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Editorial

Brain Death

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Mechanical ventilation frequently saves lives that are threatened by temporary respiratory failure; but when breathing stops due to irreversible brain damage ventilation only prolongs the process of dying, as organs serially cease to function. The possibility of extending from a few minutes to many days the interval between final failure of the brain and ultimate cardiac asystole emphasises that death is not an event, but a process.

History of Brain Death

The increasing use of ventilators for resuscitation in the mid-1950s inevitably led to the occurrence of brain death in some cases, and it was first formally described (as coma dépassé) in 1959 [11]. Ten years later the first set of diagnostic criteria were published by an Ad hoc Committee of the Harvard Medical School, which included lawyers and theologians and which also made it clear that once the brain was dead the person should be regarded as dead [19]. In many places this concept has led to the enactment of brain death laws, and it follows that the legal time of death is when brain death is diagnosed, not some later time when the heart stops. To discontinue ventilation in such circumstances is not therefore allowing someone to die, it is stopping doing something useless to a person who is already dead. Indeed to continue to ventilate such a corpse is to deprive that patient of death with dignity, and to prolong the distress of his relatives; it also misappropriates intensive care resources that should properly be freed for patients whose survival could depend on them.

Changing Concepts and Diagnostic Criteria

The original Harvard document on brain death presupposed that the entire central nervous system had to be dead – cortex, spinal cord and brain stem. It followed that diagnosis required absence of all reflex motor activity and that a flat (isoelectric) EEG was recommended. It soon became evident, however, that the crucial element of brain death was permanent cessation of function in the *brain stem*, because once this occurred the heart always stopped functioning in a matter of one or two weeks even when ventilatory and other support was maintained. This empirical observation has now been recorded in hundreds of published cases from many countries, and diagnostic criteria have therefore been adjusted to focus on brain stem function.

The first consequence of this was the recognition that spinal reflex activity in the limbs could persist long after the brain stem had ceased to function: most current sets of criteria specify that brain death can be diagnosed in the presence of such movements. It has also become evident that residual electrical activity sometimes persists in parts of the cortex for some time after brain stem death, and that patients with a dead brain stem whose cortical EEG still shows some activity develop cardiac asystole just as certainly as do those with a flat EEG [6]. This had led to progressively less emphasis on the EEG as a necessary component of the diagnosis of brain death in many countries. The criteria published in 1976 by the Conference of Medical Royal Colleges in the UK were able to take account of 20 years experience of brain death [2, 3]. These put great emphasis on distinguishing between pre-conditions and tests, and they dealt in detail with the most crucial test – that for apnoea. They also stated explicitly that the EEG was not necessary for diagnosis.

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Situations Leading to Brain Death

Most often brain death results from unsuccessful resuscitation after an acute intracranial insult; head injury accounts for half the cases in Britain and intracranial haemorrhage for almost a third [6, 7]. Cardiac arrest or profound hypotension contribute some cases and a few are due to less sudden events such as meningo-encephalitis, brain tumour or intracranial abscess. Sometimes the patient becomes apnoeic very soon after arrival at the hospital; in these circumstances, especially after head injury, extracranial factors that can depress brain function have to be considered; these include alcohol and other drugs, hypotension, and hypoxia. In other cases apnoea develops in patients who are already in hospital, due to secondary complications from head injury, or after prolonged treatment of a progressive condition, or when recurrent subarachnoid haemorrhage occurs from an aneurysm that has been diagnosed by angiography. In all of these circumstances the cause of the brain damage is not in doubt and confusing factors are not a problem. The frequency of brain death and its distribution between different hospitals and specialities depends on local policies for the care of acutely brain damaged patients and on current practice in their management (e.g. what proportion are put on ventilators). In Britain, as in most of Europe, transfer of patients to regional neuro-units is selective, favouring patients likely to benefit from the special facilities which such units provide. Consequently three quarters of the estimated 4,000 brain deaths in Britain each year occur outside of such special units [7].

Diagnostic Criteria

The *pre-conditions* require that the patient be in apnoeic coma from irremediable brain damage; this implies that reversible causes of brain stem depression have been excluded. Hypothermia and gross metabolic imbalance are readily detected; a nerve stimulator will confirm that relaxant drugs are no longer active; alcohol levels are easily measured, but it is less easy to be certain of the influence of depressant drugs – especially if several have been taken.

The *tests* for brain stem function consist of attempting to evoke reflex responses (corneal, pupillary, gag, vestibulo-ocular). The final test is to disconnect the patient from the ventilator whilst maintaining diffusion oxygenation through a tracheal catheter. Disconnection must allow an adequate rise to stimulate respiratory activity, taking account of the starting $PaCO_2$ and the reduced rate of CO_2 production in these patients – relationships that have been worked out from observations on series of such patients [20, 21].

Confirmatory laboratory tests, of cerebral circulation or of electrical activity of the brain, are still used by some doctors in some countries [6]. The equipment and expertise required for isotope or radiographic investigations are limited in availability, whilst angiography carries some risk; even in the hands of enthusiasts there are technical failures and difficulties in interpretation in some circumstances. For these various reasons it is generally agreed that it is not only impractical but it is unwise to require such investigations, quite apart from the argument that they are unnecessary.

EEG is much more widely available and in several places it has come to be regarded as a recommended, if not required, component of the criteria for the diagnosis of brain death. Within a year of the publication of the Harvard criteria there were clear statements from Boston that an iso-electric EEG was not needed for diagnosis [1, 22]; neurosurgeons from Minnesota were even more emphatic in 1971 and they have recently re-asserted their confidence in clinical criteria alone [10, 4]. Some of those who still use EEG admit that they do so for reasons of public relations rather than because they consider it medically necessary [18]. There are three reasons why EEG is now used less and less. It is irrelevant because it assesses function in the cortex not in the brain stem. It is unnecessary because it has been shown that persistent EEG activity after clinical brain stem death does not alter the prognosis [13]. And it is unreliable – both because of technical problems associated with recording in the electronically hostile environment of the intensive care unit, and because patients with recoverable coma can have an iso-electric EEG. These various points have been argued in detail by British clinical neurophysiologists [9, 14, 15, 17].

Safeguards

Occasional reports of recovery after suspicion of brain death usually prove to be due to failure to satisfy the pre-conditions rather than to inadequate testing of brain stem function. Sometimes relatives misinterpret a near-hopeless prognosis as a declaration of brain death: naturally some such patients respond to resuscitation. Other states resulting from severe brain damage, such as vegetative state or the locked-in syndrome, may lead inexperienced staff to consider the possibility of brain death, but this would be excluded as soon as formal criteria were applied [5]. Journalistic efforts to find patients in the UK or USA who had recovered after being declared brain dead reached a peak with two BBC television programmes in the winter 1980/81 [8, 5, 12], based on incidents that occurred many years ago in America.

The considerable subsequent correspondence failed to reveal any adequately documented case of mistaken diagnosis by recognized clinical criteria, and the only doctor claiming to know of such cases in Britain had to publish an unreserved retraction [16]. What did emerge was how extensively the clinical criteria had been put to the test over the years, in that ventilation had been maintained in many cases after the diagnosis of brain death until the heart stopped [6, 8, 13].

There was some evidence during this controversy that some of the supposed doubts about the reliability of brain death criteria really reflected reservations about organ transplantation. It was unfortunate that fortuitously organ transplantation and brain death developed in the same decade, because it made plausible the innuendo that brain death had been invented to facilitate the supply of organs for transplantation. But it was long after cadavers replaced live donors as the main source of organs that brain dead patients (on ventilators) become almost the only donors that transplant surgeons were willing to consider [5]. With a brain dead donor the haste and hurry is taken out of the situation, making organ removal more acceptable both to the donor's family and to his doctors and nurses, whilst the transplant surgeon has time to make arrangements so that he receives organs in the best possible condition. But if alternatives to transplantation were to be developed there would still be thousands of brain dead patients every year about whom decisions would have to be made as to when to discontinue ventilation.

The best safeguard against mistaken suspicion of brain death is a well-written set of guidelines that are applied by medical and nursing staff who are confident about the technicalities and who are also familiar with how to deal sympathetically with the relatives of brain dead persons. The diagnosis should involve two doctors whose discipline is less important than their experience and seniority; their experience is needed chiefly in assessing the pre-conditions, because the brain stem tests are quite simple to do, and their interpretation is likewise easy. It is helpful to have a standardised sheet on which the data leading to the diagnosis is recorded by the two doctors; this can act both as an aide memoire for the staff and as a permanent record in the patient's case notes.

An important safeguard is to ensure that sufficient time elapses for the preconditions to be satisfied before the brain stem tests are carried out. This could be as little as six hours, for example when apnoea develops in a patient already in hospital because there are no diagnostic difficulties, but when the cause of brain stem depression has been hypoxia at least 24 h should elapse; in cases of diagnostic doubt this should extend to 48 h or even longer [5].

Conclusions

Brain death is now a part of life in acute hospitals in technologically developed countries. Good medical practice demands that doctors in intensive care units become proficient in its diagnosis, and compassion requires that they then take appropriate action. Whatever methods are used the decision that the patient is dead has to be made by doctors at the bedside, weighing all the evidence. Published criteria provide only guidelines, as both British and American authorities responsible for them have stressed. The doctor must decide what investigations are appropriate in given circumstances, and also how long to wait before carrying out brain stem tests.

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