination of one or more of the cranial nerves impossible, and in patients otherwise meeting the criteria whose pupils are small.

Recently there have been published criteria of brain death, which do not include the electroencephalogram.[12] It is certainly true that those patients meeting the criteria of complete absence of cranial reflexes, absence of spontaneous respirations, absence of hypothermia and no overdose of drugs, and who maintain this condition for six hours, almost always have EEGs showing electrocerebral silence. Such persons, of course, also have lack of cerebral blood flow. In making a decision about a matter as serious as brain death it would seem that both a clinical and laboratory evaluation would be reasonable. Since the electroencephalographic examination can be made at the bedside and in general entails less difficulties than a test for cerebral blood flow, it would appear that the combination of the clinical examination and the electroencephalogram are adequate and useful methods for making the determination of brain death. For the physician in the hospital without EEG services, or with questionable portable EEG services, the establishment of brain death on the basis of clinical criteria alone can certainly be used as a preliminary base for a decision about transfer to another center or about the possibility of the use of organs for transplantation.

In the study of patients with possible brain death one of the most bothersome and practical problems is that of drug overdose or of medication with sedative or anticonvulsant drugs. Certainly routine laboratory screening for toxic substances should be carried out on each patient before brain death is determined. When specific drugs have been given, particularly anticonvulsant drugs, serum levels of these drugs should be measured so that it is clear that they are not at toxic levels. In the patient whose coma is originally due to drug overdose this fact alone should prohibit the diagnosis of brain death. It is true that many patients with overdose suffer secondary anoxic brain damage which is irreversible, but it is clear that patients with drug overdose may meet all the criteria for

brain death for a period exceeding twenty-four hours and still recover.

In determination of brain death, evaluation of the presence or absence of spontaneous respiration is essential. This becomes a difficult problem since removing the patient from the respirator for long periods might suggest that additional hypoxic damage might occur. If, however, intratracheal oxygen is administered, no hypoxia occurs and $Paco_2$ levels rise to a level sufficient to trigger spontaneous respiration if it can occur.[13]

As a practical matter, the test of time is sufficient for determination of brain death. In the NIH collaborative study no patient meeting the criteria of brain death survived longer than seven days. In our personal experience at the Medical College of Virginia this has also been true. Patients who meet the criteria even with attempts at support by drugs to maintain blood pressure and by respirators for breathing eventually show a drop in their blood pressure, and irreversible cardiac arrhythmias and cardiac standstill develop.

There are indeed patients who are in deep coma who survive in a vegetative state, but these patients are not ones who have met the criteria of brain death. We have seen a few patients with electrocerebral silence on EEG recording who still had cranial reflexes. Some of these patients eventually regained spontaneous respiration and continued to exist in a vegetative state. This has not happened to any of our patients who met both the clinical and electroencephalographic criteria for brain death.

Another factor that modifies decisions about brain death has to do with the underlying illness. Obviously, a patient with a clearly severe gunshot wound to the head or with an excessively large intracerebral hematoma demonstrated by computerized tomography (CT) scan or with a known rapidly progressive brain tumor has a dismal prognosis from the underlying illness regardless of any specific criteria of brain death. On the other hand, patients with cerebral anoxic damage from cardiac or pulmonary arrest may have severe or moderate brain damage and their condition may change rapidly with marked improvement over a matter of hours and days.[14] This is also true of patients with metabolic coma and, in fact, with coma of any type of unknown cause. In such patients criteria for establishment of brain death must be adhered to completely and without any question. The possibility of drug overdose must always be kept in mind. In all considerations of the literature on brain death it should be recognized that the criteria established have been for adults and that there is not a good enough or large enough series of cases to allow these criteria to be absolutely imposed on infants or young children. In general, experience has demonstrated that the same criteria are applicable to children from three to four years upward.

The many cases of deep coma which are publicized in newspapers and periodicals, some of which eventually recover, have at no time met the criteria of brain death. It is in these patients with severe but not complete brain damage that the most difficult problems of continued nursing care, life support, and the treatment of complications must be faced. No simple answers are available in this set of patients, including the great number of patients in the so-called vegetative state. Studies related to determination of brain death, including electroencephalograms,[15] and cerebral-evoked potentials[16] as well as clinical examination continue to give us more information about prognosis. The CT scan also allows improved assessment of possible structural intracranial lesions.

From this discussion, it should be recognized that the matter of determination of brain death has been extensively studied and the criteria as set forth can be applied routinely and with confidence so long as exacting clinical neurological examination is performed and a technically adequate electroencephalogram is performed. Since patients meeting these criteria almost never survive more than seven days, patients who survive longer almost certainly do not have brain death unless some additional insult to the brain occurs.

The Commonwealth of Virginia Statute concerning brain death:

§32-364.3:1. **When person deemed medically and legally dead.**—A person shall be medically and legally dead if, (a) in the opinion of a physician duly authorized to practice medicine in this State, based on the ordinary standards of medical practice, there is the absence of spontaneous respiratory and spontaneous cardiac functions and, because of the disease or condition which directly or indirectly caused these functions to cease, or because of the passage of time since these functions ceased, attempts at resuscitation would not, in the opinion of such physician, be successful in restoring spontaneous life-sustaining functions, and, in such event, death shall be deemed to have occurred at the time these functions ceased; or (b) in the opinion of a consulting physician, who shall be duly licensed and a specialist in the field of neurology, neurosurgery, or electroencephalography, when based on the ordinary standards of medical practice, there is the absence of spontaneous brain functions and spontaneous respiratory functions and, in the opinion of the attending physician and such consulting physician, based on the ordinary standards of medical practice and consid-

ering the absence of the aforesaid spontaneous brain functions and spontaneous respiratory functions and the patient's medical record, further attempts at resuscitation or continued supportive maintenance would not be successful in restoring such spontaneous functions, and, in such event, death shall be deemed to have occurred at the time when these conditions first coincide. Death, as defined in subsection (b) hereof, shall be pronounced by the attending physician and recorded in the patient's medical record and attested by the aforesaid consulting physician.

Nothwithstanding any statutory or common law to the contrary, either of these alternative definitions of death may be utilized for all purposes in the Commonwealth, including the trial of civil and criminal cases.

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