Early development of infants 1000 g or less at birth

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SUMMARY In a 4-year period the neonatal survival rate for 26 infants weighing 501-750 g was 42% and for 81 infants weighing 751-1000 g it was 61%. All 59 surviving infants have been assessed at follow-up; 39 were at least 2 years old (corrected for prematurity) and data from the remaining 20 were derived from assessment at 1 year corrected age. Five children had cerebral palsy, 4 had multiple handicaps, 4 each had a sensory handicap, 2 had developmental delay, and 1 had a dilated right ventricle without clinical hydrocephalus. Twelve of the 16 children with defined handicaps were considered to have significant functional handicaps. Therefore, of the 107 infants in this series, 48 (45%) died, 12 (11%) survived with significant functional handicaps, and 47 (44%) were considered to be developing within the normal range. No significant differences in the incidence of handicap were observed between inborn and outborn children, boys or girls, those who were small or appropriate for gestation, those who weighed ≤ 750 g or > 750 g at birth, and those who required or did not require prolonged oxygen or ventilation.

Significant improvements in the survival rate and quality of survival for very low birthweight infants > 1000 g have been reported.¹ Increasing attention is now focused on extremely low birthweight (ELBW) infants whose birthweight is 1000 g or less and in whom it is questionable whether maximum effort should be expended to achieve survival. We have reported improved survival for 107 such infants treated at the Queen Victoria Medical Centre during the 4-year period January 1977 to December 1980.² The purpose of this paper is to report on the early outcome of the 60 neonatal survivors from this series of ELBW infants, to determine whether the improved survival has been associated with change in late morbidity for the survivors.

Patients and methods

Of the 107 ELBW infants cared for in our neonatal intensive care unit 60 (56%) survived the neonatal period; 11 (42%) of 26 infants with a birthweight 501-750 g survived compared with 49 (61%) of 81 who were 751-1000 g. Neonatal survival rates for the four years were 48%, 67%, 50%, and 62%. Eighty-nine (83%) infants were inborn, 48 (45%) were boys, 8 (7%) were small for gestational age, and 26 (24%) were ≤ 750 g. Although the survival rates were higher in infants who were inborn compared with outborn (58 compared with 44%), female compared with male (64 compared with 46%),

small for gestational age compared with appropriate for gestational age (75 compared with 55%), and infants > 750 g compared with those ≤ 750 g (60 compared with 42%), none of these differences was statistically significant. The neonatal management of ELBW infants has been described in previous studies from this unit.²⁻⁶ Their pattern of respiratory failure, their morbidity attendant on respiratory management, and other major clinical and pathological characteristics which influenced outcome, have been reported previously.⁷

Of the 60 neonatal survivors, one infant who developed persistent neurological abnormality and post-intraventricular haemorrhage hydrocephalus had his life support systems withdrawn at 51 days. The 59 survivors were all being followed up at the growth and development clinic with the exception of two; one was assessed by a follow-up clinic overseas and the other by her own paediatrician. At the clinic, the children were given a clinical and neurological examination by a developmental paediatrician (A A O) and their development was assessed by a psychologist (J A) according to the Bayley scales of infant development which included a mental developmental index (MDI) and a psychomotor developmental index (PDI).⁸ Developmental data were available in 39 infants who were at least 2 years old (corrected for prematurity) at their last assessment (mean $\pm$ SD, 24.6 ± 1.1 months). Information about the remaining 20 infants was derived

from their scheduled assessment at 1 year corrected age (mean $\pm$ SD, 12.5 ± 0.5 months). The mean birthweight of the survivors was 861 (SD 96) g and the mean gestation 26.8 (SD 2.3) weeks.

Handicap was defined, similar to the definition of Stewart *et al.*,⁹ as an abnormality which in the long term was likely to affect the individual's ability to lead a normal life. Such abnormalities included cerebral palsy, developmental delay (MDI more than 2 SDs below the mean), visual deficits or sensorineural deafness, hydrocephalus, or persistent ventricular dilatation. Children who came within this definition of handicap were judged to have significant functional handicap only if the abnormality interfered with neuromotor or mental function. Mild cerebral palsy with asymmetry of muscle tone, hypotonia, or hypertonia which did not interfere with function, and hydrocephalus in a child who was otherwise physically and developmentally normal were not considered as significant functional handicaps.

Methods of collection and processing of data have been reported in detail.^{10 11} Statistical significance was evaluated using Student's *t* test and χ^2 analysis with Yates's correction as considered appropriate.

Results

There were 2 children with monoplegia, 5 with hemiplegia, and 2 with spastic quadriplegia (Table 1, Cases 1 to 9). The two children with quadriplegia had intrauterine infection from cytomegalovirus (Case 7) and rubella (Case 9). Both were small for gestational age and neither required assisted ventilation in the neonatal period. In addition to 3 children with cerebral palsy who had an MDI

scored at more than 2 SDs below the mean, a pair of twins (Cases 10 and 11) with uneventful neonatal courses had an isolated MDI of 50 and 68 respectively. Fig. 1 shows the distribution of the Bayley scores. The mean score for the MDI was 97.91 (SD 20.53) and the mean score for the PDI was 85.18 (SD 16.06).

Three children (Cases 12, 13, and 14) had cicatricial retrolental fibroplasia, 2 in the right eye and the remaining child in both. One child (Case 15) required the use of a hearing aid. Another child who was small for gestational age, had a dilated right ventricle of unknown aetiology (Case 16). Her head growth was normal and ventriculo-peritoneal shunting was not required.

The incidence of handicaps in survivors is shown in Table 2 together with their mean Bayley scores among 4 subgroups. There were no significance differences in the MDI and PDI scores between children who were inborn or outborn and those who were small or appropriate for gestational age.

Table 2 Comparison of developmental outcome between groups

Subgroups	No of survivors	No with handicap	Bayley scores (mean $\pm$ SD)	
			MDI	PDI
Inborn	51	13 (25%)	97 $\pm$ 19	94 $\pm$ 15
Outborn	8	2 (25%)	101 $\pm$ 29	90 $\pm$ 21
Male	21	8 (38%)	87 $\pm$ 29	83 $\pm$ 15
Female	38	7 (18%)	103 $\pm$ 19*	86 $\pm$ 17
Small for gestational age	6	2 (33%)	91 $\pm$ 12	78 $\pm$ 26
Appropriate for gestational age	53	13 (25%)	99 $\pm$ 21	86 $\pm$ 15
<750 g	11	3 (27%)	86 $\pm$ 26	73 $\pm$ 15
>750 g	48	12 (25%)	101 $\pm$ 18	88 $\pm$ 15*

*P < 0.005.

Table 1 Survivors with handicaps

Case	Gestation (weeks)	Birthweight (g)	Sex	Neurological function	Seizure	Abnormal vision	Bayley scores		Functional handicap
							MDI	PDI	
1	25	730	F	Right hemiplegia	—	Myopia	<50	82	Moderate
2	25	840	F	Right hemiplegia	—	—	103	50	Moderate
3	26	780	M	Left hemiplegia	—	Myopia	52	<50	Moderate
4	26	800	M	Right hemiplegia	—	—	87	78	Moderate
5	26	880	F	Right monoplegia	—	—	106	98	Mild
6	26	1000	M	Right monoplegia	—	—	79	87	Mild
7	27	700	F	Spastic quadriplegia	—	—	50	<50	Severe
8	27	960	M	Right hemiplegia	—	—	104	57	Moderate
9	32	950	M	Spastic quadriplegia	+	Blind	NT	NT	Severe
10	27	850	M	—	—	—	50	85	Moderate
11	27	880	M	—	—	—	68	85	Mild
12	24	660	F	—	—	Right eye RLF	97	93	Moderate
13	25	870	F	—	—	Right eye RLF	NT	NT	Severe
14	26	890	M	—	—	Bilateral RLF	NT	NT	Severe
15	25	89	F	Hearing impaired	—	—	112	75	Mild
16	31	730	F	Dilated right ventricle	—	—	106	<50	Moderate

NT = not tested, RLF = retrolental fibroplasia.

Fig. 1 Distribution of Bayley scores (a) MDI, (b) PDI.

Fig. 2 Outcome of ELBW infants ≤ 750 g and > 750 g.

Girls had similar PDI scores compared with boys but significantly higher MDI scores. Children with birthweights ≤ 750 g had similar MDI scores compared with those > 750 g but significantly lower PDI scores. There were no statistical differences in the incidence of handicap in any of these groups. Fifty-five (53%) of 104 infants who required oxygen and 50 (51%) of 98 infants who required assisted ventilation survived long term. The incidence of handicap in survivors who required periods of oxygen or ventilation are shown in Table 3. No significant differences in handicap rate were found between those who required and those who did not require extended periods of oxygen or assisted ventilation.

Table 3 Incidence of handicap in survivors who had varying periods of oxygen and ventilatory therapy

	No of survivors	No with handicap
Oxygen therapy		
Required	55 (93%)	14 (25%)
Not required	4	2 (50%)
> 7 days	42 (71%)	11 (26%)
≤ 7 days	17	5 (29%)
> 21 days	35 (59%)	10 (29%)
≤ 21 days	24	6 (25%)
Assisted ventilation		
Required	50 (85%)	14 (28%)
Not required	9	2 (22%)
> 7 days	34 (58%)	12 (35%)
≤ 7 days	25	4 (16%)
> 21 days	25 (42%)	9 (36%)
≤ 21 days	34	7 (21%)

Of the 16 children coming within the definition of handicap in this study, 4 had mild functional handicaps only (Cases 5, 6, 11, 15). Therefore, of the 107 infants in this series, 48 (45%) died, 12 (11%) survived with moderate or severe functional handicaps, 4 (4%) survived with mild functional handicaps, and 43 (40%) were healthy survivors. The 47 (44%) infants in the last two groups were considered to be developing within the normal range. The percentage who died, survived handicapped, or survived healthy for the 26 infants 501–750 g and for the 81 infants 751–1000 g are shown in Fig. 2.

Discussion

The reported incidence of healthy survivors has varied from 6 to 31% of the ELBW population^{12–18} (Fig. 3). The percentage of inborn infants in these published series ranged from 18 to 56% and the study with the highest number of healthy survivors consisted exclusively of outborn infants.¹⁸ With the increasing trend of intrauterine transfer of the high-risk fetus, even inborn infants can be a very selected group. In this series, 73% were either booked maternity patients or had an elective *in utero* transfer before onset of labour. The percentage of small for

gestational age infants in the total cohort or among survivors in published series ranged from 18 to 51% except in one study.¹⁴ The numbers of survivors ≤ 750 g were either unknown or fewer than 4 and therefore data on their outcome were sparse. In the present series, only 17% of the cohort were outborn and 7% were small for gestational age. In addition, with the improved survival rate of 42% in infants ≤ 750 g who made up 25% of the patient population, more information is now available on the prognosis for these smallest infants.

The incidence of retrolental fibroplasia in this cohort has previously been reported.¹⁹ Although 8 (7.5%) of 107 ELBW infants had evidence of acute changes in hospital, most had spontaneous regression of their retinopathy. At the most recent examination only 3 (5%) of the 59 survivors had grade III or more retinal disease. Our experience with this condition was therefore different from the high incidence of 13–39% reported in the other series.^{15–18} Transcutaneous oxygen monitoring, which was available during most of the study period, might have contributed to the improved ophthalmological outcome in this group at risk of retrolental fibroplasia.

Fig. 3 Outcome of ELBW infants from published series.

We did not find a statistically significant increase in the incidence of handicap among survivors who had required extended periods of oxygen or assisted ventilation, although there is a suggested trend for a poorer outcome in those who required prolonged ventilation. A recent series has reported a significantly higher handicap rate in ELBW infants treated with mechanical ventilation.¹⁷ Current ability to achieve more optimal and stable oxygenation during the critical phase of their illness might have accounted for a lower incidence of both retrolental fibroplasia and cerebral palsy.

Although the majority of survivors were over 2 years old at the most recent assessment and the remainder were aged at least 1 year, the duration of follow-up is still fairly short. It is unlikely that any major handicap had remained undiscovered but more subtle mental or behavioural handicaps cannot yet be determined. It is our intention to continue the follow-up of this cohort beyond school age.

The high cost, both financial²⁰ and emotional,²¹ of neonatal intensive care for the ELBW infant, as well as the questionable quality of life despite improved survival, have discouraged a concerted effort to provide optimal perinatal care. Although the results reported in this paper are preliminary and require confirmation from longer-term assessment which is taking place, they are nevertheless encouraging. As ELBW infants from our experience and from other reports⁹ have an improving prognosis, we believe that a policy of benign neglect for these infants is not justified in the present era of perinatal medicine. Clarification of relationship between intensive care practices and quality of survival can only be achieved by careful monitoring of the growth and development in survivors from each neonatal unit. As the prognosis for ELBW infants is still less than desirable when compared with those >1000 g, such constant monitoring is obligatory for centres which embark on the perinatal care for this high-risk group of patients.

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