Neurosensory outcome at 5 years and extremely low birthweight

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Abstract

***Objective*—To establish the stability of neurosensory outcome at 5 years of age compared with 2 years of age, and to determine whether the improving survival rate of extremely low birthweight (ELBW) (500–999 g) children has been accompanied by an increase in the number of severely impaired and disabled children in the community.**

***Methods*—A geographically determined cohort study was made of consecutive ELBW survivors born in the state of Victoria during 1985–7, and during 1979–80, inclusive. Rates of neurosensory impairments and disabilities at 2 and 5 or more years of age were measured.**

***Results*—Of 212 children surviving to 5 years of age born during 1985–7, 211 (99·5%) had been assessed at 2 years of age, and 209 (98·6%) were assessed at 5 or more years of age. Of the 208 children seen at both 2 and 5 years, 32 children had deteriorated, 23 children had improved, and 153 were unchanged, compared with their 2 year assessment. The major reason for a change in classification was an alteration in psychological test results. Compared with ELBW children born in 1979–80, those born in 1985–7 had significant reductions in hearing and intellectual impairment. The rate of severe neurosensory disability in the 1985–7 cohort was 5·7% compared with 12·4% in children born in 1979–80.**

***Conclusions*—The age of 2 is too early to be sure of neurosensory outcome in ELBW infants. The additional survivors born in the mid 1980s, compared with the late 1970s, are free of severe neurosensory disability at 5 years of age, with no increase in the absolute number of ELBW children surviving with severe neurosensory disability.**

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More and more extremely low birthweight (ELBW) (birthweight 500–999 g) infants are surviving in ever increasing numbers. In the past, adverse neurosensory impairments occurred more frequently in ELBW survivors compared with their normal birthweight counterparts. Consequently, there is concern that the improving survival rate of ELBW children will increase the number of impaired and disabled children in the community. Although reports from individual hospitals can help to determine if such concerns are real or groundless, long term follow up studies of geographically based cohorts are vital. We have already reported that the survival rate of ELBW infants rose by 50% between 1979–80 and 1985–7 in Victoria, and that the number of severely disabled children at 2 years of age had not increased, averaging eight a year in both eras.[1] Neurosensory impairments, however, and the disabilities imposed by these impairments, are not always stable, particularly if diagnosed early in childhood.

The aims of this study of ELBW children born during 1985–7 were to establish the stability of the neurosensory outcome at 5 years of age compared with 2 years of age, and to determine whether the improving survival rate of ELBW children has been accompanied by an increase in the number of impaired and disabled children in the community.

Methods

There were 560 livebirths with birthweights 500–999 g in the state of Victoria over the three year period from 1 January 1985. The subjects of this study comprised the 212 consecutive ELBW survivors (survival rate 37·9%) to 5 years of age; details of how the survival rate for these children was determined have already been reported.[1] All survivors were enrolled in a long term follow up study to determine the rates of neurosensory impairments and disabilities. The plan was to see the children at 2 years of age, and every three years thereafter; 211 of the 212 (99·5%) survivors had been assessed at 2 years of age.[1] The one child not assessed at 2 years of age was living in another country at the time, but had subsequently returned to Australia and was assessed at 5 years of age. Data could not be obtained on three children at 5 years of age because they had emigrated; they had been free of neurosensory impairments at 2 years of age. The remaining 209 children (98·6% of survivors) were assessed at 5 or more years of age, corrected for prematurity. Four children missed the 5 year appointment but were assessed at 8 years of age, and their results are included in this report.

The paediatric assessment included a neurological examination to determine outcomes such as cerebral palsy, and visual acuity was also assessed. The criteria for a diagnosis of cerebral palsy have been reported.[2] Children were considered blind if visual acuity in both

Table 1 Neurosensory impairments and severity of disability imposed on individual disabled children in 1985–7 cohort at 5 or more years of age

	Impairments leading to disability	
Disability	*Major*	*Other*
Severe (n=12)	Blindness (n=6)	Severe mixed cerebral palsy, untestable IQ (1)
		IQ score −2·5 SD and mild cerebral palsy (1)
		Untestable IQ (IQ score −4 SD) (2)
		IQ score −1·1 SD (1)
		IQ score −0·5 SD (1)
	Cerebral palsy (n=1)	Untestable IQ (IQ score −4 SD) (1)
	IQ score <−3 SD (n=5)	Moderate cerebral palsy, untestable IQ (2)
		Mild diplegia, IQ score −3·5 SD (1)
		Untestable IQ (IQ score −4 SD) (1)
		IQ score −3·7 SD (1)
Moderate (n=11)	Deafness (n=1)	IQ score −1·5 SD (1)
	Cerebral palsy (n=5)	Diplegia (1), hemiplegia (4) (one with IQ score −1·1 SD)
	IQ score −3 SD to <−2 SD (n=5)	Mild hemiplegia (1)
Mild (n=47)	Cerebral palsy (n=7)	Ataxia (2), hemiplegia (3), diplegia (1), monoplegia (1)
	Suspect IQ (IQ score −2 SD to <−1 SD) (n=39)	
	Cerebral palsy and suspect IQ (n=1)	Hemiplegia with IQ score −1·6 SD (1)

IQ=intelligence quotient.

eyes was worse than 6/60. Children had usually been screened for hearing loss earlier in childhood, but those with suspected deafness or delayed language were referred again for audiological assessment. Children were considered to be deaf if they required hearing aids. The psychological assessment included the Wechsler Preschool and Primary Scales of Intelligence-Revised (WPPSI-R) Full Scale,[3] or alternative psychological tests if the children were blind, or if they were assessed by a psychologist where the WPPSI-R was not available. Some children were able to complete only one scale of WPPSI-R (Verbal or Performance), because English was not their primary language, or because of physical disabilities. Some children not assessed at five years, completed the Wechsler Intelligence Scale for Children – Third Edition (WISC-III)[4] at 8 years of age. Psychological test results were expressed as standardised normal scores ((test score−mean)/standard deviation[SD]). Children unable to complete psychological tests because of severe intellectual impairment were given an IQ score of −4 SD.

Children were considered to have a neurosensory impairment if they had cerebral palsy, blindness, deafness, or a psychological test score more than 1 SD below the test mean. The severity of the neurosensory disability imposed by the impairment was graded as follows: severe – cerebral palsy with the child unlikely ever to walk, blindness, or a psychological test score of <−3 SD; moderate – cerebral palsy in ambulant children causing considerable limitation of movement, deafness, or a psychological test score from −3 SD to <−2 SD; mild – cerebral palsy in ambulant children with only minimal limitation of movement, or a psychological test score from −2 SD to <−1 SD. The remaining children were considered to have no neurosensory disability.

Data from all children were entered on to a computer for editing and analysis using SPSS for Windows. Outcomes were contrasted with ELBW children born in Victoria during 1979–80, the results of the 5 year assessment in this latter group having been reported before.[5] The classification of neurosensory disability in that report was different, the major differences being that neurosensory deafness requiring hearing aids, moderate cerebral palsy, and IQ scores 2 SD or more below the mean were then considered to impose a severe disability, and IQ scores of >−2 SD to −1 SD combined with one or more of mild cerebral palsy, neurosensory deafness not requiring hearing aids, or lesser visual morbidity (myopia, strabismus, and retrolental fibroplasia), were considered to impose a moderate disability. Disabilities for children in the 1979–80 cohort were reclassified to be identical with the 1985–7 cohort. Odds ratios (OR) and 95% confidence intervals (CI) for differences in proportions were computed.[6] The overall rate of neurosensory disability and psychological test scores were contrasted between groups using the Mann Whitney U test.[7] The relation between standardised psychological test scores at 2 years and 5 years of age was determined by linear regression analysis. A P value of <0·05 was considered significant.

Table 2 Neurosensory disabilities compared over time for 1985–7 births seen at both 2 and 5 or more years

	Neurosensory disability – n (%) at 2 years				
At 5 or more years	*Nil*	*Mild*	*Moderate*	*Severe*	*Total*
Nil	124	11	3	1	139 (66·8)
Mild	24	15	4	3	46 (22·1)
Moderate	0	5	5	1	11 (5·3)
Severe	0	2	1	9	12 (5·8)
Total	148 (71·2)	33 (15·9)	13 (6·2)	14 (6·7)	208*

*Excludes one child not seen at 2 years with mild disability at 5 years (IQ score −1·7), and three children not seen at 5 years, but with no disability at 2 years.

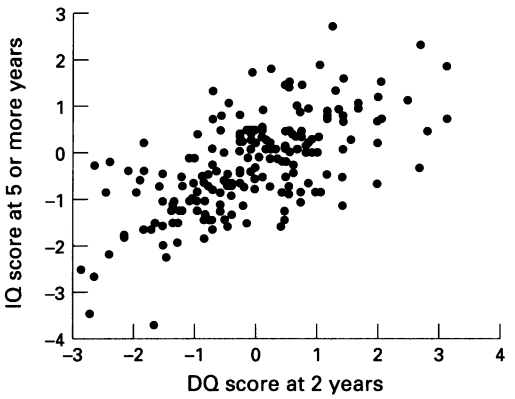
Results

Of the 209 children assessed at 5 or more years of age, 20 (9·7%) had cerebral palsy, six (2·9%) were blind, and one (0·5%) was deaf. IQ scores were skewed relative to a normal distribution, with 4·3% <−3 SD (expected 0·14%), 2·9% from −3 SD to <−2 SD (expected 2·1%), and 20·6% from −2 SD to <−1 SD (expected 13·6%). The severity of the disability imposed by these impairments is listed in table 1. Four (1·9%) children were multiply severely disabled.

Of the 208 children seen at both 2 and 5 years, compared with their two year assessment,

Table 3 Reasons for change in classification of disability between 2 and 5 or more years

	Reason for change
Improved	
From severe at 2 to no disability at 5 (n=1)	Cerebral palsy disappeared (1)
From severe at 2 to mild at 5 (n=3)	Improved vision and psychological tests (2) Improved psychological test score (1)
From severe at 2 to moderate at 5 (n=1)	Improved psychological test score (1)
From moderate at 2 to no disability at 5 (n=3)	Improved psychological test score (3)
From moderate at 2 to mild at 5 (n=4)	Moderate to mild cerebral palsy (2) Improved psychological test score (2)
From mild at 2 to nil at 5 (n=11)	Improved psychological test score (10) Mild cerebral palsy disappeared (1)
Deteriorated	
From mild at 2 to severe at 5 (n=2)	Deterioration in psychological test score (2)
From moderate at 2 to severe at 5 (n=1)	Deterioration in psychological test score (1)
From mild at 2 to moderate at 5 (n=5)	Mild to moderate cerebral palsy (4) Deterioration in psychological test score (1)
From nil at 2 to mild at 5 (n=24)	Deterioration in psychological test score (21) New cases with mild cerebral palsy (2) Known case of cerebral palsy considered not disabled at 2 (1)



Relation between intelligence quotient (IQ) at 5 or more years of age and developmental quotient (DQ) at 2 years of age (data are standardised scores).

32 children had deteriorated, 23 children had improved, and 153 were unchanged (table 2). The major reason for a change in classification was alteration in psychological test results, although changing diagnoses of the presence and severity of cerebral palsy, and improvement in visual outcome in some children thought to be blind at 2 years of age were responsible in some cases (table 3). For the 194 children able to complete psychological tests at both 2 and 5 or more years, there was a significant correlation between the scores at each age (figure; correlation coefficient=0·638, 40·7% variance explained, $F_{1,192}=131·5$, $P<0·0001$). If the children unable to be formally assessed but who were given scores of −4 SD were included in the regression, the significance increased (correlation coefficient=0·682, 46·6% variance explained, $F_{1,206}=179·6$, $P<0·0001$).

Rates of deafness and of IQ scores of <−2 SD were significantly lower for children born in 1985–7 than those born in 1979–80 (table 4). The rates of cerebral palsy and blindness in the two eras were not significantly different (table 4).

Compared with children born in 1979–80, fewer were severely disabled, but more were mildly disabled in 1985–7 (table 5). The overall rate of neurosensory disability was not significantly different between eras (table 5). The absolute number of severely disabled survivors at 5 years of age was 5·5 a year in 1979–80, 4·0 a year in 1985–7.

Discussion

It can be difficult to be certain about the presence or absence of neurosensory impairments and disabilities in very young children. Psychological, neurological, visual and audiological testing can all be affected by tiredness, lack of cooperation, and even fear. Not surprisingly, therefore, results obtained early in childhood are not necessarily identical when the same children are assessed in later life. In our current cohort some diagnoses made at 2 years of age had improved by 5 years of age. Three blind children at 2 years of age were no longer legally blind at 5 years of age, although two children were still blind in one eye, and the other had reduced vision in both eyes. Cerebral palsy disappeared in two children, one of whom was thought to be severely disabled and the other mildly disabled at 2 years of age; in retrospect, the child with presumed severe cerebral palsy was extremely uncooperative at 2 years of age. Seven children were also diagnosed with cerebral palsy for the first time at 5 years of age; one of these children sustained severe head injuries between 2 and 5 years, and had a moderate disability from cerebral palsy at 5 years of age. In the remaining six children newly diagnosed with cerebral palsy, the disability was mild in five and moderate in one. It has already been reported that cerebral palsy in ELBW infants in particular, may improve or even disappear as the children grow older,[8 9] and others have suggested that the diagnosis of cerebral palsy may not be stable until at least 5 years of age.[10] Although only a few experienced paediatricians were making the diagnosis of cerebral palsy, and they had previously agreed on the diagnostic criteria, because a diagnosis had to be made after only one assessment, which may have been less than ideal, it is not surprising that there has been a change in cerebral palsy between 2 and 5 years in some children, especially those with a mild disability. The diagnosis of cerebral palsy, and the disability it imposes, made at 5 years of age in our study might still not be stable and will change again when the children are assessed later in childhood.

The major reason for a reclassification of disability, however, was a change in psychological test scores. This is expected because we have imposed discrete cutoff points on to continuous scales to classify disability, and children are bound to change their score if retested, as can be seen in the figure. Developmental delay in the first two years of life does not

Table 4 No (%) neurosensory impairments at 5 or more years of age contrasted between eras

Impairment	*1985–7 (n=209)*	*1979–80 (n=89)*	*Statistics*
Cerebral palsy			
Any	20 (9·6%)	8 (9·0%)	OR 1·07 95% CI 0·46–2·50, NS
Severe	2 (1·0%)	3 (3·4%)	OR 0·23 95% CI 0·034–1·60, NS
Blindness	6 (2·9%)	6 (6·7%)	OR 0·37 95% CI 0·105–1·30, NS
Deafness	1 (0·5%)	5 (5·6%)	OR 0·075 95% CI 0·012–0·44, P<0·01
IQ scores			
<−2 SD*	15 (7·2%)	19 (21·3%)	OR 0·25 95% CI 0·11–0·54, P<0·01
<−3 SD*	9 (4·3%)	8 (9·0%)	OR 0·42 95% CI 0·14–1·22, NS

*Includes children too disabled to be tested; OR=odds ratio, CI=confidence interval, NS=not significant.

Table 5 Comparison of neurosensory disabilities between eras

	Neurosensory disability at 5 years or more of age				
Era	*Nil*	*Mild*	*Moderate*	*Severe*	*Total*
1979–80	64 (71·9%)	8 (9·0%)	6 (6·7%)	11 (12·4%)	89
1985–7	139 (66·5%)	47 (22·5%)	11 (5·3%)	12 (5·7%)	209

Mann Whitney U test Z=0·3, P=0·76, not significant.

always imply mental retardation later in childhood.[11] This can be seen in the figure where nine children who were tested formally had developmental delay at 2 years of age (developmental quotient <−2 SD), but three improved to the normal range, and two to the range −2 SD to <−1 SD for IQ by 5 or more years of age.

Given the limitations in diagnosing impairments and disabilities in early childhood, we feel more confident about the assessments at 5 years of age than those at 2 years of age. With respect to the stability of grading the severity of disabilities, we have been more likely to overdiagnose severe disability at 2 years that subsequently improves (5 of 14, or 35·7%) than we have been to diagnose severe disability at 5 years that was not present at 2 years of age (3 of 12, 25·0%).

The survival rate for ELBW infants rose significantly from 25·4% (89/351) in 1979–80 to 37·9% (212/560) in 1985–7.[1] The average number of survivors a year was almost 45 in 1979–80, and almost 71 in 1985–7, an increase of 26 a year. The number of severely disabled survivors at 5 years of age averaged 5·5 a year in 1979–80, but only four a year in 1985–7. Clearly, the additional 26 survivors a year in 1985–7 were free of severe disability at 5 or more years of age, and it has therefore been possible to improve the survival rate of ELBW infants without increasing the absolute number of ELBW children surviving with severe disability. Whether the improving survival rate of ELBW infants in the 1990s has also been achieved without an increase in the absolute number of ELBW children surviving with severe disability remains to be determined.

It is difficult to compare studies reported from different regions because criteria for neurosensory outcome and ages of ascertainment are not uniform. We have attempted to address the problem of differing criteria by including information in table 1 that would allow other investigators to reclassify our children to meet their own needs. With regard to divergent ages for ascertainment of outcomes, it is clear from our study that ELBW children do change as they grow older, and comparing children of different ages may be difficult.

Several other groups have reported regional data which contrast the outcome for ELBW infants in different eras. Robertson *et al* contrasted children born to residents of Northern and Central Alberta in 1978–9 with those born in 1988–9.[12] In their study, which included children with birthweights of <1251 g, the survival rate for ELBW infants rose from 13·2% (17/129) to 55·4% (97/175) between those two eras. For the 97 ELBW survivors from the 1988–9 cohort, who were assessed at 1 year of age, their rates of cerebral palsy (11·3%), blindness (4·1%), deafness (2·1%) and psychological test score <−3 SD (6·2%), were similar to our 1985–7 cohort. It is not possible to classify severe disability for ELBW infants in their study identically with ours, or vice versa, but in their study the absolute number of disabled ELBW children rose from 2·5 per year in 1978–9 to eight per year in 1988–9. Saigal *et al*, reporting the outcome at 3 years of age for children born in Ontario with a birthweight of 501–1000 g,[13] contrasted those born in 1977–80 with those born in 1981–4, and found that survival, neurosensory impairment, and severe functional disability rates were all similar between eras, although the rate of all functional disabilities fell.

In conclusion, 2 years of age is too early to be sure of neurosensory outcome in ELBW infants, particularly with respect to psychological test results, cerebral palsy, and vision. The additional survivors born in the mid 1980s compared with the late 1970s are free of severe neurosensory disability at 5 years of age, with no increase in the absolute number of ELBW children surviving with severe neurosensory disability.

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1 The Victorian Infant Collaborative Study Group. Improvement of outcome for infants of birth weight under 1000 g. *Arch Dis Child* 1991; **66:** 765–9.
2 Kitchen WH, Ford AL, Rickards AL, Doyle LW, Kelly E, Murton LJ. Five-year outcome of infants of birthweight 500 to 1500 grams: relationship with neonatal ultrasound data. *Am J Perinatol* 1990; **7:** 60–5.
3 Wechsler D. *Wechsler preschool and primary scales of intelligence – revised.* San Antonio, Texas: The Psychological Corporation. Harcourt Brace Jovanovich Inc, 1989.
4 Wechsler D. *Wechsler intelligence scale for children*; Third Edn. New York: The Psychological Corporation. Harcourt Brace Jovanovich Inc, 1991.
5 Kitchen WH, Ford G, Orgill A, Rickards A, Lissenden J, Bajuk B, *et al.* Outcome in infants of birth weight 500 to 999 g: A continuing regional study of 5-year-old survivors. *J Pediatr* 1987; **111:** 761–7.
6 Chalmers I, Hetherington J, Elbourne D, Kierse MJNC, Enkin M. Materials and methods used in synthesizing evidence to evaluate the effects of care during pregnancy and childbirth. In: Chalmers I, Enkin M, Kierse MJNC, eds. *Effective care in pregnancy and childbirth. Vol 1.* Oxford: Oxford University Press, 1989: 62–4.
7 Moses LE, Emerson JD, Hosseini H. Analyzing data from ordered categories. *N Engl J Med* 1984; **311:** 442–6.
8 Ross G, Lipper EG, Auld PAM. Consistency and change in the development of premature infants weighing less than 1501 grams at birth. *Pediatrics* 1985; **76:** 885–91.
9 Ford GW, Kitchen WH, Doyle LW, Rickards AL, Kelly E. Changing diagnosis of cerebral palsy in very low birthweight children. *Am J Perinatol* 1990; **7:** 178–81.
10 Stanley FJ. Using cerebral palsy data in the evaluation of neonatal intensive care: A warning. *Dev Med Child Neurol* 1982; **24:** 93–4.
11 Kitchen WH, Rickards AL, Ford GW, Doyle LW, Kelly E, Ryan MM. Selective improvement in cognitive test scores of extremely low birthweight infants aged between 2 and 5 years. *Aust Paediatr J* 1989; **25:** 288–91.
12 Robertson CMT, Hrynchyshyn GJ, Etches PC, Pain KS. Population-based study of the incidence, complexity, and severity of neurologic disability among survivors weighing 500 through 1250 grams at birth: a comparison of two birth cohorts. *Pediatrics* 1992; **90:** 750–5.
13 Saigal S, Rosenbaum P, Hattersley B, Milner R. Decreased disability rate among 3-year-old survivors weighing 501 to 1000 grams at birth and born to residents of a geographically defined region from 1981 to 1984 compared with 1977 to 1980. *J Pediatr* 1989; **114:** 839–46.