be achieved by increasing awareness that the condition is common and that the diagnosis can, and should, be made in most cases by careful routine palpation of the abdomen. Our experience, and that of many others, indicates that it is imperative to establish the diagnosis and initial treatment before the onset of acute symptoms or rupture if the death rate of this common disorder is to be appreciably reduced.

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Contemporary Themes

Brain death in Britain as reflected in renal donors

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Abstract

The diagnostic mix of 1228 brain-dead renal donors in Britain was similar to that of 479 cases of brain death recently reported from three neurosurgical units. About half the donors came from non-teaching hospitals without a neurosurgical unit, many of them small and distant from the centre. The different circumstances that preceded brain death were examined—namely, diagnosis and whether the fatal ictus of brain damage occurred when the patient was already in hospital—to explain why donors spend varying times on the ventilator. Head injuries accounted for half the donors, and intracranial haemorrhage for almost a third.

While many potential donors are not made available, the size of the pool has been overestimated, particularly in regard to head injury. Reduction in organ donation since "Panorama" has been very uneven, with some places increasing their yield; this suggests reluctance of doctors to initiate donation rather than relatives withholding permission.

Introduction

Cardiorespiratory function can now be maintained for several days after brain function has irreversibly stopped—that is, after

the occurrence of brain death. Meanwhile, renal transplantation has become a routine procedure that brings undoubted benefits to a high proportion of recipients. Both are now relatively frequent events, with about 4000 cases of brain death and almost 1000 renal transplant operations each year in Britain. Although these two technological developments emerged quite independently they tend to be associated with each other, and it is still sometimes supposed that they can lead to a conflict of interest at the deathbed of some brain-damaged patients.

Brain death emerged in the 1950s with the increasing availability of ventilators for resuscitation and was first formally described in 1959.¹ There is abundant evidence that once brain death has been confirmed the heart always stops within 14 days (usually much sooner) even though ventilation is maintained.² Discontinuing ventilation in these circumstances is therefore now regarded as good medical practice in order to spare the patient the indignity and the family the distress of a prolonged period of fruitless mechanical "treatment." If alternatives to transplantation emerged, brain death would be just as frequent; doctors would still need to decide in each case when it had become inappropriate to persist with mechanical ventilation because the patient was already dead.

Renal transplantation became a routine procedure some time after brain death had become well recognised, and for some years only a proportion of cadaveric kidneys came from brain-dead patients. In the West Midlands, for example, only 25% of donors offered in 1969 were receiving ventilation; by 1977 the proportion had risen to 65%,³ and since 1978 all donors have been brain dead.⁴ Relatives are more likely to consent to donation when their family member is receiving ventilation, perhaps because the process of seeking permission and arranging nephrectomy can then be conducted in an unhurried and seemingly way. The trust that had been slowly built up over recent years between the public, the donor doctor, and the transplant

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surgeon was, however, temporarily undermined by misinformed comment on BBC *Panorama* in October 1980. The programme "Transplants—are the donors really dead?" provoked a storm in the public and medical press, and the ensuing weeks saw an appreciable reduction in organ donors.⁵

Doubts about the reliability of the criteria for diagnosing brain death have now been resolved and the level of organ donation is slowly being restored. Uncertainty about some of the practicalities of brain death and organ donation seem to persist, however, especially among those who are seldom, if ever, themselves concerned in these events. We present data about the frequency and distribution of brain death in British hospitals.

Present study

SOURCES OF DATA

The frequency and distribution of brain death in Britain cannot be discovered direct. There are data about such cases in two general intensive care units^{6,7} and from the neurosurgical units in Cambridge, Glasgow, and Swansea.² Although these three centres were committed to securing organs for transplantation, fewer than one in four of their brain-dead patients became a donor. Organ donation was fairly evenly spread among different types of brain-dead patient and it seems probable that donors do reflect the whole population of brain-dead cases from which they are drawn (table I). Use can therefore be made of the data that are available for donors throughout Britain, based on returns from transplant surgeons to the United Kingdom Transplant Service in Bristol.

TABLE I—Causes of brain damage (percentages in parentheses)

	No of cases	Head injury	Intracranial haemorrhage	Other
All brain deaths in three neurosurgical units	479	263 (55)	133 (28)	83 (17)
Donors in all British hospitals	1228	613 (50)	339 (28)	276 (22)

We studied details of donors during the 33 months before October 1980. The time on the ventilator was available for 1128 (89%) of these donors, and we confined our analysis to these. We classified the hospitals from which the donors came into those that included a neurosurgical unit, other teaching hospitals, and other hospitals. The size and distance from the nearest neurosurgical unit of the "other" hospitals was also noted. Some comparisons are made with the data on all cases of brain death from the three neurosurgical units² and with donors from non-neurosurgical sources in Glasgow.

HOSPITALS SUPPLYING DONORS

Tables II and III show that of 285 hospitals that supplied one or more donors, 40 (14%) had a neurosurgical unit; these hospitals supplied 479 (39%) of the donors. The 208 hospitals (73%) in the "other" category (neither neurosurgical nor teaching) accounted for 553 (45%) of the donors. A third of these other hospitals had less than 250 beds, and these provided a fifth of the donors that came from other hospitals. Almost half of these other hospitals were more than 20 miles (32 km) from the regional neurosurgical unit and provided more than half of the donors from other hospitals. The recent West-Midlands series of 156 donors⁴ showed a similar distribution (40% from non-teaching hospitals without a neurosurgical unit). Only 39 out of

TABLE II—Distribution of donor hospitals and of donors (percentages in parentheses)

Type of hospital	Donor hospitals (n = 285)	Donors (n = 1228)
Neurosurgical	40 (14)	483 (39)
Teaching	37 (13)	192 (16)
Other	208 (73)	553 (45)

TABLE III—Features of "other" hospitals (percentages in parentheses)

	Donor hospitals (n = 208)	Donors (n = 553)
No of beds:		
> 500	64 (31)	210 (38)
250-500	79 (38)	235 (43)
< 250	64 (31)	108 (19)
Distance in miles from regional neurosurgical units:		
< 20	108 (52)	257 (46)
20-40	67 (32)	210 (38)
> 40	33 (16)	86 (16)

(1 mile = 1.6 km.)

51 cases from neurosurgical hospitals in the West Midlands came from the neurosurgeons, who therefore contributed only a quarter of all donors, even though this was a region where there were neurosurgical units in five of the 31 donor hospitals.

CAUSE OF BRAIN DAMAGE IN DONORS

Six diagnostic categories were recorded by the United Kingdom Transplant Service: road traffic and other accidents together accounted for half the cases, presumably indicating head injuries; subarachnoid haemorrhage made up 28% of cases; 5% were ascribed to cerebrovascular accident, and some of these were probably haemorrhagic strokes, as were some of the unspecified cases; the broader term "spontaneous intracranial haemorrhage" probably therefore accounted for almost a third of donors. Brain tumour and suicide were the cause in 2% and 1%, while 14% were unspecified. The distribution of head injury, intracranial haemorrhage, and "other" diagnoses (grouped together) did not vary greatly among different types of hospital (table IV). Head injury, however, was rather more common in neurosurgical units (and so also in neurosurgical hospitals); it was also more frequent in other hospitals that had fewer than 250 beds or that were more than 20 miles from the centre; fewest head injuries occurred in teaching hospitals without a neurosurgical unit. Children under 15 accounted for 10% of donors; less than 0.5% were under 5. Head injury was the diagnosis in over 70% of children, while intracranial haemorrhage accounted for only 7%.

TABLE IV—Diagnoses of donors in different hospitals (percentages in parentheses)

	Neurosurgical (n = 483)	Teaching (n = 192)	Other (n = 553)
Head injury	244 (50)	83 (43)	286 (52)
Intracranial haemorrhage	130 (27)	50 (26)	159 (29)
Other	109 (23)	59 (31)	108 (19)

TIME RELATIONS ASSOCIATED WITH BRAIN DEATH

The best safeguard against the erroneous suspicion of brain death is the passage of time. Criteria published many years ago required that signs of brain death should persist for 24 hours or more, but that period has since been steadily reduced.⁸ Of more relevance is the interval before tests are first applied. Time is needed to satisfy the preconditions, which require that the patient should be in deep coma and be apnoeic (and therefore on a ventilator); that irreversible structural brain damage should have been diagnosed; and that reversible causes of depression of brain-stem function have been excluded. How long this takes depends on how obvious is the cause of the brain damage and how readily confusing factors, in particular drugs, can be excluded. To explain how this can vary from a few hours to several days calls for a description of the more common clinical scenarios that lead to brain death.

HEAD INJURY

Overwhelming impact damage—Respiratory failure occurs just before or soon after arrival at hospital; mechanical ventilation is begun and steps taken to counter factors such as hypoxia and arterial hypotension that might be combining with trauma to depress brain

function. Time is needed to complete these resuscitation procedures, to allow the blood alcohol concentration (if raised) to fall below that which could cause deep coma, and for relevant investigative and primary therapeutic manoeuvres to be carried out. Experience is that these various activities take a minimum of six hours,⁹ though cardiac asystole may occur sooner than this. How frequently such cases of early (but secondary) apnoea are encountered will depend on how soon after injury patients reach hospital; when there is delay these cases will be included among the 50% of fatally head-injured patients who are dead before reaching hospital due to overwhelming damage in the head or elsewhere.¹⁰ Many who do reach hospital alive have had a brief episode of apnoea after impact which has recovered spontaneously; very occasionally recovery is reported when a more prolonged period of primary apnoea (five to 15 minutes) has been dealt with at the scene by artificial respiration.¹¹

Secondary brain damage is presumed when a high level of responsiveness at some stage after injury indicates that impact damage was not overwhelming but the patient later deteriorated. An intracranial haematoma has usually been diagnosed in the neurosurgical unit by computed tomography: either it has been evacuated without improvement or an operation has been considered unjustified because of the patient's condition. Those without a haematoma have deteriorated either because of diffuse swelling with high intracranial pressure, or because of fat embolism, or because of hypoxia and hypotension related to multiple injuries.

SPONTANEOUS INTRACRANIAL HAEMORRHAGE

Most patients with this condition have a ruptured aneurysm or arteriovenous malformation associated with subarachnoid and intracerebral haemorrhage. The exact nature of the underlying primary lesion is often uncertain, and some are cases of primary intracerebral haemorrhage with or without hypertension.

Initial haemorrhage overwhelming—The patient becomes deeply unconscious within minutes of suffering sudden severe headache, and soon after arrival at hospital becomes apnoeic. The flaccid areflexic patient may not have neck stiffness; the diagnosis rests on a typical story and on finding blood-stained cerebrospinal fluid, and perhaps also subhyaloid fundal haemorrhages. There may have been focal neurological signs before the patient became totally areflexic.

Recurrent haemorrhage in hospital often occurs in the neurosurgical unit when investigations (computed tomography, or angiography or both) have been completed, but it may happen sooner and elsewhere. Apnoea often occurs immediately after a severe subarachnoid haemorrhage, spontaneous recovery of respiration may occur in a minute or so, or the patient may die within a few minutes. In some patients apnoea lasts for an hour or so, and if ventilation is mechanically maintained during this time the patient may recover completely. Instituting ventilation when recurrent subarachnoid haemorrhage occurs in hospital is justified for this reason.

OTHER CAUSES OF COMA

Sometimes coma is of uncertain origin, and usually such patients are found unconscious at home or in the street, often with some external evidence of injury but with no witnesses to what happened. It is in these circumstances that ventilation may have to be maintained for as long as 24-72 hours while drug screening, metabolic tests, and other investigations are completed. Only when these have been completed, and enough time has passed for all possibly reversible influences to have disappeared, is it proper to declare brain death. Extra time (at least 24 hours) must also elapse when cerebral hypoxia has been the cause of the brain damage, such as after cardiac arrest, because recovery may be delayed for several hours.

Occasionally intracranial mass lesions (such as tumour or abscess) are already obviously hopeless when the patient presents at hospital, computed tomography showing a lesion that is inaccessible or no longer treatable at this late stage. Most patients with mass lesions who are declared brain dead have either failed to recover after a surgical attempt at removal, or have a delayed recurrence of a previously verified inoperable tumour for which no further therapeutic intervention is recommended. In the latter circumstances the only reason for using a ventilator would be to facilitate organ donation; sometimes such a course is agreed to by the family before terminal apnoea occurs.

TIME IN HOSPITAL AND ON VENTILATOR

When brain death occurs soon after head injury or intracranial

haemorrhage the time in hospital is relatively short, but almost all of it is spent receiving ventilation because resuscitation and diagnostic measures have all to be completed during the period of ventilation. When a secondary event occurs in a patient who is in hospital and already fully investigated, with no doubts about confusing factors, brain death may be declared after only a short period of ventilation (figure).

The median duration of ventilation for United Kingdom Transplant Service donors was somewhat shorter in hospitals with neurosurgical units than in other hospitals, and donors with intracranial haemorrhage in all three types of hospital spent less time on the ventilator than other types of case (table V). The median time of ventilation was longer for transplant service donors than for neurosurgical patients with brain death (table VI), and fewer donors were on the ventilator for 12 hours or less.

Time in *hospital* was more than twice as long as time on the ventilator for donors from the three neurosurgical units; the difference was much more apparent in cases of intracranial haemorrhage, reflecting secondary events in patients already in hospital (table VII). For non-neurosurgical donors in Glasgow the time spent in hospital was much less than in the neurosurgical units, especially for intracranial haemor-

Contrasting circumstances before brain death, resulting in different ventilator times.

TABLE V—Median time (hours) on ventilator until cardiac asystole

Type of hospital	All diagnoses	Head injury	Intracranial haemorrhage	Other
All hospitals (n = 1228)	48	48	23	48
Neurosurgical (n = 483)	36	48	24	36
Teaching (n = 192)	48	48	24	48
Other (n = 553)	48	48	24	48

Intracranial haemorrhage versus other types of case: $p < 0.001$ (median test).

TABLE VI—Time on ventilator before cardiac asystole (percentages in parentheses)

Time in hours	All brain death cases in three neurosurgical units (n = 476)	United Kingdom Transplant Service donors (n = 1228)
≤ 12	82 (17)	140 (11)
13-48	238 (50)	732 (60)
> 48	156 (33)	356 (29)
Median	33.5 h*	48 h*

* $p < 0.001$ (median test).

TABLE VII—Median time (hours) in hospital and on ventilator for neurosurgical and other donors

	All diagnoses	Head injury	Intracranial haemorrhage	Other
Neurosurgical (Glasgow/Swansea) (n = 69)	28 50	29 48	25 144	28 60
Other (Glasgow) (n = 47)	24 36	23 28	17 31	38 84

rhage. This is further evidence for the different kind of events that precede brain death in neurosurgical as distinct from other hospitals.

DONORS BEFORE AND AFTER "PANORAMA"

In the six months since *Panorama* the donor yield was 77% of that expected on the basis of the previous 33 months; in non-neurosurgical hospitals it was only 64% of normal. But the overall yield from neurosurgical hospitals was at the expected rate, and in four transplant centres more than the expected number of donors were provided in the period after *Panorama*. In each case the increase was mainly from the regional neurosurgical unit; in Glasgow, for example, the rate of donation more than doubled after *Panorama*, and it continues at this high rate. In the country as a whole hospitals with neurosurgical units comprised 28% of donor hospitals and contributed 50% of donors since *Panorama*, compared with 14% and 39% respectively in the previous period. Of the 285 hospitals that had a donor in the 33 months before *Panorama*, only 80 gave a donor during the next six months. But 36% of hospitals supplied only one and 19% only two donors in the preceding period; many would not therefore have been expected to provide a donor in this six months.

NUMBER, NATURE, AND LOCATION OF POTENTIAL DONORS

Many potential donors are not at present used as providers of organs, but the shortfall is not as great as nephrologists and transplant surgeons sometimes suggest. They point to the discrepancy between the number of registered deaths from head injury and subarachnoid haemorrhage in Britain and the annual yield of donors, and to the donation and transplantation rate (on a population basis) in different countries. These calculations, however, fail to take account of several important factors, especially with regard to head injury, which already accounts for more than half of all British donors. The annual incidence of fatal head injuries in Britain is less than half the rate in North America, Australia, and several European countries.¹² Moreover about half of fatally injured patients do not reach hospital alive, while only about half of those who die in hospital do so while receiving ventilation. The potential donor pool from head injury is therefore only a quarter of the registered deaths from this condition; many of these patients have multiple injuries leading to shock and other complications that may make them unsuitable as donors.

The events that commonly lead to brain death are sudden and unheralded and they are no respectors of geography. Ventilators are now available in a wide range of hospitals throughout Britain, any of which may therefore encounter brain death. In contrast, most neurosurgeons in Britain work in regional units where many neurologists are also based, and where almost all CT scanners are located. These units can provide an effective service only by operating a selective transfer policy, favouring patients likely to benefit therapeutically from specialist intervention. This therefore properly tends to exclude most that look obviously hopeless soon after admission elsewhere—the very patients most likely to become brain dead. Even so, a large neurosurgical unit, particularly if committed to caring for most of the severe head injuries in its region, encounters brain death much more frequently than does a general intensive care unit. Each of the 300 or so of these encounters about eight brain deaths a year, compared with almost 10 times as many in the Glasgow neurosurgical unit (serving 2.7 million population).

Discussion

This study confirms earlier estimates about the frequency of brain death in Britain. Two-thirds to three-quarters of cases are spread between a large number of general hospitals, some of them quite small and distant from the centre. There is no case for moving potentially brain-dead patients to regional neurosurgical centres or for neurosurgeons and neurologists becoming peripatetic pronouncers of brain death, which would be both an impracticable and an inappropriate use of specialist resources. They could more usefully help by ensuring that some identified staff in every acute hospital in their region are fully acquainted with the preconditions and confirmatory tests for brain death. They should, however, expect to be consulted when there is

doubt about the preconditions and there seems a possibility of recovery.

We have observed in our own region an appreciable variation in the yield of donors from hospitals that have similar catchment populations and admission policies, which Barnes also noted in the West Midlands,^{3,4} and also between the same hospital in different years as staff change. There is no doubt that the most important determinant of the frequency of organ donation is the willingness of medical and nursing staff caring for potential donors to initiate this process and to undertake the considerable extra work that this inevitably entails. The uneven reduction in donor supply after *Panorama*, with some places increasing the numbers provided, strongly suggests that the main cause was an increased reluctance of doctors to raise the issue of donation, rather than that relatives were more often withholding consent. Further support for this view comes from a Gallup poll conducted in March 1981 for the British Kidney Patients' Association, which showed no significant difference in public attitudes to kidney donation compared with a survey a year before.

It is to be hoped that the widespread discussion of brain death in recent months, together with the substantial amount of hard data that have been reviewed, will lead to clearer thinking on this issue. Doctors responsible for these patients may be expected to act in future with greater confidence, and this should in turn lead to more compassionate care in intensive care units. Quite secondarily there is likely to be a more plentiful supply of donors.

Information from the United Kingdom Transplant Service records was kindly made available by the director, Dr B A Bradley, and with the permission of Mr A Barnes, chairman of the committee of management. In Glasgow Mr Stuart MacPherson was most helpful in providing data about local donors outside the neurosurgical unit; Mr Robert MacMillan helped with the analysis of the data. Miss Catherine Hesselst is supported by the Medical Research Council.

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A girl aged 11 reacted badly to her second and third combined immunisation injection when she was a baby. She developed a hard tumour at the site of both injections that eventually subsided but not completely. I was told that it was probably the tetanus component that had caused this reaction. Her mother has now asked about further tetanus protection. What should I advise?

It is common for a baby to have a small lump of the size of a large pea at the site of whooping cough, tetanus, and diphtheria immunisation; these nodules may last for many months and are of no importance. Almost certainly that is what this girl had; I have seen these lumps only with the triple injection, and I assume that they are due to the whooping cough component. There is therefore no contraindication to tetanus booster injections, and it is most important that children and adults should maintain their immunity to tetanus.