

# Diagnosis of death

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## Key points

Death consists of the loss of capacity for consciousness and the loss of the ability to breathe.

Brainstem death occurs after neurological injury when the brainstem has been irreversibly damaged but the heart is still beating and the body is kept alive by a ventilator.

Two appropriately qualified clinicians are required to diagnose brainstem death after exclusion of reversible causes of unconsciousness, confirmation of the absence of brainstem reflexes, and completion of apnoea testing.

Cardiorespiratory death can be diagnosed after 5 min of observed asystole, long enough for irreversible damage to the brainstem to have occurred.

Recently updated guidelines from the Academy of Medical Royal Colleges provide guidance on the procedures governing the diagnosis of death.

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The diagnosis, confirmation, and certification of death are core skills for medical practitioners in the UK.<sup>1</sup> Although the confirmation of death remains relatively straightforward in the majority of circumstances, developments in advanced resuscitation techniques together with the continuing recognition of the medical benefits of cadaveric organ donation present the clinician working in critical care with specific challenges. Although these can largely be overcome, to do so requires a thorough understanding of the pathophysiological events that surround death within the broader societal context of what are considered the essential distinctions between what is alive and what is dead.

## Historical perspective

The historical record is littered with countless examples of failures to distinguish deep coma from death, and accounts of the obsession with premature burial and the use of phrases such as 'saved by the bell' and the 'graveyard shift'. Although the scientific foundations of modern medical practice have largely allowed these issues to be resolved, they have been replaced by even more challenging circumstances that are primarily the result of techniques of advanced resuscitation. For example, the demonstration of the effectiveness of cardiopulmonary resuscitation in maintaining cerebral perfusion has challenged the axiom that cardiac arrest is inevitably associated with death (at least temporarily). Similarly, interventions in patients with terminal respiratory arrest secondary to an intracranial catastrophe has led to the emergence of a state of profound and irreversible apnoeic coma in patients whose heart continues to beat for as long as mechanical ventilation is continued. This second group of patients, originally described as being in a state beyond coma (le coma dépassé),<sup>2</sup> has proved particularly challenging for both the medical profession and society as a whole, although eventually led to the emergence of widely accepted criteria for brain death.

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Two sets of criteria for the diagnosis of brain death have been of particular influence. The landmark Harvard code of practice sets the standard for 'whole brain' death that dominates opinion in North America and beyond, and which underpins the requirement for ancillary testing that sometimes accompanies contemporary criteria.<sup>3</sup> In contrast, the original UK criteria were based upon a conviction that the key elements of brain death—namely irreversible loss of the capacity to breathe combined with the irreversible loss of the capacity for consciousness—could be satisfied through loss of brainstem function alone and that such a state could usually be diagnosed on clinical grounds.<sup>4</sup> Regardless of the details, acceptance of the concept of brain death had two consequences. First, there emerged an understandable belief that there were now different kinds of death—brain death and cardiorespiratory or somatic death. Secondly, because transplantation outcomes from organs retrieved from heartbeating brain dead donors were superior to those from asystolic donors, brain death has become inextricably linked with organ donation.

## Fundamental concepts of death

As noted above, aspects of modern critical care have placed new demands upon the diagnostic criteria for death and even challenged our very understanding of it. Declaration of death in a corpse in an advanced stage of decay and decomposition requires little in the way of diagnostic acumen. However, the possibility of successful resuscitation in a patient who has recently suffered a cardiac arrest, together with the maintained circulation and somatic physiology in an individual who is brainstem dead, highlights the inadequacy of using cardiorespiratory criteria alone in the diagnosis of death. Furthermore, some philosophers and ethicists speculate that the loss of capacity for thought, reason, and feeling may indicate a state of death of the person that could be

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distinguished from the biological death of the organism as a whole. However, there remains a professional and indeed societal conviction that death occurs as a single phenomenon that marks the end of the biological existence of the organism and that its timing can be identified with a reasonable degree of accuracy. Recent statements from both the UK and the USA give professional credibility to these convictions. For instance, guidance from the Academy of Medical Royal Colleges (AoMRC) in the UK<sup>5</sup> states that:

Death entails the irreversible loss of those essential characteristics which are necessary to the existence of a living human person and, thus, the definition of death should be regarded as the irreversible loss of the capacity for consciousness, combined with irreversible loss of the capacity to breathe.

The President's Council on Bioethics in the USA has expanded on these ideas,<sup>6</sup> proposing that in order for an organism to be considered to be living an animal must be a *whole*, describing wholeness as follows:

Determining whether an organism remains a whole depends upon recognizing the persistence or cessation of the fundamental vital work of a living organism—the work of self-preservation, achieved through the organism's need-driven commerce with the surrounding world. When there is good reason to believe that an injury has irreversibly destroyed an organism's ability to perform its fundamental vital work, then the conclusion that the organism as a whole has died is warranted.

The statement of the Presidential Council goes on to define the essential elements of an organism's vital work of commerce with its surroundings:

- (i) openness or receptivity to the signals and stimuli that emanate from the environment—*consciousness*;
- (ii) the ability of an organism to interact with the environment to selectively obtain what it needs for survival, and an innate drive that compels an organism to do what it must to complete this interaction—for example, through *spontaneous respiration* engage in the exchange of carbon dioxide for oxygen.

Thus, the key elements of a biological standard for death are considered to be the *simultaneous and irreversible loss of both the capacity for consciousness and the capacity to breathe*. The criteria required to confirm such a state will vary according to the precise circumstances in which death has occurred and the extent to which this has resulted in the collapse of normal biochemical processes, although it is clear that neurological criteria are in most direct alignment (Fig. 1).

The recent document published by the AoMRC provides practical guidance on both the cardiorespiratory and neurological criteria for the diagnosis of death. Further details on practical management issues relating to the diagnosis of death can be found at <http://healthguides.mapofmedicine.com/choices/map/index.html>.

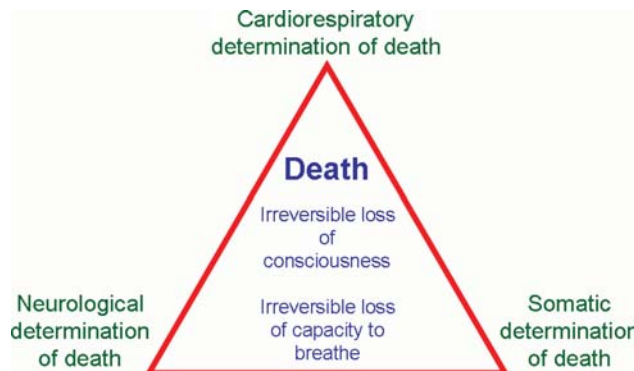


Fig 1 The relationship between the various criteria for the diagnosis and confirmation of death.

## Diagnosis of death by neurological criteria

The UK Code for the diagnosis of *brainstem death*, more recently referred to diagnosis of death by neurological criteria, has *three essential components*:

- (i) fulfilment of essential *preconditions*;
- (ii) *exclusion* of potentially *reversible* contributions to a state of apnoeic coma;
- (iii) the *formal demonstration* of *coma*, *apnoea*, and the *absence* of *brainstem* reflex *activity*.

The new guidance from the AoMRC builds on the original Codes of Practice and provides greater clarity over various elements of both patient assessment and the performance of the tests themselves. Clinical interrogation of the brainstem serves to demonstrate the absence or otherwise of brainstem functions, but it is the initial phases of assessment that indicate their irreversibility.

The tests should be *carried out by two qualified doctors* who are competent with the procedure, *one* of these should be a *consultant* and *both* should have been *fully registered* with the *General Medical Council* for at *least 5 yr*. The tests must be undertaken by the two doctors *together* and completed successfully on two occasions.

### Preconditions

- (i) The patient should be deeply unconscious, apnoeic, and mechanically ventilated.
- (ii) There should be no doubt that the patient has suffered irreversible brain damage of *known aetiology*, common causes of brainstem death including spontaneous intracranial haemorrhage, hypoxic brain injury, ischaemic stroke, and trauma. On the *rare* occasions where the primary diagnosis remains *obscure*, an *extended* period of clinical *observation* and support may be required before the irreversible nature of the pathology can be confirmed.

### Exclusion criteria

Clinicians must be sure that a patient's apnoeic coma is not the result of, either completely or in part, reversible influences such as

sedative drugs, endocrine and metabolic abnormalities, hypothermia, or cardiovascular instability (Table 1).

### Depressant drugs

Drug intoxication represents a clinically significant reversible cause of coma and may complicate assessment on occasions where the patient has received infusions of sedative drugs as part of their critical care treatment and when their brain injury is a result of drug-induced self-harm. The most problematic of circumstances are those where the identity of the intoxicating substances is unknown, where drug elimination is impaired by reduced hepatorenal function, or where agents with long half-lives have been used. Possible approaches include:

- (i) A period of observation that approximates to four times the elimination half-life of the agent involved to allow effective drug elimination. This approach is best suited to circumstances where short-acting agents such as propofol and alfen-tanil have been given to patients with normal hepatic and renal function.
- (ii) The administration of specific antagonists such as flumazenil or naloxone in circumstances where the residual effects of opioids or benzodiazepines is suspected.
- (iii) Plasma analysis to confirm that a suspected sedative is either not detected or at a subtherapeutic level. This option is particularly suited for agents with long or unpredictable half-lives such as thiopental or phenobarbital.
- (iv) A confirmatory test to demonstrate the absence of cerebral blood flow/perfusion, for example, cerebral angiography.
- (v) Despite this general guidance, the revised AoMRC Code remains permissive and gives a clinician the latitude to dismiss the influence of sedative agents in circumstances where there is independent evidence to suggest that the patient is brainstem dead, for example, on the basis of the computed tomographic (CT) head scan or a prolonged period of malignant intracranial hypertension.

### Reversible causes of apnoea

Other causes of apnoea are rare but should be actively sought if the history or clinical examination suggests their presence. Severe neuromuscular weakness of any cause can produce apnoea. After head injury, it is necessary to exclude cervical spinal cord injury as a cause of respiratory paralysis. It is also sensible to routinely use a nerve stimulator to confirm the absence of residual drug-related neuromuscular block.

### Brainstem reflex and apnoea testing

Formal testing can take place once clinicians are satisfied that the patient has satisfied the essential preconditions and that there are no significant reversible contributions to the comatose and apnoeic state. These tests are designed to be easy to perform with unequivocal results. They require no special equipment and can be performed at the bedside. Key family members should be given the opportunity to witness the tests.

The tests have two components—an examination of the integrity of a number of brainstem reflexes that are mediated by afferent and efferent components of various cranial nerves, and the apnoea test (Table 2). The apnoea test should only be performed once the total absence of brainstem reflex activity has been demonstrated and both elements of the tests must be performed twice. The time of death is recorded as the time at which the first set of tests was completed.

### Ancillary tests

The UK Code recognizes that there may be circumstances where clinicians feel unable to confirm death using neurological criteria based on clinical assessment alone. Such circumstances include:

- (i) episodes where a comprehensive neurological examination cannot be carried out, for example, after severe maxillofacial trauma;
- (ii) when the influence of residual sedation cannot be excluded;

**Table 1** Potentially reversible causes of coma and guidance for testing. Note that these limits are not prescriptive and do not replace clinical judgement when assessing their contribution (and therefore importance) to the overall condition of the patient

Factor	Lower limit	Upper limit	Notes
Temperature	34°C		Impaired consciousness below 34°C; brainstem areflexia <28°C
Biochemistry			
Sodium	115 mmol litre <sup>-1</sup>	160 mmol litre <sup>-1</sup>	Derangements that are clearly the result of brainstem death, e.g. the hypernatraemia associated with diabetes insipidus, may not require correction ahead of testing. Blood glucose should be checked immediately before testing
Potassium	2 mmol litre <sup>-1</sup>	—	
Magnesium	0.5 mmol litre <sup>-1</sup>	3.0 mmol litre <sup>-1</sup>	
Phosphate	0.5 mmol litre <sup>-1</sup>	3.0 mmol litre <sup>-1</sup>	
Glucose	3 mmol litre <sup>-1</sup>	20 mmol litre <sup>-1</sup>	
Respiratory and haemodynamic parameters			
pH	7.35	7.45	Requirement for cardiorespiratory stability is an important new element of the AoMRC guidance
P <sub>a</sub> CO <sub>2</sub>		6.0 kPa	
P <sub>a</sub> O <sub>2</sub>	10 kPa		
Mean arterial pressure	60 mm Hg		
Endocrine disturbance	The acute endocrine failure associated with brainstem death is not a cause of reversible coma. Although longstanding and profound hypothyroidism or hypoadrenalism can result in impaired conscious level, this can usually be excluded from the history		

Table 2 Brainstem death tests

Brainstem reflex tests				
Test	Cranial nerve		Test details (brainstem level)	Response in brainstem death
	Sensory	Motor		
Pupillary response	II	III	A bright light is shone into each eye in turn. Direct and consensual reflexes should be sought (mid brain)	Absence of pupillary constriction
Corneal reflexes	V	VII	The cornea is brushed lightly with a swab (pons)	No blinking
Oculo-vestibular reflexes	VIII	III, IV, VI	50 ml of ice cold saline is instilled into the external auditory meatus over 1 min. The tympanic membrane should be visualized by otoscopy before testing. Both sides should be tested, though inability to perform the test on one side does not invalidate the test (pons)	No eye movement
Response to painful stimulus	V	VII	Painful stimulus is applied to the supra-orbital ridge (pons), and also to the limbs and trunk	No motor response in the cranial distribution
Gag reflex	IX	X	The pharynx is stimulated with a spatula or similar device (medulla)	No gag or pharyngeal contractions
Cough reflex	X	X	A bronchial catheter is passed to the carina (medulla)	No cough
Apnoea test				
The apnoea test should only be performed once the absence of brainstem reflex activity has been confirmed. The aim is to produce an acidotic respiratory stimulus (pH<7.4) without inducing hypoxia or cardiovascular instability. This applies to those with chronic respiratory disease, though the PaCO <sub>2</sub> required to achieve this may be higher				
1. Increase F <sub>IO<sub>2</sub></sub> to 1.0				
2. Perform arterial blood gas analysis to calibrate P <sub>CO<sub>2</sub></sub> and SpO <sub>2</sub>				
3. Reduce minute ventilation until P <sub>CO<sub>2</sub></sub> reaches 6.0 kPa and pH is 7.4. SpO <sub>2</sub> should be greater than 95%				
4. Maintain apnoeic oxygenation by either instilling 5 litre min <sup>-1</sup> O <sub>2</sub> into the lungs with a suction catheter or with CPAP				
5. Observe for respiratory activity for 5 min				
6. Confirm an increase in PaCO <sub>2</sub> of more than 0.5 kPa using blood gas analysis				
After completion of the apnoea test, the ventilator should be reconnected. Acid–base status should be normalized before second set of tests				

(iii) high cervical cord injury where a distinction between central apnoea and the effects of cervical cord injury cannot be distinguished.

Provision is made in the guidelines for a number of confirmatory tests to be performed in order to confirm the clinical suspicion of brainstem death. These tests are generally aimed at confirming the presence or absence of cerebral blood flow or cerebral function. EEG is the most popular and best validated ancillary test worldwide, but is of little value in cases of drug intoxication since sedative drugs suppress neuronal and therefore EEG activity. Confirmation of the absence of cerebral blood flow by angiography establishes the irreversibility of coma in such circumstances, but may be more difficult to organize. CT angiography may be more readily available, but has yet to be properly validated. Expert advice should be sought from a local neuroscience unit if necessary.

Diagnosis of brainstem death in children

In children older than 2 months of age, brainstem death is diagnosed in exactly the same manner as in the adult. Also as in adults, the tests must be undertaken by two competent clinicians of whom one should be a consultant. One, however, should be a paediatrician and one should not be directly involved in that patient's care.

In infants younger than 2 months of age, the diagnosis of brainstem death becomes difficult. Coma in this age group is often multifactorial. Although hypoxic encephalopathy remains the most likely cause of devastating brain injury, it is often difficult to demonstrate structural brain damage and thus the preconditions are rarely met.

In preterm infants (gestational age below 37 weeks), there is little evidence concerning normal brainstem reflexes and as such their absence is difficult to demonstrate. Diagnosis of brainstem death is inappropriate in this age group.

Diagnosis of death by cardiorespiratory criteria

Although it is important to recognize that death is a process, there is a clear societal and professional demand for a reliable means of identifying the moment of death. Although the criteria for the diagnosis of death should be separated from matters relating to subsequent organ donation as far as possible, it is nevertheless necessary to consider the criteria for the diagnosis and confirmation of death using cardiorespiratory criteria as it relates to donation after cardiac death (DCD) since it is in this context that guidance is most required. Guidance from the AoMRC advises that death can be diagnosed and confirmed after 5 min of continuous asystole. Asystole refers to the absence of mechanical cardiac function and, although it can be identified in a number of ways (which will in part be dependent upon the monitoring modalities that are being used or are available), in practice, this will involve a combination of continuous ECG and intra-arterial pressure monitoring. Within the context of DCD, the starting point for the determination of cardiorespiratory death should be the loss of circulation as demonstrated by the absence of pulsatile flow on a correctly functioning arterial line or alternatively with echocardiography where the expertise exists,

rather than electrical silence on an ECG. However, in the absence of an arterial line, asystole on the ECG is the only reliable way of confirming 5 min of absent circulation. This diagnosis should only be made by a clinician who is familiar with the specific implications of confirming death by cardiorespiratory criteria in this fashion.

Any return of cardiac or respiratory activity during this period of observation should prompt a further 5 min observation period after asystole develops again. At the completion of 5 min of continuous asystole, the clinician should confirm the absence of pupillary reaction and motor response to corneal stimulation and supra-orbital pressure. Death is recorded at the time these observations are completed.

### Conflict of interest

None declared.

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Please see multiple choice questions 1–3.