

**DEATH DETERMINED BY NEUROLOGICAL CRITERIA: THE NEXT STEPS**

Smith M.<sup>1,2</sup>, Citerio G.<sup>3,4</sup>

<sup>1</sup>Neurocritical Care Unit, The National Hospital for Neurology and Neurosurgery  
University College London Hospitals, Queen Square, London, UK.

Email: [martin.smith@ucl.ac.uk](mailto:martin.smith@ucl.ac.uk)

<sup>2</sup>UCLH/UCL National Institute for Health Research Biomedical Research Centre

<sup>3</sup>School of Medicine and Surgery, University of Milan-Bicocca, Monza, Italy.

Email: [giuseppe.citerio@unimib.it](mailto:giuseppe.citerio@unimib.it)

<sup>4</sup>Neurointensive Care Unit, Department of Emergency and Intensive Care, San Gerardo Hospital,  
Monza, Italy.

**Corresponding author:**

Martin Smith MBBS FRCA FFICM

Neurocritical Care Unit

The National Hospital for Neurology and Neurosurgery

University College London Hospitals

Queen Square

London WC1N 3BG

UK

Tel: +44 (0)20 3448 4711

Email: [martin.smith@ucl.ac.uk](mailto:martin.smith@ucl.ac.uk)

**Keywords**

Brain death, guidelines, variability

**Conflict of interest**

GC is Deputy Editor and MS Section Editor of *Intensive Care Medicine*

No other conflicts declared

Death has important medical, legal and societal implications making it imperative that its determination is accurate, reliable and certain. Despite it being more than forty years since the concept of “brain death” was first introduced into clinical practice, many of the controversies that surround the determination of death by neurological criteria (DNC), a more focused and accurate description of the process, have not been settled and present an opportunity for future research and education to clarify outstanding issues in order to reduce professional and public disquiet [1]. While the philosophical and religious issues that surround the determination of DNC in some cultures will continue to generate debate, there has been limited success in resolving scientifically more pragmatic issues including the substantial international variation in DNC definitions and criteria, and the equivalence of DNC with an individual’s biological death,

There is broad consensus, at least in the Western world, that human death is ultimately death of the brain, but debate continues over the extent of brain functions that must cease in order to satisfy a definition of DNC [2]. Confusingly DNC can be defined in two different ways based on ‘whole’ brain and ‘brainstem’ formulations. The determination of whole brain death requires confirmation, in theory at least, of the loss of *all* brain function including, but not limited to, the brainstem. The diagnosis of brainstem death on the other hand requires only confirmation of absence of brainstem function; it does not require that all other brain functions have ceased, but that any functions that might persist should not indicate any form of consciousness. The justification for this approach is that the brainstem is responsible for consciousness, breathing and circulatory regulation, and conducts virtually all throughput to and from the brain [2]. Since the permanent loss of all measurable brainstem function equals death, and this is assessable clinically, continuing to highlight differences between whole brain and brainstem approaches to the determination of DNC is unnecessary and unhelpful [3]. Furthermore, the clinical determination of whole brain and brainstem death is identical, requiring confirmation of the absence of brainstem function by identification of unresponsive coma and absence of brainstem reflexes including the capacity to breathe.

Ancillary investigations assessing electrophysiology or blood flow may be useful in situations where clinical testing cannot be performed or when confounding or special conditions are present, but they are legally required in some countries as an essential component of the diagnosis of DNC. This adds

further confusion, inferring as it does that clinical testing alone is insufficient to confirm DNC despite a lack of evidence to support this notion [4]. Methods to confirm the absence of cerebral blood flow are less affected than electrophysiological methods by confounding factors such as residual sedation, and are preferred. Non-invasive techniques, such as CT angiography (CTA), are increasingly employed but, as with other ancillary investigations, there are limited data to confirm their applicability and reliability [4]. Although CTA has high sensitivity for the confirmation of DNC in individuals who fulfil clinical criteria for its diagnosis, there is insufficient evidence to support its use as a screening tool for DNC [5]. CT perfusion imaging appears to offer no advantages over CTA. Positron emission tomography has an evolving role in the diagnosis and prognosis of disorders of consciousness and, as it measures both regional cerebral metabolic rate for glucose in addition to regional blood flow, it has theoretical advantages as an ancillary investigation in the diagnosis of DNC. There are currently no data to support such an approach and further investigation is required to determine a role (if any) for vascular, perfusion and metabolic imaging in the screening and diagnosis of DNC.

Despite potential roles for ancillary tests, they are not universally favored and the majority of experts argue for continued reliance on clinical assessment [3]. Claims that failure to incorporate ancillary investigations results in a less rigorous determination of DNC, particularly in jurisdictions that utilize a brainstem approach, fundamentally misunderstand and misinterpret the concept of DNC [6]. All codes of practice define a clinical context involving three sequential but independent steps which, together, demonstrate absent brainstem function and confirm irreversibility. There are no false positives following the rigorous application of established clinical criteria for the determination of DNC [7]. The reliance on direct observation and examination of the patient for the determination of DNC, after preconditions have been fulfilled and confounding conditions excluded, has recently been reinforced [8].

Death is not a single event but a process, and once a threshold of irreversibility has been reached it is not necessary to wait for the death of the whole organism for the inevitable consequence of its biological death to be certain. While it is universally accepted that cessation of cardiac and respiratory function marks the death of an individual, nobody argues that the whole human organism is dead at this point. Unfortunately, the same cannot be said for DNC; reports of brain dead patients 'being kept

alive on a ventilator' are familiar, and family members (and indeed some physicians) continue to refuse to accept that brain dead patients are actually dead [9]. In a 2004 survey, over 98% of general public respondents were aware of DNC but only one-third believed that somebody who is brain dead is legally dead [10]. It is unlikely that the position is substantially different today, and there is a need to educate the public and some healthcare professionals that DNC is an appropriate place to draw the line between life and death, and that its confirmation legitimately marks the death of an individual.

Major international differences in the procedures for diagnosing DNC have recently been highlighted [11]. While some of these stem from legal, religious and cultural differences, others relate to the different ways in which DNC is defined, the variable requirement for ancillary investigations, and different approaches to the clinical diagnosis of DNC including differences in the time of observation prior to proceeding to determination of DNC, conduct of the apnea test, qualification and number of examiner(s), and the number of tests required to confirm DNC. In addition, and worryingly, there are well-documented failures to adhere to clinical practice guidelines in institutions and countries that have such guidance in place [12;13]. Such variability, from whatever cause, continues to adversely influence public and professional trust in the credibility of a DNC determination, and should motivate initiatives to standardize practice worldwide and improve training in DNC determination. Research is particularly required to validate DNC simulation methods and assessment tools, as well as the impact of simulation on performance in clinical practice [14].

Future research into DNC must include prospective studies and audit-based data collection to characterize current practice (including the use and type of ancillary tests) in detail, further assessment of the role (if any) of ancillary investigations in the screening and diagnosis of DNC, and population studies to determine the road blocks to the acceptance of DNC criteria (table 1). In addition, concerted efforts must continue to develop an international consensus to standardize practices worldwide in order to minimize variation and inconsistency in clinical practice and the application of ancillary tests [1;8]. At the same time, critical care physicians must unite with other professional colleagues and public policy makers to engage local communities and national governments in DNC related issues. Only in this way will it be possible to achieve equivalence of DNC and cardiorespiratory death in the minds of the public and professionals. As Dr Varelas so eloquently

stated in 2014, the time has come when the determination of DNC should be as easy and accepted as placing a stethoscope on a deceased patient's chest to search for a heartbeat and breath that will never come [15].

## References

1. Smith M (2012) Brain death: time for an international consensus. *Br J Anaesth* 108 Suppl 1:i6 doi: 10.1093/bja/aer355
2. Bernat JL (2013) Controversies in defining and determining death in critical care. *Nat Rev Neurol* 9:164-173. doi: 10.1038/nrneurol.2013.12
3. Wijdicks EF (2015) The clinical determination of brain death: rational and reliable. *Semin Neurol* 35:103-104. doi: 10.1055/s-0035-1547531
4. Wijdicks EF (2010) The case against confirmatory tests for determining brain death in adults. *Neurology* 75:77-83. doi: 10.1212/WNL.0b013e3181fe77fa
5. Brasil S, Bor-Seng-Shu E, de-Lima-Oliveira M, et al. Role of computed tomography angiography and perfusion tomography in diagnosing brain death: asystematic review. *J Neuroradiol* 2016; 43: 133-40. doi: 10.1016/j.neurad.2015.07.006
6. Wijdicks EF (2012) The transatlantic divide over brain death determination and the debate. *Brain* 135:1321-1331. doi: 10.1093/brain/awr282
7. Wijdicks EF, Varelas PN, Gronseth GS, Greer DM (2010) Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 74:1911-1918. doi: 10.1212/WNL.0b013e3181e242a8
8. Shemie SD, Hornby L, Baker A, Teitelbaum J, Torrance S, Young K, Capron AM, Bernat JL, Noel L (2014) International guideline development for the determination of death. *Intensive Care Med* 40:788-797. doi: 10.1007/s00134-014-3242-7
9. Magnus DC, Wilfond BS, Caplan AL (2014) Accepting brain death. *N Engl J Med* 370:891-894. doi: 10.1056/NEJMp1400930
10. Siminoff LA, Burant C, Youngner SJ (2004) Death and organ procurement: public beliefs and attitudes. *Soc Sci Med* 59:2325-2334. doi: 10.1016/j.socscimed.2004.03.029

11. Wahlster S, Wijdicks EF, Patel PV, Greer DM, Hemphill JC, III, Carone M, Mateen FJ (2015) Brain death declaration: Practices and perceptions worldwide. *Neurology* 84:1870-1879. doi: 10.1212/WNL.0000000000001540
12. Greer DM, Wang HH, Robinson JD, Varelas PN, Henderson GV, Wijdicks EF (2016) Variability of Brain Death Policies in the United States. *JAMA Neurol* 73:213-218. doi: 10.1001/jamaneurol.2015.3943
13. Shappell CN, Frank JI, Husari K, Sanchez M, Goldenberg F, Ardelt A (2013) Practice variability in brain death determination: a call to action. *Neurology* 81:2009-2014. doi: 10.1212/01.wnl.0000436938.70528
14. MacDougall BJ, Robinson JD, Kappus L, Sudikoff SN, Greer DM (2014) Simulation-based training in brain death determination. *Neurocrit Care* 21:383-391. doi: 10.1007/s12028-014-9975-x
15. Varelas P (2014) Brain death determination: still a lot to learn, still a lot to do... *Neurocrit Care* 21:373-375. doi: 10.1007/s12028-014-0075-8

**Table 1**

**A proposed research agenda for the neurological determination of death**

**UNIVERSAL DEFINITION OF DEATH DETERMINED BY NEUROLOGICAL CRITERIA**

- Development of a common, universally accepted and easy to understand terminology for death by neurological criteria.

**UNIVERSAL DETERMINATION OF DEATH BY NEUROLOGICAL CRITERIA**

- Development of a uniform procedure for the determination of death by neurological criteria worldwide.
- Formalize the identification and avoidance of confounders.
- Determine the applicability and reliability of ancillary tests, such as computed tomography angiography and perfusion scans.
- Determine the need (or otherwise) of repetition of the clinical determination of death by neurological criteria.

**EDUCATION ON DEATH DETERMINATION USING NEUROLOGICAL CRITERIA**

- Implementation of professional education strategies for the determination of death by neurological criteria.
- Development of communication and education strategies on death by neurological criteria for lay people.