Brain (2001), **124,** 1290–1298

Neuropathology of inflicted head injury in children
I. Patterns of brain damage

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Summary
Fifty-three cases of non-accidental head injury in children were subjected to detailed neuropathological study, which included immunocytochemistry for microscopic damage. Clinical details were available for all the cases. There were 37 infants, age at head injury ranging from 20 days to 9 months, and 16 children (range 13 months to 8 years). The most common injuries were skull fractures (36% of cases), acute subdural bleeding (72%) and retinal haemorrhages (71%); the most usual cause of death was raised intracranial pressure secondary to brain swelling (82%). On microscopy, severe hypoxic brain damage was present in 77% of cases. While vascular axonal damage was found in 21 out of 53 cases, diffuse traumatic axonal injury was present in only three. Eleven additional cases, all of them infants, showed evidence of localized axonal injury to the craniocervical junction or the cervical cord. When the data were analysed by median age at head injury, statistically significant patterns of age-related damage emerged. Our study shows that infants of 2–3 months typically present with a history of apnoea or other breathing abnormalities, show axonal damage at the craniocervical junction, and tend also to have a skull fracture, a thin film of subdural haemorrhage, but lack extracranial injury. Children over 1 year are more likely to suffer severe extracranial, particularly abdominal, injuries. They tend to have larger subdural haemorrhages, and where traumatic axonal injury is present, show patterns of hemispheric white matter damage more akin to those reported in adults. Diffuse axonal injury is an uncommon sequel of inflicted head injury in children.

Keywords: non-accidental head injuries; infant head injury; subdural hemorrhage; child abuse

Abbreviations: βAPP = β amyloid precursor protein; NAI = non-accidental injury; DAI = diffuse axonal injury

Introduction
The neuropathology of inflicted head injury, whether adult assault or non-accidental injury (NAI) in children, has not been fully studied. Given the central role that a neuropathologist may be asked to play in a fatal NAI case, it is surprising that since the first paper of Lindenberg and Freytag in 1969, which described 'contusional tears' in the brains of young infants who had suffered inflicted head injury with impact (Lindenberg and Freytag, 1969), there have been only a few published studies of the neuropathology of NAI in the literature (Calder *et al.*, 1984; Vowles *et al.*, 1987; Hadley *et al.*, 1989; Shannon *et al.*, 1998; Gleckman *et al.*, 1999), the largest series being 14 cases; in none of them have detailed clinicopathological correlations been attempted. This dearth of information means that much of the data needed for interpretation of findings in medicolegal situations has to be extrapolated from what is known about adult head injury, despite the fact that the majority of fatal cases fall in the very young age group, and there are many reasons why the immature brain should react differently to trauma. We have examined the brains from 53 well-documented cases of inflicted head injury with the aim of analysing patterns of neuropathology in non-accidental head injury in children of different ages to provide data for use in assessment of such cases.

Methods
Study population
The study population comprised all the cases of paediatric head injury in the files of two neuropathologists (H.L.W. and J.F.G.) that fulfilled one of a series of criteria for the diagnosis of NAI. The diagnostic criteria used were: (i) head injuries in which there had been a confession by the perpetrator

($n = 7$); (ii) cases in which non-accidental head injury had been established as a result of conviction in a criminal court, and in which there were also unexplained extracranial injuries to support this ($n = 19$); (iii) cases with unexplained injuries elsewhere in the body, in addition to the head injury, but no conviction ($n = 8$); (iv) cases in which the carer was tried and convicted of injuring the child, but in which there were no extracranial injuries ($n = 12$); and (v) cases in which there was a major discrepancy between the explanation of the incident given by the carer and significant injuries such as a skull fracture, or if the history was developmentally incompatible ($n = 7$). Cases were excluded if there was insufficient material in the form of either blocks or residual brain tissue. Full documentation, including witness statements and court papers, was available for 52 out of 53 cases; for one case only a clinical history was available, but there was sufficient detail to merit inclusion into the study.

The research proposal was scrutinized and approved by the Research Ethics Committee of the East London and City Health Authority (T/98/007).

Sampling for microscopy

The brains were systematically sampled for histology, and where initial sampling had been inadequate, further blocks were taken. In 32 cases large hemisphere blocks were used. In 52 out of 53 cases, minimum sampling included several blocks of hemispheric white matter, of corpus callosum, internal capsule, cerebellum, midbrain, pons, medulla and spinal cord. In one case only, there were no blocks of the brainstem, merely cerebrum and several segments of cervical spinal cord.

Staining methods

H & E (haemotoxylin and eosin) staining was performed on all blocks. Immunocytochemistry for β-amyloid precursor protein (βAPP) (Chemicon monoclonal, clone 22C11) was carried out using an avidin–biotin complex, peroxidase-labelling detection system (Vector Universal Elite kit). Anti-βAPP was used at a dilution of 1 : 300, with 1 h incubation at room temperature, after microwave antigen retrieval. For cases with long survival or evidence of a previous head injury, CD68 (Dako, PG-M1) was used in addition, at a dilution of 1 : 100, with 40 min incubation and microwave retrieval. Additional stains, including Perls, HVG (haematoxylin van Gieson) and immunohistochemistry for GFAP (glial fibrillary acidic protein), were performed on selected blocks.

Results

Subjects and details of injury

The data consisted of 53 cases of fatal non-accidental head injury. Details of the presentation to paramedics or doctors were: apnoea, abnormal breathing or collapse, with the child suddenly turning blue and limp (33 cases); found dead (six cases); child dropped (four cases); fell (two cases); found unconscious at the bottom of the stairs (two cases); and thrown, shaken or stabbed (one case of each). There were no details of presentation in three cases. The age at head injury ranged from 20 days (at 37 weeks' gestation) to 8 years. Since one of the aims of our analysis was to focus on the differences between younger and older NAI cases, we divided the series into those aged <1 year at presentation (who we refer to as 'infants', $n = 37$), and those aged ⩾1 year (who we refer to as 'children', $n = 16$). Outline details of the study population and findings are shown in Tables 1 and 2. Figure 1 summarizes the results in Table 2 by displaying the relative risk (and 95% confidence interval) corresponding to each factor, indicating whether the presence of the factor was more common, less common or the same in infants compared with children.

Table 1 *Summary information on 53 NAI cases*

Factor		All cases	Infants (<1 year)	Children (⩾1 year)
Sex (number)	Male	27	18	9
	Female	26	19	7
Age at head injury (days)	Number	53	37	16
	Median	124	73	630
	Mean	347	97	925
	Range	20–2920	20–273	388–2920
Survival (days)	Number	49*	37	12
	Median	1	1	0.7
	Mean	21	27.7	1.2
	Range	0–695	0–695	0–3

*Accurate survival times were not available for four cases.

General autopsy findings

Fifty-one per cent of subjects (27 out of 53) had significant extracranial injury: of these, 10 had recent or old fractures of the ribs or clavicle, four had long bone fractures, six had serious abdominal injuries, principally bleeding from hepatic and/or mesenteric lacerations. Seven had burns or extensive bruising. Evidence of previous trauma to the head was seen in 20% of cases, to the body in 8% and to both head and body in 4%.

Eighty-five per cent of subjects (45 out of 53) had signs of impact to the head at autopsy, in the form of either subscalp bruising or skull fracture. In the remaining eight cases, all infants, neither bruising nor fracture was found at autopsy. Skull fractures, present in 19 out of 53 cases, were found in the parietal and/or the occipital bones in 18 out of 19 cases. In six subjects the fractures were bilateral. The median age in those with a skull fracture was 3 months and 6 months for those without. No extradural haemorrhages were observed in cases with skull fractures.

Macroscopic neuropathology

Eighty-one per cent of the cases (43 out of 53) were found to have subdural haemorrhages, 38 of them acute. The

Table 2 *Principal details of all 53 NAI cases, comparing findings in infants with those in children*

Factor		% All cases (number)	% Infants (<1 year) (number)	% Children (⩾1 year) (number)	Relative risk	*P*-value‡
Clinical						
Apnoea or respiratory systems	No	37 (19)	22 (8)	69 (11)	1.00	0.002
	Yes	63 (33)	78 (28)	31 (5)	2.49	
General autopsy						
Significant extracranial injury	No	49 (26)	59 (22)	25 (4)	1.00	0.03
	Yes	51 (27)	41 (15)*	75 (12)†	0.54	
Earlier injury	No	68 (34)	67 (24)	71 (10)	1.00	1.00
	Any	32 (16)	33 (12)	28 (4)	1.17	
	Head	20 (10)	19 (7)	21 (3)	0.98	
	Body	8 (4)	8 (3)	7 (1)	–	
	Both	4 (2)	6 (2)	0 (0)	–	
Subscalp bruising	No	23 (10)	27 (10)	0 (0)	1.00	0.02
	Yes	77 (43)	73 (27)	100 (16)	0.63	
Macroscopic neuropathology						
Skull fracture(s)	No	64 (34)	57 (21)	81 (13)	1.00	0.12
	Yes	36 (19)	43 (16)	19 (3)	2.31	
Extradural haemorrhage	No	100 (53)	100 (37)	100 (16)	–	–
Intracranial pressure raised	No	18 (9)	19 (7)	15 (2)	1.00	0.71
	Yes	82 (42)	81 (29)	85 (13)	0.93	
Subdural haemorrhage	No	19 (10)	16 (6)	25 (4)	1.00	0.46
	Any	81 (44)	84 (31)	75 (12)	1.12	
	Old	9 (5)	8 (3)	12 (2)	1.00	
	Thin film	64 (34)	70 (26)	50 (8)	1.22	
	Mass lesion	8 (4)	5 (2)	12.5 (2)	–	
Subarachnoid haemorrhage	No	40 (21)	35 (13)	53 (8)	1.00	0.56
	Any	60 (31)	65 (24)	47 (7)	1.39	
	Old	12 (6)	14 (5)	7 (1)	2.50	
	Yes	48 (25)	51 (19)	40 (6)	1.39	
Intracerebral haemorrhage	No	94 (50)	95 (35)	94 (15)	1.00	1.00
	Yes	6 (3)	5 (2)	6 (1)	0.86	
Contusional tears	No	92 (48)	89 (32)	100 (16)	1.00	0.30
	Yes	8 (4)	11 (4)	0 (0)	3.7§	
Microscopy						
Hypoxia-ischaemia	No	19 (10)	13 (5)	31 (5)	1.00	0.17
	Any	81 (43)	87 (32)	69 (11)	1.26	
Focal infarct		4 (2)	3 (1)	6 (1)	–	
	Global hypoxia	77 (41)	84 (31)	63 (10)	–	
Vascular axonal injury¶	No	60 (31)	63 (23)	50 (8)	1.00	0.37
	Yes	40 (21)	37 (13)	50 (8)	0.72	
Focal traumatic axonal injury¶	No	58 (30)	55 (20)	63 (10)	1.00	0.01
	Central wh. m.	21 (11)	14 (5)	37 (6)	0.53	
	Craniocervical	21 (11)	31 (11)	0 (0)	7.45§	
Diffuse axonal injury	No	94 (50)	95 (35)	94 (15)	1.00	1.00
	Yes	6 (3)	5 (2)	6 (1)	0.86	
Retinal bleeding	No	29 (11)	30 (9)	25 (2)	1.00	1.00
	Yes	71 (27)	70 (21)	75 (6)	0.93	

The relative risk is estimated as the percentage of infants with the presence of the specified factor divided by the percentage of children with the same finding. Complete results were not available for all 53 cases. wh. m. = white matter. *Of these 15, nine had an old injury and six had a new injury. †All 12 had a new injury. ‡Using Fisher's exact test. §0.5 used instead of 0 when estimating the relative risk. ¶Impossible to assess in one case.

remaining five showed pigmentation and membrane formation indicative of older subdural bleeding. In 34 cases the subdural was trivial in terms of quantity of blood, almost invariably described in the post-mortem report as a 'thin film'; 28 of these were bilateral. The four haematomas that were large enough to act as space-occupying lesions occurred in four older subjects (ages 8 months, 9 months, 3 years and 4 years). Cases with a significant subdural were on average

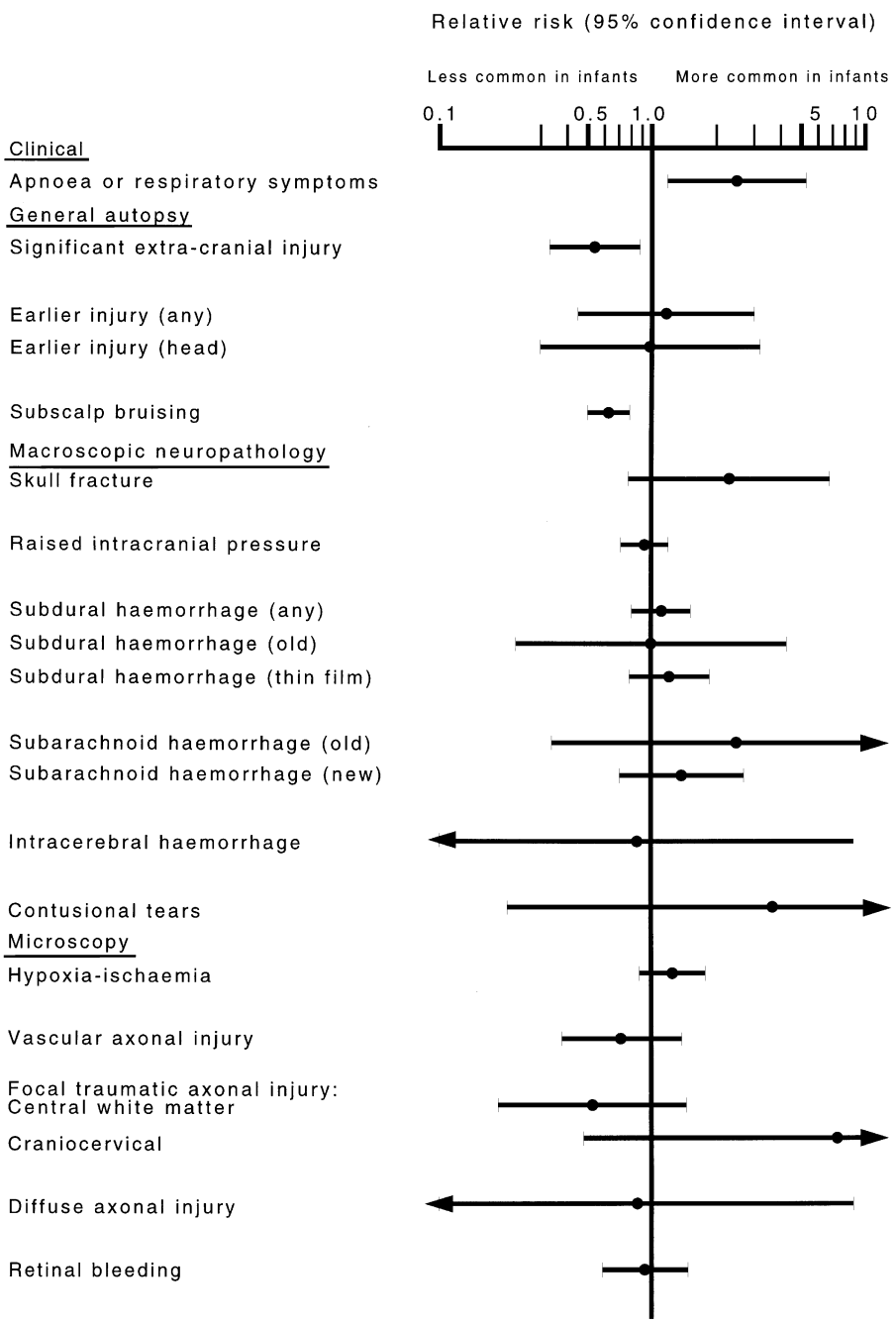

Fig. 1. The relative risk and 95% confidence interval of the presence of specified factors in infants compared with children. The relative risk is the percentage of infants with the specified finding divided by the percentage of children with the same finding. For example, from Table 2, 78% of infants presented with apnoea compared with 31% of children; the relative risk is thus 2.5 (i.e. infants were 2.5 times more likely to present with apnoea than children).

almost 2 years old, ~1.5 years older than those without any subdural haemorrhage or merely trivial bleeding ($P = 0.10$).

The brain weight was increased in 82% of the cases in which it had been recorded at post-mortem, and raised intracranial pressure was the most common cause of death.

Of other features, subarachnoid haemorrhage was present in about half the cases (25 out of 52), in association with subdural bleeding or with a fracture, or both. It did not occur on its own. Cortical contusions were seen in five cases only. Contusional tears were found in only four cases and all were <4.5 months old. Three had fractures and the fourth showed neither scalp bruising nor fracture. Intracerebral haemorrhage was seen in only three cases, of which it was trivial in one, but acted as a mass lesion in two. A layer of epidural

bleeding was seen round the upper cervical cord in three cases.

Microscopic changes

Of the 38 cases in which the eyes were examined by a pathologist, 71% (27 out of 38) had retinal haemorrhages, of which 26 were bilateral. The original sampling of the eyes had not been uniform, however, and we were unable to analyse the distribution of the bleeding further. There was a significant association between subdural bleeding and the presence of retinal haemorrhages; in all cases with intraocular bleeding there were subdural haemorrhages ($P < 0.001$). Of the 10 cases in which there were no subdural haemorrhages, five had the eyes examined and none of these showed retinal bleeding.

According to the histories given, 21 of the 49 children for whom there were accurate survival data were either found dead or died in <2 h; survival data was insufficient for any histological changes to be detectable. However, 13 of these subjects, including 11 infants, had clearly lived longer after the cerebral insult than the history suggested, since they showed widespread hypoxic changes on haematoxylin and eosin staining (generally believed to take ~4–6 h to develop in adults; Adams and Graham, 1994). Ten of them also showed foci of recent traumatic axonal damage on βAPP immunocytochemistry (not detectable in adults with <2 h survival; Geddes *et al.*, 1997), which were restricted to the corticospinal tracts in the brainstem in five cases.

The most frequent microscopic finding in the brains was global neuronal hypoxia–ischaemia, identified by routine neuropathological criteria (widespread neuronal cytoplasmic eosinophilia and shrinkage), and present in 84% of infants and 63% of older children. Damage to axons, both vascular and traumatic, was detected with βAPP immunohistochemistry in a number of cases. Vascular axonal damage was diagnosed when a 'geographic' pattern of white matter immunoreactivity was present, which was usually widespread and related to vessels. Focal geographic βAPP expression, commonly seen in the diencephalon and brainstem, was taken to be outlining areas of incipient ischaemia resulting from brain swelling (Geddes *et al.*, 2000). [Typical patterns interpreted as vascular in origin, are illustrated in Fig. 1 in the companion paper (Geddes *et al.*, 2001)]. Such appearances were seen in 37% of infants and 50% of the older children, and were assumed to be the sequelae of ischaemic white matter damage secondary to brain swelling and raised intracranial pressure—indeed, raised intracranial pressure was associated with the presence of vascular βAPP expression ($P = 0.06$).

Traumatic damage to axons was identified by finding βAPP-immunoreactive axons or bulbs, scattered or in groups in hemispheric white matter, corpus callosum and internal capsule. Where the brainstem was also involved, the case was—by definition—one of diffuse axonal injury (DAI) (see below). In cases with survival of >24–48 h, ischaemic axonal damage could be excluded by routine histopathological criteria, and with survival of 1 week or over, microglial clusters were present around foci of axonal pathology (Geddes *et al.*, 2000). The traumatic damage seen in the series varied from scattered foci in the hemispheres only, to damage severe enough to be called DAI. This is defined as widespread traumatic axonal damage occurring throughout the centrum semiovale, particularly parasagittal white matter, corpus callosum, internal capsule and cerebellar peduncles in the rostral brainstem (Adams *et al.*, 1989). In our series it was found in only three out of 53 cases: two of these were infants, who had multiple skull fractures; the other was an 8-year-old child. Lesser degrees of hemispheric axonal damage were detected in only 11 cases, five infants and six older children (see Table 2, which distinguishes between focal 'traumatic axonal injury' and the more severe 'diffuse axonal injury'; Geddes *et al.*, 2000). In one case the state of preservation of the brain made the immunohistochemistry impossible to assess.

While DAI was rare, localized axonal damage was detected in 11 subjects in the infant group, in the lower brainstem (eight cases) and in cervical cord roots (three cases). The damage in the brainstem was found to be anatomically confined to the corticospinal tracts in the lower pons and medulla, and the number of axonal swellings varied from very few in the long tracts to a large number, but were only present in these tracts, bilaterally (the worst case is illustrated in Fig. 2). In one other case survival had been sufficient for a microglial reaction to be established round the bulbs.

Patterns of injury in different age groups

Abdominal injuries were less common in infants (two out of 37 infants compared with four out of 16 children; relative risk 0.22 of infants to children; $P = 0.07$). Infants were less likely to have a significant extracranial injury (relative risk 0.54; $P = 0.03$), and they tended also to have evidence of previous traumatic damage (nine out of 15 infants had an old injury compared with none out of 12 children, $P = 0.001$).

Specific neuropathological features were also analysed according to median age at head injury (Figs 3 and 4). At 2–3 months of age, cases tended to have presented with apnoea ($P = 0.002$) and damage at the craniocervical junction, particularly in the corticospinal tracts ($P = 0.02$). There was a suggestion that they also tended to have a skull fracture and trivial subdural bleeding ($P = 0.10$). The average age differences were: cases with apnoea were 1 year younger than those without apnoea; those with corticospinal tract damage were 3 months younger than those without; those with a skull fracture were 3 months younger than those without the corresponding damage. The youngest cases also tended not to have significant extracranial injury ($P = 0.10$) and those without significant extracranial injury were ~1 month younger than those with. Finally, cases with traumatic axonal damage in the cerebrum tended to be ~15 months old on average, and ~10 months older than those without any

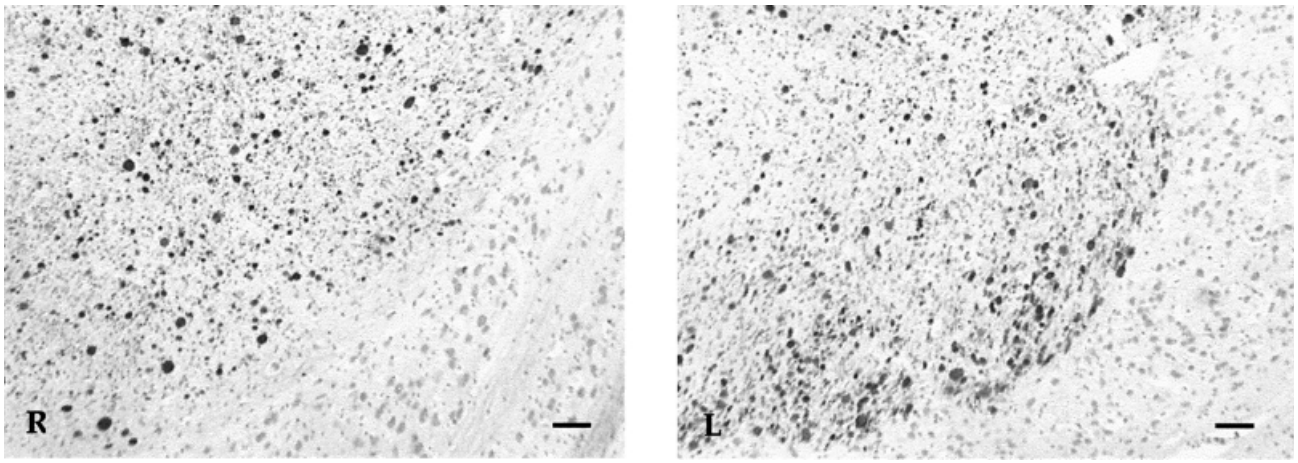

Fig. 2. A low power view of both corticospinal bundles in the caudal pons of a 20-day-old girl. Very many βAPP-immunoreactive axonal bulbs and swellings are seen. Note that there is no βAPP expression in the transverse fibres. R = right; L = left. Bar = 75 μm.

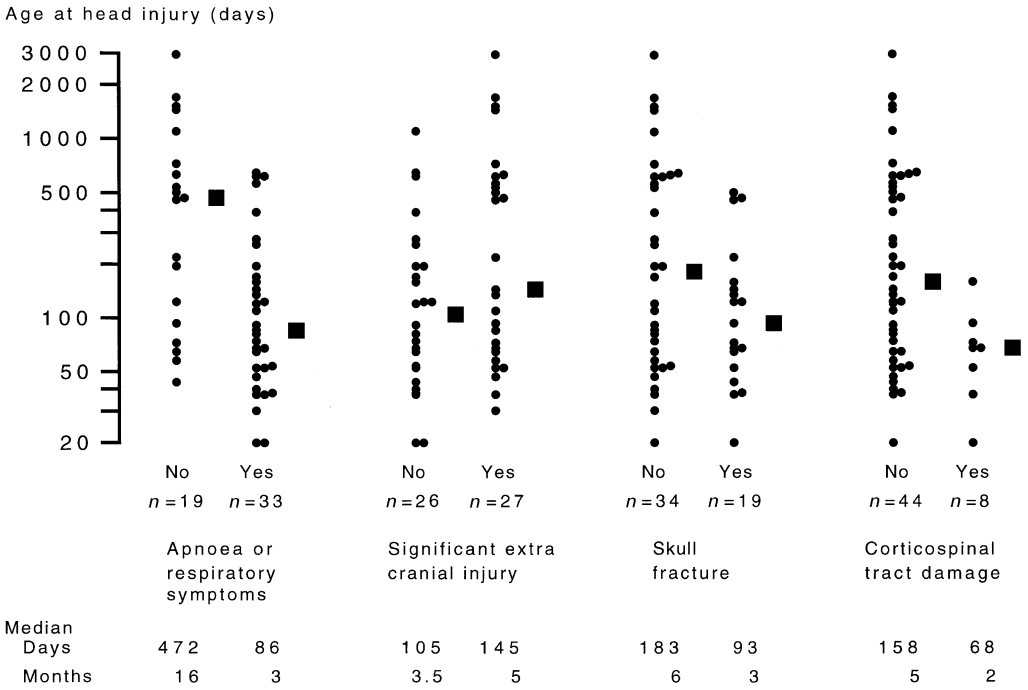

Fig. 3. The age (or approximate age) at head injury in the 53 cases of NAI according to the presence or absence of specified factors. The median in days and months (square symbols) are shown. The *P*-values for the difference between the medians (using a non-parametric Wilcoxon rank test) were $P = 0.002$ (apnoea or respiratory problems); $P = 0.10$ (significant extracranial injury); $P = 0.10$ (skull fracture); $P = 0.02$ (corticospinal tract damage). The presence or absence of apnoea at presentation was not known for one case and for another case the lower brainstem was not available.

traumatic axonal damage ($P = 0.008$). The tendency for large subdural haemorrhages to be found in older children has been recorded above.

'Shaken-only' infants versus others

The eight infants who showed no signs of impact were assumed to have been shaken, and in one case a carer had confessed to having done so. The clinical presentation of all but one of these eight 'shaken-only' cases was of collapse or respiratory arrest. In seven the brain was swollen sufficiently to cause death; the eighth child survived 5 months in hospital after his head injury with severe hypoxic–ischaemic brain damage, before dying of bronchopneumonia. One of the eight had a rib fracture, but no other extracranial injuries were seen. Seven had subdural haemorrhages, described in each case as a 'thin film' or 'small', and five of the six cases in which the eyes were examined had bilateral retinal

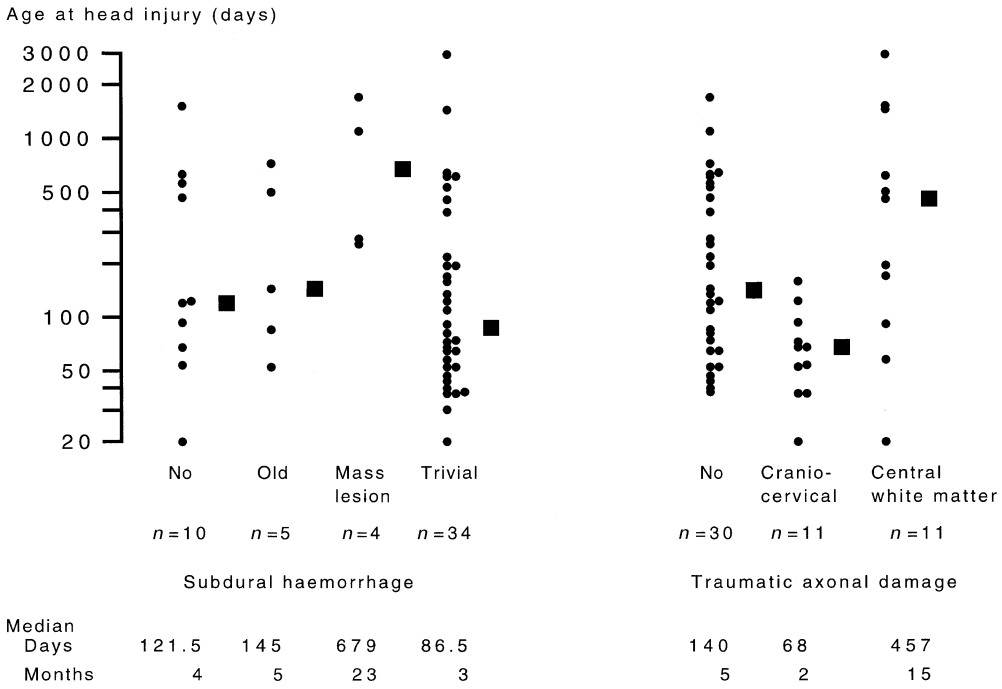

Fig. 4. The age (or approximate age) at head injury in the 53 cases of NAI according to the absence or type of subdural bleeding and traumatic white matter damage. The median in days and months (square symbols) is shown. The *P*-values for the difference between the medians (using a non-parametric Kruskal–Wallis analysis of variance) were $P = 0.10$ (subdural haemorrhage); $P = 0.008$ (traumatic axonal damage). Information on traumatic axonal damage was not known for one case.

haemorrhages. One case had corticospinal tract damage, and one had axonal damage in the nerve roots in cervical spinal cord segments. There was no evidence of differences between the pathology in this 'shaken-only' group and the 29 infants who had evidence of impact.

Discussion

While the literature contains many studies of neuropathological findings in adult head injury, there is virtually no comprehensive information from neuropathologists on brain damage in fatal paediatric head injury. The few studies that have been published have concentrated on specific features only, rather than patterns of injury, and the numbers of cases have been small. Lindenberg and Freytag reported a series of 16 head-injured infants, collected because they all demonstrated unusual impact lesions in white matter which the authors termed 'contusional tears' (Lindenberg and Freytag, 1969). These lesions were also documented by Calder and colleagues in seven out of nine infants, all <5 months (Calder *et al.*, 1984), almost all in association with skull fractures. Hadley and colleagues described damage to the craniocervical junction in a small series (Hadley *et al.*, 1989), while Hart reported on correlations between post-mortem imaging of the brain and autopsy findings (Hart *et al.*, 1996). Three further papers, which looked at microscopic brain changes in NAI, have suggested that diffuse axonal injury is a feature of non-accidental head injury (Vowles *et al.*, 1987; Shannon *et al.*, 1998; Gleckman *et al.*, 1999); their findings are discussed in more detail in a companion paper (Geddes *et al.*, 2001).

A common drawback of most of these series, particularly those relating to the question of microscopic damage, is that they contain limited additional clinical detail, and very little attention has been paid to potentially confounding factors such as artificial ventilation, brain swelling, the presence of global hypoxia and so on (Geddes *et al.*, 2000). In some, the paucity of neuropathological detail supplied undermines the validity of the authors' conclusions: this is discussed in more detail elsewhere (Geddes *et al.*, 2001). The lack of firm published data on the neuropathology is compounded by the fact that review articles or texts which mention the pathology of NAI, particularly that caused by shaking, tend merely to reiterate the neuropathological features of adult trauma (Leestma, 1988; Brown and Minns, 1993; David, 1999). Our study in fact confirms that there are significant differences not only between the pathology of non-accidental head injury in children and adults, but also between children of different ages.

The diagnosis of NAI

One of the major problems encountered in assembling cases for NAI series is that the presenting history may not be accurate, and very few confessions are obtained (seven out of 53 in our series). Often child abuse is first suspected when subdural bleeding or retinal haemorrhages are detected—i.e. on the basis of the pathology alone. However, if one aims to

produce reliable data this approach is untenable, since it may result in cases of accidental injury being included.

In an attempt to be as certain as possible that we were indeed dealing with cases of inflicted head injury, we drew up diagnostic criteria for this study (see Methods). Even so, we are aware that the 12 cases in one category (where a conviction was obtained, in the absence of extracranial injuries), might conceivably include cases that were not in fact NAI, even though they had the pathology widely taken to be pathognomonic or at least 'highly suggestive' of child abuse. Lack of firm objective grounds for concluding that cases were NAI is another drawback of many series in the literature, including clinical and forensic series.

Distinctive features of inflicted head injury in children

Despite the frequency of skull fractures, extradural haematomas are rarely reported in NAI. There were none in our series. This may be because the common sites of skull fracture [almost exclusively parietal or occipital in our series, as in others (Duhaime *et al.*, 1998)], are ones that would not be expected to compromise a major artery, but the fact that the dura is very densely adherent to the undersurface of the infant skull, and not easily stripped from the bone, probably also contributes. Extradural haemorrhage around the cervicomedullary junction, however, while not a common feature in adult head injury, has been reported in NAI (Hadley *et al.*, 1989), and was noted in three of our cases.

In a general review of the pathology of what he first described as the 'whiplash shaken infant syndrome', Caffey talked of 'massive traumatic intracranial bleeding' resulting from shaking (Caffey, 1974). In point of fact, subdural haemorrhages in NAI in young children are materially different from those seen in adults, and are rarely 'massive' (Carter and McCormick, 1983; Duhaime *et al.*, 1998; David, 1999). They are almost invariably bilateral thin films of blood over the cerebral hemispheres, which do not require neurosurgical intervention—indeed, they may be missed on scans, even by magnetic resonance imaging, and only found at post-mortem (Hart *et al.*, 1996; Feldman *et al.*, 1997). Of themselves they do not usually cause mass effect, and may be survivable—as the occasional finding of organizing haematomas at autopsy shows. In our series, the few cases in which the subdural acted as a significant mass lesion were seen in the older infants and children. The question that needs answering is: given the differences between 'adult'-type subdurals and those seen in infants in NAI, are the conditions or forces that produce the two necessarily the same?

Subarachnoid bleeding is also rarely clinically significant in NAI. Most occurs over the hemisphere, associated with fracture sites or underlying subdurals, where it presumably results from rupture of veins crossing the subarachnoid space. Contusions, superficial foci of haemorrhagic necrosis which characteristically affect the base of the brain and areas of cortex underlying skull fractures, are seldom seen in infants, although common in older children. This difference is probably explained in part by the fact that the floor of the infant skull is smooth, and in part by the soft consistency of the incompletely myelinated brain.

Macroscopically, the majority of brains showed merely swelling, manifest as increased brain weight. Histological study revealed that a significant proportion of the children who had been reported to have been found dead or died rapidly had survived an insult sufficiently long for neuronal cytoplasmic or axonal pathology to be detectable. In all brains in which there were microscopic changes, global hypoxia was the most usual finding. While prolonged ventilation might be thought to account for this in a proportion of cases, the clinical notes for our cases generally indicate that brain swelling and hypoxic changes were evident when the child was scanned on arrival at hospital. In terms of microscopic brain damage, we took great care to sample the brain adequately, using large brain blocks where possible, and to attempt to distinguish between axonal damage caused by trauma and axonal damage secondary to hypoxia–ischaemia, raised intracranial pressure and/or brain shift. Our experience has always been that DAI is a rarity in NAI. In the present series it was only found in three out of 53 cases: in an 8-year-old child (in whom one might reasonably expect neuropathology akin to that seen in a young adult) and in two infants, both of whom had very severe head injuries with bilateral skull fractures. These findings would tend to confirm the study of Duhaime and her colleagues (Duhaime *et al.*, 1987) which suggested that shaking does not reproduce the forces necessary for DAI to occur. The localized axonal damage demonstrated in corticospinal tracts in the lower brainstem, similar to that reported in adults with non-disruptive cervical cord damage due to a hyperextension neck injury (Lindenberg and Freytag, 1970; Geddes *et al.*, 2000), may in fact be more significant. Injury at this point, presumably caused by stretch to the neuraxis produced by cervical hyperextension, might provide an explanation for the frequent occurrence of apnoea at presentation. We have discussed this finding, and the general question of what our study has revealed of the nature of diffuse brain damage and mechanisms of injury, elsewhere (Geddes *et al.*, 2001).

Contusional tears, the traumatic lesions peculiar to the brains of young infants (Lindenberg and Freytag, 1969; Calder *et al.*, 1984), which are occasionally detected by neuro-imaging (Hausdorf and Helmke, 1984; Jaspan *et al.*, 1992), were found in four of our infant cases at post-mortem. Because these tissue tears are believed to be the result of shearing of the interface between grey and white matter, the conditions have been assumed by authors in the NAI literature to be the same as those that cause DAI and the tissue tears reported in adult head injury (Graham and Gennarelli, 1996). However, this may not necessarily be true: the severe angular or rotational acceleration, with or without deceleration, necessary to produce widespread 'shearing' forces to axons

throughout the brain may well be quite different from the forces necessary to produce localized 'shearing' between grey and white matter (two regions of very different consistency in the infant), after impact injury.

Retinal haemorrhages, the detection of which in a moribund child so frequently first raises suspicions of NAI—for which they are thought to be an important marker (OCA Working Party, 1999)—were found in 71% of our cases, a figure comparable with findings of clinical series (Duhaime *et al.*, 1998). They were seen both in cases in which impact had occurred, and in cases in which there was no macroscopic evidence of impact. There was, however, a statistically significant association between subdural and retinal bleeding, mentioned above, and we found no cases of retinal haemorrhages without subdural bleeding. A discussion of the aetiology of retinal haemorrhages, characteristic of the young population who are biomechanically particularly vulnerable to shaking-type injuries, is beyond the scope of this paper.

Acknowledgements

The authors are grateful to Mrs Georgina Lindop for administrative work. The study was supported by a grant from Action Research.

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Received February 5, 2001.
Accepted February 22, 2001