

Late Neurologic and Cognitive Sequelae of Inflicted Traumatic Brain Injury in Infancy

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ABSTRACT. *Objective.* There is limited information regarding the long-term outcome of inflicted traumatic brain injury (TBI), including shaken infant syndrome. The purpose of this study was to describe the long-term neurologic, behavioral, and cognitive sequelae seen in this population.

Methods. A cross-sectional and prospective longitudinal study was conducted of 25 children with inflicted TBI in Scotland between 1980 and 1999. After consent was obtained, neurologic and cognitive examinations were performed on all participants and sequentially in the prospective cohort. Two global outcome measures were used: Glasgow Outcome Score (GOS) and Seshia's outcome score. Cognitive outcome was assessed using the Bayley Scales of Infant Development, British Ability Scales, and the Vineland Adaptive Behavior Scales.

Results. The mean length of follow-up was 59 months. A total of 68% of survivors were abnormal on follow-up, 36% had severe difficulties and were totally dependant, 16% had moderate difficulties, and 16% had mild difficulties on follow-up. A wide range of neurologic sequelae were seen, including motor deficits (60%), visual deficits (48%), epilepsy (20%), speech and language abnormalities (64%), and behavioral problems (52%). There was a wide range of cognitive abilities: the mean psychomotor index, 69.9 (SD: ± 25.73); and mean mental development index, 74.53 (SD: ± 28.55). Adaptive functioning showed a wide range of difficulties across all domains: communication domain (mean: 76.1; SD: ± 25.4), Daily living skills domain (mean: 76.9; SD: ± 24.3), and socialization domain (mean: 79.1; SD: ± 23.1). Outcome was found to correlate with the Pediatric Trauma Score and the Glasgow Coma Score but did not correlate with age at injury or mechanism of injury.

Conclusions. Inflicted TBI has a very poor prognosis and correlates with severity of injury. Extended follow-up is necessary so as not to underestimate problems such as specific learning difficulties and attentional and memory problems that may become apparent only once the child is in school. Behavioral problems are present in 52% and begin to manifest clinically between the second and third years of life, although the consequences of frontal lobe injury may be underestimated unless follow-up is extended into adolescence and early

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ABBREVIATIONS. TBI, traumatic brain injury; CI, confidence interval; MREC, Multicenter Research Ethics Committee; GCS, Glasgow Coma Score; PTS, Pediatric Trauma Score; GOS, Glasgow Outcome Score; BSID-II, Bayley Scales of Infant Development—Second Edition; BAS II, British Ability Scales II; VABS, Vineland Adaptive Behavior Scales—First Edition; DQ, developmental quotient.

Head injuries are a common cause of death in childhood, and an important cause of traumatic brain injury (TBI) leading to death in infancy is inflicted (nonaccidental) TBI.^{1,2} Between 24% and 33% of TBI admissions in children <2 years of age are from inflicted TBI, and up to 42% require admission to the ICU.^{3,4} The various forms of inflicted TBI (including shaken infant syndrome) are now well recognized and diagnosed in most countries. The incidence in Scotland is 24.6 infants per 100 000 person-years (95% confidence interval [CI]: 14.9–38.5), which is comparable with epidemiologic data in the United States, where the incidence of severe inflicted TBI is 29.7 infants per 100 000 person-years.^{5,6}

There is very limited research on the outcome of inflicted TBI in childhood. The available literature was summarized in a recent publication.⁷ Most of the studies have been retrospective, and the source of the cases differs. Some report the outcome of children who had been admitted to either the ICU or high-dependency unit, where it is reasonable to assume that these children are the more severely injured and likely to have a worse prognosis.^{8,9} The reported mortality rate ranges from 13% to 36%, which is higher than accidental head injuries in a similar age range, 6% to 12%.^{3,5,8,10–12} A total of 106 of the 489 documented cases in this literature died (excluding the Scottish epidemiologic cohort), with an overall mortality rate of 21.6%. The Scottish cohort documented a mortality rate of 11%. Although relatively low, this is likely to reflect the mortality rate of the full spectrum of inflicted TBI in early childhood.^{2,5,8,11,13}

The method of attainment of outcome in the literature varies and includes chart reviews, telephone follow-up, and a few with patient interview. The outcome measures that are used also vary (perhaps

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in part because of a lack of consensus on a suitable outcome score of head injury in children), and most of the studies report short-term outcomes. One prospective study of 28 children reported that 16% had a severe outcome, 61% had a moderate outcome, and 25% had a good outcome at a mean follow-up of 3 months.¹⁴ The overall morbidity in reports of a total of 292 survivors is 74% (range: 59–100%), with only 25% being “normal” on follow-up.⁷ No long-term follow-up studies have reported the outcome of the whole spectrum of inflicted TBI.¹⁵

A cross-sectional and prospective longitudinal study was undertaken (1) to examine the outcome of all children who were admitted to the hospital and for whom there was enough evidence to support a diagnosis of inflicted TBI; (2) to observe the evolving neurologic picture of this population through the period of maximal brain growth; (3) to document the cognitive, behavioral, and adaptive skills of these children; and (4) to document any changes over time in the prospective group.

METHODS

Study Design

The cross-sectional group consisted of all children who were admitted to the Royal Hospital for Sick Children (Edinburgh, UK) since 1981 and received a diagnosis of inflicted TBI. The prospective group consisted of all children who were admitted to a hospital in Scotland between January 1997 and July 1999 with inflicted TBI.

Patient Identification

The cross-sectional cohort was identified using diverse sources such as neurology and neurosurgical admission records, emergency department attendance reports, intensive care admission records and chart reviews from hospital records, or a combination of these methods. As part of an epidemiologic study in Scotland, a register of all cases of inflicted TBI has been established since 1998. This source was used to identify potential cases for the prospective arm.

Inclusion Criteria

Inclusion criteria were (1) a diagnosis of inflicted TBI that satisfied a predetermined algorithm that inflicted TBI was the most likely mechanism of injury and (2) consent of both the physician and the legal guardian of the child. The algorithm used was based on similar ones to Duhaime and Goldstein.^{2,8} An encephalopathy plus at least 2 of the following features had to be seen: intracranial hemorrhage including subdural hemorrhages, retinal hemorrhages, rib fractures, skeletal injuries, malicious injuries (eg, cigarette burns, torn frenulum, bite marks), and a history that was inconsistent with the observed injuries and/or changing histories with time.

Consent

The study was approved by and conducted in concordance with the protocol of the Multicenter Research Ethics Committee (MREC). Written informed consent to participate was obtained from the legal guardian. This was done at least 3 months after discharge from the hospital at the request of the MREC. There was a high refusal rate, 48%, and this was attributable to the complex medicolegal and social issues encountered in these cases. Reasons for refusal to participate in the study included refusal to accept the diagnosis, mistrust of the medical profession, anxiety about bringing up issues that the family were trying to forget, and 2 children who could not enter as the local research ethics committee was concerned about possible legal ramifications.

Clinical Details

Medical records were reviewed to ascertain demographic and birth details, the likely mechanisms of injury, acute admission

details such as the lowest postresuscitation Glasgow Coma Score (GCS), ventilation, hypoxia, hypotension, lowest blood pressure in the first 24 hours, clinical seizures, and details of injuries. The Pediatric Trauma Score (PTS) was determined for each case on the basis of clinical details within the first 24 hours of acute admission. This score uses 6 categories of assessment: weight, systolic BP, level of consciousness, airway, wound, fracture. A score of +2, +1, or –1 is awarded for each. The final score is the sum of these, with a maximum score of +12 and minimum score of –6. A lower score indicates a more severe injury. This score has been shown to have good intraobserver reproducibility, is easy to use in children, and has been shown to correlate significantly with outcome in other traumatic injuries.^{16,17}

Neurologic and Neuropsychologic Examinations

Both qualitative and quantitative outcome measures were used. Neurologic histories and examinations were performed by 1 pediatric neurologist (K.M.B.) in the child's home, and a standard proforma was completed. Visual acuity scores were used to measure impairment; severe visual impairment is a visual acuity <20/200. Standard questions about the child's behavior and function were asked as part of this examination. The examinations took place at least 3 months after discharge from the hospital (this was at the request of the MREC) and thereafter every 6 to 12 months in the prospective group. All children's cognitive, behavioral, and adaptive skills were assessed at least once by 1 of 3 clinical psychologists.

Qualitative Assessment of Outcome

Two qualitative outcome scores were used as there is no well-accepted universal outcome score with childhood head injury. The Glasgow Outcome Score (GOS) modified for children was used because most pediatricians are familiar with this score.¹⁸ This is a 5-point outcome score in which a “good” outcome was assigned when there were age-appropriate levels of functioning and, for school-aged children, functioning in school full time without special educational services. “Moderate” disability was assigned on the basis of significant reduction in cognitive functioning, special education therapy, and/or motor deficits interfering with activities of daily living. “Severe” disability was assigned when cognitive functioning was in the deficient range and/or severe motor deficits that require substantial assistance with self-care skills were present. “Persistent vegetative state” was assigned when there was no evidence of ability to communicate, verbally or nonverbally, or to respond to commands, and the fifth outcome was “dead.” Because a significant proportion of children who have moderate and severe TBI and a “good outcome” using the GOS score have significant neuropsychologic abnormalities and go on to fail grades in school or require modified educational programs, a second outcome score was also used.¹⁹

Originally, a 5-point outcome scale, Seshia's outcome score, was updated to a 6-point scale in 1994.^{20,21} The score awarded is dependent on the (1) recorded neurologic deficits (eg, hemiparesis, cranial nerve deficits, visual deficits, microcephaly, seizures) and (2) a calculated developmental quotient of gross motor, fine motor and hand function, communication, and language abilities. These were calculated by comparing achieved ability with median age at which that ability occurs in the normal population. A developmental quotient of 79 to 71 was classified as mild impairment, 70 to 51 was classified as moderate impairment, 50 to 26 was classified as severe impairment, and ≤ 25 was classified as profound impairment. A score of 1 is normal, 2 is mild, 3 is moderate, 4 is severe, 5 is vegetative, and 6 is dead. There are inherent difficulties sometimes in matching the functional outcome with the neurologic deficit to arrive at a score. When there was functional/neurologic dissociation, the most severe outcome level was chosen. Similar methods of assessing outcome have been used by others.^{22,23}

Quantitative Outcome Measures

The cognitive tests used depended on the age of the child. The Bayley Scales of Infant Development–Second Edition (BSID-II) was used for children between birth and 2.5 years. These are normed scales that yield mental and psychomotor development indices with a mean index score of 100 and an SD of 15. It also includes a Behavior Rating Scale, which is primarily oriented

toward the functions of attention and arousal before 6 months of age. Beyond 6 months of age, the Behavior Rating Scale becomes increasingly concerned with orientation toward and interactions with the examiner and the caregiver, quality of movement, and emotional regulation during testing. The Total Score is thought to reflect neurobehavioral integrity in younger children and adaptation to the environment in older children. The Total Score can fall into 1 of 3 descriptive categories: within normal limits (scores ranking at or above the 26th percentile), questionable (scores from 11th to 25th percentiles for age), or nonoptimal (below the 10th percentile).²⁴

The British Ability Scales II (BAS II) was used for children aged 2.5 to 17.5 years. This is an individually administered intelligence test that yields 3 major intelligence scores (general, visual, and verbal) as well as a short-form score. These are carefully normed using a representative sample of British children, and the norms give both T scores and percentiles corresponding to the Rasch ability scores within the appropriate age groups. The scales are classified into 5 general areas: (1) reasoning (formal operations, similarities, matrices, and social reasoning); (2) spatial imagery (block design level and power, rotation of letter-like forms, and visualization of cubes); (3) perceptual matching (copying, matching letter-like forms, and verbal-tactile matching); (4) short-term memory (immediate and delayed visual recall, recall of designs, recall of digits, and visual recognition); and (5) retrieval and application of knowledge (basic number skills, naming vocabulary, verbal comprehension, verbal fluency, word definitions, word reading, and conservation items).

Adaptive behavior was measured using the Vineland Adaptive Behavior Scales—First Edition (VABS), which assesses the social competence of handicapped and nonhandicapped individuals from birth through age 19. Norms are provided from birth to 18 years, 11 months with a standard score mean of 100 and SD of ± 15 . Using this scale, adaptive behavior is measured in 4 main domains that include communication, daily living skills, socialization, and a composite adaptive level. A fifth score that gauges motor skills is measured for children who are < 6 years of age. An adaptive level is designated to be “high” with a standard score of > 131 (± 2 SD), “moderately high” with a standard score of 116 to 130, “adequate” with a standard score of 85 to 115, “moderately low” with a standard score of 70 to 84 (-1 SD), and “low” with a standard score of ≤ 69 (-2 SD).²⁵

Statistical Analysis

Fisher exact test (2-tailed) was used to compare demographic and injury variables between those who did not consent to be in the study and participants. The Mann-Whitney *U* test was used to compare the outcome between these 2 groups. Fisher exact test (2-tailed) was used to compare injury with and without clinical evidence of impact and outcome in the study group. Nonparametric statistical analysis using Kendall rank correlation method was used to analyze the relationship between age at injury, GCS and PTS, and the 2 global outcome measures (GCS and Seshia's outcome score).

RESULTS

Fifty-five patients were identified during the study period between 1997 and 1999: 31 children in the cross-sectional group and 24 children in the prospective group. Six children died, 1 of whom was in the prospective group. Twenty-five children took part in the study: 12 in the prospective group and 13 in cross-sectional group. The average length of follow-up was 59 months (median: 40 months). In the prospective group, the mean age at the first examination was 16 months (SD: ± 9.9 months) and the last examination was 25.3 months (SD: ± 9.1 months). The mean age at follow-up in the cross-sectional group was 90 months (SD: ± 50 months). The perpetrator was known in 19 of the cases (biological father, 14; boyfriend, 3; other male, 1; mother, 1). A total of 36% of children were in foster care.

Acute Admission Details of the Study Group

The median age at admission was 2.3 months (range: 2 weeks to 34 months). The male:female ratio was 3:2. Clinical findings of the acute admission included subdural hemorrhages (84%), subarachnoid hemorrhage alone (16%), retinal hemorrhages (64%), evidence of an impact injury (44%), rib fractures (24%), other skeletal fractures (24%), bruising (24%), acquired coagulopathy (16%), ventilated and admitted to the ICU (32%), documented hypovolemia and/or shock (40%), raised intracranial pressure (48%), neurosurgical intervention (28%), and early posttraumatic seizures (68%). One child had a congenital craniofacial dysmorphic syndrome. The median length of admission was 26 days (range: 3–57).

Twenty-four families did not participate in the study. There were no statistical differences in the characteristics of those who did not consent and the participants. The mean age at admission was the same in both groups (3.5 months), and there was no statistical difference in other demographic or injury profiles: gender ($P = .76$), geographic area ($P = .49$), ICU admission ($P = .76$), fluid resuscitation ($P = .18$), ventilation ($P = .51$), and documented hypoxia ($P = .74$). Socioeconomic circumstances could not be obtained in the majority of those who refused consent. Outcome (based on chart review) was available for 12 of the children for whom consent was not obtained. There was no difference in outcome between this group and the participants ($P = .32$). The main difference between these groups was that the perpetrator was known more frequently in the participants ($P < .01$).

Neurology

Many children had acquired dysmorphism: 8 developed an acquired microcephaly (32%), whereas 5 (20%) were macrocephalic. Two children with severe neurologic impairment on follow-up developed a high arched palate. Asymmetric growth with dwarfing of 1 side, in association with a hemiparesis, was found in 3 children. The neurologic deficits at each examination are summarized in Table 1. Ten (40%) had an unchanging normal neuromotor pattern. The predominant abnormal neuromotor patterns included hemiparesis (4), ataxia (8), tetraplegia (2), and mixed (4). The first signs of an evolving cerebral palsy in infancy was frequently central hypotonia with delay in motor milestones followed by the emergence of other signs such as spasticity, eg, an ataxic diplegia (patient 8) and a monoplegia (patient 2) became apparent in the second year of life. A variety of cranial nerve abnormalities were found. Third cranial nerve palsy was found in 1 child, upper motor neurone seventh was found in 2, sensorineural deafness was found in 2, and lower motor 12th was found in 1. Pseudobulbar palsy was seen in 3 children. No peripheral sensory abnormalities were detected (Table 1).

Vision

Twelve (48%) children had abnormalities of visual function. Cortical blindness was observed in 4 chil-

TABLE 1. Clinical Details at Acute Admission Are Displayed Together With the Neurologic and Behavioral Findings at Follow-up Examinations

Patient	Clinical Findings	Age at Follow-up, Months	Neurologic Findings	Gross Motor DQ	Fine Motor DQ	Speech and Language DQ	Social Function DQ	Other	Seshia Outcome Score	Modified GOS
1	AI = 1.5, male, SAH, SDH, CO, RH, bruising, inconsistent history, PTS = 4, PPP, decreased BP, apnea, ventilated, increased ICP (Mon), Sz, SIS (held by the neck), perp (F) convicted	11	Microcephaly, left hemiparesis left UMN VIIth, left homonymous hemianopia, heterotropia	63	72	63	72	Placid, no separation anxiety	3	Moderate
		21	Microcephaly, left hemiparesis, left UMN VIIth, left homonymous hemianopia, heterotropia	48	71	66	71	Placid	3	Moderate
		30	Microcephaly, left hemiparesis, left UMN VIIth, left homonymous hemianopia, heterotropia	50	60	55	80	Temper tantrums, self-injurious behavior (head banging)	3	Moderate
2	AI = 3, female, SDH, CO, RH, inconsistent history, PTS = 5, PPP, apnea, ventilated, increased ICP, Sz, NS (SD drain), SIS, perp (F) convicted	10	Microcephaly, truncal hypotonia, severe visual impairment, left esotropia	60	80	60	60	Placid infant	3	Moderate
		16	Microcephaly, truncal ataxia, left esotropia	63	63	88	75		3	Moderate
		23	Microcephaly, truncal ataxia, right lower limb monoparesis, left esotropia	65	78	78	78	Temper tantrums, self-injurious behaviors (head banging and self-biting)	3	Moderate
3	AI = 2, male, SDH, ICH, CO, RH, PTS = 2, PPP, apnea, ventilated, increased ICP, Sz, SIS, perp (F) convicted	8	Ataxic tetraparesis Blind Infantile spasms	12	12	12	12		4	Severe
		17	Ataxic tetraparesis, cortical blindness	6	6	6	6	Cries irritably, settling for short periods to voice	4	Severe
4	AI = 1, female, SAH, ICH, bruising, R# PTS = 5, apnea, ventilated, increased ICP, NS (IVD), impact	12	Normal	100	100	100	100	Normal	1	Good
		18	Truncal hypotonia	83	100	100	100	Normal	2	Good
5	AI = 8, male, craniofacial syndrome, SDH, RH, bruising (genitalia), inconsistent history, PTS = 7, Sz, SIS, perp (uncle)	14	Craniofacial syndrome	79	79	79	79	Temper tantrums, self-injurious behaviors, sleep disturbance	1	Good
		20	Craniofacial syndrome	75	75	75	75		2	Good
6	AI = 18, female, SDH, bruising, PTS = 10, narcotics, perp (BF), impact	31	Normal	97	90	77	97	Normal	1	Good
7	AI = 7, male, SDH, CO, RH, skull#, skeletal#, rib#, PTS = -4, PPP, apnea, ventilated, increased ICP (Mon), GCS = 3, Sz, NS (SD drain), impact \pm WSIS	18	Blind, sensorineural deafness, truncal hypotonia, symptomatic partial epilepsy	27	22	22	22		4	Severe
		28	Microcephaly, cortical blindness, sensorineural deafness, spinocerebellar ataxia, symptomatic partial epilepsy	26	19	15	15	Self-injurious injury (head banging, eye poking); self-stimulation	4	Severe
8	AI = 1, male, SDH, SCWT, CO, bruising, GCS = 5, PTS = 3 PPP, apnea, ventilated, increased ICP (Mon), Sz, NS (SD drain), impact \pm WSIS, perp (F) convicted	8	Microcephaly, truncal hypotonia	50	50	50	75		3	Moderate
		12	Microcephaly, high arched palate, cerebellar ataxia	50	50	50	75		3	Moderate
		20	Microcephaly, high arched palate, ataxic diplegia	45	75	75	75	Sleep disturbance	3	Moderate
9	AI = 2, male, SDH, RH, GCS = 13, PTS = 8, Sz, SIS, perp (F) convicted	37	Dyspraxic dysarthria	97	89	67	100		2	Good
		44	Dyspraxic dysarthria	95	82	82	84	Hyperactive, impulsive, rage reactions	2	Good
10	AI = 1, female, SDH, RH, GCS = 13, PTS = 9 Sz, WSIS, perp (F) convicted/confession	4	Normal	100	100	100	100	Normal	1	Good
		11	Normal	100	91	109	100	Normal	1	Good
11	AI = 1.5, female, SDH, CO, RH, bruising, rib#, skeletal#, PTS = 0, apnea, PPP, ventilated, increased ICP (Mon), NS (SD drain), Sz, impact + WSIS, perp (F) convicted	16	Microcephaly, truncal hypotonia, left hemiparesis, possible diplegia	52	81	81	100		3	Severe
		26	Microcephaly Ataxic diplegia Left hemiparesis Dysarthria	46	69	58	69	Temper tantrums	4	Severe

TABLE 1. Continued

Patient	Clinical Findings	Age at Follow-up, Months	Neurologic Findings	Gross Motor DQ	Speech and Language DQ	Social Function DQ	Other	Seshia Outcome Score	Modified GOS
12	AI = 1, male, SDH, CO, CC, bruising, PTS = 3, PPP, Sz, compression injury, perp (F)	24 36	Spinocerebellar ataxia, bilateral 8th	50 50	63 50	75 67	Mild temper tantrums Severe temper tantrums, impulsive, self-injurious behavior, poor sleep pattern	3 4	Severe Severe
13	AI = 4, male, premature 29/40, SDH, R#, GCS = 14, PTS = 8 increased ICP (Mon), NS (SD drain), WSIS, perp (F)	37	Normal	97	100	100	Normal	1	Good
14	AI = 3, male, SDH, RH, inconsistent history, rib#, skeletal#, skull#, PTS = 0, Sz, ventilated, PPP, increased ICP, NS (SD drain), impact \pm WSIS	39	Microcephaly, heterotopia	100	100	100	Normal	1	Good
15	AI = 2, female, SDH, bruising, PTS = 7, Sz, perp (F), impact + WSIS	60	Microcephaly, left homonymous hemianopia, left CN 3rd, left esotropia, left lower limb monoplegia, severe expressive dysphasia, good nonverbal communication, intractable epilepsy	60	80	40	Marked hyperactivity, severe concentration difficulty, impulsivity, disruptive behavior	4	Severe
16	AI = 3, male, SDH, RH, MI, skull#, R#, S#, PTS = 1, apnea, ventilated, increased ICP (Mon), Sz, NS (SD drain) impact \pm WSIS, perp (F)	78	Macrocephaly, mild optic atrophy, decreased visual acuity, visual sensory inattention, heterotopia, mild cerebellar ataxia, dyspraxia, 12th CN abnormality	76	92	90	Impulsive, loses temper easily, moderate verbal and numeric memory difficulties	2	Good
17	AI = 22, female, SDH, RH, bruising, GCS = 11, PTS = 9, Sz, Coag, impact + WSIS	80	Macrocephaly, normal, heterotopia	90	100	100	Normal (initially fearful of men)	1	Good
18	AI = 19, male, SDH, RH, MI, bruising, skeletal#, PTS = 7, increased ICP, Sz, impact \pm WSIS	78	Macrocephaly, normal	92	100	100	Normal	1	Good
19	AI = 2, female, SDH, ICH, CC, RH, bruising, skeletal#, apnea, PTS = 5, increased ICP, Sz, perp (F), SIS	128	Right hemiparesis	63	76	89	Normal behavior, special educational support in mainstream	3	Moderate
20	AI = 6, male, SDH, RH, Sz PTS = 0	52	Microcephaly, cortical blindness, severe language impairment, spinocerebellar ataxia, lower limb monoplegia, epilepsy	31	23	27	Autistic features, self-injurious behaviors, hyperkinetic reactions, sleep disturbance	4	Severe
21	AI = 1, male, SDH different ages, PTS = 7, Sz, SIS	252	Macrocephaly, spastic tetraplegia, pseudobulbar palsy, cortical blindness, intractable epilepsy	4	4	4	Total dependence, no active rolling, 24-h care	4	Severe
22	AI = 7, female, SDH, RH, Sz, PTS = 0	96	Ataxic diplegia, left hemiparesis, pseudobulbar palsy, UMN 7th CN, visual impairment, intractable epilepsy	10	38	25	Severe speech and language delay, poor attention span, placid, sleep disturbance	4	Severe
23	AI = 3, male, SDH, RH, skull#, PTS = 5, Sz, increased ICP (Mon), NS (SD drain), impact \pm WSIS	71	Spastic diplegia with mild bilateral upper limb involvement and dystonia, pseudobulbar palsy, dysarthria, mild visual impairment	17	68	76	Temper tantrums, impulsivity, poor attention span	4	Severe
24	AI = 2, male, SDH, rib#, skeletal#, bruising, GCS = 13, PTS = 5, increased ICP, WSIS, normal	59	Macrocephaly	115	115	110	Normal, comparable with twin	1	Good
25	AI = 3, female, SDH, skull#, PTS = 9, impact \pm WSIS	146	Normal	100	100	100	Sexual behavioral problems, multiple foster homes	1	Good

Prospective cohort: patients 1 to 12; cross-sectional cohort: patients 13 to 25. AI indicates age at admission (mo); SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage; CO, cerebral edema; Sz, seizure; RH, retinal hemorrhages; PPP, decreased peripheral perfusion; Perp, perpetrator; F, father; BF, boyfriend; BP, blood pressure; ICP, intracranial pressure; (Mon), monitored; SIS, shaken infant syndrome; SD drain, subdural drain; NS, neurosurgery; ICH, intracerebral hemorrhage; #, fracture; WSIS, whiplash-shaking injury; Coag, coagulopathy; UMN, upper motor neuron; CN, cranial nerve.

dren.^{3,7,20,21} Visual field defects were observed in 2 children (patients 1 and 15), and visual agnosia was observed in 1 child (patient 16). Visual acuity deficits were observed in 3 other children; these deficits were always bilateral. Patient 2 had a marked visual acuity deficit initially at 6/96 with ocular abnormalities, but this improved to normal at the end of follow-up. Seven children had abnormal extraocular movements with heterotropia. It was associated with visual acuity or visual field abnormalities in 5 children; 2 children had no other abnormalities detected. One patient had paralytic heterotropia (patient 15). Four children were treated with intermittent eye patching, and 2 had corrective surgery (Table 1).

Epilepsy

Two children (patients 1 and 3) were initially on antiepileptic drugs, having had seizures in the acute illness, but these were stopped without additional seizures during the follow-up period. Five (20% children) had symptomatic partial epilepsy with secondary generalization. Three of these children had intractable multifocal seizures with multiple daily seizures despite 2 or more antiepileptic drugs with persistent epileptiform activity demonstrated by electroencephalogram. Patient 3 developed infantile spasms at 8 months of age and a hypsarrhythmic electroencephalogram that responded to nitrazepam (Table 1).

Functional Mobility and Praxis

Ten (40%) children had normal gross motor function, 2 (8%) had mild, 3 (12%) had moderate, 6 (24%) had severe, and 4 (16%) had profound difficulties. Functional mobility was normal in 15 (60%) children; 3 were mobile within the home, 3 were mobile with therapeutic aids and 3 were nonambulatory (1 had active rolling). Seven children required orthotics such as ankle-foot orthoses, rolators, standing frames, and K-walkers. Eleven (44%) patients had normal praxis, 4 (16%) had mild, 5 (20%) had moderate, 1 (4%) had severe, and 4 (16%) had profound manipulative difficulties (Table 1).

Speech and Language

Speech and language function was normal in 9 (36%) patients. Seven (28%) children had mild difficulties. Patient 6 had a mild developmental dysarthria with normal cognitive function. Patient 9 had a marked dyspraxic dysarthria without evidence of corticospinal tract or cerebellar or bulbar involvement but with evidence of cognitive impairment (Table 2). Two (8%) children had moderate speech and language delay. Two (8%) had severe speech and language delay all associated with cognitive impairment and marked behavioral abnormalities (patients 15 and 20). Patient 20 had an autistic spectrum disorder. Patients 8 and 12 had relative paucity of speech, which was slow and dysarthric in association with a bilateral sensorineural deafness and a spinocerebellar ataxia. Four (16%) had profound language problems, all associated with profound cognitive impairment (patients 3, 7, 21, and 22; Table 1).

Developmental Arrest

The developmental quotient (DQ) in speech and language is a better indicator of cognitive development than the DQ in fine and gross motor skills. The DQ in speech and language fell in 5 of the 11 children with prospective examinations (patients 1, 3, 7, 11, and 12); in 2, it was associated with developmental arrest (patients 3 and 7), in whom no developmental progress was seen. In patient 8, the DQ for speech and language increased significantly, from 50 to 75; this was associated with a change of caregiver.

Behavioral

Self-injurious behaviors were seen in 6 (24%) children; these behaviors were mainly head banging but also included eye poking and biting. These behaviors all occurred in children who had neurologic abnormalities (patients 1, 2, 5, 7, 12, and 20), and these behaviors appeared toward the end of the second year of life. Nine children developed severe temper tantrums, 3 of whom had been placid, quiet infants (patients 1, 2, and 12). Rage reactions were reported in 2 children: patient 9 had expressive language problems and cognitive dysfunction on neuropsychologic testing and demonstrated evidence of frontal lobe dysfunction with hyperactivity, impulsivity, and rage reactions; patient 18 had an autistic spectrum disorder. Other behavioral problems included marked problems with attention (patients 9, 15, 16, and 22), impulsivity (patients 9, 12, 15, 16, and 23), hyperactivity (patients 9, 15, and 20), and ritualistic behaviors (patients 15 and 20). These were noted in the older children in the cross-sectional group (5–6 years of age). Six (24%) children had problematic sleep disturbance (Table 1).

GOS

Using Seshia's global outcome score, 8 (32%) children were normal at follow-up, 4 (16%) had mild difficulties, 4 (16%) had moderate difficulties, 9 (36%) fell in the severe outcome category, and no children were in a vegetative state. Four of the 11 children with sequential examinations changed outcome categories; all were 37 months or younger at the age of the first assessment and 44 months or younger at the last examination. All changed to a more severe outcome category. Two changed from normal to mild (patients 4 and 5), and 2 changed from moderate to severe (patients 11 and 12).

Cognitive Development

BSID-II

Fourteen children had the BSID-II administered. The mean Psychomotor Development Index score was 69.93 with an SD of ± 25.73 . There was a wide range of scores among this group (<50 –121), and the median was 50 (0.1th percentile). The mean of the Mental Developmental Index score was slightly higher 74.53 (SD: ± 28.55) also with a wide range of scores (<50 –112), with a median of 58.5 (0.7th percentile). Figure 1 displays the distribution of percentile rank equivalents, which is markedly skewed to the left. Eight of the 14 children scored in the abnor-

TABLE 2. Cognitive Development After Inflicted TBI

Patient	Age, mo	BSID-II, Developmental Index					VABS Standard Score, Percentile			
		Mental MDI (Percentile)	Psychomotor PDI (Percentile)	Behavior, Percentile		Motor Quality, n	Communication, n (%)	Daily Living, n (%)	Socialization, n (%)	Motor, n (%)
				Total, n	Orientation, n					
1	23	62 (1%)	<50 (<0.1%)	7	12	11	77 (6)	82 (12)	84 (14)	73 (4)
2	24	62 (1%)	<50 (<0.1%)	13	15	38	79 (8)	77 (6)	87 (19)	75 (5)
3	9	<50 (<0.1%)	<50 (<0.1%)	1	1	1	74 (2)	78 (8)	65 (1)	69 (2)
4	17	80 (10%)	55 (<0.1%)	21	27	38	99 (47)	95 (37)	101 (53)	79 (8)
5	22	74 (4%)	60 (<1%)	2	6	13	78 (7)	91 (27)	96 (39)	86 (18)
6	32	112 (79%)	121 (92%)	10	6	21	88 (21)	90 (25)	104 (61)	81 (10)
7	28	<50 (<0.1%)	<50 (<0.1%)	1	1	6	63 (1)	68 (2)	55 (<0.1)	57 (<1)
8	10	50 (<0.1%)	<50 (<0.1%)	3	2	5	91 (27)	96 (39)	93 (32)	77 (6)
9	40	55 (2%)	93 (30%)	32	23	38	62 (1)	59 (<1)	69 (2)	92 (30)
10	11		Refused neuropsychological testing as now "normal"							
11	29	55 (<0.1%)	<50 (<0.1%)	1	2	4	76 (5)	87 (19)	81 (10)	61 (1)
12	36	<50 (<0.1%)	<50 (<0.1%)	3	8	7	57 (<1)	74 (4)	68 (2)	77 (6)
13	37	111 (75%)	120 (91%)	54	27	51	100 (50)	97 (42)	105 (63)	109 (73)
14	40	101 (53%)	88 (21%)	37	16	59	121 (92)	101 (53)	102 (55)	106 (66)
15	60	<50 (<0.1%) age equivalent = 18	<50 (<0.1%) age equivalent = 35	—	—	—	48 (<0.1)	66 (1)	61 (1)	59 (<1)
WPPSI-R Scaled Scores, Percentiles										
		Full-Scale IQ, Percentile	REY Complex Figure	Vocabulary	Block Design	Raven's Colored Matrices	Similarities			
16	60	WPPSI 89 (23%) VIQ 79 PIQ 89	1% Story recall < 2 SD	3 (1%)	6 (9%)	<5%	93 (32)	95 (37)	90 (25)	87 (19)
17	68	WPPSI 78 (7%) VIQ 71 PIQ 78	28% Story recall < 3 SD	5 (5%)	7 (16%)	25%	112 (79)	101 (53)	94 (34)	93 (32)
BAS-II T Score, Percentiles										
		General T Score, Percentile	Recall of Designs	Word Definition	Pattern Construction	Matrices	Verbal Similarities			
18	78	100 (50%)	46 (34%)	58 (79%)	48 (42%)	47 (38%)	101 (53)	100 (50)	102 (55)	109 (73)
19	128	74 (4%)	37 (10%)	30 (2%)	30 (2%)	36 (8%)	78 (7)	78 (8)	81 (10)	73 (4)
20	52	BAS-II Untestable	U	U	U	U	42 (<0.1)	39 (<0.1)	45 (<0.1)	31 (<0.1)
21	252	BAS-II Untestable	U	U	U	U	<20 (<0.1)	<20 (<0.1)	<20 (<0.1)	<20 (<0.1)
22	96	BAS-II Untestable	U	U	U	U	39 (<0.1)	22 (<0.1)	52 (<0.1)	<20 (<0.1)
23	71	BAS-II Untestable	U	U	U	U	—	—	—	—
24	60	Lost to follow-up; doing "normally" in school								
25	146	Doing well in a normal school, refused neuropsychologic testing, sexual behavioral problems								

U indicates untestable; MDI, Mental Development Index; PDI, Psychomotor Development Index.

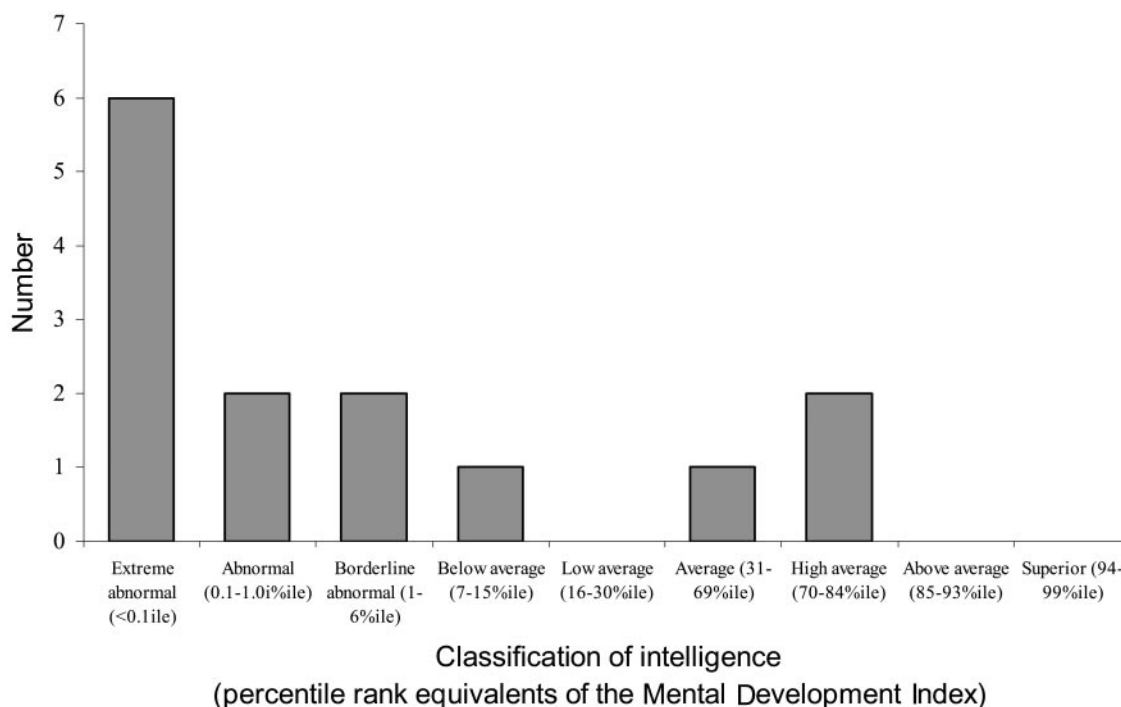


Fig 1. Distribution of the percentile rank equivalents of the Mental Development Index scores. The median was in the 0.7th percentile.

mal range, ie, below the 1st percentile, and 2 children fell in the borderline range (1st–6th percentiles; Table 2).

BAS-II

Six children had the BAS-II administered (patients 18–23), and 2 children (patients 16 and 17) had cognitive testing performed as part of another study. These included the Wechsler Preschool and Primary Scale of Intelligence–Revised, REY Complex Figure Test, Ravens Colored Matrices, and Logical Memory, and these results were included as part of the overall data set. Four children were able to complete these tests with overall scores ranging from the 4th to 50th percentiles. The results are shown in Table 2. Two children (patients 16 and 17) whose IQ fell within the normal range, 89 and 78, respectively, were found to have previously unrecognized memory deficits. Patient 16, who had a mild cerebellar ataxia and visual inattention, was found to have severely impaired visual memory with no recall or recognition of a complex visual figure. His verbal memory for verbal prose was also impaired with a loss of information over a delay. Patient 17 had a normal neurologic examination. Her IQ was in the 8th percentile, and she was found to have moderately impaired visual memory with poor recall and recognition of a complex visual figure. Her memory for verbal prose was also impaired, with a loss of information over a delay. This was associated with moderate difficulty in focusing and sustaining attention.

Adaptive Behavior

Behavior Rating Scales of the BSID-II (N = 14)

The total raw score was a mean of 21.85 (SD: ± 22.75), and the median was at the 7th percentile. Seven children scored in the “nonoptimal range,” ie,

below the 10th percentile, 1 in the “questionable” range, ie, between the 11th and 25th percentiles. The orientation raw score was a mean of 19.6 (SD: ± 24.96 ; median: 8th percentile). Six children were in the “nonoptimal range,” indicating a low level of initiative and involvement in tasks and reluctance to engage socially. Three additional children were in the “questionable” range. The emotional scale raw score indicates irritability and emotional lability with easy frustration and poor adaptability (mean: 24.77; SD: ± 18.79 ; median: 13th percentile; range: 1st to 58th percentiles). Four children scored below the 10th percentile, and 3 children scored in the “questionable” range. Motor scale raw score was a mean of 15.08 (SD: 15.04). The median was on the 9th percentile with range between the 1st and 48th percentiles. Seven children scored in the “nonoptimal” range, indicating neuromotor dysfunction, and 4 scored in the “questionable” range.

Twenty-one caregivers completed the VABS (Fig 2). In the communication domain, the mean was 76.1 (SD: ± 25.4); 1 (5%) child scored in moderately high category (patient 14), 7 (33%) children scored in the “adequate” category, 6 (28%) scored in the “moderately low level” category, and 7 (33%) scored in the “low level” category. In the daily living skills domain, the mean was 76.9 (SD: ± 24.3). In this domain, 10 (48%) scored in the “adequate” category, 5 (24%) scored in “moderately low” category, and 6 (28%) scored in the “low” category. In the socialization domain, the mean was 79.1 (SD: ± 23.1). Eleven (52%) children scored in the “adequate” category, 2 (10%) scored in the “moderately low” category, and 8 (38%) scored in the “low” category. In the motor skills domain, the mean was 73.1 (SD: ± 25.4). Seven (33%) children scored in the “adequate” category, 7 (33%)

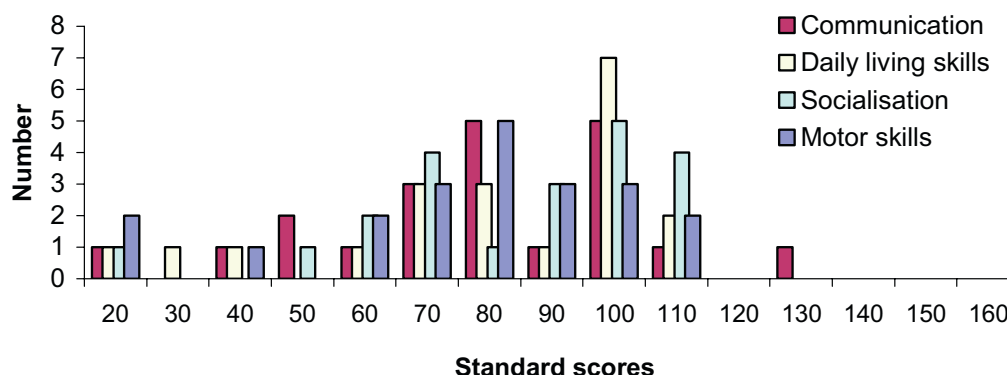


Fig 2. Distribution of standard scores on the VABS, the mean for each domain ranging between 73 and 79, which is well below the normal mean of 100.

scored in the “moderately low” category, and 7 (33%) scored in the “low” category.

Losses to Psychologic Evaluation

Patient 10 (11 months) in the prospective group withdrew from the study because the family believed that she was normal and did not require additional testing or follow-up. In the cross-sectional group, patient 24 (5 years) was lost to follow-up because the caregivers moved to other parts of the United Kingdom with no forwarding address or contact information. At this time, he was thought to be normal and functioning well in the first year of school. Patient 25 (12 years) declined neuropsychologic evaluation. She was doing well academically in an age-appropriate class in a mainstream school; however, there were significant difficulties with inappropriate sexual behaviors. Patient 21 (21 years) was tested with the BAS-II but was untestable at the entry level of the test (2 years of age). Using the VABS, his adaptive behavior was in the “below average” range for the supplementary norm for nonambulatory mentally handicapped adults in all domains. Patient 22 (8 years) was untestable because of frequent seizures during the examination. Using the VABS, she attained a level of 18 months in the communication domain, 23 months in the daily living skills domain, 34 months in the socialization domain, and 33 months in the motor skills domain. These all are below the 1st percentile.

Correlates of Outcome

Mechanism of Injury

Twelve (52%) patients had a whiplash shaking injury as the most likely mechanism of injury with no evidence of impact. There was no statistical difference between Seshia’s global outcome score of those with a pure whiplash shaking injury and those who had evidence of impact ($P = .188$).

Age at Acute Admission

The age at acute admission was not found to correlate with Seshia’s global outcome score within this cohort ($\tau = -0.197$; $P = .207$).

Severity of Injury

The PTS and the GCS were used as indicators of severity of injury. Seshia’s global outcome score correlated significantly with the PTS ($\tau = -0.37$; $P = .029$). This indicates that children with lower PTSs (ie, more severely injured and unwell) had a worse outcome. The GCS was documented accurately in 9 cases and was found to correlate significantly with outcome in these cases ($\tau = -0.793$; $P = .01$).

DISCUSSION

This study significantly adds to the literature on the outcome of inflicted TBI and confirms the high morbidity rate in the survivors: 68%. The wide range of neurologic sequelae is displayed and mirrors the variety and the extent of pathologies seen in these children. A total of 36% had severe neurologic disabilities and will require substantial long-term nursing and caregiver support in the community. Speech and language abnormalities were present in 64%, usually in association with other neurologic abnormalities. For some, these are profound language difficulties, including 1 child with autism. Epilepsy was common (20% in this cohort) and is often intractable when present.¹³ Many of the children had complex disabilities with varying combinations of cognitive, motor, language, and behavioral abnormalities.

A previous study reported that 25% of 56 children with shaken infant syndrome had some degree of visual impairment.²⁶ Forty percent of patients in the current study were found to have significant visual deficits. It is a limitation that the visual assessments were not made by a pediatric ophthalmologist, and one would assume that the number of abnormalities may be underestimated here. The types of visual impairment were varied, including cortical blindness (16%), visual field deficits, visual agnosia, and decreased visual acuity. Although there are many possibilities for the cause of the abnormal visual function in these children (eg, injury to the occipital cortex, optic radiation, optic nerve, and retina), in most cases, it is attributable to injury to the cortex and optic radiation.^{27,28} Additional studies on the long-term visual outcome are necessary as the extent of these problems are likely to have been previously underestimated, and when they occur, they un-

doubtedly will have a significant impact on learning and quality of life.

This study highlights for the first time the frequent occurrence of behavioral (52%) and sleep abnormalities (24%) in this population of children. The behavioral abnormalities included self-injurious and self-stimulatory behaviors, hyperactivity, impulsivity, temper tantrums, and rage reactions. Psychologic testing mirrored the parental reports as 47% (10 of 21) of children scored in or below the "moderately low" category of the socialization domain of the VABS, suggesting problems with interactions with others, including play, use of free time, and responsibility and sensitivity to others. Many of the children did not develop these problems until the second or third year of life, and one third of the children who developed severe behavioral problems in the prospective group had been described as "quiet, placid" infants. This is in keeping with a recent report in which children with an inflicted TBI, examined 1.6 months after injury, showed significant reduction in social and cognitive domains in comparison with control subjects, and the authors suggested that early brain injury causes significant disruption in behaviors that regulate initiation and responsiveness in social contexts.²⁹

The behavioral problems are likely to be attributable to varying combinations of frontal lobe injury, speech and language abnormalities, and genetic and environmental factors. As the consequences of damage to the frontal lobe may not manifest until puberty or even later, it is possible that substantially more than 50% will have problems when follow-up is extended into adolescence and early adulthood.^{30,31} On a practical note, many caregivers (both adoptive and biological parents) reported that they had the most difficulty in dealing with these problems and that they perceived professional help and advice in this area to be limited.

Twenty-one children had psychologic evaluation. Cognitive performance fell below the 1st percentile for 10 children, and 3 children were in the borderline intelligence range (1st–6th percentiles). Thirty-two percent scored above the 7th percentile on cognitive testing. Three patients who attended mainstream school without learning support had IQs within the normal range and were able to complete a more comprehensive evaluation. Two of these children were found to have significant memory deficits that had not been identified in the classroom.

Bonnier described a "sign-free interval" in 6 of 13 cases of pure whiplash-shaking injury lasting between 6 months and 5 years.³² In her study, 2 children were thought to be normal at 3 years of age, and of these 2 children, 1 was found to have learning disabilities at 5 years. Five of the 11 children with multiple, prospective examinations in this study demonstrated a falling DQ in speech and language, and 4 of these children also changed outcome categories. This is not surprising as learning disabilities are typically not found until school age. Two children, as mentioned above, who were performing normally at school at 5 years of age were found to have significant memory deficits on psychologic

evaluation. Thus, it is advisable that cognitive testing, including specific tests of memory, be performed during the early school years even for children who are thought to be progressing normally.

The age at injury did not correlate with outcome within this cohort. This is contrary to other many studies that have examined predictors of outcome in older children after TBI, in which it was found that younger children have a poorer outcome.^{33,34} One other study recently found age not to be predictive of outcome in young children, and here the authors comment that their findings are "contrary to expectations."³⁵ A larger study is required to confirm our findings that age does not seem to influence outcome within the subpopulation of inflicted TBI. A major determinant of outcome in young children is the cause of the TBI.³⁵ It is not surprising that the external evidence of impact did not correlate with outcome as it is acknowledged that external evidence of impact does not determine that impact did not occur.³⁶

The main factors that did correlate with outcome were the severity of injury as assessed by the PTS and the GCS. Only 9 children had accurate documentation of the GCS, however, which also reflects how difficult this score is to use in infancy. Other determinants of outcome from previous reports have included the severity of the early posttraumatic seizures, lower cerebral perfusion pressures, and the extent of parenchymal injuries on computed tomography during the acute encephalopathy.^{13,14,37,38}

The postinjury environment influences outcome from a TBI; this has been found in both in humans and in animals, where it has been demonstrated that environmental enrichment improves the recovery in rats.^{39,40} In this study, the speech and language development in 1 patient was shown to improve markedly after a change of major caregiver. This was not investigated systematically here. The social situations in many of these families were complex; 36% of these children were in foster care, and several children had many foster placements. Additional studies are required to investigate how postinjury environmental factors influence outcome in this population.

Methodologic Issues

Although this is primarily a descriptive study, it should be noted that for some children there are some confounding factors that may also explain neurologic abnormalities. Patients 7, 13, and 23 were born prematurely. They all had relatively uneventful neonatal courses and did not have retinopathy of prematurity, cranial ultrasound scans were normal during their neonatal admission, and their caregivers reported normal development at the time of acute admission. Patient 20 may have had significant exposure to alcohol in utero, although he did not have the classical dysmorphic features of fetal alcohol syndrome. Some of the children in foster care had had multiple foster homes, including 1 girl who had marked problems as a result of inappropriate sexual behaviors. This study lacks a control group. This is a very difficult population to control for as there are multiple potential confounding factors. Previous

studies have used children with an accidental TBI as control subjects, but these children are usually older (the number occurring in a similar age group is prohibitively small) and have a much better outcome even when controlling for injury severity.^{8,41} This is attributable in part to the different mechanism of injury in inflicted TBI, the extent of axonal injury, and the frequent presence of hypoxic ischemic injury.^{42,43} Children who have sustained nonneurologic physical abuse would not be suitable control subjects as they score significantly lower in cognitive, motor, and social skills in comparison with control subjects, and the occurrence of a previous neurologic insult cannot be ruled out.⁴⁴ The postinjury environment is likely to influence outcome and is difficult to control for. In the present study, it was variable, and foster home placements could change frequently.

CONCLUSIONS

Sixty-eight percent of survivors of inflicted TBI are abnormal on follow-up. The outcome is related to severity of injury. At least 40% have severe deficits and will never live independently in the community. Deficits in preschool children are often underestimated, and impairments can become apparent over time as a child fails to meet expected developmental milestones. We report for the first time the frequency of behavioral problems in this population (52%). These issues cause marked family concern and have a large impact on the child's educational and social development. The burden of the injury on family members and caregivers is great and particularly important as these people provide the long-term support for these children and is currently being assessed in an ongoing study. This study emphasizes the need for prolonged follow-up into the school years and probably adolescence before the consequences of infantile TBI can be fully appreciated.

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