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Which clinical features distinguish inflicted from non-inflicted brain injury? A systematic review

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ABSTRACT

Aim: A systematic review of the scientific literature to define clinical indicators distinguishing inflicted (iBI) from non-inflicted brain injury (niBI).

Methods: An all language literature search of 20

electronic databases, websites, references and bibliographies from 1970-2008 was carried out. Relevant studies were independently reviewed by two trained reviewers, with a third review where required. Inclusion criteria included primary comparative studies of iBI and niBl in children aged <18 years, with high surety of diagnosis describing key clinical features. Multilevel logistic regression analysis was conducted, determining the positive predictive value (PPV) and odds ratios (OR) with p values for retinal haemorrhage, rib/long bone/skull fractures, apnoea, seizures and bruising to head/neck. Results: 8151 studies were identified, 320 were reviewed and 14 included, representing 1655 children, 779 with iBI. Gender was not a discriminatory feature. In a child with intracranial injury, apnoea (PPV 93%, OR 17.06, p<0.001) and retinal haemorrhage (PPV 71%, OR 3.504, p = 0.03) were the features most predictive of iBI. Rib fractures (PPV 73%, OR 3.03, p = 0.13) had a similar PPV to retinal haemorrhages, but there were less data for analysis. Seizures and long bone fractures were not discriminatory, and skull fracture and head/neck bruising were more associated with niBI, although not significantly

Conclusions: This systematic review shows that apnoea and retinal haemorrhage have a high odds ratio for association with iBl. This review identifies key features that should be recorded in the assessment of children where iBl is suspected and may help clinicians to define the likelihood of iBl.

In 1974, radiologist John Caffey published his paper "The whiplash shaken infant syndrome: manual shaking by the extremities with whiplash induced intracranial and intraocular bleedings, linked with residual permanent brain damage and mental retardation". The title captured a proposed mechanism for the most serious form of physical child abuse and referred to the association of intracranial and retinal haemorrhages. The article described the diagnostic challenges of identifying a condition where there are often no external signs of trauma to the head, skull fractures or a history of trauma of any kind, and associated injuries may be subtle or occult, particularly in the case of coexisting fractures. Caffey recognised that these children were often subjected to repeated traumatic episodes. Despite advances in investigative neurology and widespread awareness of this condition, inflicted brain injury (iBI) is commonly

What is already known on this topic

- ► Considerable scepticism is being expressed as to how to distinguish inflicted (iBI) from non-inflicted brain injury (niBI).
- Varying weight has been given to specific clinical features of iBI in previous publications.
- Apnoea, retinal haemorrhages and rib fractures are felt to be important but there is no comprehensive statistical estimate of predictive power regarding iBI.

What this study adds

- ► The finding of apnoea and/or retinal haemorrhage in a child with a brain injury is more strongly associated with iBI than niBI.
- ► Children where iBI may be a differential diagnosis should undergo fundoscopy by an ophthalmologist and if <2 years old should have a skeletal survey.
- Infants less than 6 months of age with a brain injury are more likely to have sustained an iBI than older infants.

under-recognised $^{\mbox{\tiny 8}}$ and remains a diagnostic challenge.

Children with iBI often present with significant intracranial injury in the context of a history of a minor fall, trivial injury or no reported trauma. Clinical symptoms and signs vary from the most non-specific, for example vomiting or irritability, to those that clearly point to a central neurological insult such as reduced consciousness.4 Some may present with other inflicted injuries, such as bruising or fractures, as the primary indicator. For some children with a non-specific clinical presentation, the possibility of an iBI may not be considered.35 As in most cases of physical child abuse there is no diagnostic test for iBI, the diagnosis is made on a balance of probability and after careful exclusion of other possible causes of the clinical presentation which include accidental injury and medical conditions such as rare metabolic conditions (glutaric aciduria⁶), coagulation disorders, 7-9 infective encephalopathies, etc. It has been recognised that up to 50% of children with iBI had presented previously with signs of physical abuse that were missed.2 3

Although well recognised as a condition that is prevalent in infants and babies, the estimated

Box 1 Databases and websites searched

Databases

- All EBM Reviews ACP Journal Club (ACP), Cochrane Database of Systematic Reviews (COCH), Database of Abstracts of Reviews of Effects (DARE), Cochrane Central Register of Controlled Trials, Health Technology Assessment, National Health Service Economic Evaluation, Cochrane Methodology Register
- ► ASSIA (Applied Social Sciences Index and Abstracts)
- ► ChildData
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- ► EMBASE
- ▶ MEDLINE
- ► MEDLINE In-Process & Other Non-Indexed Citations
- ▶ SCOPUS
- ► Open SIGLE (System for Information on Grey Literature in Europe)*
- ► Social Care Online
- ► TRIP Plus
- Web of Knowledge ISI Proceedings
- ▶ Web of Knowledge ISI Science Citation Index
- ▶ Web of Knowledge ISI Social Science Citation Index

Websites

- The Child Brain Injury Trust (CBIT), www.cbituk.org
- Child Welfare Information Gateway (formerly National Clearing House on Child Abuse and Neglect), http://www.childwelfare. gov/
- International Society for Prevention of Child Abuse and Neglect (ISPCAN), http://www.ispcan.org/
- ► The National Center on Shaken Baby Syndrome, http://www.dontshake.com/

*Up to 2005 when the database ceased indexing.

incidence of inflicted head injury is 21-24 per 100 000 infants under the age of 1 year. 10 11 Cases may present regularly to specialist neurology units but present infrequently to general paediatric units. Clinicians in all settings need to be aware of the clinical indicators for this condition to make evidence based decisions as to when they should consider investigating an infant where iBI is a possible cause and to inform a final diagnosis. Many are asked to present their professional or expert opinion in the family or criminal courts as part of the child protection process and they must be able to cite relevant evidence to back up their statements. Although there is a considerable amount of published scientific literature in this field, there have been few attempts to systematically review and critically appraise the world literature. We have attempted to repair this deficit and have addressed the question: "What are the clinical features that distinguish inflicted from non-inflicted brain injury?". The neuro-radiological features of iBI/niBI are the subject of a separate review.

METHODS

We conducted an all language literature search from 1970–2008, searching 20 databases, websites, references and bibliographies, using over 100 keyword combinations (box 1, table 1). This yielded 320 studies for review by reviewers, drawn from paediatricians, paediatric neurologists, neuro-radiologists and ophthalmologists, designated and named doctors/nurses in child

protection. All reviewers underwent standardised critical appraisal training, based on the NHS Centre for Reviews and Dissemination critical appraisal standards, ¹² supported by a dedicated electronic critical appraisal module. All studies underwent two independent reviews and a third if there was disagreement (fig 1).

Inclusion/exclusion criteria and quality standards

We defined the term "brain injury" as extra-axial haemorrhage (subdural, extradural, subarachnoid) and/or injury to the brain (hypoxic ischaemic injury, parenchymal injury, contusion, diffuse axonal injury, cerebral oedema). Inclusion/exclusion criteria are listed in box 2. Inflicted brain injury (iBI), the item of interest, refers to children who had sustained brain injury from physical child abuse. Those with non-inflicted brain injury (niBI) had other causative mechanisms including accidental trauma, and medical causes of intracranial lesions.

Given the nature of this research field, our optimal study type was population based studies that compared the clinical features of iBI and niBI with consecutive case ascertainment. As only studies with both niBI and iBI cases could be used for any analysis of predictive power of the features identified, many oft cited (non-comparative) studies were not eligible for inclusion. The included studies detailed the clinical features of interest but did not rely solely on these for the determination of diagnosis (iBI vs niBI). Only studies after 1970 were considered for inclusion, as radiological techniques prior to this would not be relevant to current practice. Included studies had a high surety of diagnosis of iBI¹³ and confirmation of cause in niBI. To determine a high surety of abuse, we implemented our previously published "ranking of abuse", that is, children stated as "abused" in the study had had that outcome confirmed by multi-agency child protection teams, legal decision, witnessed abuse or perpetrator admission (rank 1-2)13 (table 2). Studies where the decision of abuse had relied solely on clinical features were excluded to minimise selection bias and circularity. Where studies included a category "aetiology indeterminate", these cases were excluded from the final analysis.

Statistical analysis

The analysis was limited by the items that the authors chose to report and we were able to analyse the following features:

- apnoea
- retinal haemorrhages
- rib fractures
- ▶ long bone fractures
- ▶ bruising to the head and/or neck
- seizures
- ▶ skull fractures.

We were dependent on the primary authors' definitions of the above terms. "Apnoea" reflects either recorded or reported apnoea in the two studies that recorded this item. "Seizures" were not always defined, but some authors did record that some children presented in status epilepticus. "Long bone fractures" included any fracture to the femur, tibia, fibula, radius, ulna or humerus. Likewise, "skull" or "rib fractures" included any type or location of fracture, respectively.

We included only data from studies where a key feature was explicitly mentioned by the authors. Further, even when a feature was included in the study, not all children in each group were examined for the feature in question. For example, not all children in the niBI group had a fundoscopy examination to look for retinal haemorrhages. We have elected to adopt an

Table 1 Keywords and search strategy				
Keywords				
Set 1				
battered child	child protection	non-accidental injury		
shaken baby	children	non-accidental trauma		
battered baby	inflicted brain injury	physical abuse		
battered infant or shaken infant	inflicted cerebral injury	shaking baby syndrome		
child	inflicted traumatic head injury	shaking impact syndrome		
child abuse	inflicted traumatic brain	soft tissue injury		
child maltreatment	intentional abuse			
Set 2				
abusive head trauma	growing skull fracture	intraventricular hematoma		
bleeding into brain	haematoma	laceration		
blow to the head	haemorrhagic retinopathy	laminar necrosis		
brain	head injuries	leptomeningeal cyst		
brain damage	head trauma	multiple skull fracture		
brain haemorrhages	hematoma	neurologic injury in child abuse		
brain hemorrhages	hemorrhagic retinopathy.af.	neuropathology		
brain injuries	hydrocephalus	non-accidental head injury		
brain swelling	hygroma	parafalcine		
brainstem	hypoxic-ischaemic injury	parenchymal contusion, laceration		
central nervous system	hypoxic-ischemic injury	retinal haemorrhage		
cerebral	impact injury	retinal hemorrhage		
cerebral atrophy	infarction	sciwora		
cerebral edema	inflicted brain injury	shaking impact syndrome		
cerebral injuries	inflicted cerebral injury	shearing injury		
cervical lumbar	inflicted traumatic brain injury	skull fractures		
cervical spine injury	inflicted traumatic head injury	spinal cord injury		
cervical spine	interhemispheric	subarachnoid hematoma		
neuropathology	intracerebral bleeding	subdural hematoma		
contusion	intracerebral haemorrhage	subdural haematoma		
contusional tear	intracerebral hemorrhage	subdural hygroma		
cranial injury	intracranial haemorrhage	thoracic lumbar sacral		
craniocerebral trauma	intracranial hemorrhage	traumatic effusions		
craniocervical	intracranial injuries	ventricular haemorrhage		
diagnostic triad	intraparenchymal tear	ventricular hemorrhage		
diffuse axonal injury	intraparenchymal haemorrhage	whiplash impact syndrome		
eggshell fracture	intraparenchymal hemorrhage	whiplash injury		
encephalomalacia		whiplash shaken infant		
encephalopathy				

Search strategy

extracranial CNS injury extradural haemorrhage extradural hemorrhage

2. (child: or infant: or toddler:).af.

3. 1 or 2

4. non-accidental injur:.af.

5. non-accidental trauma.af.

6. (non-accidental: and injur:).af.

7. soft tissue injur:.af.

8. physical abuse.af.

9. (inflicted brain injur: or inflicted cerebral injur:).af.

10. (inflicted traumatic head injur: or inflicted traumatic brain injur:).af.

11. (or/4-10) and 3

12. (child abuse or child maltreatment or child protection).af.

13. (battered child or shaken baby or battered baby).af.

14. (battered infant or shaken infant).af.

15. Shak: Baby Syndrome.af.

16. shak: impact syndrome.af.

17. Caffey-Kempe syndrome.af. 18. battered child syndrome.af.

54. (retinal hemorrhage or retinal haemorrhage).af.

55. skull fracture:.af.

56. (spinal cord injury adj3 radiologic abnormality).af.

57. spinal cord injur:.af.

58. (subdural haematoma or hemotoma).af.

59. (subarachnoid hematoma or subarachnoid haematoma).af.

60. (subdural haemorrhage or subdural hemorrhage).af.

61. (ventricular haemorrhage or ventricular hemorrhage).af.

62. whiplash impact syndrome.af.

63. whiplash injur:.af.

64. whiplash shaken infant.af.

65. infarction.af.

66. (hypoxic-ischemic injur: or hypoxic-ischaemic injur:).af.

67. (contusion: or contusional tear).af.

68. (hematoma or haematoma).af.

69. laceration:.af.

70. shearing injur:.af.

71. traumatic effusion:.af.

Table 1 Continued

Search	h strategy
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- 19. *"Child Abuse"/di [Diagnosis]
- 20. infant traumatic stress syndrome.af.
- 21. parent-infant traumatic stress syndrome.af.
- 22. or/12-21
- 23. 11 or 22
- 24. abusive head trauma.af.
- 25. bleeding into brain.af.
- 26. blow to the head.af.
- 27. brain damage.af.
- 28. (brain haemorrhage: or brain hemorrhage:).af.
- 29. (brain swelling or cerebral edema).af.
- 30. cerebral injur:.af.
- 31. cervical spine injur:.af.
- 32. cervical spine neuropathology.af.
- 33. cranial injur:.af.
- 34. craniocerebral trauma.af.
- 35. diffuse axonal injur:.af.
- 36. extracranial CNS injur:.af.
- 37. extracranial Central Nervous System injur:.af.
- 38. central nervous system injur:.af.
- 39. (extradural haematoma or hematoma).af.
- 40. extradural haemorrhage.af.
- 41. haemorrhagic retinopathy.af.
- 42. (head inur: or head trauma).af.
- 43. impact injur:.af.
- 44. intracerebral bleeding.af.
- 45. (intracerebral haemorrhage or intracerebral hemorrhage).af.
- 46. (intracranial haemorrhage or intracranial hemorrhage).af.
- 47. intracranial injur:.af.
- 48. (intraventricular hematoma or intraventricular haematoma).af.
- 49. (multiple skull fractur: or eggshell fractur:).af.
- 50. (neurological injur: adj3 child abuse).af
- 51. neuropathology.af.
- 52. non-accidental head injur:.af.
- 53. (parenchymal contusion or laceration).af.

- 72. subdural hygroma.af.
- 73. hygroma.af.
- 74. interhemispheric.af.
- 75. parafalcine.af.
- 76. (brain or brainstem).af.
- 77. cerebral.af.
- 78. intraparenchymal.af.
- 79. sciwora.mp.
- 80. spinal cord injury without radiologic abnormality.af.
- 81. cervical lumbar.af.
- 82. thoracic lumbar sacral.af.
- 83. leptomeningeal cyst.af.
- 84. growing skull fracture.af.
- 85. hydrocephalus.af.
- 86. laminar necrosis.af.
- 87. encephalomalacia.af.
- 88. cerebral atrophy.af.
- 89. craniocervical.af.
- 90. encephalopathy.af.91. (intraparenchymal hemorrhag: or intraparenchymal
- 91. (intraparenchymal hemorrhag: or intraparenchymal haemorrhag:).af.
- 92. Haemorrhagic retinopathy.af.
- 93. hemorrhagic retinopathy.af.
- 94. (Haemorrhagic retinopathy adj3 retinal haemorrhages).af.
- 95. Extradural haemorrhage.mp. or Extradural hemorrhage.af.
- 96. (extradural haemorrhag: or extradural hemorrhag:).af.
- 97. (extradural spinal haemorrhag: or extradural spinal hemorrhag:).af.
- 98. (Haemorrhagic retinopathy adj3 retinal haemorrhag:).af.
- 99. (Hemorrhagic retinopathy adj3 retinal hemorrhag:).af.
- 100. (retinal hemorrhag: or retinal haemorrhag:).af.
- 101. or/24-100
- 102. 23 and 101

extremely conservative imputation approach to account for this missing information.¹⁷ For example, if we are analysing a feature that we suspect may be associated with iBI, for instance, retinal haemorrhages: in the group of children with iBI, if only 6/10 iBI children underwent fundoscopy, we made the assumption that the four children who were not examined would not have had the feature.

By contrast, in the group of children with niBI, if an investigation for this feature was not performed, for example, if only 2/10 niBI children underwent fundoscopy, we made the assumption that the eight children who were not examined would have had the feature. Only in the case of skull fractures, a feature whose presence we suspect to be associated with niBI, was the opposite imputation performed. We believe that by approaching the missing data in this way, we err on the side of caution, and risk underestimating, rather than overestimating, the strength of the discrimination provided by this feature. We have specifically employed this technique to avoid reinforcing any prior assumptions, but rather to determine a valid estimate of the significance of each of the features under analysis.

These imputations being given, we then conducted a multi-level logistic regression analysis, ¹⁸ allowing not only the prevalence of abuse to vary between studies, but also the odds ratios (OR) for the features in question. By allowing the odds

ratio to differ between studies, we again aim to minimise the risk of circularity, where an individual study may have overly relied upon a particular feature in order to arrive at the diagnosis of abuse. For each feature, we report the estimated odds ratio for the feature in discriminating between iBI and niBI, together with a 95% confidence interval (95% CI). We also provide a p value to determine if this odds ratio is significantly different from 1, and a positive predictive value (PPV), the estimated probability of abuse given the presence of this feature in a child with brain injury, together with a 95% CI.

RESULTS

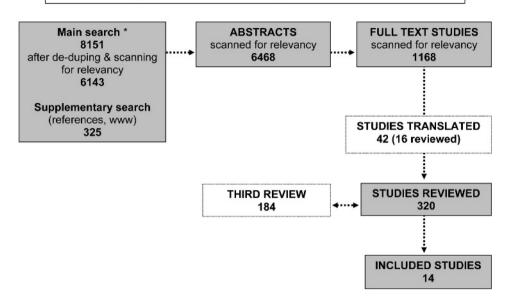
Of 320 reviewed studies, 14 met the inclusion criteria. ^{14–16} ^{19–28} All were published after 1995. Six were cross-sectional studies, ¹⁹ ²² ²⁴ ^{27–29} five case series, ¹⁴ ¹⁶ ²⁰ ²³ ²⁵ two case—control studies ¹⁵ ²⁶ and one a longitudinal cohort study. ²¹ Eight studies involved prospective enrolment of cases. ¹⁴ ¹⁶ ²⁰ ²³ ²⁵ The six retrospective studies achieved full case ascertainment from hospital inpatient coding and/or radiology databases. Full study details are given in online appendix A.

Of the 306 studies excluded, the most common reasons for exclusion were the lack of comparative data or a rank of abuse of less than 1 or 2. A small number (11 studies) were excluded

Figure 1 Main phases and number of studies identified at each stage.

* DATABASES SEARCHED 1970-2008

All EBM Reviews, ASSIA, ChildData, CINAHL, EMBASE, MEDLINE, MEDLINE In-Process, SCOPUS, SIGLE, Social Care Online, TRIP Plus, ISI Proceedings, ISI Science Citation Index, ISI Social Science Citation Index



Box 2 Inclusion and exclusion criteria

Inclusion criteria

- ► children aged 0 to <18 years
- observational comparative study (cross-sectional/case control/case series/longitudinal cohort)
- children with inflicted brain injury diagnosed on CT/MR: intracranial haemorrhage (extra-axial with or without additional brain injury — ± intra-parenchymal haemorrhage, ± diffuse axonal injury ± hypoxic ischaemic injury ± cerebral contusion ± cerebral oedema)
- ranking of abuse 1 or 2 for inflicted brain injury (iBI)
- non-inflicted brain injury (niBI): non-inflicted aetiology confirmed
- ► children who were alive at presentation
- ▶ all language studies
- relevant clinical details given for each group

Exclusion criteria

- studies about complications, management or prognosis of iBI/ niBI
- consensus statements or personal practice studies
- non-comparative studies
- studies addressing exclusively post mortem neuropathological findings
- studies with mixed adult and child data, where the children's data cannot be extracted
- methodologically flawed studies (eg, significant bias, where iBI was not adequately confirmed or where inadequate clinical details were given)
- studies that only addressed head injury where there was no intracranial abnormality
- studies with a low surety of diagnosis of inflicted injury (rank 3–5 abuse)

due to study design (expert opinion/review article, etc) and a further 10 included mixed adult and child data. Many studies were excluded on more than one basis (eg, rank of abuse/noncomparative/lack of detail on features for analysis).

Studies represented combined data on 1655 children, 779 of whom had suffered iBI and 876 niBI. Eleven of 14 studies included children less than 3 years of age. 14-16 19 20 22 24 25 27-29 Seven studies ascertained all children who were hospitalised with traumatic head injuries, 19-22 25 26 29 six studies included all children with subdural haemorrhage of any aetiology (trauma, coagulopathy, metabolic disorder or post infection, etc) 14-16 23 25 28 and one study included children with subdural or extradural haemorrhage. 27 The majority (seven) were conducted in the USA, 19-22 24 26 27 five were European 14 15 23 25 29 (three UK 14 15 23) and one each was from Australia 28 and Hong Kong. 16 In nine studies, children were included solely on the basis of age and confirmation of cause. However, five had specific exclusion criteria (table 3).

Gender was recorded in 980 cases and was not a distinguishing feature. More boys than girls sustained brain injuries, regardless of aetiology (PPV of iBI if the child is a boy 0.397 (95% CI 0.277 to 0.530), OR 0.697, p>0.2).

It was not possible to undertake a formal analysis of age as a discriminating feature as each study reported it differently. Eight studies confirmed that children with iBI were significantly younger than those who sustained niBI. 15 16 20 21 23 24 26 28 Of the

Table 2 Abuse ranking

Tubic 2	Abuse runking
Ranking	Criteria used to define abuse
1	Abuse confirmed at case conference or civil, family or criminal court proceedings or admitted by the perpetrator, or independently witnessed
2	Abuse confirmed by stated criteria including multi-disciplinary assessment
3	Diagnosis of abuse defined by stated criteria
4	Abuse stated as occurring, but no supporting detail given as to how it was determined
5	Abuse stated simply as "suspected", no details on whether it was confirmed or not

Table 3 Additional exclusion criteria of included studies

Author/year	Additional exclusion criteria	
Ewing-Cobbs L, Kramer L, Prasad M, et al (1998) ²¹	Prior traumatic brain injury, metabolic abnormality, preterm (<32 weeks)	
Hettler J, Greenes DS (2003) ²²	Coagulopathy, neonatal neurological abnormality, structural abnormality, surgery or previous intracranial haemorrhage	
Fung ELW, Sung RYT, Nelson EAS, et al (2002) ¹⁶	Subdural haemorrhage due to infection or surgery	
Pierre-Kahn V, Roche O, Dureau P, et al (2003) ²⁵	Cardiopulmonary resuscitation, coagulation abnormality, severe dehydration or delayed eye examination	
Ettaro L, Berger RP, Songer T (2004) ²⁰	Concussion, cerebral lacerations or contusions	

eight studies addressing children less than 3 years of age, where mean ages were available, $^{15\ 16\ 19\ 20\ 22\ 24\ 28\ 29}$ three studies found no significant difference between iBI and niBI. $^{19\ 22\ 29}$ Five studies $^{15\ 16\ 20\ 24\ 28}$ stated that children with iBI were significantly younger than those with niBI. Four of these studies $^{15\ 16\ 24\ 28}$ gave the mean ages of children with iBI as less than or equal to 6 months, while the niBI groups ranged between 7.5 and 12.4 months. $^{15\ 16\ 24\ 28}$

Combined feature analysis

It was not possible to identify which children had specific combinations of features, as this level of detail was not given.

Apnoea

Apnoea appeared to be a highly discriminatory finding, with a PPV of 93% (97.5% CI 0.733 to 0.986) and an OR of 17.062 (97.5% CI 5.018 to 58.011, p<0.001). However, it was one of the least recorded clinical items, only being analysed by two authors (405 children), perhaps reflecting that its significance has only been recognised more recently. 15 80

Retinal haemorrhage

Although 1283 children were included in studies that considered this feature, only 998 had fundoscopy (670 iBI and 328 niBI). Many children presenting with witnessed trauma did not have formal fundoscopy, whereas the majority of children with iBI did. Therefore, to account for studies where this was not explicit, $^{20\ 21}$ we used the conservative approach described above. Retinal haemorrhages were strongly associated with iBI, with a PPV of 71% (97.5% CI 0.483 to 0.868) and an OR of 3.504 (97.5% CI 1.088 to 11.280, p = 0.03). A child with an intracranial injury who has co-existent retinal haemorrhages is significantly more likely to have iBI than niBI.

Rib fractures

Rib fractures were considered in studies representing 1002 children, and data were available on 903 children. Rib fractures were associated with inflicted injury, with a PPV of 73% (97.5% CI 0.500 to 0.882) and an OR of 3.027 (97.5% CI 0.716 to 12.799). The wide confidence interval reflects the fact that relatively few children had data recorded on this item. Our conservative analysis therefore results in lower significance.

Seizures

Seizures were considered in studies involving 760 cases, and results were documented in 758. Seizures were more associated with iBI than niBI, but not significantly so, with a PPV of 66% (97.5% CI 0.454 to 0.821) and an OR of 2.924 (97.5% CI 0.731 to 11.694, p=0.13).

Long bone fractures

One of the difficulties in analysing fractures as recorded in studies, is knowing whether the author is counting individual fractures, or individual children who have sustained fractures. In studies where this was not explicit, 20 we made the assumption that the number of children with fractures was recorded, a conservative approach. Studies considering long bone fractures represent 1020 children, of whom 921 underwent skeletal imaging. Overall, the PPV of long bone fractures for iBI was 59% (97.5% CI 0.48 to 0.69), OR 1.722 (97.5% CI 0.824 to 3.601, p = 0.14). Therefore a long bone fracture in association with an intracranial injury was a weak predictor for iBI, but not significantly so.

Skull fractures and bruising to the head and neck

Skull fractures were considered in studies representing 1014 children, and documented as present or absent in 916 children. Skull fractures were more strongly associated with niBI than iBI, with a PPV for iBI of 44% (97.5% CI 0.223 to 0.678), OR 0.852 (97.5% CI 0.316 to 2.301, p>0.2). Likewise, bruising to the head and neck was more common in the niBI children, but it was the least recorded item, weakening its significance. Only 212 cases had this feature considered, and overall the PPV of head and/or neck bruising for iBI was 37% (97.5% CI 0.035 to 0.906), OR 0.811(97.5% CI 0.070 to 9.410, p>0.2). No specific mention was made of the use of 3D reconstruction techniques to define such fractures; the authors simply recorded their presence or absence when looked for.

DISCUSSION

Making the clinical distinction between iBI and niBI in children is always going to be challenging. By producing a multilevel logistic regression of specific clinical features on over 1600 children, we have shown that there is scientific evidence to support the distinction between iBI and niBI, and we are able to offer positive predictive values and odds ratios for individual clinical indicators in children hospitalised with brain injury. The published literature does not allow an analysis of combined features.

This review is the largest of its kind, and offers for the first time a valid statistical probability of iBI when certain key features are present (eg, retinal haemorrhages). Although in some instances, for example, rib fractures, the sample size limits our statistical power to detect the full effect of this feature, as with any systematic review, we are of course limited by the amount of high quality data available in the published literature. However, even with this limited data set, the presence of rib fractures (PPV 73%, OR 3.027) is still indicates an association with iBI rather than niBI, and emphasises how important it is to conduct appropriate imaging to determine if such fractures are present.

It appears that the younger the child, the greater the likelihood that an intracranial injury is due to abuse.

However, children as old as 10 years with severe iBI have also been described in isolated case reports.^{31–34}

Apnoea appears to be a critical distinguishing feature (PPV for abuse 93%, OR 17.06, p<0.001). There is increasing evidence that hypoxic ischaemic injury and its attendant complications are an integral part of the cascade in iBI.⁴ The presence or absence of apnoea must be recorded in all cases of head injury in children.

Retinal haemorrhages are a valuable discriminator, reinforcing the need for fundoscopy on any child with unexplained intracranial injury, or suspected iBI. Indirect ophthalmoscopy should be conducted by an ophthalmologist, as studies have shown that other clinicians are either unable to conduct an accurate examination, or when they do, may miss up to 13% of retinal haemorrhages present.³⁵

Fractures in physical abuse are often occult.³⁶ ³⁷ Therefore, in line with the Royal College of Paediatrics and Child Health/Royal College of Radiologists standards for the radiological investigation of suspected physical abuse, any child aged less than 2 years in whom an inflicted injury is considered, should have a full skeletal survey, including oblique views of the ribs.³⁸ Seizures were not a valuable discriminatory finding. Perhaps an analysis of specific patterns of seizures (eg, status epilepticus, complex, focal) would be more informative.

It was not possible to analyse the value of history given as a predictor, as a number of studies had used absence of a history of trauma or inconsistent explanation as part of their definition of abuse.^{20 21} Only one large study set out to estimate the value of the initial history in predicting whether the head injury was inflicted or non-inflicted.²² Study design ensured that the history did not contribute to the decision as to whether the child belonged to the iBI or niBI group. The study concluded that having no history of trauma had a high specificity (0.97) and high PPV (0.92) for inflicted injury.

Although many studies addressed encephalopathic features, the differing classifications that were used (altered consciousness, coma, irritability, Glasgow Coma Score (GCS)) precluded any combined analysis of this information. It is recognised that performing a GCS on young infants is imprecise; a study²⁴ that noted an increased relative risk of this item for iBI (RR 1.7, 95% CI 0.9–3.2) did not attach weight to this feature.

We did not address social features which are more culturally specific, and less suited to meta-analysis. There is also the risk of introducing bias by undue reliance on social features, as shown by Jenny,³ who noted that white infants from two parent families were more likely to have their iBI missed than ethnic minority children or those living with one parent.

This review did not address biomechanical features. It is recognised that iBI can occur as a consequence of shaking, ^{39 40} impact, ⁴¹ shaking and impact, ^{39 42} water intoxication, ^{43 44} suffocation or strangulation. ⁴⁶ In our review skull fracture and bruising to the head/neck were more strongly associated with niBI than iBI, suggesting blunt trauma as a common mechanism of niBI. Clinical evidence of impact may only be found on post mortem, ⁴² so conclusions as to whether an impact injury has occurred or not in iBI cannot reliably be drawn from the clinical features alone.

It is recognised that subdural haemorrhage (SDH) can occur in infancy from other causes, and consideration must be given to possible organic disease, such as metabolic disorders (eg, glutaric aciduria),⁶ albeit this has characteristic MRI findings. While coagulopathy may cause intracerebral haemorrhage,⁷⁻⁹ it may also be secondary to an iBI,⁴⁷ highlighting the need for thorough investigations in this group. It is recognised that SDH in particular, may occur as a consequence of birth, particularly

following instrumental delivery, $^{\rm 48-50}$ although a neonatal SDH without skull fracture has also been described where the mother was assaulted ante-natally. $^{\rm 51}$

While this review has highlighted certain clinical features that in association with intracranial injury have a high positive predictive value and odds ratio for iBI, such as retinal haemorrhage, apnoea or rib fractures, none of these features are exclusive to iBI. It is essential that the diagnosis of iBI is only made after taking into consideration full details on history (birth, medical, family, developmental, social, details of any reported trauma) and a detailed examination, and having actively excluded other relevant organic diseases. It is vital that future work should endeavour to collect data on all the features above, with detailed recording of precise abnormalities found, for example, on ophthalmology, if we are to refine these statistical correlations.

Baroness Kennedy has made it abundantly clear that clinicians must be able to cite scientific evidence to support their clinical opinions when providing evidence to the courts, ⁵² and it is challenging for any clinician to keep up to date with all the current evidence (in the year 2007 alone 242 studies relating to iBI were published). Therefore, we feel that this unique, rigorously conducted systematic review will be a valuable resource for clinicians and other professionals in the field, providing, as it does, odds ratios of abuse for seven easily documented clinical features.

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APPENDIX A

Publication details	Case details	Relevant results	Critical appraisal comments
Author(s): Bechtel K, Stoessel K, Leventhal JM, et al ¹⁹	Ascertainment: all children aged <2 years admitted to a single unit with head injuries, and who had CT. Prospective	82 met inclusion criteria, 15 abuse, 67 accident. No difference in mean age, gender, ethnicity. Accidental (niBI) – 65 witnessed falls, 47 were <4 ft. 2 MVA. Of abuse (iBI) – 12 no history of trauma, 1 perpetrator admission, 1 history of falling 3 inches, 1 "self inflicted". SDH more likely in iBI than niBI (p<0.001). No difference in SAH, skull fracture, EDH. All children had fundoscopy. RH commoner in iBI (9/15) vs niBI (7/67) (p<0.001). Good detail on RH given, unilateral RH in 6/7 niBI, single haemorrhage in 3/7. Seizures commoner in iBI (8/15) vs niBI (4/67) (p<0.001), same for abnormal mental status (defined) – iBI (8/15) vs niBI (7/67) (p<0.001). In contrast, scalp haematoma commoner in niBI (34/67) vs iBI (1/15) (p<0.001). "Abnormal mental status" defined as unresponsive/poorly responsive to painful stimuli/gaze palsies/flaccidity – iBI 53% vs niBI 9% (p<0.001). NB: given sample size, 85% power to detect differences of 41%, at error of 5%. iBI had more seizures requiring anticonvulsants but NS	Raw data provided by authors
Title: Characteristics that	Ranking of abuse: 2 (criteria+social worker)	anticonvulsants, but NS	Good study, standardised ascertainment, all had ophthalmology, but small numbers, particularly in
distinguish accidental from abusive injury in hospitalized young children with head trauma	Worker		abuse group. Only includes TBI, but rank of abuse not dependent on type of intracranial injury
Year: 2004	Exclusion of abuse: explicit history of accidental trauma		Confirms predictive power of RH and seizure. No
	accidental trauma		difference in skull fracture surprising, but scalp haematoma commoner in accidents. Unfortunate that data on bruising/apnoea not recorded
Country: USA	No. of examiners: N/A. Gender split: 47 boys, 35 girls		
Aim: to describe clinical features distinguishing accidental from abusive head trauma in hospitalized children aged <2 years	Ethnicity: 47 white, 7 African American, 18 Hispanic (no difference between iBl and niBl)		
Study design: prospective cross- sectional	Socio-economic group: N/A		
Time period: 1 August 2000–31 October 2002	Age: 0-2 years, no difference in mean age between iBI and niBI		
Author(s): Ettaro L, Berger RP, Songer T ²⁰	Ascertainment: all children admitted to a single unit with traumatic head injury, included intracranial haemorrhage and skull fracture, excluded concussion and cerebral lacerations or contusions. Retrospective	Unfortunate that presumptive and suspected cases combined, but raw data allow separation. 377 cases, 61 iBI, 316 niBI based on raw data, where suspected added to niBI. iBI cases were younger and of lower economic status than niBI. Good information on history given at presentation, 33/89 (37%) iBI no history of trauma vs 1/288 (0.3%) niBI. 97% iBI vs 54% niBI gave a history of no or minor trauma on presentation (p<0.001). 46 (52%) iBI vs 174 (61%) niBI had skull fractures, NS. Rib fractures and long bone fractures more common in iBI (p<0.001), long bone also more common (p \leqslant 0.01) than in niBI	Raw data provided by authors, and abuse confirmed by multidisciplinary assessment
Title: Abusive head trauma in young children: characteristics and medical charges in a hospitalized population	Ranking of abuse: 2. Duhaime "presumptive" abuse added "suspected" abuse to this for analysis but was separated in raw data	Mortality greater in iBI $-$ 10.1% vs 2.1%, also more disability (NS) $-$ 9% vs 3.7%	Good study, but weakened in published form by combining the "presumptive" and "suspected" for analysis
Year: 2004	Exclusion of abuse: MVA, fall, struck	A lot of detail on increased cost	Raw data very valuable, allowed us to separate "suspected" abuse
Country: USA	No. of examiners: N/A. Gender split: 53/ 89 (60%) iBl boys, 169/288 (59%) niBl boys	No detail on altered consciousness or seizures	Highlights age, SE difference. Interestingly, no difference in skull fractures, but some of the cases had only fractures, not given in paper, thereby making it difficult to compare with other studies
Aim: to examine differences in clinical features and hospital charges between iBI and niBI	Ethnicity: 69 iBl (80%) vs 234 (83%) niBl white		Cases from 1996/7 did not routinely have a skeletal survey or retinal examination

APPENDIX A Continued

Publication details	Case details	Relevant results	Critical appraisal comments
Study design: comparative case series	Socio-economic group: 63 (74%) iBI were Medicaid or self-pay vs 139 (49%) niBI (p<0.001)		
Time period: 1995–1999	Age: 0-3 years 78 (87%) iBl vs 121 (42%) niBl <1 year (p<0.001)		
Author(s): Ewing-Cobbs L, Kramer L, Prasad M, et al ²¹	Ascertainment: all TBI (iBI or niBI) in children admitted to 2 centres, moderate or severe TBI, no prior neurological or metabolic abnormalities, no prior TBI, gestation >32/40. 88% of iBI and 71% niBI enrolled	20 each in iBI and niBI groups	Useful prospective study, with clear detail on outcome, significantly worse outcome for iBI vs niBI (p $<$ 0.05). Clear difference in ICH pattern, weakness is that skull fractures determined on CT
Title: Neuroimaging, physical, and developmental findings after inflicted and noninflicted traumatic brain injury in young children	Ranking of abuse: 2	iBI cases were younger than niBI (see age for data). No differences in birth history, good detail on perpetrators. Type of ICH differed, 16/20 iBI vs 9/20 (p<0.005) SDH, no EDH (p<0.005), 4 SAH vs 7/20 niBI. 11/20 iBI vs 16/20 niBI had soft tissue swelling. 30% niBI vs 5% iBI had parenchymal involvement. Multiple, linear and depressed skull fractures same in each group (NB: only on CT). RH 13/20 iBI vs 0 niBI (p<0.001). Differences between rib, tibia/fibula, femoral fractures commoner in iBI vs facial commoner in niBI. Considerable detail on neurological outcome	Suggested that 40–45% of iBI had cerebral atrophy or ventriculomegaly but none of those with niBI
Year: 1998	Exclusion of abuse: history \pm investigations	Seizures commoner in iBI 13 vs 3 (p<0.001), no detail given. $5/20$ iBI history of being dropped by caregiver, $5/20$ fall <4 ft and 10 no history vs $2/20$ with fall <4 ft in niBI and none dropped or no history of trauma	
Country: USA	No. of examiners: N/A	GCS measured – NS, also no difference in levels of hemiparesis at admission (6/16 iBl vs 10/20 niBl) or cranial nerve abnormalities	
Aim: to describe clinical and radiological features of iBI and niBI to help determine aetiology	Gender split: 3/20 iBI boys, 10/20 niBI	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
Study design: longitudinal	Ethnicity: NS difference, recorded all relevant groups		
Time period: N/A	Socio-economic group: NS difference Age: 1 month to 6 years iBI mean 11 vs 35 months niBI (p<0.001)		
Author(s): Fung ELW, Sung RYT, Nelson EAS, et al ¹⁵	Ascertainment: identified all SDH by ICD-9 codes and neurosurgical database, in a single hospital. Excluded SDH due to infection/surgery		Study questions the assumption that RH and SDH equals abuse. They show a very large increase in the number of SDH cases in 1 year, with no real explanation
Title: Unexplained subdural hematoma in young children: is it always child abuse?	Ranking of abuse: 2	Noted 4 confirmed abuse, but no perpetrator identified, no legal proceedings. Among iBI, 2/4 no history of trauma, 1 fall from sibling's arms, 1 three recent falls, no details. Among niBI, 3 no history of trauma, 1 fall from chair, 1 fall while standing (age 10 months). 2/4 iBI had RH, 3/5 niBI had RH, one of whom had extensive RH, no explanation for niBI other than (?) fall and parents shook to rouse (?). All had severe ICH, 1 NAI had co-existent SAH, niBI also had EDH. All skeletal surveys and coagulation screens normal. 3/4 had severe disability as a consequence, 4/5 niBI also had. NB: 5-month-old baby with iBI had had facial petechiae 2 weeks prior to admission. 2/4 iBI had loss of consciousness/crying vs 3/5 niBI with loss of consciousness. Noted status epilepticus in one case, others "convulsions", "twitching of limbs"	
Year: 2002	Exclusion of abuse: for 2 there was a case conference, 2 unclear		Raises valid concerns over how a diagnosis of iBI is reached, but offers little substantial evidence for their own suggestion that minor trauma may cause this
Country: Hong Kong Aim: to evaluate clinical indicators for confirming NAHI in Hong Kong	No. of examiners: N/A Gender split: 8 boys, 1 girl (4 iBl boys)		

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Publication details	Case details	Relevant results	Critical appraisal comments
Study design: case series	Ethnicity: N/A		
Time period: 1995–1998	Socio-economic group: N/A Age: 1–24 months, mean iBI 6 months vs 10 months for niBI		
Author(s): Hettler J, Greene DS ²²	Ascertainment: all children presenting to a single children's hospital/trauma centre with TBI. Excluding coagulopathy, perinatal and structural intracranial abnormality, including previous surgery or ICH. Retrospective	Determined abuse without reference to history at presentation, but this was retrospective. 20/49 abuse cases had RH and fractures, 19 RH alone, 6 fractures alone, 3 skin (1 bite, 1 slap to face, 1 linear bruises to chest), 1 witnessed abuse. 1 non-abuse had RH. 92/114 (81%) niBl had social work assessment, 31/114 (27%) had skeletal surveys, 28 (25%) had ophthalmology, 11 (10%) child protection services notified. iBl more likely than niBl to present with apnoea 9 vs 3, seizure 17 vs 5 (not defined), vomiting 23 vs 23, lethargy 25 vs 23 (all p<0.001). More likely to have neurological abnormalities at discharge 26 vs 8	Raw data provided by author, allowing inclusion, as all also confirmed by social work team
Title: Can the initial history predict whether a child with a head injury has been abused?	Ranking of abuse: 2	34/49 (69%) iBI had no history of trauma vs 3 (3%) niBI, PPV of 92 for abuse. Only in those with persistent abnormal neurology, a history of no or low impact trauma PPV of 1.0 for abuse. Overall, 34/49 (69%) iBI no history of trauma vs 3/114 (3%) (p<0.001). 2 iBI witnessed high impact trauma. Among all cases history of no or low impact trauma NS between iBI and niBI	In order to separate history from diagnosis of abuse, the definition relied heavily on a single clinical feature (eg, RH or fracture). However, surety of abuse shown by the fact that only 1/49 abuse cases went home with original carer
Year: 2003	Exclusion of abuse: clinical and 81% social work assessment	Lethargy $-$ 25/49 (51%) iBl vs 13/114 (20%) niBl (p \leqslant 0.001). Also "initial neurologic abnormality" 32/49 (65%) iBl vs 28/114 (25%) (p \leqslant 0.001)	Important paper to try and address historical features
Country: USA	No. of examiners: N/A. Gender split: 27/49 (55%) iBl boys, 65/114 (57%) niBl boys		
Aim: to determine the diagnostic value of presenting history in identifying abuse	Ethnicity: N/A		
Study design: cross-sectional	Socio-economic group: N/A		
Time period: 1993–2000	Age: 0-3 years Mean 6 months for iBI vs 9.1 months for niBI, NS		
Author(s): Hobbs C, Childs A-M, Wynne J, et al ¹⁴	Ascertainment: used BPSU reporting system to identify all cases of SDH/ effusion of any cause in children aged <2 years, also checked Statistics Office for fatal cases. Retrospective	106/186 were iBI. Apnoea was reported/recorded. Annual incidence SDH 12.5/100 000, age 0–2 years, 24.1 age 0–1 year. For iBI 7.1/100 0000 for 2 years (95% CI 6.4 to 9.31), 14.2 for 0–1 year, 0.3 for 1–2 years. Minor injury history in 41/97 iBI and 2/16 undetermined. 99/106 abuse cases had child protection investigations, relied on raw data here	Raw data provided by author
Title: Subdural haematoma and effusion in infancy: an epidemiological study	Ranking of abuse: 2/3 (used raw data to analyse high rank cases)	NB: 55/106 (52%) iBI had RH, 2/7 accidental, 2/26 perinatal, 0/30 disease, 0/17 undetermined. 51/106 abuse cases had fractures (full details in raw data), other fractures only perinatal and accidental	Gives UK incidence figures for those aged $<$ 2 years, relied on local centre diagnosis of abuse and radiology interpretation. However, large scale study, with no excluded patients
Year: 2005	Exclusion of abuse: variable Ix	A history of minor trauma in 41/97 iBl but no data on niBl. Seizures not defined	Interesting prevalence of RH in other causes of SDH. Limited data on the intracranial injury itself
Country: UK	No. of examiners: N/A. Gender split: 120/186 (65%) all cases, 74/106 (70%) iBl	data on mon. ocizares not defined	Emiliar data of the interchinal injury reserv
Aim: to determine incidence, aetiology and clinical features of SDH/effusion in the British Isles	Ethnicity: N/A		
Study design: case series Time period: 1998–1999	Socio-economic group: Townsend niBl 0.3 vs 2.1 for iBl (p<0.007), ie iBl commoner in lower socio-economic groups Age: 0-2 years, mean age iBl was 16		
Author(s): Hoskote A, Richards P, Anslow P, et al ²³	weeks, others varied Ascertainment: all children attending a single unit, from ICD-9, neurosurgery, radiology and social services databases with subdurals	36 children, 14 iBI, 22 other including 6 RTA, 1 assault, 4 iatrogenic, 1 medical, 2 accidental, 6 unexplained (5 neonates), 1 each head injury and assault	All SDH, age range to 16 years includes MVC etc, good detail on iBl and on 9 medical/unexplained causes. 39% of SDH were due to abuse. Probably lower than other studies because of the wide age range

APPENDIX A Continued

Publication details	Case details	Relevant results	Critical appraisal comments
Title: Subdural haematoma and non-accidental head injury in children	Ranking of abuse: 2	All iBI had an inconsistent history, were aged 4–28 weeks (12 between 4 and 16 weeks), 12/14 had RH, 3 skull fracture, 5 multiple fractures (2 including skull). 4 bruising, 6 seizures, 11 bilateral SDH, 3 unilateral, 6 interhemispheric with loss grey/white diff. 2 died.	The authors derived a probability tool based on the presence of up to 5 features – age <12 weeks, inconsistent history, RH, fractures, unexplained bruising, and gave the presence of ≥3 PPV of 100%, ≥1 PPV of 82%, but based on a very small data set, without confidence intervals
Year: 2002	Exclusion of abuse: witnessed accident or obvious cause	niBI – age 1.5–13 months for "unexplained" and medical/accidental causes (9), none of whom had RH or fractures. 2 birth trauma, no details on motor vehicle collisions, 3 accidents/ assault aged 9–14 years. 51/80 (64%) iBI had no history vs 0/72 niBI. No difference in number dropped (6/80, 7% iBI vs 8/72, 11% niBI) or fell (12/80, 15% vs 15/72, 21%)	Good radiological detail (added value of MRI, and proton density images) and possibility of missing or misinterpreting imaging
Country: UK Aim: to study presentation, management and outcome of SDH in children and evaluate NAHI cases	No. of examiners: N/A Gender split: N/A		
Study design: case series Time period: 1995–1998	Ethnicity: N/A Socio-economic group: N/A Age: 0–16 years Mean iBI 3.4 months vs 7.2 months for niBI		
Author(s): Keenan HT, Runyan DK, Marshall SW, et al ²⁴	Ascertainment: all children with serious/ fatal TBI admitted to PICU/high dependency prospectively identified in all 9 hospitals within one state (including checking the 3 closest out-of-state hospitals which residents could have been admitted to). Also checked deaths register	152 cases, 80 inflicted 72 niBl. Median age iTBl 4 months, niTBl 7.5 (p<0.001). Good detail on presenting complaints of both groups, non-MVC niTBl, 44% (13/29) had swelling/redness face/head or asymptomatic after fall vs 8.3% (6) iTBl asymptomatic with bruise/limb deformity (p<0.001). iTBl more likely to have rib, long bone, metaphyseal fractures than niTBl. 1 niTBl with metaphyseal after MVC, which was an old fracture along with rib and long bone fractures. 56% (17) non-MVC niTBl had skull fractures. Skull fractures commoner in niTBl (59% vs 17.5%; p<0.001). Only 24/72 niTBl had retinal examination, 6 (24%) had RH (4 were MVC). Old injury in 28 (35%) of iTBl vs 1 (1.4%) of niTBl. Good detail on type of ICH. SDH iTBl more than niTBl (94% vs 61%; p<0.01), EDH commoner in niTBl (18.2% vs 1.3%, p<0.001). Data on outcome also, overall worse for iTBl than niTBl	Very large study, with good ascertainment. Overall, 53% of TBI in children aged <2 years was inflicted, with a high rank of abuse (30% admitted by perpetrator). RH, fractures and SDH were main associations, but 10% of iTBI had no RH or fractures. 35% of iTBI had no overt clinical signs of trauma (eg, bruising, palpable fracture or limb deformity). In this group of severe/moderate TBI, all niTBI had a history of trauma, although almost self-fulfilling, in contrast to niTBI
Title: A population-based comparison of clinical and outcome characteristics of young children with serious inflicted and noninflicted traumatic brain injury	Ranking of abuse: 1 and 2	GCS of 9–12 commoner in iBI (15/80) than niBI (7/72), relative risk 1.7 (0.9 to 3.2), but measure "imprecise". Lethargy, irritability, unresponsive also recorded in each, NS	Although only a third of niTBI cases had ophthalmology, other investigations seem complete
Year: 2004	Exclusion of abuse: witnessed, determined on evaluation		
Country: USA	No. of examiners: 2 for data analysis		
Aim: to compare inflicted TBI and niTBI in terms of presenting complaints, clinical features and hospital outcomes	Gender split: 87/152 (57.2%) boys		
Study design: prospective cross- sectional	Ethnicity: N/A		
Time period: 2000–2001	Socio-economic group: N/A Age: 0–2 years Median for iBI 4 months vs 7.5 months for niBI (p<0.001)		
Author(s): Kemp AM, Stoodley N, Cobley C, et al^{15}	Ascertainment: all children attending 2 regional hospitals with SDH, identified from the WPSU, inpatient data, neurology and neurosurgery databases. Retrospective	Apnoea was either reported or recorded. 4/14 had bleeding around and damage to cervical spinal cord/brain stem on post mortem. 23/65 iBl apnoea 1/25 controls. 31/65 iBl had fractures	Raw data provided by authors
Title: Apnoea and brain swelling in non-accidental head injury	•	Concluded that apnoea significantly associated with poor outcome (p $<$ 0.005)	Published study focussed on apnoea, high prevalence of cervical abnormality at post mortem, and co-existent injuries
Year: 2003	Exclusion of abuse: witnessed accident or medical causes		We have used raw data for meta-analysis, highlights the importance of apnoea

APPENDIX A Continued

Publication details	Case details	Relevant results	Critical appraisal comments
Country: UK	No. of examiners: N/A. Gender split: 58 boys (40 iBl boys)		
Aim: to identify if infants with inflicted SDH have apnoea leading to HIE, relationship to prognosis, and degree of trauma to cause NAHI	Ethnicity: N/A		
Study design: case–control Time period: 1992–98	Socio-economic group: N/A		
	Age: 0–23 months Mean age iBI 5.2 months vs 8/12 months for niBI		
Author(s): Pierre-Kahn V, Roche O, Dureau P, et $a\ell^5$	Ascertainment: all children consecutively admitted to a single unit with SDH. Excluded if CPR, coagulation abnormality, delayed eye exam or severe dehydration	Primarily ophthalmology study, refers to 7 accidental cases, but cannot extract any data other than RH (none) from them. 231 total, 153 rank 1 or 2, which we included	Of limited value for this review as there is only comparative information on RH, and only 7 children in this group
Title: Ophthalmologic findings in suspected child abuse victims with subdural hematomas	Ranking of abuse: 1 and 4	Did note seizures, SDH with associated SAH/ intracerebral and EDH. Fractures and bruises noted, no breakdown by abuse/accidental. Coagulation studies normal on all	Excellent ophthalmology detail
Year: 2003	Exclusion of abuse: proven severe accidental trauma		
Country: France	No. of examiners: N/A. Gender split: 165 boys in total group, 66 girls		
Aim: to determine the pattern and evolution of abusive intraocular haemorrhages and distinguishing features	Ethnicity: N/A		
Study design: prospective comparative case series	Socio-economic group: N/A		
Time period: 1996-2001	Age: 0–29 months Median age for iBI 1.5 months, range 0.9–3.9. For "shaken only" or "unwitnessed or denied trauma" median 4.6 and 5.5 months, respectively		
Author(s): Ruppel RA, Kochanek PM, Adelson PD, <i>et al</i> ²⁶	Ascertainment: 16 children admitted to ITU with severe TBI (2 with DAI alone excluded)	16 included, 4 iBI remainder MVC, fall (1), pedestrian (3), bike (1)	Limited data for use in this review
Title: Excitatory amino acid concentrations in ventricular cerebrospinal fluid after severe traumatic brain injury in infants and children: the role of child abuse	Ranking of abuse: 2	Three of iBI had RH, none of the niBI. 1/4 iBI had skull fracture, 5/12 niBI	Given the severity of injury at presentation, ophthalmology and skeletal survey data low in niBl
Year: 2001	Exclusion of abuse:	One from each group had long bone fracture	
Country: USA	No. of examiners: N/A. Gender split: N/A	Main results relate to cerebral metabolic markers, showing peak CSF glutamate (p<0.007) and glycine (p<0.002), but not aspartate, are increased in severe iBI compared to controls. Higher in younger and abuse cases. Also appears to be linked to severity of injury	
Aim: to evaluate if CSF glutamate, aspartate and glycine are increased in TBI, and evaluate associated features	Ethnicity: N/A		
Study design: case-control	Socio-economic group: N/A		
Time period: N/A	Age: 0.2–16 years, mean age for group 5.5 years		
Author(s): Shugerman RP, Paez A, Grossman DC, et al ²⁷	Abuse cases 0.1–0.2 years Ascertainment: all children admitted to two regional hospitals (one is the only level 1 trauma centre for the region) with SDH or EDH using trauma registry (1 unit) or case records (1 unit)	Study focussed on SDH or EDH probability of abuse. 93 children in total, 59 SDH, 34 EDH. No difference in skull fracture between two groups. 56/93 niBl, 30/93 iBl, 1 neglect (47-month-old fell from bonnet of car while parent drunk), 6 undetermined	Objective was to determine the relative probabilities of abuse for SDH or EDH, however no power calculation given, numbers of EDH much lower, and it is clear that full abuse work-up was more frequent in SDH, possibly reinforcing the finding that this is a less common finding in iBl
Title: Epidural hemorrhage: is it abuse?	Ranking of abuse: 2	Of EDH, 6/34 had associated injuries vs 29/59 SDH	
Year: 1996	Exclusion of abuse: clinical or social work assessment (no details)	All iBl cases had a history of minor trauma vs 35/56 niBl	

APPENDIX A Continued

APPENDIX A Continued			
Publication details	Case details	Relevant results	Critical appraisal comments
Country: USA	No. of examiners: N/A. Gender split: N/ A	6% of EDH were iBI vs 47% of SDH	
Aim: To determine the probability of abuse for EDH compared to SDH	Ethnicity: N/A	All 46 iBI had history of minor trauma vs 35/56 (62%) niBI	
Study design: cross-sectional Time period: 1985–1991	Socio-economic group: N/A Age: 0–3 years, no breakdown by aetiology		
Author(s): Tzioumi D, Oates RK ²⁸	Ascertainment: all children attending a single children's hospital with SDH	21 (55%) iBI, 17 niBI (15 accidental, 2 illnesses). iBI group aged 4 weeks to 20 months, mean 5.3 months, 2 history of shaking, 3 "violent" injury. Age of accidental cases 2–23 months, mean 12.4 months, older than iBI (p<0.02). More boys than girls in each group, NS	This study was limited by small numbers and spanning a long time span, with use of CT scanning alone, and incomplete data on some children. However, high surety of diagnosis of iBI due to strict criteria used
Title: Subdural hematomas in children under 2 years. Accidental or inflicted? A 10-year experience	Ranking of abuse: 1 and 2	5 had inadequate histories, concede may have been abuse. Also 1 of medical cases, subdural effusions, no detail on RH at presentation, from 1987, may have been iBl. Of niBl, 5 MVC, 5 falls >8 ft	Confirms that the commonest cause of SDH is iBI, but not as high a percentage as in other studies (54%), and also confirms significance of RH (limited by only 1/3 of niBI having eyes examined) and rib/ long bone fractures (NB: not stated if all niBI had skeletal survey)
Year: 1998	Exclusion of abuse: mixed, some MVC, long falls, some unclear, organic disease	Bilateral SDH in 58% iBl vs 27% niBl, NS. 19/21 iBl had ophthalmology (5/15 niBl), RH in 84% iBl none of niBl ($p<0.002$). 4/21 iBl rib fractures (0 niBl), 8/21 long bone fracture (0 niBl), p<0.002 for one or both of these fractures. Skull fracture 4 (iBl) vs 3 niBl. 11/21 iBl presented with seizures (vs 3/15 niBl), 6/15 iBl vomiting vs 6/17 niBl, 5/15 iBl with loss of consciousness vs 4/17 niBl. None of these significant. 2 iBl admitted shaking infants, and 3 admitted to "violent injury" out of 21. 5/15 niBl were MVC, 5 falls $>$ 8 ft, others no clear history. Irritability/drowsiness/loss of consciousness/vomiting — NS difference between iBl and niBl	Two cases of admissions of shaking (one unilateral SDH) and 3 of "violent injury", unfortunately precise details of these cases not given
Country: Australia	No. of examiners: N/A. Gender split: 30	between ibi and ilibi	
Aim: to determine the causes and distinguishing characteristics of SDH in children	boys, 8 girls Ethnicity: N/A		
Study design: cross-sectional	Socio-economic group: N/A		
Time period: 1987–1996	Age: 0-2 years Mean iBI 5.3 months vs accidental mean 12.4 months		
Author(s): Vinchon M, Defoort- Dhellemes S, Desurmont M, et al ²⁹	Ascertainment: all children (recruited	150 cases, for which we have the raw data. 60/103 SDH were boys vs 47 girls. 57 abuse cases	Raw data from authors, with full explanations
Title: Accidental and nonaccidental head injuries in infants: a prospective study	Ranking of abuse: 2	niBI were household accidents, birth injury, MVC or haemophilia. 4 idiopathic macrocranium. 73 SDH, 46 (64%) were abuse	Very valuable prospectively collected data, with all participating teams trained at the outset. Strong ppv for RH, significantly worse outcome
Year: 2005	Exclusion of abuse: witnessed or reported trauma, also a few cases with pre-existing macrocranium with possible minor trauma	Full clinical data on raw data spreadsheet	
Country: France	No. of examiners: N/A. Gender split: 103 boys, 47 girls	RH in 42/56 iBI, 5/73 niBI. Abuse cases 38% of total, but 90% of severe morbidity and 71% of mortality	
Aim: to examine the epidemiology of head injury in infants, the value of RH in abuse, and factors predisposing to SDH	Ethnicity: N/A	Impaired consciousness significantly associated with iBI vs niBI (p<0.001)	
Study design: cross-sectional Time period: 2001–2004	Socio-economic group: N/A Age: 0–2 years, mean 5.3 months		
	difference between iBI and niBI, NS		

BPSU, British Paediatric Surveillance Unit; CPR, cardiopulmonary resuscitation; CSF, cerebrospinal fluid; CT, cat scan; DAI, diffuse axonal injury; EDH, extradural haemorrhage; GCS, Glasgow coma score; HI, head injury; HIE, hypoxic-ischaemic encephalopathy; iBI, inflicted brain injury; ICD-9, International Classification of Diseases, 9th edn; ICH, intracerebral haemorrhage; iTBI, inflicted traumatic brain injury; ITU, intensive care unit; MRI, magnetic resonance imaging; MVA, motor vehicle accident; MVC, motor vehicle collision; N/A, not available; NAI, non-accidental injury; niBI, non inflicted brain injury; niTBI, non-inflicted traumatic brain injury; NS, not significant; PICU, paediatric intensive care unit; PM, post mortem; PPV, positive predictive value; RH, retinal haemorrhage; RTA, road traffic accident; SAH, subarachnoid haemorrhage; SDH, subdural haemorrhage; SE, socio-economic group; TBI, traumatic brain injury; WPSU, Welsh Paediatric Surveillance Unit.