Brain damage in fatal non-missile head injury

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The most important factor governing the outcome in a patient who sustains a non-missile head injury is the damage sustained by the brain. Some of this may occur at the moment of impact and may be so severe that the patient never recovers consciousness; but in many patients who experience a lucid interval after their original injury and then become unconscious it is clear that the principal brain damage has not occurred at the moment of impact. This is because the original injury—sometimes apparently of no great severity—has initiated a dynamic process that has led to further, or secondary, potentially fatal brain damage.

There are therefore two principal reasons for undertaking comprehensive neuropathological studies on patients who die as a result of a head injury. The first of these is to define as precisely as possible the sequence of events that has led to the fatal outcome. It is only by this means that one can separate immediate impact injury, which by definition is not amenable to treatment no matter how good the medical services are, from brain damage brought about by a complication of the original injury, and at least some of which might have been preventable had the complication been recognised earlier. The second reason is that it is only by defining the wide spectrum of brain damage that may be present in a fatal head injury that one can gain some insight into the types of damage that may be present in patients who remain permanently brain-damaged after a head injury. Certainly one of the principal objectives of the present study was to establish as close clinicopathological correlations as possible in the hope that more comprehensive neuropathological information might to some extent contribute to patient management.

Numerous valuable studies have been published in the course of the past 20 years1–7 on the types of brain damage that are likely to be encountered in patients who have died as a result of a non-missile head injury. They are, however, open to certain criticism since they fall into two distinct and rather disparate groups: the first is composed of large numbers of cases subjected only to macroscopic assessment of the brain when inevitably much of the brain damage remains unrecognised, while the second consists of small series, albeit subjected to a detailed neurohistological study, but too selective clinically to be of much general value.

The reasons for the paucity of comprehensive neurohistological studies are not hard to find since a full histological analysis of a brain requires the examination of many large sections, preferably embedded in celloidin. This is a time-consuming exercise which requires considerable specialist expertise on the part of both the technician and the pathologist. There has therefore inevitably been a tendency, often contributed to by forensic pressures, for pathologists to lay particular stress on the readily identifiable macroscopic abnormalities such as fracture of the skull, intracranial haematoma, and cerebral contusions. Indeed, only too often is death ascribed to fracture of the skull and cerebral contusions when neither of these may even have contributed to the patient’s loss of consciousness! We, however, have become increasingly aware of the more subtle types of brain damage that are almost impossible to identify macroscopically if the brain is sliced cursorily in the postmortem room and that can account for severe cerebral dysfunction and death in head injured patients. Yet a better understanding of these not uncommon types of brain damage would be of considerable help to the general pathologist and to the forensic pathologist faced with an almost normal looking brain in a patient known to have been unconscious for varying periods of time after a head injury.

The brief account of brain damage due to a non-missile head injury that follows is based on a comprehensive neuropathological study8–12 of a consecutive series of fatal cases, and, as a result of these studies, our current approach to the pathology of brain damage in non-missile head injury is as follows:

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Immediate impact injury
- Contusions and lacerations
- Diffuse damage to white matter
- Other types of diffuse brain injury

Primary complications
- Intracranial haemorrhage
- Brain swelling

Secondary complications
- Brain damage secondary to raised intracranial pressure
- Hypoxic brain damage
- Infection

Material and methods

During the five-year period 1968-72, 151 necropsies were undertaken on patients with head injuries who had been managed by the Department of Neurosurgery in the Institute. Since all of the patients had survived their injury long enough to be referred to a neurosurgical unit, there are very few patients in the series who survived less than 12 hours. There were 123 males and 28 females; the age range was 8 months to 86 years; and the duration of survival ranged from 6 hours to 21 months (Figs 1 and 2). The majority of the injuries were attributable to road traffic accidents (46%) or to falls (43%). Blows to the head accounted for 9%, while the remaining 2% were crush injuries.

The clinical records were assessed independently by the Department of Neurosurgery with particular reference to any deterioration in the conscious level after a lucid interval, defined as whether or not the patient had talked after the injury. If the patient had talked but had not been completely rational, the lucid interval was defined as being partial. As a result of this study it was established that 58 (38%) of the 151 cases had experienced a complete (25; 16%) or partial (33; 22%) lucid interval after injury.

The brains and spinal cords were fixed in 10% formal saline for at least three weeks before dissection. After transection of the mid-brain, the cerebral hemispheres were cut in the coronal plane into slices 1-0 cm thick. Large representative blocks of the cerebral hemispheres and the cerebellum were embedded in celloidin, and 30 μm thick sections were stained by Nissl's method with cresyl violet and by Woelke's modification of Heidenhain's technique for myelin. The brain stem was cut into seven to nine blocks. One block each of mid-brain, pons, and medulla were embedded in celloidin, and 30 μm thick sections were stained by the Nissl and Woelke methods. Frozen sections were cut from the remaining blocks and stained with oil red O and by the Marchi technique to demonstrate the breakdown products of myelin. These blocks were then embedded in paraaffin wax, and sections were stained with haemalum and eosiin, by Luxol fast blue/cresyl violet, by the Glee's or Palmgren techniques for axons, and by the Naumenko and Feigin technique for microglia.

The sections were examined with a Watson zoom stereo-microscope with transmitted light at a magnification between ×10 and ×50. Much of the analysis could be done at these magnifications, particularly in the longer surviving patients when it was easy to recognise loss of neurons and reactive changes. In shorter surviving patients, however, where there were foci suggestive of early neuronal necrosis, the lesions were accepted as genuine only if the specific cytological abnormalities of ischaemic nerve cell change with or without encrustations could be identified by conventional light microscopy. It was also possible in each case to assess whether or not the intracranial pressure had been high during life on the basis of the histological criteria we have already defined.

All macroscopic and histological abnormalities identified in the brains were charted on a series of line diagrams of the cerebral hemispheres, the cerebellum, and the brain stem, and these diagrams formed the basis of the present analysis.
Results

Fracture of the Skull

There was a fracture of the skull in 120 of the 151 cases (79%); thus about one in five of the patients in this series who died as a result of a non-missile head injury did not have a fracture of the skull. Of the 120 fractures, 69 were centred on the mid-line of the calvaria (55) or were restricted to the base of the skull (14) and therefore gave no indication as to the site of injury. In 51 patients the fracture was restricted to one side of the calvaria or was predominantly unilateral, and in 30 of these there was a corresponding laceration or bruising of the scalp. It seemed reasonable to assume that in these 30 patients the site of the fracture was a fairly accurate indication of the site of the injury, and that from these cases one could gain some indication as to the distribution of brain damage in relation to the site of injury.

Immediate Impact Injury

Cerebral contusions and lacerations

These are the hallmark of a head injury and occur as haemorrhagic lesions, particularly at the crests of gyri. In an attempt to assess contusions more precisely, we have developed a contusion index (Figs 3, 4 and 5) which has allowed the depth and extent of contusions in various regions of the brain to be expressed quantitatively. The regions chosen—the anatomical locators—were the frontal, temporal, parietal, and occipital lobes, the cortex above and below the Sylvian fissures, and the cerebellum. Contusions in each anatomical locator are graded according to depth—0 (absent) to 3 (extending into

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Figs 3, 4, and 5 Three representative line diagrams of the cerebral hemispheres to show how the contusion index (Cl) is derived for six of the anatomical locators referred to in the text (ie, left and right frontal lobes, cortex adjacent to left and right Sylvian fissures, and left and right temporal lobes). The Cl for each locator is obtained by multiplying depth (the first digit) by extent (the second digit) and can range from 0 (0 x 0) to 9 (3 x 3) (from Adams et al.12).
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the white matter)—and extent—0 (absent) to 3 (very extensive). The contusion index (CI) for each anatomical locator is derived by multiplying depth by extent and can therefore range from 0 (contusions absent) to 9 (deep and extensive contusions). The total contusion index (TCI) for a given brain is obtained by adding the CIs of all the locators, left and right, and can range from 0 to 108. Mean contusion indices (MCI) for specific anatomical locators and mean total contusion indices (MTCI) can be derived for the whole group or for subsets.

An analysis of cerebral contusions in the present series12 showed that the MTCI (whole brain) was 16-6. In seven of the 151 fatal head injuries the MTCI was 0, while in 13 patients contusions were minimal, that is, a CI not more than 1 in any of the locators. The 15 patients (ie, 10% of the series) with the highest MTCIs were classified as having severe contusions (all had an MTCI of > 32). The MCIs for the various anatomical locators are given in Table 1, the distribution of contusions in the 30

Table 1 Distribution of contusions in entire series (n = 151: from Adams et al.13)

<table>
<thead>
<tr>
<th>Locator</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal lobe</td>
<td>5-7</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>5-4</td>
</tr>
<tr>
<td>Sylvian fissure</td>
<td>2-7</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>1-2</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td>0-7</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0-9</td>
</tr>
<tr>
<td>MCI for cerebral hemispheres</td>
<td>15-7</td>
</tr>
<tr>
<td>MTCI (whole brain)</td>
<td>16-6</td>
</tr>
</tbody>
</table>

Table 2

(a) Contusions in patients with localising fractures (n = 30: from Adams et al.13)

<table>
<thead>
<tr>
<th>MCI</th>
<th>Fracture on left (n = 16)</th>
<th>Fracture on right (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Frontal lobe</td>
<td>2-9</td>
<td>2-5</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>3-3</td>
<td>2-2</td>
</tr>
<tr>
<td>Sylvian fissure</td>
<td>1-0</td>
<td>1-7</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>1-1</td>
<td>0-3</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td>0-1</td>
<td>0-0</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0-7</td>
<td>0-1</td>
</tr>
</tbody>
</table>

(b) Contusions in patients with predominantly frontal or occipital fractures

<table>
<thead>
<tr>
<th>Site of fracture</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frontal</td>
</tr>
<tr>
<td>Frontal (n = 23)</td>
<td>7-9</td>
</tr>
<tr>
<td>Occipital (n = 44)</td>
<td>7-5</td>
</tr>
</tbody>
</table>

patients with localising fractures as defined above and in the 67 patients with predominantly frontal or occipital fractures in Table 2, and a comparison between the MTCIs in patients with and without skull fracture, lucid interval,13 and diffuse damage to white matter as defined below is given in Table 3.

Statistical assessment of the results, using a non-parametric test, discloses that in the present series contusions were more severe in patients with a fracture of the skull (p < 0.001) and less severe in patients with diffuse damage to white matter (p < 0.001). There is no evidence to suggest that there is any difference in the severity of the contusions in patients who do or do not experience a lucid interval after head injury. In the 30 patients with lateralising fractures, there is no evidence that contusions are more severe in the cerebral hemisphere contralateral to the fracture, while in patients with predominantly frontal or occipital fractures contusions are more severe in the frontal lobes than in the occipital lobes.

Of the 15 cases with severe contusions defined above, the age range was 9 to 65 years and the duration of survival ranged from less than 12 hours to seven days. Of these 15 cases, 10 were unconscious from the time of injury until death, and five were lucid (3 partial and 2 total). A fracture of the skull was present in every case, and in 13 there was evidence of raised intracranial pressure. In only three of these cases were there no other types of severe brain damage, and each case had a particularly extensive depressed fracture of the skull.

Diffuse damage to white matter

The cases in the present series with this type of brain damage have been described in detail elsewhere10 where the relevant literature is also reviewed. The hallmarks of this type of brain damage that can be seen macroscopically are focal lesions in the corpus callosum and in the dorsolateral quadrants of the rostral brain stem. In patients who die soon after their injury these lesions are usually haemorrhagic (Figs 6 and 7), but if the patient survives for some weeks or longer these lesions come to be represented by shrunken, sometimes cystic, and usually small
Fig. 6  Diffuse damage to white matter (six-day survival after injury): there is a recent haemorrhagic lesion in the corpus callosum. Compare with Fig. 8 (from Adams8).

Fig. 7  Diffuse damage to white matter (12-day survival after injury): there is a recent haemorrhagic lesion in the dorsolateral quadrant of the rostral brain stem. Compare with Fig. 9 (from Adams8).

Fig. 8  Diffuse damage to white matter (21-month survival after injury): there is a shrunken cystic area (arrow) in the corpus callosum. The corpus callosum is also thin (from Adams et al.10).

Fig. 9  Diffuse damage to white matter (nine-month survival after injury): there is a shrunken cystic area (arrow) in the dorsolateral quadrant of the rostral brain stem (from Adams et al.19).

scars (Figs 8 and 9). In patients who survive for many months after their injury, there is characteristically some loss of bulk of the white matter of the cerebral hemispheres and an associated increase in the size of the ventricles (Fig. 10). Histological examination will disclose widespread evidence of damage to nerve fibres, as shown by the presence of axonal retraction balls, particularly in the corticospinal tracts and medial lemnisci, in short survivors (Fig. 11), multiple microglial stars (Fig. 12) in those of intermediate survival, and long tract degeneration stainable by the Marchi technique in patients who survive for more than two or three months (Fig. 13). Other common abnormalities associated with this type of brain damage are small petechial haemorrhages throughout the brain, which are presumably attributable to the rupture of small blood vessels, and linearly disposed haemorrhagic lesions in the subcortical white matter at the dorsal angles of the cerebral hemispheres, particularly in the posterior frontal and parietal regions. 

In the present series there were 19 patients with diffuse damage to white matter: all were unconscious from the moment of impact, that is, none experienced a lucid interval, and remained so or in a vegetative state18 until death. The duration of survival ranged from 12 hours to 21 months. In eight of these cases there was no neuropathological evidence of there having been a significantly high intracranial pressure during life; in this group there was a fracture of the skull in only one (12.5%) patient, and the
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MTCI was low—3.9. In the remaining 11 the intracranial pressure had been high during life because of a complicating expanding lesion; there was a fracture of the skull in five (45%) of the group and the MTCI was 10.7. 

Thus in this group of 19 cases there was a much lower incidence of lucid interval than in the rest of the series (0% compared with 44%; p < 0.001), a high intracranial pressure (58% compared with 87%; p < 0.005), and fracture of the skull (32% compared with 86%; p < 0.001). Contusions were also considerably less severe (MTCI of 7.8 compared with 17.8 for the rest of the series; p < 0.001).

Other types of diffuse brain injury
In the series of 151 cases there were two young adults, each of whom was unconscious from the

![Fig. 10](image1) Diffuse damage to white matter (21-month survival after head injury): there is a reduction in the bulk of the white matter and enlargement of the ventricular system (from Adams et al.).

![Fig. 12](image2) Diffuse damage to white matter (six-week survival after injury): there are numerous clusters of microglia in the white matter (from Adams et al.; cresyl violet × 250).

Fig. 10 Diffuse damage to white matter (21-month survival after head injury): there is a reduction in the bulk of the white matter and enlargement of the ventricular system (from Adams et al.).

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Other types of diffuse brain injury
In the series of 151 cases there were two young adults, each of whom was unconscious from the
moment of impact and died within 12 hours of injury. Both had a fracture of the skull, no histological evidence to suggest that the intracranial pressure had been high during life, and innumerable petechial haemorrhages throughout the cortex and white matter of the cerebral hemispheres and in the mid-brain of the rostral pons. The petechial haemorrhages in the cortex were construed as superficial but extensive contusions, with the result that the MTCI in these two cases was high—41 and 55, respectively.

**PRIMARY COMPLICATIONS**

*Intracranial haemorrhage*

This was classified as follows:

(a) Extradural haematoma

(b) Intradural haematoma

   i. Subdural haematoma

   ii. Discrete intracerebral or intracerebellar haematomas not in continuity with the surface of the brain

   iii. ‘Burst’ lobe, i.e., an intracerebral or intracerebellar haematoma in continuity with a related subdural haematoma (Fig. 14).

Only haematomas thought to be sufficiently large to act as significant intracranial expanding lesions were recorded. Thus thin films of blood in the subdural space were excluded from the analysis; so also was subarachnoid haemorrhage since in any acute head injury in which there are cerebral contusions there is almost inevitably some subarachnoid haemorrhage. Furthermore, no circumscribed subarachnoid haematomas were encountered in the present series although they do occasionally occur. The great majority of the haematomas recorded had been evacuated surgically before death.

Ninety-seven patients had intracranial haematomas; they were supratentorial in 88, infratentorial in five, and both supratentorial and infratentorial in four. The distribution of the supratentorial haematomas was as follows:

*Extradural haematoma* was present in 16 patients. In six there were no other intracranial haematomas, and in one of these six patients there were bilateral extradural haematomas. In the 10 other patients with extradural haematoma there were also intracerebral haematomas—seven with ipsilateral supratentorial subdural haematomas (2 cases) or intracerebral haematomas (5 cases), one with a contralateral ‘burst’ temporal lobe, and two with haematoma in the posterior fossa (one patient with a subdural haematoma and one with both extradural and intracerebellar haematomas). There was a fracture of the skull in relation to the extradural haematoma in 15 of the 16 patients. Of the 16 patients with extradural haematomas, eight experienced a lucid interval—three of the six patients with an extradural haematoma only and four of the 10 patients with an intradural haematoma as well.

*Subdural haematoma* occurred in 30 patients. Ten of these patients experienced total lucid intervals and seven partial lucid intervals. Six patients with subdural haematoma did not have a fracture of the skull. Of the 51 patients with lateralisising fractures, 10 had subdural haematomas. In five of these the haematoma was contralateral to the fracture.

One of the 30 patients with subdural haematoma had an ipsilateral extradural haematoma, two had contralateral ‘burst’ lobes (one frontal and one temporal), while two had contralateral frontal intracerebral haematomas.

*Intracerebral haematoma* was found in 33 patients. There were 46 discrete haematomas, 23 in the frontal lobes, 13 in the temporal lobes, four in the parietal lobes, four centred on the basal ganglia, and two in the occipital lobes. Twenty-three patients had single haematomas, eight had two, one had three, and one had four. Five of the 33 patients also had an extradural haematoma and two a subdural haematoma. Seven patients had a total lucid interval, eight a partial lucid interval, and 18 no lucid interval. Four of the 33 patients did not have a fracture of the skull.

‘Burst lobes’ were present in 33 patients, 15 being frontal and 19 temporal. One patient had ‘burst’ frontal and temporal lobes. A contralateral subdural haematoma was present in two patients and an ipsilateral extradural haematoma in one. There was no fracture of the skull in three of the 33 patients.
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Fig. 15 Brain swelling (24-hour survival after injury): there is swelling of the white matter adjacent to contusions affecting the orbital surface of the left frontal lobe.

Of the total of 33, four experienced a total lucid interval, nine a partial, and 20 no lucid interval.

In the 51 patients with lateralising fractures there were 17 with ‘burst lobes’. Of these, nine were ipsilateral to the fracture of the skull and eight contralateral.

Infratentorial haematomas occurred in nine cases—three intracerebellar haematomas, two subdural haematomas, two ‘burst lobes’, and two extradural haematomas. Four of these cases had supratentorial haematomas as well. There was a fracture of the skull implicating the posterior fossa in six of these nine cases, and it was unilateral to the haematoma in every case.

Brain swelling

Brain swelling is used in preference to ‘cerebral oedema’ since cerebral vasodilatation may produce swelling without there being any increase in water content.

Localised brain swelling occurs adjacent to cerebral contusion (Fig. 15) and may therefore contribute to any increase in intracranial pressure.

Unilateral brain swelling, that is, diffuse swelling of one cerebral hemisphere (Fig. 16), was present in 17 patients. There was a fracture of the skull in every case. Of the 51 cases with lateralising fractures there was unilateral brain swelling in five. Swelling was ipsilateral to the fracture in two and contralateral in three. The contusion index for the ipsilateral hemisphere was 11·8, and for the contralateral hemisphere 4·3.

In seven of the 17 cases with unilateral brain swelling an ipsilateral acute subdural haematoma had been evacuated; this association just attains statistical significance (p < 0·025) in comparison with cases with unilateral brain swelling without a subdural haematoma.

Bilateral brain swelling, that is, diffuse swelling of both cerebral hemispheres (Fig. 17), was seen in nine patients. Six of these cases were aged 16 or under, and there was no fracture of the skull in four. One patient, a child aged 4, who developed an extradural...
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haematoma which was evacuated, had a complete lucid interval. Two others had partial lucid intervals. Of the remaining six who did not have lucid intervals, two were examples of diffuse brain damage of immediate impact type, while a third came into the category of multiple small haemorrhages throughout the cortex. The MTCI in the nine cases was 20-9, and contusions were symmetrical (left 10-0; right 10-9). For the five patients aged 15 years or less the MTCI was 11.2; in three of these five it was 0, 2, and 3 respectively, that is, contusions were minimal.

SECONDARY COMPLICATIONS

Brain damage secondary to raised intracranial pressure

It was difficult in the past for the neuropathologist to decide whether or not a patient had experienced a high intracranial pressure during life since, during the period of spatial compensation when the intracranial pressure is not significantly high, there can be considerable brain shift and the development of internal herniae.19 As a result of the introduction of continuous monitoring of intracranial pressure, however, we17 have been able to define certain criteria which allow the neuropathologist to state with a considerable degree of certainty if a supratentorial expanding lesion has been sufficiently large to elevate the intracranial pressure during life even when it has not been monitored clinically. The principal criterion is pressure necrosis in one or both parahippocampal gyri (Figs 18-20). This necrosis can probably be equated with a pressure differential between the supratentorial and infratentorial compartments. The criteria defined, however, have two possible fallacies: if the intracranial pressure is high because of an infratentorial expanding lesion there will be no tentorial herniation and therefore no pressure necrosis in the parahippocampal gyrus; and if the pressure has been high for only a very short period of time, the latter may be insufficient to allow the occurrence of even localised tissue necrosis. Necrosis in the parahippocampal gyrus is therefore indicative of a high intracranial pressure, probably

Fig. 18 Raised intracranial pressure: there is a small wedge of haemorrhagic pressure necrosis (arrow) in the right parahippocampal gyrus along the line of a tentorial hernia.

Fig. 19 Raised intracranial pressure: there is a wedge of pale pressure necrosis (arrow), which could not be seen macroscopically, in the right parahippocampal gyrus (from Adams and Graham17).

Fig. 20 Raised intracranial pressure: there is a small old cystic lesion (arrow) in the right parahippocampal gyrus indicative of previous raised intracranial pressure and tentorial herniation (from Adams and Graham17).
of at least some hours' duration, caused by a supratentorial expanding lesion.

Of the 151 cases there was evidence of a high intracranial pressure in 125 (83%) patients. The causes were usually intracranial haematoma or brain swelling. Thus brain damage—usually haemorrhage or infarction in the brain stem—secondary to a high intracranial pressure and shift and herniation of the brain was an important factor leading to death. This type of damage was, however, not a common cause of the vegetative state since only five of the 125 patients survived for more than four weeks after their injury and, of these, two had diffuse damage to white matter and two severe hypoxic brain damage in addition. In none of the five cases was there severe brain stem damage secondary to the high intracranial pressure.

Of the 26 cases with no evidence of the intracranial pressure having been high during life, eight had evidence of diffuse damage to white matter, seven had severe hypoxic brain damage, and two had multiple small haemorrhages throughout the brain. The causes of death in the remainder were cardiac and/or renal failure (3), meningitis (2), fulminating fat embolism (1), a high cervical spinal injury (1), and severe chest injury (1). One patient had an isolated extradural haematoma in the posterior fossa.

**Hypoxic brain damage**

The incidence and distribution of this type of brain damage in the present series have been described in detail elsewhere where the relevant literature is also reviewed. Of the total of 151 cases, there was hypoxic damage in the Ammon’s horns in 122 (80%), in the basal ganglia in 119 (79%), in the cerebral cortex—excluding infarction in the medial occipital cortex secondary to a high intracranial pressure and tentorial hernia—in 70 (46%), and in the cerebellum in 67 (44%). There were only 13 cases in the entire series in which there was no hypoxic brain damage.

The hypoxic damage in the cerebral cortex took several forms; in the commonest type (33 cases) it was centred on the boundary zones (Fig. 21) between the major cerebral arterial territories, particularly between the anterior and middle cerebral arterial territories, but also in the lateral part of the occipital lobe in the common boundary zone of the anterior, middle, and posterior cerebral arterial territories. The hypoxic damage was bilateral in 27 of these 33 cases. In another group of 14 cases the hypoxic damage was centred on the territories supplied by the anterior and/or the middle cerebral arteries. This type of damage was bilateral in eight. In 10 cases there were multiple foci of necrosis throughout the cerebral cortex, while in eight there was severe and diffuse necrosis of the cortex (Fig. 22).
80 mm Hg for at least 15 minutes, or a PaO₂ of less than 50 mm Hg at some time after the injury) than in those who had not (p < 0·005). It was also commoner in patients who had experienced a high intracranial pressure as defined above than in those who had not (p < 0·005).

Many of the patients in this study were included in another study in which the angiographic findings were correlated with the presence of hypoxic brain damage.
contusions are indicative of focal damage to the brain. Diffuse damage to white matter is probably the most important single factor governing the outcome in a patient with head injury since it occurs at the moment of impact and is therefore neither preventable nor reversible in the course of further clinical management. None of the 19 patients with this type of brain damage experienced a lucid interval, and there were significantly fewer cases with a fracture of the skull, contusions, and a high intracranial pressure compared with the remainder of the series. Indeed, the brains of patients with this type of brain damage may appear virtually normal externally. This is the commonest type of brain damage we observe in brains submitted to us by pathologists in other hospitals because they have found it difficult to reconcile the clinical picture of severe brain damage resulting from a head injury with the external appearance of the brain. It is also, in our experience, the commonest cause of the vegetative state after head injury. As we have discussed before,10 there has been some controversy in the past as to the pathogenesis of this type of brain damage but since it clearly occurs at the moment of impact it seems likely that it is brought about by shear-strains engendered in the white matter which are sufficiently intense to cause disruption of nerve fibres. Rotational movements are probably of greater importance than translational forces in its pathogenesis. Although the clinical picture may be that of primary brain stem damage, damage is never restricted to the brain stem. The C-T scan is often normal23 in patients with diffuse damage to white matter but it is sometimes possible to identify the focal lesions in the corpus callosum and in the brain stem.24

The two cases with multiple small haemorrhages throughout the cortex are difficult to classify. Since both patients were unconscious until they died within 12 hours of injury, it seems likely that this is another type of diffuse immediate impact injury. It may be commoner than the present series suggests since we encounter very few patients who die within 12 hours of injury.

Intracranial haematoma is a common and well-recognised complication of head injury.22 25 It is perhaps worth emphasising that only 50% of the patients with extradural haematoma experienced a lucid interval, that 57% of the patients with a pure subdural haematoma did experience a lucid interval, and that in 50% of the patients with a lateralising fracture and a subdural haematoma the haematoma was contralateral to the fracture.

Brain swelling is an important complication of head injury since it may lead to a considerable increase in the volume of the intracranial contents. It is of particular significance in two contexts—diffuse swelling of one cerebral hemisphere and diffuse swelling of both cerebral hemispheres. The occurrence—or perhaps persistence—of swelling of a cerebral hemisphere after evacuation of an ipsilateral acute subdural haematoma is generally recognised but the association just attained statistical significance in the present series. Unilateral oedema is not restricted to patients with subdural haematoma, and in such cases contusions were more severe in the ipsilateral hemisphere. The occurrence of diffuse brain swelling in children is also well recognised,23 24 and six of the nine patients in the present series with diffuse brain swelling were aged 16 years or less. That this can occur in the absence of severe contusions is clearly established by the fact that in three of the children in the present series with diffuse brain swelling the MTCI was very low. The pathogenesis of brain swelling in association with acute head injury has not been clearly defined but it seems possible, at least in children, that it may be contributed to by loss of vasomotor tone, which in turn leads to vasodilatation.26 27 Vasodilatation itself will produce brain swelling, and if the vasodilatation persists the blood-brain barrier may become defective, this in turn leading to true vasogenic extracellular cerebral oedema. Other causes of diffuse brain swelling are diffuse damage to white matter and severe hypoxic brain damage.

Of the secondary complications of head injury, brain damage secondary to a high intracranial pressure and distortion and herniation of the brain is well recognised, and analysis of the present series does not yield any new information. It is, however, worth emphasising that, despite the frequency of secondary damage to the brain stem, this was not a common cause of prolonged coma since every patient with severe secondary brain stem damage died within four weeks of injury.

It is also clear from the present analysis that hypoxic brain damage is common in patients dying as a result of a head injury. Perhaps the principal reason why this high incidence has not been emphasised in the past is that much of it can be identified only microscopically.14–16 Furthermore, the incidence may be particularly high in the present series since all the patients survived long enough to be transferred to a neurosurgical unit. We have already argued11 that it is unlikely that the hypoxic damage occurs at the moment of impact and that the damage may therefore be potentially preventable since it is significantly more common in patients known to have experienced an episode of hypoxia in the post-injury period and in patients in whom the intracranial pressure has been high. From the distribution of the brain damage it seems likely that much of it is due to a reduction in cerebral perfusion pressure—hence
the need to preserve cerebral blood flow and arterial oxygenation in patients who have sustained a head injury. Severe hypoxic brain damage in a patient with head injury can also be associated with a normal C-T scan.23

The distribution of hypoxic damage is most easily assessed in large histological sections. It is hardly feasible for a general pathologist to undertake a comprehensive neurohistological analysis in every case of fatal head injury but it is usually possible to establish that a patient has experienced an episode of hypoxia sufficiently severe to produce brain damage by the histological examination of quite small, bilateral blocks from the ‘selectively vulnerable areas’, viz, the arterial boundary zones, the Ammon’s horns, the thalamus, and the cerebellum.15 16

Meningitis is another well recognised complication of a head injury, and it occurred in four cases in the present series. In every case there was a fracture of the base of the skull, and in one of the cases meningitis did not develop until four weeks after the injury.

There were two cases in the present series with fulminating fat embolism. This was the only other type of severe brain damage encountered, and in each case it was entirely unexpected since there was no macroscopic evidence suggestive of cerebral fat embolism.

This series of cases forms part of a systematic study of the pathology of brain damage that occurs in fatal non-missile head injury and is associated with the MRC Head Injury Research Programme being undertaken in the University Department of Neurosurgery. That study has been recording for 11 years clinical data about all severe head injuries in this Institute as well as cases from centres in other parts of the world.28 The cases reported in the present series were collected some 10 years ago, so that a study of more recent cases might reveal a different incidence of brain damage since changing patterns of admission and management may have produced some alterations in the types and distribution of secondary complications. A computerised data collection system has now been developed so that as close clinicopathological correlations as possible can be established. Special attention is being paid to factors that might have been avoided,29 30 particularly in patients who were known to have talked some time after their injury.13 These studies have highlighted the importance of hypoxia and hypotension, and of reducing delay in the treatment of intracranial haematoma. These factors have all been implicated as events leading to a fatal outcome, and it seems likely that they are also factors contributing to persistent brain damage in patients who survive their injury.

The present study would not have been possible without the willing co-operation of the forensic pathologists in the West of Scotland who allowed us to fix the brains intact before dissection. We are particularly indebted to Emeritus Professor G Forbes, Professor WA Harland, Dr A Dick, Dr WDS McIay, Dr AA Watson, and Dr WP Weir. We are also indebted to the staff of the Department of Neurosurgery for access to their clinical records. It is a pleasure to thank the Department of Medical Illustration of the Southern General Hospital for their help in preparing the illustrations, and Mrs J Rubython for typing the manuscript.

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