

17.11 Diagnosis of death and organ donation 3918 P

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ESSENTIALS Death is the permanent loss of the capacity for consciousness and respiration, both of which are functions of the brain-stem. Death can be diagnosed by somatic, circulatory, or neurological criteria, which vary between countries and are influenced by prevailing attitudes towards death, legal frameworks, and available medical technologies. When organ retrieval is planned after circulatory death, there is need for a time-critical schedule for the diagnosis of death using circulatory criteria. These require the absence of consciousness and respiratory effort to be demonstrated, and emphasize the need for explicit clarity that resuscitation should not be instigated or continued, how the absence of the circulation should be identified, and the minimum period of observation that is required to be assured that the possibility of spontaneous return of the circulation has passed.

Introduction Death is usually a process rather than an instantaneous event. However, putting aside the complex and interwoven religious, cultural, sociological, and legal perspectives on death, there is a clear clinical requirement to determine with confidence when an individual has died. Historically, there was a practical necessity to be able to sanction the prompt disposal of a corpse before the onset of putrefaction and decay while avoiding the possibility of the premature burial of someone who was in deep coma but still alive. Clinicians now face additional problems, some of which have required a fundamental review of the essential features of life and death. Is the irreversible loss of brain function sufficient to satisfy criteria for the determination of death even though the circulation persists for as long as the patient is artificially ventilated? Can there remain clear distance between the diagnosis of death and organ donation for the purposes of transplantation, particularly with regards to donation after circulatory death following withdrawal of life support such as mechanical ventilation?

Diagnosis of death

Overarching professional concepts While death is essentially a biological phenomenon that is the same for all humans, the diagnostic criteria for its recognition have been developed by individual countries and jurisdictions rather than by international clinical consensus. As a result, the

diagnostic criteria for the diagnosis of death vary between countries and are influenced by prevailing attitudes towards death, legal frameworks, and available medical technologies. A group assembled by the World Health Organization has sought to provide an international consensus on death, defining it as 'the permanent loss of capacity for consciousness and loss of all brain-stem functions, as a consequence of permanent cessation of circulation and/or catastrophic brain injury' (the term 'permanent' meaning loss of function that cannot resume spontaneously and will not be restored through intervention). Such an approach provides an overarching definition of death that is applicable to all circumstances and also avoids the suggestion that there are different kinds of death as implied by terms such as brain death or cardiorespiratory death. There is only one kind of death; the differences lie in how the state is reached and how it can be recognized (Fig. 17.11.1). The diagnosis of death by somatic criteria Somatic criteria for the diagnosis of death are primarily used by emergency medical staff to recognize circumstances in which attempts at resuscitation should not be made. They represent a list of conditions which are unequivocally associated with death and require no further investigation or assessment (Box 17.11.1). The diagnosis of death by circulatory criteria Although clinicians across the world have for many years used circulatory criteria to diagnose death, very often this has been in the absence of any clear professional guidance on how the diagnosis should be made. When practised in this way, the safety of the circulatory standard for the determination of death has depended, more or less explicitly, upon allowing sufficient time to elapse to ensure 17.11 Diagnosis of death and organ donation Paul Murphy

17.11 Diagnosis of death and organ donation 3919 that circulatory arrest is permanent and has resulted in irreversible anoxic brain damage. However, the possibility of successful transplantation using organs retrieved from patients whose death follows circulatory arrest, which requires organs to be retrieved as soon as possible after death, has required the schedules for the diagnosis of death by circulatory criteria to be completely reviewed. The overarching definition of death is based upon permanent loss of the capacity for consciousness and respiration, both of which are functions of the brain. A robust time-critical schedule for the diagnosis of death using circulatory criteria requires clarity over the relationship between the loss of circulation and the failure of brain function as well as the factors that determine the permanence of such changes. It must also be able to accommodate the very different circumstances in how death occurs and whether continued resuscitation is appropriate. The key dynamic relationships between loss of circulatory and brain function are shown in Fig. 17.11.2. Although brain function is lost within seconds of circulatory arrest, it is possible that some brain activity could return were cerebral perfusion to be restored within the minutes that follow asystole. It follows that the permanence of loss of brain function is dependent upon whether resuscitation is to be attempted or whether there remains a possibility for myocardial function to return spontaneously. Within the context of abandoned cardiopulmonary resuscitation, the longest period of continuously monitored asystole that has been followed by spontaneous return of the circulation (the Lazarus phenomenon) is seven minutes. In contrast, when asystole follows withdrawal of life-sustaining treatments from intensive care (ICU), this interval is just 65 seconds. Although it is important to recognize the need to always confirm the absence of both neurological and circulatory function, there will be many occasions on which clinicians can continue to adopt a cautious approach to the diagnosis of death—for example, when donation is not a possibility or when minimal monitoring is available. However, a more robust approach is required when organ retrieval is planned, with the key elements of such a time-critical schedule for the diagnosis of death using circulatory criteria being listed in Table

17.11.1. They emphasize the need for explicit clarity that resuscitation should not be instigated or continued, how the absence of the circulation should be identified, and the minimum period of observation that is required to be assured that the possibility of spontaneous return of the circulation has passed. They also benefit from a clear requirement for the absence of consciousness and respiratory effort to be demonstrated, thereby providing a Neurological criteria Somatic criteria Circulatory criteria Permanent loss of the capacity for consciousness Permanent loss of the capacity to breathe Death Fig. 17.11.1 A unifying medical concept of death. Death is regarded as the permanent loss of the capacity for consciousness and respiration, both of which are functions of the brain-stem. The criteria best suited to diagnose death are determined by how it has occurred. Box 17.11.1 Recognition of life extinct The following conditions are unequivocally associated with death in all age groups 1 Massive cranial and cerebral destruction 2 Massive truncal injury that is incompatible with life, including traumatic hemicorporectomy and decapitation 3 Decomposition/putrefaction 4 Incineration (charring involving >95% of body surface) 5 Post-mortem hypostasis (purple discolouration of the dependent areas of the body that is the result of gravitational pooling of deoxygenated blood) 6 Rigor mortis In the newborn, fetal maceration is also a contraindication to resuscitation. Circulatory arrest Circulation Brain Latest recorded return of circulatory function following treatment withdrawal Latest recorded return of circulatory function following abandoned CPR Complete loss of brain function; isoelectric EEG Limit for successful restoration of normal cerebral function in laboratory animals Limit for successful restoration of any brain activity Limit for successful restoration of cardiac activity (e.g. after transplantation) hours 60 min 15 sec 11 min 65 sec 7 min Fig. 17.11.2 Dynamic relationships between loss of circulatory and brain function (not to scale). Laboratory evidence suggests that full neurological function may be restored in experimental animals after up to 11 minutes of continuous normothermic circulatory arrest. However, it is not clear how this relates to clinical circumstances, particularly those where anoxia is superimposed upon pre-existing brain injury.

Section 17 Critical care medicine 3920 direct link between loss of circulatory function and the emergence of the essential features of death. The diagnosis of death by neurological criteria Although circulatory collapse usually precedes failure of cerebral perfusion and loss of brain function, it has been known for many years that this pathophysiological sequence may be reversed when death is the result of acute intracranial pathology. While emergency ventilatory support may prevent the progression from brain-stem ischaemia to hypoxic cardiac arrest, the patient may nevertheless still display the essential features of death, namely the permanent loss of the capacity for consciousness and respiration (Fig. 17.11.3). The emergence of this state, popularly referred to as brain death, is an inevitable consequence of the development of mechanical ventilation and related critical care services. Most countries have well defined and professionally accepted schedules for the diagnosis of death using neurological criteria. There are variations in both how the diagnosis is required to be made, and also the state they seek to confirm. Thus, while the schedules for some countries seek to establish a state of 'whole brain' death (e.g. Australia, United States, mainland Europe), other criteria are based upon the view that permanent loss of function of the brain-stem is sufficient to indicate death (e.g. United Kingdom, Canada). Regardless of these differences, there are more similarities than differences between these various protocols. Although clinicians must always take a cautious approach to the neurological determination of death, particularly when excluding reversible causes of coma and Table 17.11.1 Key elements to the time-critical diagnosis of death using circulatory criteria Decision not to attempt resuscitation The clinical circumstances may be such that the decision not

to attempt or continue resuscitation is straightforward. However, caution should be exhibited in the presence of potentially reversible systemic causes of cardiorespiratory arrest such as hypothermia, severe biochemical abnormalities, and so on. Reliable identification of circulatory arrest Aystole is the absence of mechanical cardiac function, not electrical activity. When clinicians are seeking to confirm death as expeditiously as possible, asystole is best identified by echocardiography or intra-arterial pressure monitoring rather than by continuous ECG monitoring. Digital palpation of a central pulse is unreliable in such circumstances. Minimum period of observation to confirm continuous asystole, apnoea, and unconsciousness Brain function is lost within seconds of asystole. Providing that resuscitation is not being considered, the permanence of this state is determined by the possibility of spontaneous return of the circulation having passed. If asystole follows withdrawal of life-sustaining therapies in an ICU this period may be as short as 65 seconds, although in practice protocols require a somewhat longer period of observation. This ranges from 2 minutes in some institutions in Australia and the United States, 5 minutes in Canada and the United Kingdom, and 20 minutes in Italy. Should there be any return of circulatory or respiratory function during this period of observation then the period should be halted and re-started only when asystole returns. Demonstration of the lack of capacity for consciousness and respiration It is mandatory for the period of observation to be followed by a formal neurological examination that confirms unconsciousness and loss of brain-stem function. In addition to observing continuous apnoea, the UK Code of Practice also requires the demonstration of absent papillary response to light, absent corneal reflex, and absent motor response to supraorbital pressure. Prohibition of post-mortem interventions that might restore cerebral perfusion Any intervention that might re-establish cerebral perfusion would invalidate the diagnosis of death while the brain would remain responsive to its restoration. ECG, electrocardiogram; EEG, electroencephalogram. Myocardial infarction absent pulse & heart sounds absent pulse & heart sounds fixed & dilated pupils; coma fixed & dilated pupils; coma absent breath sounds absent breath sounds Cardiovascular collapse Brain(stem) ischaemia Brain(stem) ischaemia Brain(stem) ischaemia Respiratory arrest Respiratory arrest Respiratory arrest Cardiac arrest Cardiac arrest Death determined using circulatory criteria Death determined using neurological criteria Intracranial catastrophe Intracranial catastrophe Fig. 17.11.3 Death determined using neurological criteria. Death from a massive acute coronary syndrome is the result of circulatory collapse that leads to brain failure. In comparison, an untreated and rapidly progressive intracranial pathology causes apnoea and unconsciousness through direct compression of the brain-stem, with hypoxic cardiac arrest and circulatory collapse being secondary to this. Although interruption of the later process may halt the progression from brain-stem ischaemia to cardiac arrest, the essential features of death—permanent loss of the capacity to breathe and the capacity for consciousness—may nevertheless emerge. What results is a patient who displays the essential features of death but who has a persistent circulation while ventilatory support is maintained.

17.11 Diagnosis of death and organ donation 3921 apnoea, the clinical literature confirms the neurological standard for the determination of death to be safe. The key stages for the diagnosis of death using neurological criteria are shown in Table 17.11.2, and the causes of brain-stem death in Table 17.11.3. Deceased organ donation Organ transplantation saves and transforms lives and, for kidney transplantation at least, represents the most cost effective treatment for end-stage organ failure. Although living donation programmes make important contributions to kidney and liver transplantation, deceased donation remains the mainstay of many transplantation programmes. The 'standard' model for deceased donation in many countries is donation after brain

death (DBD). However, improved road safety and more effective treatments for subarachnoid haemorrhage, ischaemic stroke, and traumatic brain injury are reducing the pool of potential DBD donors. As a result, many countries are now turning to donation after circulatory death (DCD) to increase donor numbers and improve access to transplantation. Details of the various types of deceased donation are given in Table 17.11.4. The healthcare services of nearly 100 countries around the world support organ transplantation, although rates of deceased donation vary widely (Fig. 17.11.4). The World Health Organization has called upon all such countries to work towards self-sufficiency in organ transplantation. Key to self-sufficiency is not only public support for donation (which is reflected in a country's consent rate), but also a systematic approach to the identification and referral of potential donors whenever and wherever organ retrieval is a possibility. These hospital processes need to be supported by adequate education and training, audit and governance, and operate within nationally agreed frameworks of practice. Such an approach has recently resulted in a 63% increase in deceased donation in the United Kingdom, with a corresponding increase in transplantation and reduction in transplant waiting lists (Fig. 17.11.5). It is noteworthy that this was achieved without any increase in family consent rates.

Table 17.11.2 The four key stages for the diagnosis of death using neurological criteria (based upon the UK Code for the diagnosis and confirmation of death using neurological criteria)

1. Satisfying essential preconditions Patients must:
 - be deeply unconscious (Glasgow Coma Score 3), mechanically ventilated and exhibit no sign of brain-stem reflex activity, including respiration.
 - have suffered a structural brain injury that is irremediable and a recognized cause of brain-stem death. This stage is designed to identify patients who should be considered to be possibly brain-stem dead.
 2. Exclusion of reversible causes of coma and apnoea This stage is designed to exclude potentially reversible causes/contributions to coma and apnoea, including:
 - cardiorespiratory instability
 - hypothermia
 - profound endocrine, biochemical, and metabolic disorders
 - sedative drugs and muscle relaxants
 - high cervical spinal cord injury
 3. Clinical demonstration of the absence of brain-stem function
 - a. Brain-stem reflexes
 - b. Apnoea test
 - a. The following reflexes are examined:
 - pupillary light reflex
 - corneal reflex
 - peripheral and central response to deep supraorbital pressure
 - vestibulo-ocular reflex
 - gag reflex
 - tracheal reflex
 - b. apnoea test The patient is disconnected from the mechanical ventilator and observed continuously for signs of respiratory effort. The period of observation should be a minimum of 5 minutes, during which time a respiratory acidosis sufficient to stimulate respiration should be confirmed.
 4. Ancillary/confirmatory tests A variety of additional investigations are used around the world to consolidate the clinical diagnosis. They include assessments of cerebral function such as EEG and evoked potentials and measurements of cerebral perfusion and blood flow such as transcranial Doppler, radio-isotope perfusion scanning, and cerebral angiography. Although mandatory in some countries, they are only used in the United Kingdom when the clinical diagnosis is in doubt. Additional notes: The UK Code requires the tests to be performed by two experienced doctors, one of whom must be a Consultant. The tests can only be performed when the clinicians are satisfied that the various conditions in stages 1 and 2 have been met. Although two sets of tests must be completed, the time of death is that of completion of the first set of tests.
- Table 17.11.3 Common causes of brain-stem death in the United Kingdom, 2014–2015: note that trauma

as a cause of brain-stem death has more than halved in the last two decades Cause of death Incidence (%) Spontaneous intracranial haemorrhage 54.0 Hypoxic ischaemic encephalopathy 24.7 Ischaemic cerebrovascular accident 6.1 Trauma 6.2 Meningitis 2.4 Brain tumour 1.5 Other 5.1

Section 17 Critical care medicine 3922 Spain Croatia Malta Belgium Portugal USA France Austria Estonia Slovenia Italy Norway UK Czech Rep. Ireland Uruguay Belarus Finland Latvia Australia Lithuania Sweden Canada Hungary Poland Netherlands Luxembourg Switzerland Argentina Brazil Iceland Slovak Rep. Germany Denmark Israel Iran South Korea New Zealand Cyprus Colombia Romania Chile Panama Hong Kong Greece Turkey Costa Rica Ecuador Paraguay Venezuela Mexico Kuwait Peru Bulgaria Russia Saudi Arabia Trinidad & Tob. Lebanon Dom. Rep. Japan Malaysia 0 5 10 15 20 Donors per million population, 2013 25 30 35 40 Fig. 17.11.4 Worldwide rates of deceased donation, 2013 (expressed as donors per million population).

17.11 Diagnosis of death and organ donation 3923 Table 17.11.4 Models of deceased donation

Type	Description	Notes
Donation after brain death (DBD)	Organ retrieval from patients whose death is confirmed using neurological criteria. Donation is considered after death has been confirmed.	<ul style="list-style-type: none"> Established form of donation in many countries. Supports the retrieval of kidneys, liver, small bowel, pancreas, heart and lung, as well as composite allografts such as facial tissue and limbs. Physiological optimization of the heart beating donor after the diagnosis of death may increase both the number and quality of organs that are retrieved. Minimal warm ischaemic injury to transplantable organs because the circulation is maintained during organ retrieval until the point of cold perfusion. Pool of potential DBD donors is decreasing in many countries.
Donation after circulatory death (DCD)—controlled	Organ retrieval from patients whose death follows planned withdrawal of 'futile' life-sustaining treatments in an ICU. Donation considered after the decision to withdraw life-sustaining treatments but before death is confirmed using circulatory criteria.	<ul style="list-style-type: none"> Extends the option of donation to another group of dying patients but has important implications for their end-of-life care. Organ retrieval must begin within minutes of the onset of irreversible asystole. Retrieval teams may be 'stood down' if the patient does not die within a predetermined time after treatment withdrawal (typically 1–4 hours). Although it is possible to successfully transplant both abdominal and cardiothoracic organs from controlled DCD donors, worries over warm ischaemic injury limit the number of organs that are retrieved. Long-term outcomes for DCD kidney grafts match those from DBD donors, although there is a higher incidence of delayed graft function. Outcomes for DCD liver grafts are inferior, but nevertheless superior to remaining on a transplant waiting list. Controlled DCD is well established in Australia, Belgium, Canada, the Netherlands, United States, and the United Kingdom. There may be professional, ethical, and legal obstacles to introducing this type of donation in other countries.
Donation after circulatory death—uncontrolled	Organ retrieval from patients whose death follows an unexpected circulatory arrest. Donation is considered after death has been confirmed using circulatory criteria.	<ul style="list-style-type: none"> Donation from Emergency Medicine Departments rather than an ICU. Cardiopulmonary resuscitation is used to maintain perfusion of the transplantable organs until they are perfused with cooled preservation solution of oxygenated blood using aortic and caval cannulae introduced via the femoral vessels. Supports kidney and liver transplantation. Established in parts of mainland Europe and United States.

Number 2396 2003–04 2004–05 2005–06 2006–07 2007–08 2008–09 2009–10 2010–11 2011–12 2012–13 2013–14 770 751 764 793 809 899 959 1010 1088 1212 1320 2241 2196 2385 2381 2552 2645 2695 2912 3112 3514

8000 7000 6000 5000 4000 3000 2000 1000 0 5673 6142 6698 7219 7655 7877 7800 7636 7288
7026 7997 Donors Transplants Transplant list Fig. 17.11.5 Deceased donors, organ transplants, and
transplant waiting list in the United Kingdom, 2003-2014. It is noteworthy that the increase in
donor numbers from 2007 to 2008 onwards were achieved without any increase in the family
consent rates for donation and were the result of improved rates of donor identification and referral
and expansion of DCD transplant programmes.

Section 17 Critical care medicine 3924 FURTHER READING Academy of Medical Royal Colleges
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