ABC of Brain Stem Death

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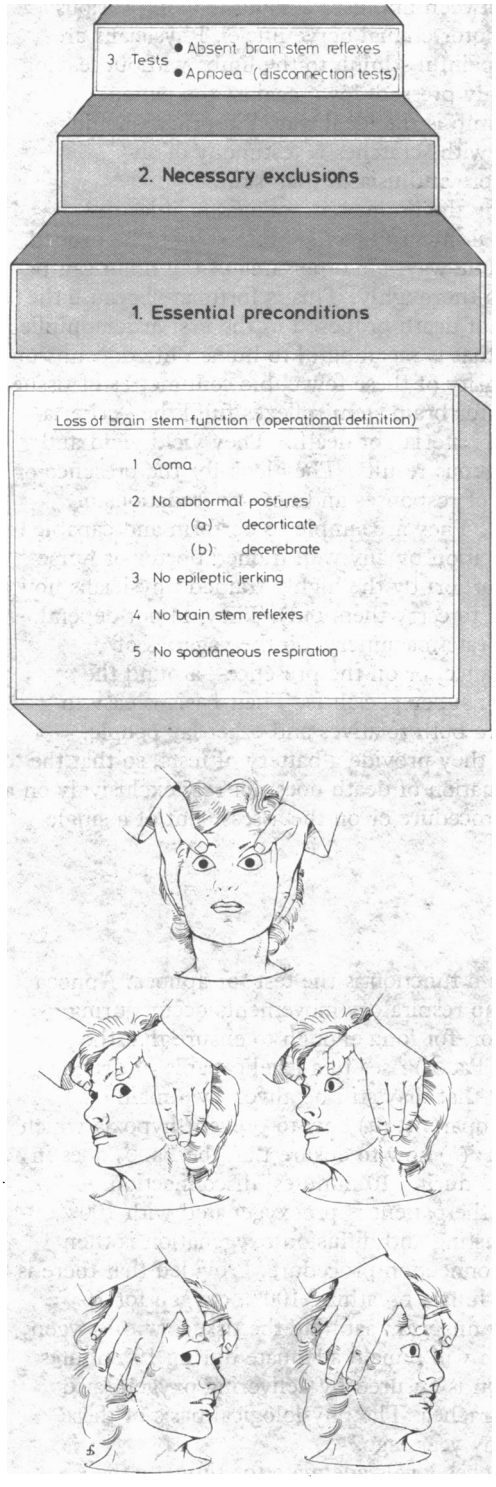
DIAGNOSIS OF BRAIN STEM DEATH—II

Tests



The tests necessary to show that the brain stem is not functioning take only a few minutes to carry out. They centre on proving that the brain stem reflexes have been lost and on scrupulous confirmation of persistent apnoea. If the preconditions for testing have been strictly adhered to, and if reversible causes of brain stem dysfunction (such as hypothermia, drug intoxication, or metabolic disturbance) have been excluded, the demonstration that the brain stem is not functioning is equivalent to asserting that the loss of function is irreversible—that the brain stem is dead.

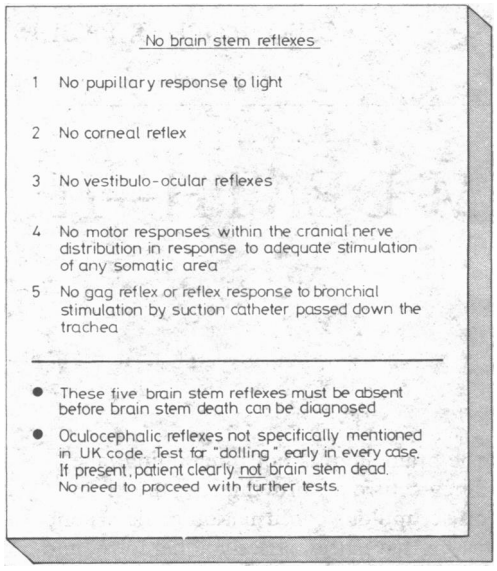
As the physician approaches the bed he may notice signs which will immediately warn him that the patient's brain stem cannot possibly be dead—and that testing for brain stem death is therefore inappropriate. These signs will always be associated with retention of one or more of the brain stem reflexes, but detecting obviously relevant clues before formal testing is embarked on will prevent the physician wasting time.

A *seizure*, generalised or focal, implies the passage of nervous impulses through the brain stem and therefore proves that this part of the nervous system is still viable.

Abnormal postures—either "decorticate" (with flexed forearms and extended legs) or "decerebrate" (with extended and hyperpronated forearms and extended legs)—likewise imply live neurones in the brain stem. Trismus has much the same importance.

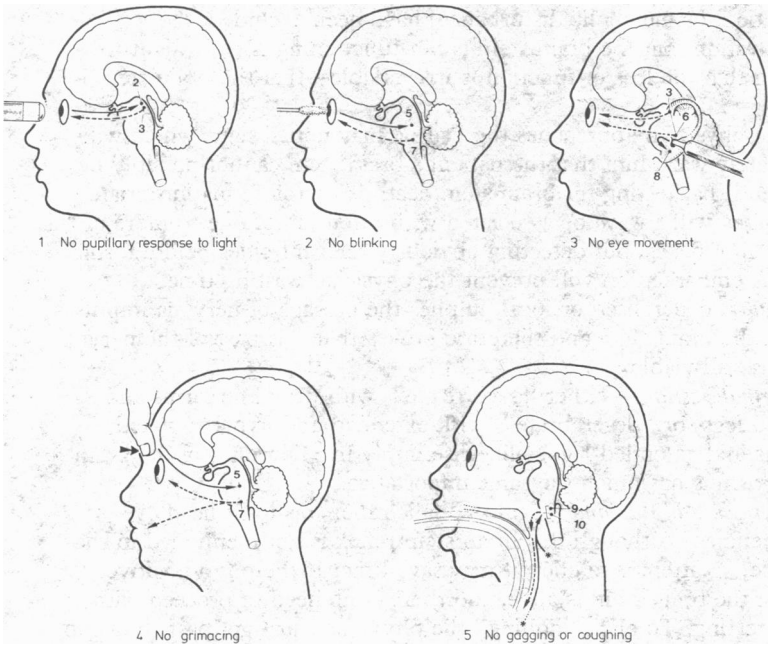
The presence of "dolling" (oculocephalic reflex, or doll's head eye phenomenon)—Although this brain stem reflex is not mentioned in the UK code, an attempt to elicit it may save time. If there is a positive response the brain stem is alive, and there is no need to proceed with further testing. To elicit "dolling" the physician must get past the various "lines" to the top of the bed and insert himself between the wall and the patient's head. He then holds the patient's head between his hands and gently raises the lids with his thumbs. The head is then rotated first to one side (and kept there for three or four seconds, while a close watch is kept on what happens to the eyes) and then, through 180°, right over in the opposite direction. (The test should not, of course, be done if there is any suspicion of cervical fracture, as there will be in some patients after recent trauma.) In a fully alert individual the eyes will, within a fraction of a second, orient with the head. In the cadaver the head and eyes will likewise move together. (In practice, there is no difficulty in distinguishing these two states.) If the patient has damaged cerebral hemispheres and a lively brain stem the latter may show certain "release" phenomena. There will, for a second or two, be quite obvious deviation of the eyes to the opposite side, as the head is rotated, followed by a prompt realignment of the eyes with the head. A similar dissociation will also occur when the head is then turned in the other direction. During each rotation the eyes are, for a short while, "out of phase" with the head. In the context of suspected brain death it is easier to perform the test properly if the patient is disconnected from the respirator for 20-30 seconds.

The brain stem reflexes



Five brain stem reflexes should then be tested systematically. There are certain basic requirements: a bright light for the pupillary responses, a strong stimulus for the corneal reflexes, and a clear external auditory canal for caloric testing. The loss of response to stimulation as suction catheters are passed through the larynx and trachea will usually first have been detected by the nursing staff but should be confirmed in the presence of the examining physician.

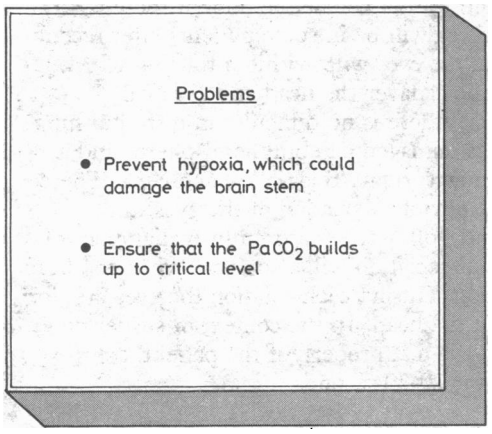
The prescription that there should be "no motor response within the cranial nerve distribution" on "adequate stimulation of any somatic area" means, in practice, that there should be no grimacing in response to painful stimuli applied either to the trigeminal fields (firm supraorbital pressure) or to the limbs. Such grimacing implies that contact has been established in the brain stem between impulses coming in along various sensory pathways and cells in motor cranial nerve nuclei. Physicians are often unaware of how to apply painful stimuli to the limbs without leaving marks. The side of a pencil firmly pressed down against the patient's fingernail by the examiner's thumb is the ideal way. Pin pricks should never be used. A body covered with scratches is testimony of an examination carried out with more enthusiasm than skill.



Testing the brain stem reflexes enables the functional integrity of the brain stem to be probed in a unique way. No other area of the brain can be tested so thoroughly. This is fortunate because the concept of death proposed in the first article implies that all that is meaningful to human life depends on the integrity of these few cubic centimetres of tissue.

Tests for brain stem reflexes fulfil the "criteria for good criteria" of death.[1] They yield vivid and unambiguous results. They look for the presence or absence of responses and not for gradations of function. They are simple to perform and capable of interpretation by any well trained doctor or nurse (and a fortiori by the highly trained physicians now required to carry them out). They do not depend on elaborate machinery, on the vagaries of maintenance, or on the presence—around the clock—of superspecialists. Their basis is easy to convey to both relatives and other lay people. Finally, they provide a battery of tests, so that the determination of death does not rely exclusively on a single procedure or on the assessment of a single function.

Testing for apnoea



The ultimate test of brain stem function is the test for apnoea. Apnoea is established by showing that no respiratory movements occur during disconnection from the ventilator, for long enough to ensure that the arterial carbon dioxide tension ($Paco_2$) rises to a level capable of driving any respiratory centre neurones that may still be alive. Two main problems will immediately be apparent: (*a*) how to prevent hypoxia which could of itself damage the brain; (*b*) how to ensure that the $Paco_2$ does in fact build up to the critical level during 10 minutes' disconnection.

Hypoxia can be prevented if the patient is preoxygenated with 100% oxygen for 10 minutes before testing and diffusion oxygenation is then maintained throughout the disconnection procedure. Provided that there is no gross diffusion defect in the lungs, breathing 100% oxygen for 10 minutes will wash out the body nitrogen, saturate the tissues with oxygen, and build up a high Pao_2, which will remain adequate during 10 minutes of apnoea. Diffusion oxygenation is ensured by delivering oxygen (at 6 l/min) by a catheter down the trachea. The physiological basis of these procedures was established many years ago.[2–4]

To ensure that the $Paco_2$ reaches levels adequate to stimulate the

Testing for apnoea

1 Preoxygenate with 100% oxygen for 10 minutes

2 Administer 5% CO_2 in 95% oxygen for a further 5 minutes to ensure starting $PaCO_2$ of 5·3 kPa (40 mmHg)

3 Disconnect. Insufflate trachea with 100% oxygen at 6 l/min through intratracheal catheter passed to carina

4 Maintain disconnection for 10 minutes If possible check final $PaCO_2$

Recent physiological data in brain dead subjects

	Milhaud *et al*[5]	Schafer and Caronna[6]	Ropper *et al*[7]
Year	1978	1978	1981
Tests	22	7	51
Mean rise in $PaCO_2$ on disconnection (kPa/min)	0·36	0·43±0·05	0·34±0·11
Mean fall in apH (units/min)	0·018	0·024	0·020
Mean apH/$PaCO_2$ change	–	–	0·02±0·01/min
CO_2 production per kg	–	–	1·84±0·23 (ml/min/kg)
CO_2 production v $PaCO_2$ rise	–	–	r=0·58
Initial apH v $PaCO_2$ rise	–	–	r=-0·40
Initial apH v apH drop	–	–	r=-0·49

Retesting

Retesting

	EEG Clinical	EEG Angiogram	Interval	EEG Clinical	EEG Angiogram
Harvard, 1968	+	+	– 24h	+	+ –
Minnesota, 1971	+	–	– 12h	+	– –
Japan, 1973	+	+	– 6h	+	+ –
ACS, 1977	+	+	– 30min	+	+ –
Ingvar and Widén (Sweden, 1972)	+	+	+ 25min	–	– +
UK Code, 1976 (retesting "customary")	+	–	– Up to 24h (depends on primary pathology)	+	– –

respiratory centre during 10 minutes off the ventilator the patient must not be hypocapnic at the time of disconnection. Patients in intensive care units tend to be overventilated. They may run continuous $Paco_2$ levels well below 4 kPa (30 mm Hg). There are two ways of overcoming this hypocapnoea: by slowing the rate of the ventilator, or having the patient breathe 5% CO_2 in 95% oxygen for five minutes before disconnection. This will raise the $Paco_2$ to at least 5·3 kPa (40 mm Hg).

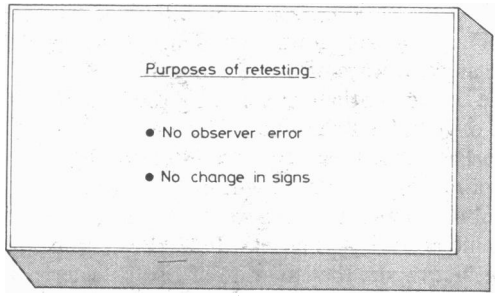
During the 10 minutes of disconnection the $Paco_2$ will increase still further. The rise is slow in immobile, moderately hypothermic patients who often have depressed metabolic rates, but is at least 0·27 kPa (2 mm Hg) per minute. Most authors in fact report that the rate of rise is faster than this.[5–7] Ten minutes' disconnection will raise the $Paco_2$ by at least another 2·7 kPa (20 mm Hg). A $Paco_2$ of 8·0 kPa (60 mm Hg) will have been reached, which is more than enough to drive a respiratory centre capable of responding to a hypercarbic stimulus. When the $Paco_2$ can be estimated (at the end of the period of disconnection) the actual level reached should be recorded.

The UK code recommends that during disconnection the $Paco_2$ should rise to at least 6·65 kPa (50 mm Hg) before the patient is deemed is incapable of breathing. A recent study has re-emphasised that this is an adequate level.[7] The continuous administration of 5% CO_2 for a few minutes before disconnection will in fact ensure that the $Paco_2$, at the end of disconnection, will have risen to at least 8·0 kPa (60 mm Hg). The administration of 5% CO_2 in oxygen for a few minutes before disconnection is strongly recommended when there are no facilities for blood gas analysis.

The test for apnoea may be the most critical of all tests of brain stem function. Testing for apnoea without ensuring an appropriate rise in $Paco_2$ has been likened to "testing the pupils without a battery in the torch."[8] Some patients in coma due to structural brain damage may have lost all their brain stem reflexes, yet may (for a short while) retain their capacity to take a few spontaneous breaths when suitably stimulated.[6] So long as this capacity persists the brain stem cannot be said to be dead. This should lead one to question some of the conclusions drawn from studies which were not scrupulous (or constant) in their definition of apnoea—for instance, work defining apnoea as the patient making "no effort to override the respirator"[9] or leaving the duration of disconnection "to the judgment of the attending physician."[10] It is even harder seriously to assess work which states that the operational concept of apnoea (in patients being tested to ascertain brain death) "does not in any way imply absent respiratory centre function."[10]

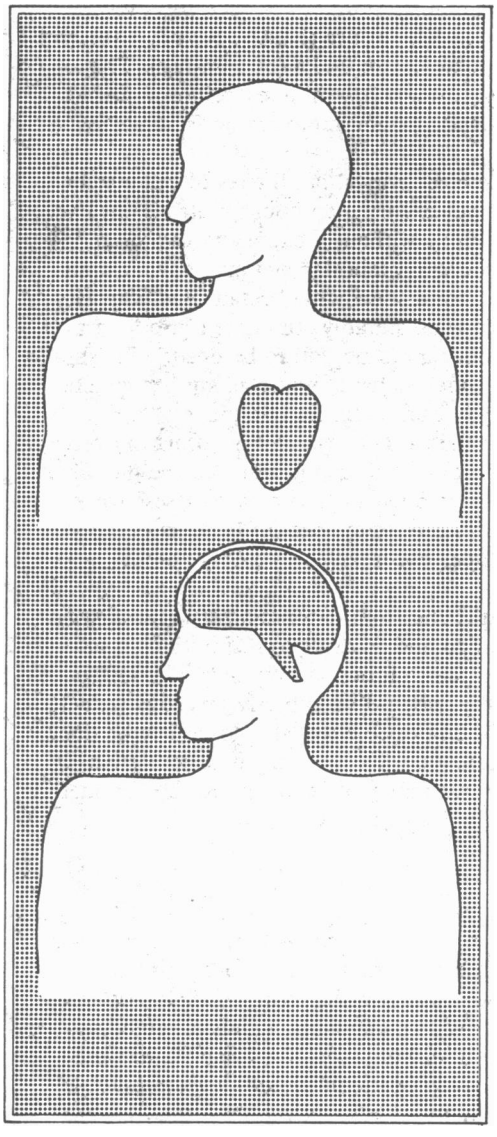
There remain a few patients suffering from chronic obstructive airways disease who may be dependent on an anoxic drive to respiration. It is difficult to assess their respiratory centre function properly. The UK code describes them as special cases who "should be expertly investigated with careful blood gas monitoring." When possible this should clearly be done, but it is probably a counsel of perfection, for on many occasions such facilities will not exist. Most such patients will probably not be considered for a diagnosis of brain stem death.

Virtually all codes urge that testing be carried out twice. The recommended intervals between the relevant tests have progressively shortened. There are several reasons why this has happened. Firstly, the objections to ventilating corpses have become more widely accepted. Secondly, when the first and second examinations for brain death were separated by as long as 24 hours several patients would develop asystole before the second examination. Finally, it became widely recognised that provided scrupulous attention was given to the preconditions and exclusions the second examination always confirmed the first. In other words, the more time spent in ascertaining the irremediable nature of the structural brain damage causing the coma the less important does the interval between tests become.



What is the purpose of retesting in a patient with a non-functioning brain stem due to well established, irremediable, structural brain damage? The UK code claims that it is to ensure that there has been no observer error. This is entirely praiseworthy, although no properly documented case has been published where the diagnosis of brain stem death has been revised after repeat testing. In my opinion retesting usually has a different purpose. It ensures that the non-functioning of the brain stem is not just a single observation at one point in time but that it has persisted. For how long? For a period several hundredfold that during which brain stem neurones could survive the total ischaemia of a non-perfused brain. At Hammersmith Hospital we like to separate our tests by two to three hours, which is more than enough to ensure that the findings are irreversible.

Brain stem death and cardiac death: one standard or two?



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Like the stopping of the heart in classical death the irreversible loss of brain stem function is ascertained by simple bedside tests. Their very simplicity seems to render them suspect in a technological age. This is not the case in relation to "cardiac" death. What is the rationality behind such a double standard?

A heart stops and its inability to function as a pump is diagnosed by an absent pulse, an unrecordable blood pressure, and the absence of audible contractions. McMichael has recently drawn attention to William Harvey's careful observations of what is happening as the hearts of many animals cease to beat.[9] "The ventricle ceases to beat before the auricles, so that the auricles may be said to outlive it. . . . With all other parts inactive and dead, the right auricle goes on beating, so that life appears to linger longest in this auricle." But knowledge of this electrophysiological fact (namely, that death of the heart as a whole may in normal individuals without heart disease precede death of the whole heart) has never really altered clinical practice. After clinical asystole has been present for several minutes few doctors would ask for an electrocardiogram to confirm that every part of the heart has really ceased to generate electrical signals. Still fewer would request that the trace be recorded at maximum amplification, using intracardiac probes. And strictly no one would suggest that the clinical findings be corroborated by non-perfusion on coronary angiography, or by biopsy evidence of necrosed cardiac muscle. Yet equivalent procedures have been suggested in relation to brain death.

If the context is known doctors have never objected to equating permanent loss of function with death. "To live is to function: that is all there is to living" Oliver Wendell Holmes said. The argument is about permanence more than about pathology. And here the evidence can only be empirical. The first patient to speak again after having shown unequivocal evidence of a dead brain stem will create as great a sensation as if the decapitated head of Louix XVI had started berating his executioners.

[1] Task Force on Death and Dying of the Institute of Society, Ethics and Life Sciences. Refinements in criteria for the determination of death: an appraisal. *JAMA* 1972;**221**:48-53.
[2] Enghoff H, Holmdahl MH, Risholm M. Diffusion respiration in man. *Nature* 1951;**168**:830.
[3] Frumin MJ, Epstein RM, Cohen G. Apnoeic oxygenation in man. *Anaesthesiol* 1959;**20**:789-98.
[4] Payne JP. Apnoeic oxygenation in anaesthetised man. *Acta Anaesth Scand* 1962;**6**:129-42.
[5] Milhaud A, Riboulot M, Gayet H. Disconnecting tests and oxygen uptake in the diagnosis of total brain death. *Ann NY Acad Sci* 1978;**315**:241-51.
[6] Schafer JA, Caronna JJ. Duration of apnoea needed to confirm brain death. *Neurology* 1978;**28**:661-6.
[7] Ropper AH, Kennedy SK, Russell L. Apnoea testing in the diagnosis of brain death. Clinical and physiological observations. *J Neurosurg* 1981;**55**:942-6.
[8] Whitwham JG. Brain death. *Lancet* 1980;ii:1142.
[9] Anonymous. An appraisal of the criteria of cerebral death. *JAMA* 1977;**237**:982-6.
[10] Bennett DR, Hughes JR, Korein J, *et al. Atlas of electroencephalography in coma and cerebral death*. New York: Raven Press, 1976.
[11] McMichael J. History of atrial fibrillation 1628-1819. *Br Heart J* 1982;**48**:193-7.