

ABC of Brain Stem Death

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REAPPRAISING DEATH

In view of the importance of and continuing interest in brain stem death and its criteria the "BMJ" has invited Dr Christopher Pallis to write (in a personal capacity) a series of articles on the subject. These nine articles are shortened versions of a fuller text that we will publish in book form at the beginning of next year. The articles concentrate on the more practical aspects of diagnosing brain stem death; the book explores the wider aspects, including some of the neurological controversies.

People have been alarmed for centuries at the prospect of being declared dead when they were still living. There was generalised anxiety about the subject 140 years ago, after Edgar Allan Poe had published various short stories, such as *Premature Burial*, in which people had been interred alive. Towards the end of the last century Count Karnice-Karnicki of Berlin patented a coffin of a particular type. If the "corpse" regained consciousness after burial he or she could summon help from the surface by a system of flags and bells. Recent controversies have revived this longstanding fear of premature or mistaken diagnosis of death.

The need to reappraise death

A dead brain in a body whose heart is still beating is one of the more macabre products of modern technology. During the past 30 years techniques have developed that can artificially maintain ventilation, circulation, and elimination of waste products of metabolism in a body whose brain has irreversibly ceased to function. Such cases begin to appear in all countries as their intensive care facilities reach a certain standard. What we do when confronted with such circumstances raises important questions. Brain death compels doctors (and society as a whole) to re-evaluate assumptions that go back for millennia.

Brain death was described as early as 1959.^{1 2} Renal transplantation was then in its infancy, whole-body irradiation being the only means of modifying the immune response. It is important to emphasise this, because some critics seem to believe that brain death was invented by neurologists to satisfy the demands of transplant surgeons. If transplantation were superseded tomorrow by better methods of treating end-stage renal failure brain dead patients would still be produced in large numbers in well run intensive care units in many parts of the world.

Over half a million people die each year in Great Britain. Whether at home or in hospital, they "die their own death." No machines are concerned. Their heart stops and that is the beginning and end of it. Epidemiological data suggest that brain death relates to perhaps 4000 deaths a year³—well under

1% of all deaths. These people have sustained acute, irreparable, structural brain damage, which has plunged them into the deepest coma. The brain damage includes permanent loss of the capacity to breathe. But prompt action by doctors has ensured that ventilation is taken over by a machine before the resulting anoxia can stop the heart.

These articles have three objectives: firstly, to emphasise that it is legitimate to equate brain death with death (this is now widely accepted in medical and legal circles throughout the world); secondly, to suggest that the necessary and sufficient component of brain death is death of the brain stem (this is less widely accepted, largely because it is a relatively new concept); and, thirdly, to emphasise that a dead brain stem can reliably be diagnosed at the bedside.

The acceptance of these ideas would lessen human distress, lead to more rational use of our limited intensive care facilities, and radically alter the life expectancy of thousands of patients with end-stage renal failure. It would also require that we change the words we use and start speaking systematically of *brain stem death*, if that is what we mean.

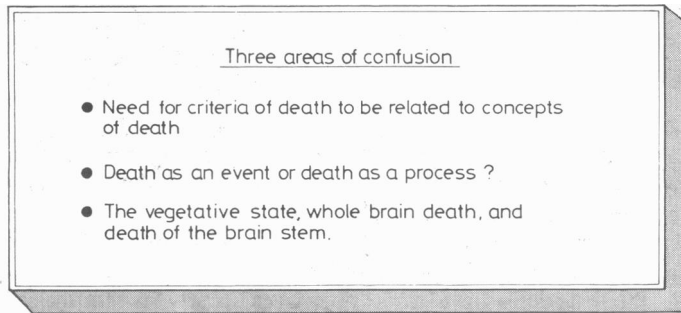
Why it is bad to ventilate corpses

- Distress to relatives
- Bad for morale of nursing staff
- Denial of limited facilities to those who might benefit from them
- The cost-effectiveness equation

On ventilating corpses

There are several reasons why it is bad to "ventilate a corpse" (to use the words of a Liverpool coroner a few years ago). The order of importance varies according to the cultural context in which one practises. I would emphasise the damaging effect on the morale of highly trained staff asked to clean the mouths or treat the pressure areas of patients who are already dead. When decisions were taken to "ventilate-to-asystole" (and we did this often in the limbo of the early 1970s) the plight of the relatives was pitiful: they became emotional hostages to uncomprehending machines. In countries where the next of kin were then asked to bear the cost of such "care" the situation was truly appalling.

Whereas the functions of the lungs and heart may be taken over by machines, those of the brain cannot. A person is therefore not dead unless his brain is dead. Arrest of the heart and circulation indicate death only when they persist long enough for the brain to die. Despite wide acceptance of these simple propositions there is still much woolly thinking about brain death. Three main areas of confusion need to be addressed before discussing the neurophysiological basis of the condition, the clinical problems of diagnosis, and the practical aspects of management.



Concepts and criteria

All talk of the criteria of death—and ipso facto all arguments about better criteria—must be related to some overall concept of what death means. When we consider death the tests we carry out and the decisions we make should be logically derived from conceptual and philosophical premises. There can be no free-floating criteria, unrelated to such premises.

The box lists several concepts that have prevailed from time to time. In the middle ages, if one entered certain monasteries one ceased to enjoy the limited rights and heavy duties of the outside world. One would be considered “dead” by civil society. The appropriate criterion for such a concept of death would presumably be a certificate from the father superior of the monastery confirming that one had entered it. Esoteric concepts may be met by esoteric criteria.

Both Hellenic and Judeo-Christian cultures identified death with the departure of the soul from the body. In 1957 Pope Pius XII, speaking to an international congress of anaesthetists,⁴ raised the question of whether one should “continue the resuscitation process despite the fact that the soul may already have left the body.” I would find it difficult to identify this particular state or to formulate relevant criteria.

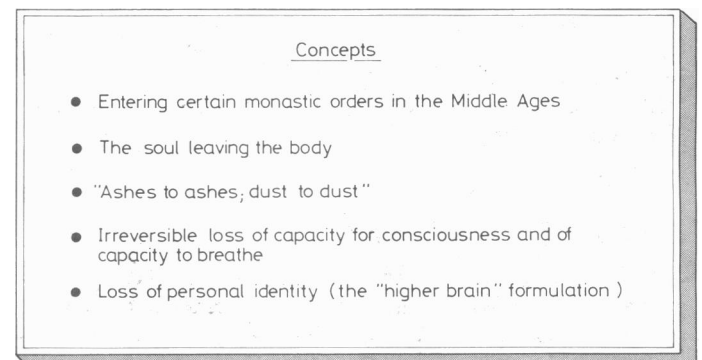
Some people have held that the surest notion of death is the biblical one: “Ashes to ashes, dust to dust.” The appropriate criterion for such a concept would be putrefaction, but no one would argue today that this is necessary before a person can be pronounced dead. We all readily grasp the difference between “Is this woman dead?” and “Has every enzyme stopped working, in every cell of her body?” The controversy is between those who think of death as “dissolution of the organism as a whole” and those who insist that it can mean only “dissolution of the whole organism.”

Asked what they mean by death, most people will probably talk about the heart “having stopped for good.” This is indeed a mechanism of death (and, until brain death appeared on the scene, it was also a universal attribute of a cadaver) but is it really a concept of death? When asked whether an individual is dead whose cardiac function has been permanently taken over by a machine many people begin to realise that a beating

heart is not an end in itself but a means to another end: the preservation of the brain. This has been unconsciously perceived by people with little or no knowledge of physiology: we have been hanging and decapitating for centuries.

I conceive of human death as a state in which there is irreversible loss of the capacity for consciousness combined with irreversible loss of the capacity to breathe (and hence to maintain a heart beat). Alone, neither would be sufficient. Both are essentially brain stem functions (predominantly represented, incidentally, at different ends of the brain stem). The concept is admittedly a hybrid one, expressing both philosophical and physiological attributes. It corresponds perhaps to an intermediate stage of current concerns, seeking to maintain a footing on both types of ground. Although seldom explicitly formulated, this view of death is, I believe, widely shared in the West. It is the implicit basis for British practice in diagnosing “brain death.”

Some people, particularly in the USA, have gone further and proposed a concept of death that would equate it with the loss of personal identity, or with the “irreversible loss of that which is essentially significant to the nature of man.”⁵ “Cognitive death” is already being evaluated as part of the “next generation of problems.”⁶ I am opposed to “higher brain” formulations of death because they are the first step along a slippery slope. If one starts equating the loss of higher functions with death, then, which higher functions? Damage to one hemisphere or to both? If to one hemisphere, to the “verbalising” dominant one, or to the “attentive” non-dominant one? One soon starts arguing frontal versus parietal lobes.



Over the past 100 years modern man has “secularised his philosophical understanding of his nature” and has sought to find “more biological formulations of what it meant to be dead.”⁷ When we strike these existential chords, however, the responses are likely to be implicitly philosophical. If we understand this we will be more tolerant of the diversity of answers people will give when asked, “What is it that is so central to your humanity that when you lose it you are dead?”

Death: an event or a process?

In 1968 the 22nd World Medical Assembly in Sydney stated: “Death is a gradual process at the cellular level, with tissues varying in their ability to withstand deprivation of oxygen. But clinical interest lies not in the state of preservation of isolated cells but in the fate of a person. Here the point of death of the different cells and organs is not so important as the certainty that the process has become irreversible, whatever techniques of resuscitation may be employed.”⁸ In thus defining death the delegates in Sydney were endorsing—

whether they knew it or not—one of the options offered by the *Concise Oxford Dictionary*, which describes death both as “dying” (a process) and “being dead” (a state).

It has, of course, been thought for centuries that growth of the hair and nails might continue after the heart had stopped. Surgeons discovered years ago that they could harvest skin 24 hours after irreversible asystole and transplant it. A bone graft or an arterial graft would “take” even if the tissue had been collected 48 hours after death. In the light of such observations, the classical signs of death (permanent cessation of breathing and of the heartbeat) will be perceived rather differently: they will be seen as major and easily detectable events, triggering a final, rapid sequence of biological changes. They are the usual points of no return in the dissolution of the organism as a whole and proof positive that the process leading to death of the whole organism has indeed become irreversible.

Legal constraints and dictionary definitions have probably delayed acceptance of the notion of death as a process. Fifteen years ago the editorial of a leading American journal⁹ talked of the “end point” of existence “which ought to be as clear and sharp as in a chemical titration.” In fact the simultaneous destruction of all tissues—death as an event—is rare indeed. The sudden carbonisation of the whole body by a nuclear explosion is the only example that readily comes to mind.

In the heat of the public controversy about brain death two years ago a limerick was written which summed up the simple wisdom that death is a process:

In our graveyards with winter winds blowing
There's a great deal of to-ing and fro-ing
But can it be said
That the buried are dead
When their nails and their hair are still growing?

I think all cultures capable of asking such a question would answer it with an unequivocal “yes”—whether the premises were true or not.

But there are other points of no return. One type of event epitomises the fact that these may in fact precede cessation of the heart beat—decapitation. Once the head has been severed from the neck the heart continues to beat. Is that individual alive or dead? If those who hold that a person can be truly dead only when the heart has stopped believe that a decapitated individual is still alive, simply because his heart is still beating, they have a concept of life so different from mine that I doubt if bridges could be built. If, however, they accept that such an individual is dead they should extrapolate this awareness to a similar situation, extended over hours or days (because of a closed circulation). They will be thinking about brain death.

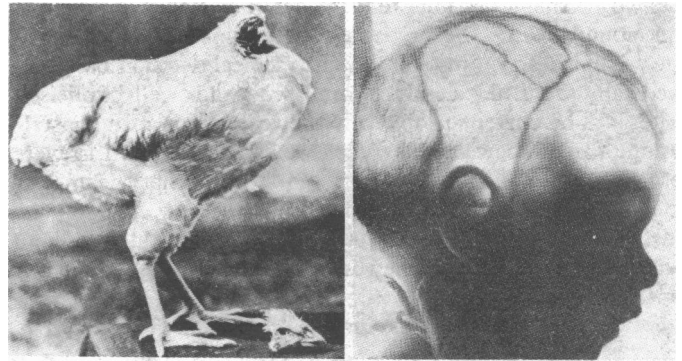
The vegetative state, whole brain death, and death of the brain stem

About 10 years ago this picture of an unsuccessfully decapitated chicken appeared in a leading magazine. The forebrain has been amputated and lies on the ground. The brain stem is still in situ. The bird, still breathing, was fed with a dropper for several weeks. Was it alive or dead?

The chicken must be considered alive so long as its brain stem is functioning. Let us transfer the argument to a child with hydranencephaly. There is a spinal cord, a brain stem, and perhaps some diencephalic structures but certainly no cerebral hemispheres. The cranial cavity is full of cerebrospinal fluid and transilluminates when a light is applied to it. The child can breathe spontaneously, swallow, and grimace in response to painful stimuli. Its eyes are open. The heart can

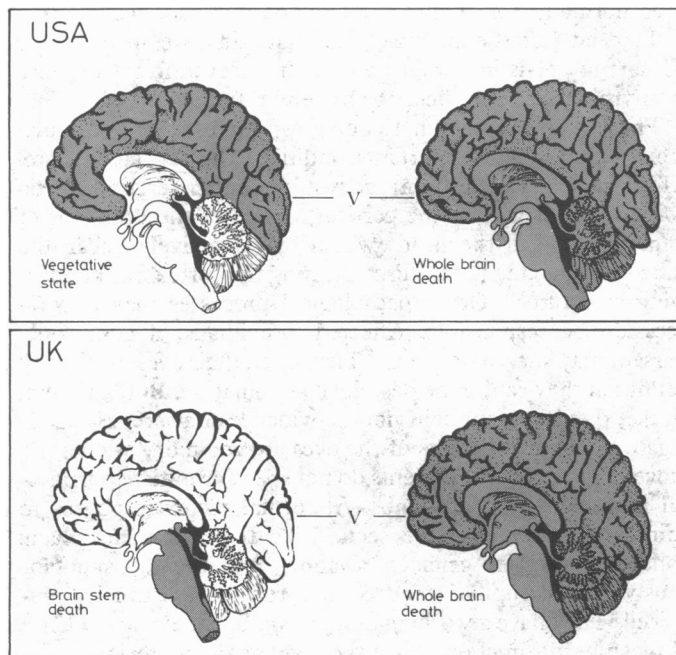
beat normally for months. No culture would declare that child dead. This emphasises the centrality we instinctively allocate to persisting brain stem function, even in the absence of anything we could describe as cerebration.

These examples may help one grasp the essence of a much more common and important condition: the vegetative state. This is a chronic condition, the result of either cerebral anoxia (which may devastate the cortical mantle of the brain) or of impact injury to the head (which may massively shear the subcortical white matter, disconnecting the cortex from underlying structures). Other pathological processes may also on occasion be responsible. Affected individuals, if adequately nursed, may survive for years. They open their eyes, so that by definition they cannot be described as comatose. But, although awake, they show no behavioural evidence of awareness. Conjugate roving movements of the eyes are common, orientating movements rare. The patients do not speak or initiate purposeful movement of their limbs. Abnormal motor responses to stimulation may often be seen. Like the hydranencephalic child, the patients grimace, swallow, and breathe spontaneously. Their pupillary and corneal reflexes are usually preserved. They have a working brain stem, but show no evidence of meaningful function above the level of the tentorium.



I have described the vegetative state so that I can contrast it with whole brain death. Brain dead individuals show no signs of neural function above the level of the foramen magnum. Even homeostatic functions, dependent on central neural mechanisms, are affected. The patients are in deep irreversible coma, and have irreversibly lost the capacity to breathe. Brain stem death is the physiological kernel of brain death, the anatomical substratum of its cardinal signs (apnoeic coma with absent brain stem reflexes) and the main determinant of its invariable cardiac prognosis: asystole within hours or days.

The figure over the page illustrates a controversy developing in the United States between those who have accepted death as synonymous with “death of all structures above the foramen magnum,” and others tentatively suggesting that death of large parts of both cerebral hemispheres (the vegetative state) might be enough. Very few informed physicians in the United States, it must be emphasised, subscribe to the latter view. A different disagreement smoulders on, meanwhile, both within the United Kingdom and to some extent between British and American neurologists, about whether we can clinically identify death of the brain stem and about what flows from such an identification. When people engaged in one discussion are suddenly parachuted into the other communication is bound, for a while, to be difficult.



Determining death and "allowing to die"

Two further questions tend to get muddled when people talk about death. The first is the determination of death: Is the patient dead? This should be a medical decision based on medically defined, clearly formulated, and well-publicised criteria. The current problem is the recognition of a constellation of neurological signs which we can equate with irreversible loss of function of the brain stem. To say that the answer should be medical does not mean that society, through its laws, should not seek to reflect public opinion and outline an acceptable conceptual framework within which its doctors can work.

Discussions about "allowing to die" are different. They

seek to answer very difficult questions about how society copes with severely brain-damaged patients who still have some brain stem function (the Karen Quinlan dilemma). There are patients of this kind in long-term care units all over the world. They are an enormous social problem. Decisions have to be taken about them. But these are social decisions, with important cultural, ethical, religious, and economic implications. There are medical implications too, but doctors should not try to play God: their function is to give an early prognosis (if they can). There have been important advances in this subject.^{10 11} Different societies at different times have taken different attitudes to this problem, which abuts on to the whole subject of euthanasia. But I am not discussing euthanasia. "The uncomfortable dimensions of the care of the dying"¹² have nothing to do with identifying a dead brain stem.

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The photograph of a child with hydranencephaly was reproduced from Kaloss W, Kuhnlein E. *American Journal of Diseases of Childhood* 1962;103:178.

- ¹ Mollaret P, Goulon M. Le coma dépassé (mémoire préliminaire). *Rev Neurol* 1959;101:3-15.
- ² Wertheimer P, Jouviet M, Descotes J. A propos du diagnostic de la mort du système nerveux dans les comas avec arrêt respiratoire traités par la respiration artificielle. *Presse Médicale* 1959;67:87-8.
- ³ Jennett B, Hesse C. Brain death in Britain as reflected in renal donors. *Br Med J* 1981;283:359-62.
- ⁴ Pope Pius XII. Prolongation of life. *Pope Speaks* 1957;4:393-8.
- ⁵ Veatch R. Brain death. *Hastings Center Report* 1972;iii:10-3.
- ⁶ Beresford HR. Cognitive death: differential problems and legal overtones. *Ann NY Acad Sci* 1978;315:339-48.
- ⁷ Veatch RM. The definition of death: ethical, philosophical and policy confusion. *Ann NY Acad Sci* 1978;315:307-21.
- ⁸ Gilder SSB. Twenty-second World Medical Assembly. *Br Med J* 1968;iii:493-4.
- ⁹ Anonymous. What and when is death? *JAMA* 1968;204:219-20.
- ¹⁰ Levy DE, Bates D, Caronna JJ, et al. Prognosis in nontraumatic coma. *Ann Int Med* 1981;94:293-301.
- ¹¹ Jennett B, Teasdale G, Braakman R, et al. Predicting outcome in individual patients after severe head injury. *Neurosurgery* 1979;4:283-8.
- ¹² Lewis HP. Machine medicine and its relation to the fatally ill. *JAMA* 1968;206:387-8.

For two years a woman has been taking 1 g of ascorbic acid daily. She claims it improves her mental and physical wellbeing and when she stops she suffers from lassitude and depression. Is this a psychological response, and what risk is there of continuing to take ascorbic acid?

The value of high doses of vitamin C in preventing or reducing the severity of the common cold remains controversial. Nevertheless, daily doses of 1 g or more are widely used, and there is no good evidence that they are harmful. Many possible hazards of prolonged use of such high doses have been postulated but their importance appears to be small, at least in otherwise healthy individuals.¹ Excretion of urinary oxalate is increased, and there may be an increased risk of stone formation in patients who already have an inborn error of oxalate metabolism. Doses of 4 g daily or more increase the renal clearance of uric acid and may also acidify the urine, thus increasing the risk of uric acid stones. In patients with glucose-6-phosphate dehydrogenase deficiency vitamin C can produce haemolysis. Very large doses have been reported to increase serum cholesterol concentrations. Suggestions that prolonged use of high doses may interfere with bone growth in children, destroy vitamin B₁₂ in food and thereby produce B₁₂ deficiency, reduce fertility in women, and predispose to diabetes have not been confirmed. It has been suggested that prolonged use of high doses may induce a temporary increase in need for the vitamin, and there have been occasional reports of overt scurvy after sudden withdrawal of doses greater than 1 g daily. Confirmatory evidence is lacking, however, and the risk of this occurring is unknown. Physical and mental tiredness have also been reported after withdrawal,² but whether

this has a pharmacological basis is unknown.—LINDA BEELEY, consultant clinical pharmacologist, Birmingham.

- ¹ Dukes MNG, ed. *Meyler's side effects of drugs*. 9th ed. Amsterdam: Excerpta Medica, 1980:635-7.
- ² Wilson CWM. Ascorbic acid and the common cold. *Practitioner* 1975;215:343-4.

What is "hogweed," why does contact with it produce unpleasant skin reaction, and why does scarring persist for several weeks? What treatment is advised?

The hogweeds are a large cosmopolitan genus of flowering plants, known to botanists as heracleum, and many species of heracleum contain photosensitising furanocoumarins. The giant hogweed *H. mantegazzianum*, which was introduced into Britain from the Caucasus, is now a widespread weed. Its large size (it may exceed 12 ft (3.6 m) in height) attracts children, who often play with the hollow stems and thus bring the sap of the plant into close contact with many areas of the skin. If the contaminated skin is then exposed to sunlight the photodynamic properties of the furanocoumarins result in the development of erythema and blisters that heal slowly to leave persistent pigmentation. Gardeners should wear gloves and avoid handling the plant in sunny weather.—A J ROOK, consultant dermatologist, Cambridge.

- Mitchell JC, Rook AJ. *Botanical dermatology*. Vancouver: Greengrass, 1979.
Murray RDH, Meindz J, Brown SA. *The natural coumarins*. New York: John Wiley and Sons, 1982.