Prediction of Inflicted Brain Injury in Infants and Children Using Retinal Imaging

AUTHORS: Robert A. Minns, FRCP(Edin), FRCPCH, PhD,[a] Patricia A. Jones, M App Sci,[a] Anamika Tandon, FRCOphth,[b] Brian W. Fleck, MD, FRCOphth, FRCSEd,[b] Alan O. Mulvihill, FRCSI, FRCSEd,[b] and Robert A. Elton, PhD[c]

[a]Department of Child Life and Health, and [b]Department of Pediatric Ophthalmology, Princess Alexandra Eye Pavilion, Royal Hospital for Sick Children Edinburgh, Edinburgh, Scotland; [c]Department of Medical Statistics, University of Edinburgh, Edinburgh, Scotland

KEY WORDS

inflicted brain injury, infants and children, retinal hemorrhages, predictive probability

ABBREVIATIONS

ATBI—accidental traumatic brain injury
IR—intraretinal
ITBI—inflicted traumatic brain injury
NFL—nerve fiber layer
"other" NTE—"other" nontraumatic etiology
RH—retinal hemorrhage
TNTC—to numerous to count

Dr Minns obtained the research grant, designed the project, obtained ethics approval and patients' consent, obtained clinical data and substantially contributed to the analysis and interpretation, literature search, manuscript writing and submission; Dr Jones obtained patients' consent, obtained clinical data and substantially contributed to the analysis and interpretation, literature search, manuscript writing, submission, and prepared figures and tables; Dr Tandon undertook clinical (photographic) data collection, categorization of imaging data, and manuscript review; Dr Fleck obtained ancillary funding, undertook clinical (photographic) data collection, and manuscript editing and review; Dr Mulvihill undertook clinical (photographic) data collection, manuscript editing and review; and Dr Elton provided statistical advice and analysis, and critical review of manuscript.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-3274

doi:10.1542/peds.2011-3274

Accepted for publication Jul 2, 2012

Address correspondence to Robert A. Minns, FRCP(Edin), FRCPCH, PhD, Emeritus Professor of Pediatric Neurology, College of Medicine and Veterinary Medicine, Child Life and Health, University of Edinburgh, 20 Sylvan Place, Edinburgh, EH9 1UW Scotland. E-mail: robert.minns@ed.ac.uk

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

(Continued on last page)

WHAT'S KNOWN ON THIS SUBJECT: Retinal hemorrhages occur in accidental and inflicted traumatic brain injury (ITBI) and some medical encephalopathies. Large numbers and peripherally located retinal hemorrhages are frequently cited as distinguishing features of ITBI in infants, but the predictive value has not been established.

WHAT THIS STUDY ADDS: This prospective retinal imaging study found that a diagnosis of ITBI in infants and children can be distinguished from other traumatic and nontraumatic causes by the presence of >25 dot-blot (intraretinal layer) hemorrhages (positive predictive value = 93%).

abstract

BACKGROUND: Retinal hemorrhages (RHs) occur in inflicted traumatic brain injury (ITBI), accidental traumatic brain injury (ATBI), and some medical conditions, although the reported number, distribution, type, and frequency vary greatly between these different etiologies. We hypothesize that these RH characteristics reliably help to distinguish ITBI from ATBI and nontraumatic etiologies.

METHODS: A 6-year prospective observational study using wide-field retinal imaging (RetCam) was conducted within 24 hours of admission to PICU, on serially recruited children with traumatic and nontraumatic encephalopathies. "Definite" and "probable" ITBI cases were confirmed by multiagency child protection case conferences. Image analysis used digital color and grayscale images for retinal "zoning" and "layering" of hemorrhages.

RESULTS: Significant differences were found between the mean numbers of hemorrhages in ATBI/ITBI, and ITBI/nontraumatic etiologies for the 3 retinal zones (range, P = .003–.009) and for the dot-blot hemorrhages (range P = .001–.002). The mean numbers of RHs per ITBI patient in the peripapillary, macula, and peripheral zones were 14, 28, and 31 respectively. RHs in ATBI were near the optic disc and more superficial than in ITBI, where hemorrhages involved deeper layers (range, P = .003–.039) and were more peripheral (P = .03). The positive predictive value for ITBI in children <3 years with >25 dot-blot (intraretinal) hemorrhages was 93%.

CONCLUSIONS: This prospective study, which included all potential causes of RHs, with objective retinal methodology, has confirmed that a young age and a high dot-blot count are strong predictors of ITBI. This high predictive value may support medicolegal deliberations. *Pediatrics* 2012;130:e1227–e1234

Retinal hemorrhages (RHs) are a recognized accompaniment of both accidental and inflicted childhood trauma and of many other nontraumatic encephalopathies. Most investigators have only recognized differences in the retinal findings in inflicted, compared with accidental traumatic brain injury, by the presence or absence of RHs,[1,2] or if there were very large numbers of hemorrhages described as "too numerous to count" (TNTC), but few have defined precise RH characteristics.

Three prospective studies[3–5] have assessed RHs from funduscopy with or without retinal drawings sketched by the examiner in traumatic brain injury in children. Pierre-Kahn et al[3] studied children presenting only with a subdural hematoma and found that RH characteristics were not statistically different in those patients presumed to have been shaken in comparison with those with signs of head trauma without a relevant history, and additionally found no RHs in 7 accidental traumatic brain injury cases. Bechtel et al[4] included only children with accidental and inflicted trauma and found RHs in abuse were more frequent, more bilateral, more pre-retinal, and more extending to the periphery. Vinchon et al[5] included all causes of traumatic injury to children from birth to 24 months and found that the sensitivity value for those patients with inflicted head injury who have a RH (presence or absence) was 75%, and specificity was 93.2%. A number of other retrospective clinical and autopsy studies have been reported,[6–15] including 2 studies that used retinal photographs.[9,15]

We aimed, by means of a prospective study of infants and children admitted to a PICU, to determine, by RetCam examination within 24 hours of admission, the frequency with which RHs occur in serious accidental traumatic brain injury (ATBI) and inflicted traumatic brain injury (ITBI) and those children admitted with "other" nontraumatic etiologies ("other" NTEs). We further aimed to document the number of RHs, their retinal location/s and retinal layer involved, and any other retinal injury from the first retinal image obtained after admission. We sought to estimate the relative risk of these RH characteristics for predicting ITBI in comparison with ATBI and other nontraumatic diagnoses.

METHODS

This prospective observational study was conducted over a 6-year period, at the Royal Hospital for Sick Children Edinburgh, in the PICU and Neurosciences Department, on serially admitted children with traumatic and nontraumatic encephalopathies. Children were excluded if there was a previous history of head injury or preexisting eye disease, a clinical contraindication (eg, a clinical necessity for pupil responses where intracranial pressure was being monitored, imminent neurosurgery, etc), an inability to recruit or undertake RetCam examination within 24 hours of admission (eg, the child's clinical state dictated early withdrawal of ventilation/sedation), early demise, and refusal or withdrawal of consent. Newborns postdelivery (from the maternity hospital) were not routinely included. Initial and sequential RetCam imaging was undertaken after fully informed parental consent.

All photographic imaging was done by using a hand-held digital retinal camera (RetCam, Clarity Medical Systems, Pleasanton, CA), with a 120° lens, while the patient was being ventilated as part of their management. The pupils were dilated, and a local anesthetic and coupling agent (carbomer gel) used. For each eye, a standard selection of views was chosen to cover as much of the retina as possible. Routine practice was indirect ophthalmoscopy before all RetCam imaging, and all suspected ITBI cases were attended by a pediatric ophthalmologist. All RetCam images were downloaded unchanged to a dedicated computer for morphometry and counting by using Photoshop7.0 and routinely applying a green filter to produce a grayscale version of each image in Scion Image Analysis software.

In this study, each RH was allocated a retinal zone and layer. We used a previously published zonal classification, with high interrater κ values, namely the peripapillary circle (zone "D"), posterior pole/macula (zone "M"), and the remainder zone "P," that is, all the peripheral area, including the midperiphery outside zone M.[16]

A retinal layer was ascribed to each hemorrhage as previously described (vitreous; pre-retinal; nerve fiber layer [NFL]; intraretinal [IR] (dot-blot)/subretinal)[17] by a single ophthalmologist investigator (A.T.), to eliminate any potential interobserver error that might result from multiple raters. Previous studies have highlighted a consistent lack of agreement on identification of subretinal hemorrhages in particular.[17,18] Subretinal hemorrhages have been counted separately from intraretinal hemorrhages in this article. For the purposes of analysis, RHs were counted from the single best quality image that showed all 3 zones and were expressed as either RHs per eye or RHs per patient. Any retinal injuries were recorded.

A "centrality score" was devised for each subject, where a score of 1 indicated "adjacent to the disc," 2 at the macula, and 3 at the periphery. An average value was calculated for each subject, weighted by the number of RHs in each zone, giving a score ranging from 1 (all RHs adjacent to the disc and none elsewhere) to 3 (where all RHs are peripheral and none elsewhere).

Ethical approval (LREC 2004/6/2) was granted by the Lothian Research Ethics Committee. All analyses were performed with the use of SPSS (version 14.0.1, Inc; Chicago, IL) and PASW Statistics Package (version 17.0.2; Chicago, IL). Mann-Whitney *U* tests were used for all analyses, except tests for asymmetry of RHs (Wilcoxon signed rank tests); primary brain injury and presence/absence of RH (χ^2); correlation of "severity" of brain and retinal injury (Spearman rank); and multiple logistic regression for investigating predictive factors for ITBI.

RESULTS

We recruited 114 children to this study of whom 79 (69%) were boys. The median age of all patients was 47.8 months (range, 0.01–212.3 months).

Twenty-one cases were designated ITBI after a convened multiagency Child Protection Case Conference[19] recommended making provision for the immediate safety of the child. They were ascribed a degree of medical surety of diagnosis[20–23] by the authors as either "definite" (n = 11) or "probable" (n = 10). It is difficult to be certain that a diagnosis of ITBI would have been confirmed by the Child Protection Case Conference, and subsequent legal proceedings, if RHs were not taken into consideration. We reviewed the 21 ITBI cases and found that 3 cases did not have RHs, and, of the remaining 18, 12 would likely have been diagnosed ITBI, without reference to RHs.

The median age for all patients who had any RHs (n = 34) was 5·9 months (range, 0.01–176.5 months). Two of the 34 were unable to proceed to RetCam examination, and RHs were detected and characterized only by indirect ophthalmoscopy. Details of the various etiological groups (ATBI, ITBI, and other NTEs) with the frequency of RHs, are shown in Table 1. Accidental injuries were of similar severity to other non-included traumatic admissions to PICU (P = .08), and occurred in 57 children (7 with RHs). Those with RHs were due to (1) motor vehicle accidents (pedestrian 3/15, passengers 1/11, or bicycle accidents, 2/10) and (2) high falls, 1/9. There were no RHs in 12 cases (6 infants with "low" [<1 m] household falls, 3 sports injuries, 2 struck on the head, and 1 other domestic accident).

RHs

There were a total of 1867 RHs in 49 eyes where RHs could be numerically counted from RetCam images. There were 16 RHs in 3 eyes counted by indirect ophthalmoscopy. In 6 eyes, the hemorrhages were initially deemed TNTC. However, by factoring up the number of hemorrhages in a radial segment of these eyes (where they were evenly distributed), the total number of RHs could be estimated. The mean number of RHs in these TNTC cases was 303 (range, 146–565).

RH Distribution

The maximum number of RHs in each zone for each patient (from either the right or left eye, which ever was the greater for that zone) was summated and compared with etiological groups (Table 2). The analysis excluded data from the TNTC cases, because RHs in these cases could not be confidently ascribed a retinal zone, because retinal zoning required clear retinal landmarks (optic disc and vascular arcades). The clinically more relevant arithmetic mean values for any individual patient, in the different etiological groups, are seen in Table 3.

The centrality score gave a mean value of 1·72 for ATBI and 2·11 for ITBI (P = .033), confirming that RHs in ITBI are more peripheral than in ATBI. The mean for the other NTE group was 2·09, and therefore, in this respect, ATBI RH distribution was different from ITBI and other NTEs.

Regardless of cause, in this series, NFL hemorrhages were predominately peripapillary in location, whereas most

TABLE 1 Patient Characteristics

Etiology	No. of Patients in Group	Mean Age, mo(Median)	Age Range of Group	Gender, F/M	GCS or % Intubated/Sedated	No. of Patients With RHs	Unilateral RHs	Bilateral RHs	Mean Age of Those With RHs, mo(median)
ATBI	57	93.74 (107)	0.2–188.94	F = 16	Sev = 27 (47.4%)	7 (12·2%)	3	4 (57.1% patients with RH)	102.91 (110.66)
				M = 41	Mod = 24 (42.1%) Mild = 6 (10.5%)				
ITBI	21	5.65 (3.12)	1.25–30.21	F = 9	Sev = 7 (33.3%)	18 (85·7%)	4	14 (77.7% patients with RH)	5.85 (2.96)
				M = 12	Mod = 6 (28.6%) Mild = 8 (38.1%)				
Other NTEs	36	62.56 (11.61)	0.01–212.32	F = 10	n = 33/36 (91.6% intubated/sedated)	9 (25%)	3	6 (66.6% patients with RH)	44.17(15.39)
				M = 26					

There is a significantly greater number of patients with RHs in the ITBI group in comparison with the other 2 groups (χ^2, P < .0001). F, female; M, male; GCS, Glasgow Coma Score; Sev, severe head injury, with E1, V2 or less, and M5 or less, GCS 3–8; Mod, moderate head injury, GCS 9–12; Mild, GCS 13–15.

TABLE 2 Significant Comparisons Between ITBI and ATBI, ITBI and Other NTEs, ITBI and a Combined Group (ATBI + Other NTEs) for RH Numbers, RH Zones, and RH Layers

	P
ITBI > ATBI: (RHs by zone: *n* = 22 patients)	
Total[a] RHs in zone D (238: 42)	.039
Total[a] RHs in Zone M (463: 36)	.009
Total[a] RHs in zone P (519: 13)	.009
ITBI > ATBI: (RHs per layer, per patient: *n* = 25 patients)	
Total[b] RHs in intraretinal layer (1906: 30)	.001
ITBI > ATBI: (RH layers by zone: *n* = 22 patients)	
Intraretinal layer	
Total[a] RHs in zone D (77: 5)	.039
Total[a] RHs in zone M (365: 20)	.005
Total[a] RHs in zone P (500: 7)	.003
Pre-retinal RH: ITBI > ATBI	
Total[a] RHs in zone M (25: 0)	.047
ITBI > other NTEs (RHs by zone: *n* = 24 patients)	
Total[a] RHs in zone D (238: 29)	.003
Total[a] RHs in zone M (463: 73)	.008
Total[a] RHs in zone P (519: 51)	.004
ITBI > other NTEs (RHs per layer, per patient: *n* = 27 patients)	
Total[b] RHs in intraretinal layer (1906: 116)	.002
ITBI > combined (ATBI + other NTEs) (RHs by zone: *n* = 31 patients)	
Total[a] RHs in zone D (238: 71)	≤.005
Total[a] RHs in zone M (463: 109)	≤.005
Total[a] RHs in zone P (519: 64)	≤.005
ITBI > combined (ATBI + other NTEs) RHs layer by zone (*n* = 31patients)	
RHs in intraretinal layer (942: 153)	.001
Total[a] RHs in zone D (77: 9)	≤.011
Total[a] RHs in zone M (365: 86)	≤.011
Total[a] RHs in zone P (500: 58)	≤.011
Pre-retinal Hs	.03
Total[a] RHs in zone M (25: 1)	.015

[a] Calculated as the number of RHs in the eye with the greatest number in that layer or zone.

[b] Calculated as the sum of the maximum numbers of RHs from each zone (from whichever eye had the greatest number).

intraretinal hemorrhages were in the macula and periphery (96%). Within the limits of our imaging technique, very few preretinal hemorrhages were seen to be exclusively in the peripheral zone "P" (0.5%). This is exemplified in the 7 ATBI cases with RHs, in which there were no vitreous hemorrhages, and almost all (ie, 98.9%) the RHs were in the NFL (65·3%) and IR (33·7%) layer. Their density was not only greatest near the optic disc (46%), they were also more superficial than in ITBI. In the same way, in the 15 ITBI patients (excluding the TNTC cases), the deeper layer IR RHs occurred in the periphery (in 93.1% of all peripheral hemorrhages) and in the macula (in 74.4% of all macula hemorrhages), that is, in ITBI, the numbers of RHs were not only greatest in the peripheral zone (43%) but also involved deeper layers (Fig 1A and 1B)

Retinal Layer of Hemorrhage

Total numbers of RHs in the 4 retinal layers in each etiological group were compared by including those seen on funduscopy (3 eyes), and including the 3 patients (6 eyes) that were from "TNTC" cases, that is, a total of 58 eyes. Based on the summated values of all patients entered into this study, Table 2 shows the significant associations between ITBI and ATBI, and also ITBI and other NTEs for the different RH layers involved. Again, the clinically more relevant arithmetic mean values for each individual patient are shown in Table 4.

ITBI Cases Compared With "Non-ITBI" Cases

There were 10 times as many RHs in ITBI as in all other cases in this study combined. In patients with a RH in at least 1 eye, significant differences exist between the maximum (and mean) RH counts between ITBI and the other 2 combined etiological groups (listed in Table 2).

RHs in Nontraumatic Encephalopathy

For the 9 other NTE cases there were no vitreous hemorrhages, and only 1 preretinal hemorrhage. 75% of other NTE RHs were deeper-layer hemorrhages (IR), and 97% of these were in the macular or peripheral region. Table 5 shows details of the other NTE cases with RHs.

Asymmetry of RH Distribution

In this study, unilateral RHs occurred more frequently in the left eye (7 cases) compared with the right eye (3 cases), and there was a nonsignificant greater number of hemorrhages in the left eye than in the right in a ratio of 1:5.2. For all cases in this study with RHs, an "asymmetry ratio" of the number of RHs in left to right eyes, when combining unilateral cases with asymmetry in bilateral cases, was not significant (1:1.16).

Primary Brain and Retinal Injury

The more severe the ATBI (lower Glasgow Coma Score), the greater the likelihood of having a RH ($P = .012$), and the more severe the ITBI, the greater the severity of RH injury, here defined as total numbers of RHs in both eyes ($P = .030$).

Other retinal injuries can be difficult to determine in ITBI patients, because the severe hemorrhagic appearance often masks additional injury (15 eyes in this study). Retinal injuries, in addition to the RHs, were seen in 7 cases of ITBI, some with up to 3 retinal injuries. For the purposes of our study, retinoschisis was recognized as traumatic splitting of the NFL, or separation by blood of the inner limiting membrane from the NFL, and occurred in ITBI in 7 eyes. Other ITBI injuries included retinal folds (2 eyes) and choroidal tears (3 eyes); 1 eye had an avulsed optic nerve. One 14-year-old child, who died of a very severe injury from a motor vehicle/bicycle collision, had a large macular schisis (left eye) in zone D, with a well-defined cystic appearance and fluid level. A small preretinal hemorrhage (right eye, zone M) was also noted.

TABLE 3 Mean Number (and Range) of Retinal Hemorrhages Counted by Zone and Etiological Group for an Individual Patient, and *P* values and Confidence Limits for the Difference in Medians

	Peripapillary (D)	Macula (M)	Periphery (P)
ATBI	4.3 (1–17.5)	4.0 (0–11.5)	1.5 (0–4)
ITBI	14 (0–33)	27.5 (0·5–105)	31.3 (0–150)
Other NTE	2.3 (0–13·5)	6.2 (0–31)	4.1 (0–25)
ITBI > ATBI (*P* values and confidence limits)	.08 (0, +25)	.007 (+2, +39)	.014 (+1, +44)
ITBI > other NTEs (*P* values and confidence limits)	.007 (+1, +26)	.01 (+2, +38)	.003 (+2, +36)

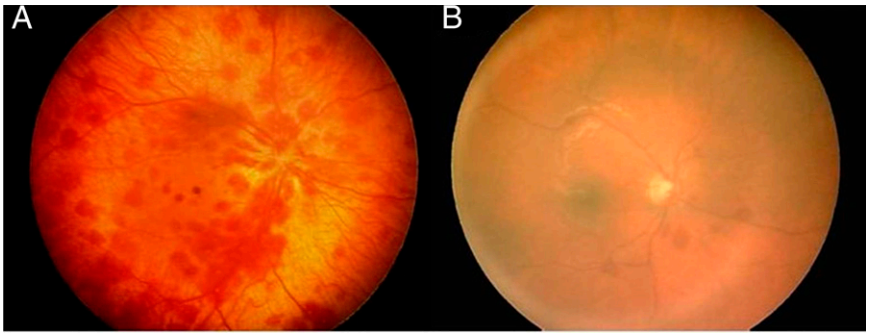

FIGURE 1
A, The RetCam image from the right eye of a 5-week-old child with ITBI showing extensive hemorrhagic retinopathy involving all retinal zones and predominantly in the intraretinal and nerve fiber layers. B, The retinal image from the right eye of a 10-year-old boy with severe traumatic brain injury from motor vehicle contact (struck by a wing mirror) shows 12 small and moderately sized hemorrhages in the NFL and IR layer that extend into the peripapillary, macula, and nasal peripheral zones.

TABLE 4 Mean Number (and Range) of RHs in Different Layers for an Individual Patient for the Different Etiological Groups, and *P* Values and Confidence Limits for the Difference in Medians

	Vitreous H	Pre-retinal Hs	NFL Hs	Intraretinal Hs
ATBI	—	0.07 (0–0.5)	6.4 (1–27.5)	3.28 (0–10.5)
ITBI	0.11 (0—1)	2.47 (0–7.5)	13.91 (0–66.5)	94.97 (2–444)
Other NTEs	—	0.22 (0–2)	3.06 (0–19)	9.77 (0–50.5)
ITBI > ATBI (*P* values and confidence limits)	NS	0.11 (0, +5)	0.57 (−2, +15)	0.001 (+14, +111)
ITBI > other NTEs (*P* values and confidence limits)	NS	0.07 (0, +16)	0.046 (0, +16)	0.002 (+5, +102)

H, hemorrhage; NS, not significant; —, no cases.

Prediction of ITBI

The presence of RHs was a very strong diagnostic factor for ITBI in the whole study sample (Table 6). Among those with RH, both young age and high dot-blot count were strongly diagnostic, with young age having greater sensitivity and high dot-blot count greater specificity. A high dot-blot count remained independently significant ($P = .017$) among those with both RH and young age.

DISCUSSION

This study has confirmed a frequency of RHs in children with severe ITBI (43% in PICU) of 85.71%. Published frequencies from other prospective studies report 37.5% to 77.5%.[1–3,5] We have also found a highly significant greater number of RHs in all retinal zones and retinal layers in ITBI in comparison with cases of ATBI. Average number of RHs in each zone and layer for each individual patient has been tabulated in Tables 3 and 4, and may be useful bedside indicators for further investigation of possible abuse. TNTC is the description used to indicate the extreme end of the hemorrhagic retinopathy appearance in ITBI, and an estimate of the numbers of RHs in the 3 cases in this study show a mean RH count of 303 (range, 146–565).

RH Characteristics in ITBI

In ITBI cases, 93% of all the peripheral hemorrhages were in the IR layer, as were 74% of all macula hemorrhages. Only 2 subretinal hemorrhages were recognized in this study, both located in the same eye (zones M and P) of an 18-month-old child with ITBI. A centrality score was devised, and this confirmed that the RH distribution was significantly more peripheral (ie, a centrifugal pattern) than the more central location in ATBI cases. Bechtel et al[4] and Gilliland[10] reported a similar peripheral distribution in ITBI. RHs in ITBI cases are therefore more peripheral and involve the deeper layers. The distribution of RH is also influenced to some extent by the retinal layer involved. It is known that the NFL diminishes in thickness toward the ora serrata, and we have found that, regardless of cause, NFL hemorrhages are predominately peripapillary, and 96% of the intraretinal hemorrhages are found in the macula/peripheral zone, all suggesting that the distribution and layer are dictated by factors other than solely the mechanism of injury.

Bilateral RHs are known to be a feature of ITBI,[4,24,25] and this study confirms bilateral RHs in 78% of cases, similar to frequencies reported by other investigators.[4,26] Unilateral RHs are also described in ITBI,[4,9,12,24,25,27–29] and they occurred in 4 cases in this study, but were additionally seen in 3 ATBI cases and in 3 medical patients. The unilateral RHs more often involved the left eye (7/10 cases), a figure similar to the

TABLE 5 NTE Cases With RHs

Etiology	No. of Patients	Mean Age, mo (Range)	Patients with RHs. n (%)	No. of Patients With Unilateral RHs	No. of Patients With Bilateral RHs
Meningococcal meningitis	7	43 (7–154)	4 (57) (a mean of 7 RHs/patient)	2 (predominantly IR in macula zone)	2 (predominantly IR in macula zone)
Blocked ventriculoperitoneal (CSF) shunt	6	148 (3–212)	1 (17)	0	1 (4 moderate-sized pre-retinal, in peripapillary and macula zones)
Cardiorespiratory arrest and cardiopulmonary resuscitation	5	34 (1–167)	2 (40)	1 (1 small discal RH)	1 (4 small RHs, IR in peripheral and macula zones).
Neonatal brain tumor	1	1 d old	1	—	46 RHs in right eye, and 93 in left. 75% were IR, and remainder in NFL. 50/139 (36%) RHs were in peripheral zone

CSF, cerebrospinal fluid; —, not applicable.

TABLE 6 Estimates (95% Confidence Intervals) for Diagnostic Properties of Selected Factors in Different Study Samples in Predicting ITBI in Comparison With the Other 2 Groups

Study	Factor	PPV	NPV	Sensitivity	Specificity
All cases	RH present	18/34 = 53% CI, 35–70	77/80 = 96% CI, 89–99	18/21 = 86% CI, 64–97	77/93 = 83% CI, 74–90
RH present	Age <3 y	18/25 = 72% CI, 51–85	9/9 = 100% CI, 66–100	18/18 = 100% CI, 81–100	9/16 = 56% CI, 30–80
	>25 dot-blots	13/14 = 93% CI, 68–99	15/20 = 75% CI, 11–47	13/18 = 72% CI, 47–90	15/16 = 94% CI, 70–99
RH present and <3 y	>25 dot-blots	13/14 = 93% CI, 68-99	6/11 = 55% CI, 23–83	13/18 = 72% CI, 47–90	6/7 = 86% CI, 42–99

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value for children <18, 12, and 6 months was 92%.

65% reported by Arlotti et al.[27] We have found a nonsignificant greater number of RHs in the left eye in unilateral cases, in bilateral RH cases, and in ITBI cases. An asymmetry ratio combining RH counts from unilateral cases with bilateral RH cases showed little asymmetry (left to right ratio of 1.16:1).

RHs have been reported in ATBI with a frequency range of 0% to 15%.[2,4,5,7,30–33] These have been described as few in number, unilateral, at the posterior pole, and involving pre-retinal and intraretinal layers. We report a RH rate of 12.2% in ATBI (90% in PICU); 98% of these were either in NFL (68%) or in the IR layer (33%). Again, the average numbers of RHs seen in children after ATBI in the different retinal zones and layers (Tables 3 and 4) could be clinically helpful. RHs in ATBI therefore were near the optic disc (ie, centripetal pattern) and predominantly superficial.

RHs occurred in children with nontraumatic medical encephalopathies in 9/36 (25%) in this series, including 1 child with a blocked ventriculoperitoneal shunt and raised intracranial pressure, 2 children after cardiorespiratory arrest and cardiopulmonary resuscitation, and 4 with meningococcal meningitis. Dinakaran et al[34] described RHs in 5/12 children with meningococcal septicemia. These were flame shaped and dot-blot, and they numbered <20 in each fundus, compared with a mean of 7 intraretinal hemorrhages per patient counted in the macula zone in our study. The large number of RHs in multiple layers (much greater than 25), in a neonate with a large congenital brain tumor (one of the other NTE cases), was the reason the prediction rate for ITBI in our study was not higher than that which we report. RH numbers in these other NTE cases combined with RH numbers in ATBI cases were still significantly fewer than the RHs occurring in ITBI.

Predictive Probability

A predictive algorithm based on RH characteristics indicated that the chance of a particular case being due to ITBI, if RHs are observed and if the maximum number of IR layer hemorrhages (predominantly dot-blot) was >25, is 93%; and chance of a particular case being due to ITBI is 92% if the patient is <18 months of age. A young age and a high dot/blot (IR) count are therefore strong indicators of ITBI. The relatively low sensitivity value for these characteristics is a reflection of the fact that ITBI may be diagnosed from other clinical features and a different pattern of retinal findings.

Although children with previous head injuries were excluded from entry into this study, no child with ITBI and only 1 with ATBI were actually excluded on this basis. Underreporting of abnormalities may occur in all zones,[18] but it was a consistent technical limitation for counting from zone P (and ora serrata) when using the 120° RetCam lens, because of the inherent fading and reduced contrast of the image toward the periphery owing to the oblique viewing angle, and from using a single "centered" photographic image. Future developments in imaging software

may allow a combination of multiple images from 1 eye to be used. In future Optical coherence tomography should clarify the depth of the hemorrhages within the retina more accurately than two-dimensional retinal photographs. This article presents the first prospective study with objectively measured RHs from all possible etiologies in children and predicts inflicted brain injury from certain RH characteristics alone.

ACKNOWLEDGMENTS

We are grateful for the support of the Trustees of the R. S. Macdonald Charitable Trust, and thank the medical and nursing staff of PICU and Neurosciences ward at Royal Hospital for Sick Children Edinburgh, Ophthalmology registrars and fellows, parents/guardians of children recruited to the study, and child protection specialists over the 6-year study period.

REFERENCES

1. Duhaime AC, Alario AJ, Lewander WJ, et al. Head injury in very young children: mechanisms, injury types, and ophthalmologic findings in 100 hospitalized patients younger than 2 years of age. *Pediatrics*. 1992;90 (2 Pt 1):179–185
2. Ewing-Cobbs L, Kramer L, Prasad M, et al. Neuroimaging, physical, and developmental findings after inflicted and noninflicted traumatic brain injury in young children. *Pediatrics*. 1998;102(2 pt 1):300–307
3. Pierre-Kahn V, Roche O, Dureau P, et al. Ophthalmologic findings in suspected child abuse victims with subdural hematomas. *Ophthalmology*. 2003;110(9):1718–1723
4. Bechtel K, Stoessel K, Leventhal JM, et al. Characteristics that distinguish accidental from abusive injury in hospitalized young children with head trauma. *Pediatrics*. 2004;114(1):165–168
5. Vinchon M, Defoort-Dhellemmes S, Desurmont M, Dhellemmes P. Accidental and nonaccidental head injuries in infants: a prospective study. *J Neurosurg*. 2005;102 (4 suppl):380–384
6. Betz P, Puschel K, Miltner E, Lignitz E, Eisenmenger W. Morphometrical analysis of retinal hemorrhages in the shaken baby syndrome. *Forensic Sci Int*. 1996;78(1):71–80
7. Binenbaum G, Mirza-George N, Christian CW, Forbes BJ. Odds of abuse associated with retinal hemorrhages in children suspected of child abuse. *J AAPOS*. 2009;13(3): 268–272
8. Budenz DL, Farber MG, Mirchandani HG, Park H, Rorke LB. Ocular and optic nerve hemorrhages in abused infants with intracranial injuries. *Ophthalmology*. 1994; 101(3):559–565
9. Gilles EE, McGregor ML, Levy-Clarke G. Retinal hemorrhage asymmetry in inflicted head injury: a clue to pathogenesis? *J Pediatr*. 2003;143(4):494–499
10. Gilliland MGF. Extent and distribution of retinal hemorrhages in abusive and nonabusive head injury. In: Proceedings of the 55th. Annual Meeting of the American Academy of Forensic Sciences; Chicago, IL, February 17–22, 2003; Abstract G86:232–233
11. Kivlin JD, Simons KB, Lazoritz S, Ruttum MS. Shaken baby syndrome. *Ophthalmology*. 2000;107(7):1246–1254
12. Morad Y, Kim YM, Armstrong DC, Huyer D, Mian M, Levin AV. Correlation between retinal abnormalities and intracranial abnormalities in the shaken baby syndrome. *Am J Ophthalmol*. 2002;134(3):354–359
13. Munger CE, Peiffer RL, Bouldin TW, Kylstra JA, Thompson RL. Ocular and associated neuropathologic observations in suspected whiplash shaken infant syndrome. A retrospective study of 12 cases. *Am J Forensic Med Pathol*. 1993;14(3):193–200
14. Riffenburgh RS, Sathyavagiswaran L. Ocular findings at autopsy of child abuse victims. *Ophthalmology*. 1991;98(10):1519–1524
15. Wilkinson WS, Han DP, Rappley MD, Owings CL. Retinal hemorrhage predicts neurologic injury in the shaken baby syndrome. *Arch Ophthalmol*. 1989;107(10):1472–1474
16. Fleck BW, Tandon A, Jones PA, Mulvihill AO, Minns RA. An interrater reliability study of a new 'zonal' classification for reporting the location of retinal haemorrhages in childhood for clinical, legal and research purposes. *Br J Ophthalmol*. 2010;94(7):886–890
17. Mulvihill AO, Jones PA, Tandon A, Fleck BW, Minns RA. An inter-observer and intra-observer study of a classification of RetCam images of retinal haemorrhages in children. *Br J Ophthalmol*. 2011;95(1):99–104
18. Tandon A, McIntyre S, Yu A, et al. Retinal haemorrhage description tool. *Br J Ophthalmol*. 2011;95(12):1719–1722
19. Mok JYQ, Busuttil A, Hammond HF. The joint paediatric-forensic examination in child abuse. *Child Abuse Rev*. 1998;7(3):194–203
20. Keenan H. Nomenclature, definitions, incidence and demographics of inflicted childhood neurotrauma. In: Reece RM, Nicholson CE, eds. *Inflicted Childhood Neurotrauma*. Elk Groove City, IL: American Academy of Pediatrics; 2002:3–11
21. Thomas SA, Rosenfield NS, Leventhal JM, Markowitz RI. Long-bone fractures in young children: distinguishing accidental injuries from child abuse. *Pediatrics*. 1991;88(3): 471–476
22. Maguire S, Pickerd N, Farewell D, Mann M, Tempest V, Kemp AM. Which clinical features distinguish inflicted from non-inflicted brain injury? A systematic review. *Arch Dis Child*. 2009;94(11):860–867
23. Maguire S, Moynihan S, Mann M, Potokar T, Kemp AM. A systematic review of the features that indicate intentional scalds in children. *Burns*. 2008;34(8):1072–1081
24. Bhardwaj G, Chowdhury V, Jacobs MB, Moran KT, Martin FJ, Coroneo MT. A systematic review of the diagnostic accuracy of ocular signs in pediatric abusive head trauma. *Ophthalmology*. 2010;117(5):983–992.e17
25. Shaw AD, Watts P, Maguire S, Holden S, Mann M, Kemp AM. Are retinal findings in abused children different from those who suffer accidental head trauma? Results of a systematic review. *J AAPOS*. 2010;14(1): e27
26. Togioka BM, Arnold MA, Bathurst MA, et al. Retinal hemorrhages and shaken baby syndrome: an evidence-based review. *J Emerg Med*. 2009;37(1):98–106
27. Arlotti SA, Forbes BJ, Dias MS, Bonsall DJ. Unilateral retinal hemorrhages in shaken baby syndrome. *J AAPOS*. 2007;11(2):175–178
28. Barry GP, Romero KE, Forbes BJ, Christian CW, Binenbaum G. Pathologic brain and head findings associated with retinal hemorrhages in young children with abusive or accidental head injuries. *J AAPOS*. 2010;14(1):e11
29. Healey K, Schrading W. A case of shaken baby syndrome with unilateral retinal hemorrhage with no associated intracranial hemorrhage. *Am J Emerg Med*. 2006;24(5):616–617

30. Sturm V, Knecht PB, Landau K, Menke MN. Rare retinal haemorrhages in translational accidental head trauma in children. *Eye (Lond)*. 2009;23(7):1535–1541
31. Trenchs V, Curcoy AI, Morales M, Serra A, Navarro R, Pou J. Retinal haemorrhages in-head trauma resulting from falls: differential diagnosis with non-accidental trauma in patients younger than 2 years of age. *Childs Nerv Syst*. 2008;24(7):815–820
32. Vinchon M, Noizet O, Defoort-Dhellemmes S, Soto-Ares G, Dhellemmes P. Infantile subdural hematomas due to traffic accidents. *Pediatr Neurosurg*. 2002;37(5):245–253
33. Vinchon M, de Foort-Dhellemmes S, Desurmont M, Delestret I. Confessed abuse versus witnessed accidents in infants: comparison of clinical, radiological, and ophthalmological data in corroborated cases. *Childs Nerv Syst*. 2010;26(5):637–645
34. Dinakaran S, Chan TK, Rogers NK, Brosnahan DM. Retinal hemorrhages in meningococcal septicemia. *J AAPOS*. 2002;6(4):221–223

(Continued from first page)

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

FUNDING: Funding was obtained from the R.S. Macdonald Charitable Trust Edinburgh, from the Royal College of Surgeons Edinburgh (Ophthalmology Grant), and from the Friends of The Sick Kids Foundation, Edinburgh, Scotland. The funders had no role in study design; in the collection, analysis, and interpretation of data; or in the writing of the report or the decision to submit the article for publication.