Updates in the Determination of Brain Death

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SUMMARY – The concept of brain death must be accurately determined and defined, especially in the light of the latest legislation on brain blood flow measurements.

Introduction

The concept of brain death merits assessment from different standpoints, the most significant of which are its historical background, definition, pathophysiology, Italian and international legislation and lastly brain blood flow measurements.

Historical Background

Up until the mid-20th century death was defined by thanatological criteria, i.e. decomposition of the corpse or irreversible cessation of heart and breathing functions.

Advances in science and medicine in the second half of the 20th century led to the development of life support equipment to replace respiratory and cardiocirculatory functions, giving rise to the need for a new definition of death. As a consequence there were the first clinical cases of patients in deep coma with irreversible brain damage who managed to maintain normal cardiopulmonary activity using mechanical ventilation systems. These patients who had lost consciousness, all brain stem reflexes, spontaneous breathing and cortical electrical activity were said to be in “coma dépassé”¹. Inevitably these patients would die after varying time intervals from cardiocirculatory arrest with brain liquifaction.

The concept of “brain death”, or rather death defined by neurological criteria, was fostered by both transplant medicine and by a medical setting allowing treatments replacing vital functions to be removed in some patients undergoing mechanical ventilation. In 1968 the Harvard criteria² were delineated to identify irreversible coma. According to these guidelines, death was ascertained in a patient with unreceptivity and unresponsiveness, no movements (observed for one hour), apnea (three minutes without breathing), no reflexes (both brain stem and spinal) and flat electroencephalogram which was an important confirmatory tool. In addition it was compulsory to rule out hypothermia (body temperature ≥32º C) and the use of CNS depressants. All tests had to be repeated after 24 hours.

Definition of Death

Following developments in philosophical and scientific thought which have also been assimilated by both West and East countries, the definition of death has been modified. Firstly it was defined as “coma dépassé”¹, secondly as central nervous system death according to the 1969 Harvard criteria², thirdly as brain stem death as defined in the United Kingdom in 1972 ³ and finally as total brain failure as defined by the United States presidential commission in 1981. The latter was subsequently adopted by Italian legislation ⁴. Although the definition of death varies partially from one country to the next, certain essential points must be defined:

– The first is the concept of the uniqueness of death, i.e. death of the brain so that the definition of “brain death” must refer only to the diagnostic criteria and not to the intrinsic concept of death. Whereas the United Kingdom defines death as brain stem death for which an EEG is not obligatory, the United States and Italy equate death with total brain failure so that the electroencephalogram is a compulsory
confirmatory test. Even though the definition of death as total brain failure may be outdated, it does guarantee all the safety criteria required to avoid disorienting public opinion.

– The second essential point is the concept of death as a dynamic process. A process that lasted a few hours in the past but even many years at present so that the task of specialists is to pinpoint the exact moment in the process corresponding to an unquestionable prognosis of death. In the past, death would occur in an instant, sometimes preceded by protracted suffering, it was always well recognizable and the moment of death could be readily identified. At present the numerous artificial life support systems maintaining heart, respiratory and nutritional functions can sustain the body’s systems almost indefinitely.

Pathophysiology

As intracranial pressure values increase due to the oedema of brain tissue within the rigid confines of the skull, there is a progressive fall in the intracranial pressure gradient until intracranial pressure equals or even exceeds systemic arterial pressure thereby stopping the nutritional blood supply to brain tissue resulting in intracranial circulatory arrest at entry into the skull (so-called “carotid siphon arrest”).

International Legislation

The problem of consensus on the diagnostic criteria for brain death has been faced by different countries finding different facets depending on the historical, anthropological and cultural setting. In short, medicolegal criteria for brain death in adults have been established in 55/80 countries (69%). In addition, guidelines for “brain death” in adults are present in 70/80 countries (88%) while confirmatory tests for brain death (EEG, angiography, transcranial doppler, scintigraphy) are compulsory in 28/70 guidelines (40%) especially in Europe and Asia. Such confirmatory tests are not required in many developing countries.

Italian Legislation

Italy is the only country in the world to have death defined by law: “death is identified by the irreversible cessation of all brain functions” (Law no. 578 dated 29/12/1993.). The Ministerial Decree relating to the modalities of ascertaining and certifying death (no. 582 dated 22/09/1994) was recently updated by Ministerial Decree dated 11/04/2008 according to which death can be defined by cardiac (cardiocirculatory arrest) or neurological criteria. Specialists serving on the National Advisory Committee on Organ Transplantation which included intensive care experts (Giordano, Lusenti, Martini, Procaccio, Pintaldi, Testasecca), neurologists (Ottonello, Ragazzoni), neuroradiologists (Beltramello, Di Paola) and forensic scientists (Gianelli, Castiglioni) recently drafted guidelines for the application of instrumental cerebral blood flow evaluation, updated to 20/02/2009. According to the Ministerial Decree, in certain conditions the diagnostic-therapeutic work-up aimed at establishing the certainty of the aetopathogenetic diagnosis of brain injury must include instrumental tests designed to disclose the existence or absence of cerebral blood flow. Such special conditions, specified under paragraph 2 of article 2 of the Decree dated 11/04/2008, include:

– infants less than one year of age;
– the presence of CNS depressants likely to interfere with the overall clinical-instrumental findings;
– clinical situations which do not allow a definite aetopathogenetic diagnosis or prevent testing of brain stem reflexes, the apnea test or recording of brain electrical activity.

Instrumental tests designed to establish the existence or absence of cerebral blood flow must be specified and carried out by the intensive care specialist during diagnosis of death when the overall diagnostic-therapeutic work-up defined by law. Execution of such tests constitutes a state of necessity (art. 54 Italian Criminal Code) according to which action must be taken even without the patient consent. However this does not exempt physicians from giving the patient’s relatives detailed information.

Blood Flow Measurements

Recent studies recommend the following methods for the measurement of brain blood flow: cerebral angiography, cerebral scintigraphy, transcranial Doppler and CT angiography. Historically, cerebral angiography has been the method most widely used by neuroradiologists for instrumental confirmation of brain death. Angiography can be performed by selective catheterization of the epiaortic vessels, or bet-
Figure 1  Angiography of the epiaortic vessels through the ascending aorta: note the good opacification of the internal and external carotid arteries in addition to the extracranial portion of the vertebral arteries bilaterally (A). No opacification of the intracranial vessels is evident at 7 s or at 20 s (“carotid siphon arrest”) with good opacification of the external carotid arteries bilaterally (B).
ter by angiography of the epiaortic vessels using a pigtail catheter positioned in the ascending aorta. Preference for the latter method of instrumental assessment of blood flow for the diagnosis of brain death is based essentially on the broader application of this procedure even in settings that are not strictly neuroradiological. In addition it avoids dissecting vascular lesions that could have a negative impact on the diagnostic criterion when resorting to selective angiography of the epiaortic vessels. For the purposes of ascertaining brain death, the assessment must be made in a patient without hypotension and must document the absence of filling of the intracranial arteries at their point of entry into the skull (at the petrous portion of the internal carotid arteries for the anterior circulation and at the foramen magnum for the vertebral arteries of the posterior circulation). Opacification of the superior longitudinal sinus – possible through the meningeal branches or emissary veins – will not affect a positive result.

Figure 2 Brain SPECT: no intracerebral tracer uptake ("empty skull" sign).
due to cerebral blood flow arrest. The criterion for correct examination must be the normal opacification of the external carotid arteries (figure 1). To demonstrate cerebral blood flow arrest, cerebral scintigraphy, performed in a patient without hypotension, must document the absence of intracerebral tracer uptake (so-called “empty skull” sign)⁸⁹. When available, it is preferable to carry out this test using brain SPECT (Single Photon Emission Computed Tomography (figure 2)).

The criterion of examination accuracy may include detection of liver tracer uptake.

Transcranial Doppler can be used to demonstrate cerebral blood flow arrest provided there are the following conditions:

a) The area above the tentorium must be explored bilaterally (using the temporal bone window) together with the area below the tentorium (using the occipital window) so as to assess both the bilateral anterior circulation and the posterior circulation;

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Figure 3 Transcranial Doppler: diastolic reflux (also called reverberating or oscillating flow): the blood tends to move during systole following its normal flow direction, whereas during diastole flow is inverted.

Figure 4 Skull and brain CT angiography with volume rendering reconstruction: no filling of the intracranial arteries (A) with good display of the superficial temporal artery, a branch of the external carotid artery (B).
b) The test must be performed in a patient without hypotension to rule out hypotension-induced transient arrests in the cerebral circulation; c) The following patterns must be considered evidence of blood flow arrest:

I) Signal inversion in diastoles with respect to systoles (“reverberating signal”, “oscillating signal”) (figure 3);
II) Presence of “systolic spikes” characterized by strongly reduced velocimetry and duration with no diastolic signal;
III) No signal in either systole or diastole only in the following two cases:
   • When the signal of at least one vessel is found through each of the three bone windows (left temporal, right temporal, occipital) with one of the four patterns described under points I and II so that the patency of the three windows is demonstrated;
   • When patency of the bone windows has been demonstrated by the same operator on the same patient disclosing the Doppler signal of the intracranial arteries usually assessed with transcranial Doppler.

The patterns described under point c) must be detected in at least two examinations performed at least three minutes apart. CT angiography can yield the same blood flow measurements as catheter angiography offering the same reliability when the same criteria are adopted, i.e. the examination must be conducted in a patient without hypotension, documenting the absence of filling of the intracranial arteries at their point of entry into the skull (at the petrous portion of the internal carotid arteries for the anterior circulation and at the foramen magnum for the vertebral arteries of the posterior circulation). Opaquification of the superior longitudinal sinus – possible through the meningeal branches or emissary veins – will not affect a positive result due to cerebral blood flow arrest. The criterion for correct examination must be the normal opaquification of the external carotid arteries (12-21) (figure 4). For the purpose of ascertaining cerebral blood flow, the report by the specialist performing the instrumental tests described must include a diagnosis of absence or presence of cerebral blood flow.

References
15 Directives medico-ethiques de l’ASSM: Diagnostic de la mort dans le contexte de la transplantation d’organes, 2005.

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