Int. J. Prenatal and Perinatal Studies (1991) 31–43

Infants at Triple Jeopardy: Preterm, BW < 1000 g and Small for Gestational Age

J. Astbury

Department of Community Medicine, University of Melbourne, Carlton, Victoria, Australia

Abstract

It has been suggested that with the adoption of modern, active obstetrics and neonatal intensive care, the outcome of preterm, extremely low-birthweight (ELBW) small for gestational age (SGA) infants would improve significantly. All 22 such infants admitted to the neonatal intensive care unit of the Queen Victoria Medical Centre, Melbourne over a four year period (1 January 1979 – 31 December 1982) were included in the study. 73% survived the neonatal period, significantly more than their appropriately grown counterparts. However, by five years of age, impairment rates for the preterm, ELBW, SGA infant were higher, although the difference just failed to reach statistical significance, more than a third of the long term survivors had multiple major impairments, more than half had an attention deficit disorder and all children had some type of minor impairment by five years of age. Weight for the group remained below the 10th centile. These findings do not support the view that the advent of modern obstetrics and neonatal care, is accompanied by reduced impairment rates in this group of multiply at risk children.

Introduction

In the 1980's reported survival rates for ELBW infants have ranged from 30% to 67% and impairment rates have ranged from 13% to 35% [21,23,43]. The majority of infants in this group are, by definition, infants who are appropriately grown for gestational age (AGA). Small for gestational age (SGA) infants are defined as those whose birthweight is less than the expected 10th centile for week of gestational age and sex.

Correspondence to: J. Astbury, PH.D, Key Centre for Women's Health in Society, Department of Community Medicine, University of Melbourne, 209 Grattan Street, Carlton, Victoria, Australia

There are around 60,000 births each year in Victoria, Australia. Infants weighing less than 1000 g at birth comprise only 0.6% of total births but account for 32% of perinatal deaths. Approximately 360 extremely low birth weight infants (ELBW, BW < 1000) are born in Victoria each year.

If only 10% of all ELBW infants were also SGA then some 36 such infants would be born in Victoria each year. However, reported rates for SGA infants amongst populations of ELBW infants have ranged between 7% and 40% [8,28,29].

Although a numerically small group, ELBW, SGA infants may be considered to be at high risk for adverse neurodevelopmental outcome. Such infants are likely to be susceptible to the multiple hazards of prematurity, extremely low birthweight and growth retardation.

Pre-term, small for gestational age infants are considered to be especially vulnerable. Perinatally their problems may include fetal distress during labour, perinatal asphyxia, meconium aspiration, pulmonary haemorrhage, hypothermia, polycythaemia, hypoglycaemia and hypocalcaemia [1].

The combination of insults received by preterm, ELBW, SGA infants is seen as having potentially hazardous effects on their neurologic and developmental outcome [35]. Chiswick [14] has reported these infants have a much higher incidence of major handicap than their term counterparts and argued that the degree of their prematurity strongly influenced their outcome. However, evidence from animal and human studies suggests that somatic growth retardation is a significant independent risk factor for an adverse outcome. Growth retardation is accompanied by an alteration in the normal growth and development of the brain including myelination, cell proliferation, cell size and connectivity [17,19,32].

Biochemical alterations, particularly of the cerebellum have been found in the brains of SGA infants [13]. Berg [7] has suggested that growth retarded infants may be less able to tolerate perinatal stress than normally grown infants. In her study, infants with intrauterine growth retardation exhibited a stronger association between perinatal stress and childhood neurological abnormalities than their appropriately grown peers. However, Berg accepts that the presence of stress may be evidence of abnormalities and damage present prior to delivery, rather than perinatal stress itself being the cause of damage.

Given the small number of preterm ELBW, SGA infants born, it is not surprising that outcome studies which concentrate primarily on SGA infants are few in number, with small sample sizes and inconsistent findings. None of the studies published so far, have reported on cohorts of infants whose birthweight was less than 1000 g.

There are several published studies on very low birthweight (VLBW, BW < 1500 g) SGA infants. Commey and Fitzhardinge, 1979, in their study of outborn infants found that 49% had a major neurological defect or a Bayley score less than 80 by two years of age. Others have reported that SGA infants had similar intellectual abilities and cerebral palsy rates at five years to their appropriately grown counterparts but had two and a half times more minor neurodevelopmental disorders [39,40]. Tudehope et al. [38] found no difference between SGA and AGA infants at 12 months of age on head circumference, neurological morbidity or sensory handicap. Ounsted [30] also reported normal intellectual functioning at

7 years amongst the 14 pre-term SGA children in her study. Most recently, Hack et al. [20] in a comparison of AGA and SGA infants weighing less than 1500 grams at birth, found no significant differences in neurological impairment or performance on the mental scale of the Bayley Scales of Infant Development at 20 months of age.

Commey and Fitzhardinge [15] reported that subsequent handicap in the preterm SGA group they studied, was strongly related to the condition of infants on admission to the neonatal intensive care unit. Early antenatal diagnosis of intrauterine growth retardation and delivery in a centre with neonatal intensive care facilities was advanced as a way of improving neurodevelopmental outcome. Similarly, Ounsted [31] argued that the poor developmental outcome of SGA infants born in the 1960's was a function of their passive obstetric and neonatal care which resulted in hypothermia, hypoglycaemia and convulsions. Ounsted suggested that when pathological factors are operating "elective delivery before full term may enhance the chances of these children achieving their full developmental potential in later childhood".

Hack et al. [20] believe the effects of intrauterine brain growth failure are different from and less severe than those of neonatal brain growth failure. They argue that postnatal undernutrition is confounded by the effects of anoxic encephalopathy which has a more significant impact on neurodevelopmental outcome than the alteration of brain growth in utero caused by undernutrition. It has even been suggested that optimal conditions postnatally may correct prenatal biochemical alterations associated with growth retardation in utero and serve as a form of postnatal rehabilitation [13].

To date, no published studies have specifically concentrated on the outcome of ELBW, SGA infants, who were recipients of active obstetric care including early elective delivery and modern neonatal intensive care, including improved parenteral nutrition. Consequently, there is no way of ascertaining whether or to what extent, such practices have been associated with a marked improvement in the neurodevelopmental outcome of preterm, ELBW, SGA infants.

Indeed, Allen [1] has argued that it is the aetiology of growth retardation, including its timing and duration in pregnancy which is the single most predictive factor in determining outcome. Aetiology may not be able to be conclusively established. Estimates of the number of infants with IUGR of unknown aetiology have ranged from 34% to 50% [2,9].

The current study is a first step towards establishing a knowledge of the long term neurodevelopmental outcome of this numerically small but potentially very high risk group of ELBW, SGA infants. All infants in this study were recipients of active, obstetric and neonatal care of the kind suggested by Commey and Fitzhardinge [15] and Ounsted [31] to be optimal for improving outcome.

The study has 3 major aims:

1. To determine if the provision of active obstetric and neonatal care to preterm, ELBW, SGA infants was positively related to improved neurodevelopmental outcome.

2. To document over a five period period from birth to school age the physical, behavioural and neurodevelopmental outcome of a 4 year cohort of ELBW, SGA infants born between January 1, 1979 and December 31, 1982.
3. To ascertain to what extent, if any, these infants showed "catch up" growth in weight, height or head circumference over this time.

Methods

All infants born over a four year period from January 1, 1979 to December 31, 1982 at the Queen Victoria Medical Centre, Melbourne, whose birthweight was less than 1000 g and also less than the 10th centile for gestation and sex, were included in the study. Twenty two ELBW, SGA infants were born during this time. Eleven were male and 11 female. Conception was achieved through artificial insemination by donor in 4 infants and 1 of these also required in vitro fertilization. Possible teratogenic effects of artificial insemination by donor have been documented [18].

Infants were followed prospectively from birth to school age and comprehensive medical, psychological, and neurodevelopmental assessments were carried out at 1, 2 and 5 years of age all corrected for prematurity as described previously [4]. Intrauterine growth charts, derived from a similar population of Victorian infants, were used to assign the percentiles for growth at birth [24,25]. At follow-up, weight, height and occipitofrontal head circumference were measured in a standard fashion [26,33]. Norms derived from an urban Australian population were used to evaluate growth in weight and height [22].

At one and two years of age, the psychological assessment comprised the Bayley Scales of Infant Development [6]. These were administered by a psychologist who was "blind" to the children's neonatal history.

Behaviour, especially that expressive of attentional deficit disorder (ADD), impulsivity and hyperactivity was observed and recorded during psycholgical assessment as described elsewhere [4]. This assessment provides an opportunity to gauge the presence of an ADD because it is a structured situation involving demands from the examiner to the child, to focus on a series of tasks, to sustain concentration and where necessary to flexibly shift attention from one type of task to another, while inhibiting impulsive responses.

At five years of age the Wechsler Pre-School and Primary Scale of Intelligence (WPPSI) was administered [41].

The paediatric examination consisted of a complete physical and neurological examination and a detailed medical history. Parental concerns over aspects of physical, mental and behavioural development were also ascertained. At five years an assessment was also made of minimal cerebral dysfunction with 10 items administered according to Touwen [37]. A score greater than 10 is indicative of minimal cerebral dysfunction. Gross and fine motor development at five years was assessed on the Bruiniks Oseretsky Scale of Motor Proficiency [10]. Hearing was assessed with full scale audiometry by the National Acoustic Laboratory and vision was screened clinically. Children with a suspected strabismus or a visual acuity of less than 6/12 in either eye were re-evaluated by an ophthalmologist.

Impairments were defined as cerebral palsy of any type or severity, bilateral blindness, sensorineural deafness or mixed sensorineural-conductive deafness requiring hearing aids and developmental delay defined as a mental score more than 2 standard deviations below the mean on the Bayley Scales of Infant Development or on the WPPSI.

Data from one, two and five year assessments were added to the computer file containing obstetric and perinatal data and analysed using SPSSX package programs. The statistical significance of the differences between group means were tested by tests and between-group proportions were obtained by the test. The case to variable ration was too low to permit multivariate analyses of the data.

Results

6/11 (54.5%) male infants survived compared with 10/11 (91%) female infants. This difference was not statistically significant. Neonatal survival for the total group was therefore 16/22 (73%). There were 2 late deaths, one at 5 and a half months of an infant with fulminating necrotizing enterocolitis and grade three retrolental fibroplasia and one at two years as a result of drowning, leaving a total of 14/44 (64%) long term survivors.

The mean BW of survivors was 835 g (sd 142) compared with 735 g (sd 131 g) for those who died and 850 g (sd 94 g) for the 66 ELBW survivors born during the same time period who were appropriate for gestational age (AGA). None of these differences were statistically significant. The mean gestation of survivors was 31 w (sd 2.4 w) compared with 30 w (sd 1.2 w) for non survivors and 26 w (sd 1.6 w) for AGA ELBW survivors. The difference in gestation between ELBW, SGA and ELBW, AGA survivors was highly statistically significant ($p < 0.0001$).

SGA and AGA ELBW infants also differed significantly on a number of variables in the neonatal period as shown in Table 1. All differences favoured the SGA infants, who were in better condition at birth, regained their birthweight sooner and spent fewer days in the Neonatal Intensive Care Unit.

Table 1. Neonatal differences between SGA and AGA ELBW infants

Variable	SGA	AGA	P <
1 min apgar	4.9 (2.7)	3.5 (2.3)	.05
5 min apgar	6.7 (2.4)	5.0 (2.7)	.01
Days to regain birthweight	12.5 (7.0)	19.8 (8.4)	.001
Days in NICU	26.4 (15.9)	47.3 (25.5)	.001

SGA infants had a significantly better survival rate than AGA infants with 16/22 (72.7%) being discharged home to their parents compared with 66/142 (46.4%) of AGA infants. This difference was highly statistically significant ($p < 0.0001$). Overall, ELBW, SGA infants comprised 13.4% of the total number of ELBW infants born in this four year period. The difference between the two

groups in the incidence of major impairments at five years of age just failed to reach statistical significance ($p < 0.06$). There were two late deaths in each group of children, leaving 14 long term SGA survivors. 5/14 (36%) had major impaiments compared with 9 (14%) had major impairments.

No further comparisons were made between the two groups of children because the five week mean difference in their gestation and their significant differences neonatally meant that the AGA ELBW children could not be considered an appropriate control group for the ELBW, SGA children and it was not possible to use matched gestational controls as appropriately grown infants of such gestation are not part of the hospital's follow up programme.

The mean maternal age at delivery amongst mothers of SGA infants was 27.6 y (sd 6.5) which is close to the Australian average and the mean maternal height was 160.4 cm (sd 6.5) which is 5 cm below average for Australian women. The mean number of cigarettes smoked during pregnancy was 11.8 (sd 12.9) cigarettes. Seven mothers (32%) had pre-eclampsia during pregnancy.

Elective delivery by caesarean section was carried out in 17/22 deliveries. 13/16 (81%) infants who survived the neonatal period were delivered by ceasarean section and 4/6 (67%) of those who died.

Four of the survivors and 3 of the infants who died had congenital anomalies. For survivors, congenital anomalies included Russell Silver dwarfism, congenital dislocation of hip and knee, cleft lip and hypospadius. The anomalies of the three infants who died included tracheo-oesphageal fistula, duodenal atresia, oesphageal atresia, scoliosis and cleft lip and palate. In addition, one child had a disorder, Lennox Gastaut's syndrome, an epileptic encephalopathy of unknown aetiology, diagnosed for the first time at 3 years of age.

Table 2 presents the children's performance on the Mental Development Index (MDI) and the Psychomotor Development Index (PDI) at one and two years of age corrected for prematurity. At the one year assessment, gross motor development lagged significantly behind mental development. At two years, there was a significant decline in mental development scores which was largely attributable to the high numbers of low scoring children with an attention deficit disorder. At the same time there was a slight increase in the motor score, so no difference in mental and motor performance was discernible by two years.

Table 2. Performance on the Bayley scales of infant development

Age	MDI	PDI
1 year	n = 14 98 (6.7)	n = 12 77.5 (15.4)**
2 years	n = 13 85 (17.6)*	n = 12 84 (17.7)

* $p < 0.02$
** $p < 0.001$

By five years of age, the mean verbal, performance and full scale IQ of the group on the WPPSI were all within the normal range. The mean verbal intelligence score was 106.8 (sd 21.2) mean performance intelligence was 101 (sd 21.2) and the full scale score was 104.4 (sd 20.8). None of these differences were statistically significant. It should be noted that only 10 children were able to be given this test. Three children were too developmentally delayed to receive formal psychometric testing. Thus the scores are an overestimate of the intellectual functioning of the whole group of children.

Table 3. Attention deficit disorder at 1, 2 and 5 years

Age	Present	Absent	Other
1 year	2 (13%)	12 (80%)	1 (7%)
2 years	11 (73.3%)	2 (13.3%)	2 (13.3%)
5 years	8 (57%)	3 (21.4%)	3 (21.4%)

As shown in Table 3 the diagnosis of attention deficit disorder was rarely made in one year olds, was most common in two year olds and persisted in a significant proportion of five year olds. Major impairments included spastic quadriplegia [2], deafness requiring hearing aids [3] and developmental delay [3]. The incidence of major impairments was 57%, but 5 children (36%) had multiple major impairments as shown in Table 4.

Table 4. Major impairments at 5 years

	n
Cerebral palsy	
Spastic quadriplegia	2
Deafness	
Sensorineural	2
Mixed	1
Developmental delay	3
Total n of impairments	8 (57%)
Total n of children with impairments	5 (36%)

All children had one or more minor impairments at 5 years. Visual impairments were common. Six children had squint, 3 had myopia, 1 hypermetropia, 1 astigmatism and 4 children required corrective lenses. Disorders of tone and reflexes included hypotonia and hyporeflexia in 3 children and hyperreflexia in 3. Poor muscle development was documented in 9 children. A further 2 children had a conductive hearing loss and 5 children were found to have an abnormal head shape. Four of these had a head circumference below the 10 centile at five years of age. 3/4 of these children had severe developmental delay and major impairments.

The mean centile score on the Bruiniks Oseretsky test of Motor Proficiency was 39 (sd 23) some 11 centiles below average for children of this age. The mean cerebral dysfunction score for them was 16 (sd 11) when a score greater than 10 is indicative of cerebral dysfunction. Abnormal findings were commonest on heel toe walking (both forwards and reverse), heel walking, the finger to nose test (opposition) with eyes open and closed, and the Romberg test, especially with eyes closed.

In their first five years of life these children spent 11 days (sd 19) in hospital. They were toilet trained by 3 years and 3 months (sd 1 month) during the day and by 3 years and 8 months (sd 1 month) at night. Eleven children were attending normal schools at five years of age. Three children with major impairments attended special schools.

The results of the psychological and medical/neurological exam generally accord with the parents' own perceptions of problems expressed at the five year visit. 54% of parents had concerns about their child's vision; 46% expressed concerns over hearing, behaviour and language development and 38% were concerned by their child's growth and weight gain, general health, learning and development.

Table 5 reveals that from birth to school age no significant catch up growth occurred in weight centiles. By five years, only 3 children were at or above the 10th centile for weight, while 11/14 (78.5%) were below the 10th centile. Seven of these children were also below the 3rd centile. For length, 5 children were above the 10th centile while 8/14 (57.1%) were below the 10th centile. For head circumference the majority of children, 9/14 (64.2%), were above the 10th centile.

Table 5. Weight, height and head circumference percentiles from birth to 5 years

Age	Weight	Height	Head Circumference
Birth	.46 (1.1)	na*	6.5 (12.7)
Discharge	**	13.3 (32)	24.4 (24)
1 year	2.7 (2.8)	8.3 (14.1)	31.5 (31.3)
2 years	4.0 (+4.6)	5.3 (+6.8)	37.8 (+27.9)
5 years	8.6 (+16.7)	21.5 (+25.8)	44.7 (+33.2)

* Insufficient measurements taken to compute means and standard deviations.

** Mean weight on discharge at a mean gestational age of 41 weeks (sd 2 w) was 1950 g (sd 401 g). This was too low to be presented in centile form.

Discussion

Earlier studies of pre-term SGA infants have suggested that poor developmental outcome might be attributed to the passive obstetric and neonatal care charac-

teristic of the 1960's and early 1970's. Postnatal growth failure has been emphasized by some as a more potent cause of poor neurodevelopmental outcome than intrauterine growth failure [17,20].

All infants in the present study were born from 1979 onwards. All were recipients of modern, active neonatal intensive care, all but one were inborn and all but two had early, elective caesarean delivery.

SGA infants regained their birthweight by twelve days, some seven days earlier than their AGA counterparts. Despite the early catch-up in weight suggestive of a beneficial nutritional environment postnatally, weight at discharge was too low to be expressed in centile terms. Although there were demonstrable gains in weight from discharge to one year and a doubling of the centiles from the 4th centile at 2 years, to more than the 8th centile at five years, the group still remained below the 10th centile for weight. Indeed, more than three quarters of the children who were growth retarded at birth (weight under 10th centile) remained so at five years of age. Seven children or 50% of the total group had a weight less than the 3rd centile. The prevalence of severely impaired growth was therefore some 16 times expectation. These findings contrast with those of Kitchen et al. [27] of 14 year old VLBW children, born before the era of assisted ventilation and parenteral nutrition, of whom only a quarter of those who were SGA at birth, remained so in adolescence. In the present study, some catch up growth did occur in length, which was around the 22nd centile and in head growth which was on the 45th centile by five years. Small head size was related to an adverse developmental outcome, with 3/4 children with a head circumference below the 10th centile having major impairments.

Despite a high neonatal (73%) and long term (64%) survival rate, preterm, ELBW, SGA infants who survive are an extremely high risk group for a poor developmental outcome, including major and minor physical impairments, attentional deficits and neurological dysfunction. The 57% incidence of major impairments in this study is even higher than that reported in previously published studies on infants born in the early 1970's. The 36% of survivors with major impairments is also markedly higher than the 14% impairment rate found at two years in appropriately grown ELBW survivors from the same hospital although this difference was not statistically significant. Of the four children conceived through artificial insemination by donor (AID), all survived the neonatal period and three were long term survivors. However, 2/3 of these long term survivors had multiple major impairments. Both children were deaf and had severe developmental delay. Thus 2/5 (40%) survivors with multiple major impairments were conceived through AID. The high risk of a poor outcome associated with preterm, ELBW, SGA infants is augmented by the tendency to repeat small for gestational age deliveries in successive births [5,11,36].

While the mean scores on the Bayley Scales at one and two years and the WPPSI at five years were completely within the normal range for children who could be tested, there was a significant decrease in MDI scores between 1 and 2 years of age. This decrease has also been found in another study of VLBW, SGA infants [35]. In the current study, the decrease in scores was related to a corresponding increase in the number of children with ADD between 1 and 2 years

of age, confirming the findings from a previous study of VLBW infants[3]. While the findings on the various psychometric tests were within the normal range on all three testing occasions, it must be stressed that they do not accurately reflect the intellectual functioning of the group as a whole. Not all children were able to be given standard psychometric testing. Three children were too severely impaired to be given standard testing and all three were attending special schools at five years of age. The principle of integration of children with impairments into mainstream schooling has been accepted in Victoria, but the severity of impairment in these children prevented them being accepted into normal schools.

As a group, these ELBW, SGA children had below average fine and gross motor coordination skills for their age, a high number of neurological signs and an elevated score on tests of minimal cerebral dysfunction. Cerebellar signs were commonly found on the tests derived from Touwen[37]. These findings are consistent with those of Chase et al.[13] concerning cerebellar biochemical alterations in the brains of SGA infants.

Even the children with 'minor' impairments, which involved all the children in this study, exhibited what Denckla[16] has called 'pastel classic' neurological signs. These are neurological signs which are abnormal at any age such as hyper- or hypotonia or reflexia and tremor of the fingers during skilled acts. In this cohort of children, these signs coexisted with visual deficits and marked attentional difficulties which persisted into school age for the majority. This constellation of difficulties have been documented repeatedly in previous studies[1,35,39]. Taken together these difficulties have been found to be associated with poorer intellectual and visuo-motor functioning and teacher rated behaviour problems in 8 year old ELBW children[12]. The children's short stature, low weight, poor muscle development and coordination problems are also likely to prevent them from participating fully in the physical activities of organized sport or in the informal playground activities which can be so important in the development of self esteem, friendships and social acceptability for the primary school aged child.

It is the practice in some studies to exclude children with congenital anomalies from follow up. None of the children with a congenital anomaly were excluded from the current study and none exhibited a major physical impairment or developmental delay at follow up. However, the child with Lennox-Gastaut's syndrome, conceived through in-vitro fertilization and artificial insemination by donor, was deaf, physically disabled and mentally retarded at five years of age. The onset of this disorder is between 3 and 6 years of age. This raises questions over the criteria used for exclusion from studies and whether the timing of that exclusion should be confined to conditions diagnosable at birth.

The small number of children in the present study precluded the use of multivariate analyses in delineating the relationship between neurodevelopmental outcome and a number of risk factors suggested by the research literature to be important. These risk factors include intrauterine growth retardation, degree of prematurity, type and severity of perinatal stress, type of obstetric and neonatal care provided, including nutrient supply, and the adequacy of growth in the neonatal period and beyond. Further, the small numbers of preterm, ELBW, SGA children born in any given population of live births, points to the neces-

sity for a multicentre collaborative study to be undertaken, so that the relative contribution of these factors may be elucidated.

In summary, the findings of the current study cannot be seen to support the argument that active obstetric and neonatal intensive care is necessarily associated with a significant improvement in the impairment rate of preterm, ELBW, SGA infants.

It is possible that without such care the children in this study may have had an even worse outcome. However, if as Allen [1] has suggested, it is the aetiology of intrauterine growth retardation which is crucial in determining outcome, then this will set a definite limit on the size of the contribution which perinatal care is able to make to these children's neurodevelopmental outcome.

References

1. Allen, M. (1984). Developmental outcome and follow up of the small for the gestational age infant. *Semin. Perinatol.* **8**, 123–156
2. Andreasson, B., Svenningsen N. W. and Nordenfelt, E. (1981). Screening for viral infections in infants with poor intrauterine growth. *Acta Pediatr. Scand.* **70**, 73–76
3. Astbury, J., Orgill, A. A., Bajuk, B. and Yu, V. Y. H. (1983). Determinants of developmental performance in very low birthweight survivors at 1 and 2 years of age. *Dev. Med. Child Neuro.* **25**, 709–716
4. Astbury, J., Orgill, A. A., Bajuk, B. and Yu, V. Y. H. (1987). Two years behaviour and outcome at five years of VLBW survivors. *Dev. Med. Child Neurol.* **29**, 370–379
5. Bakketeig, L. S., Bjerkedal, T. and Hoffman, H. J. (1986). Small-for-gestational age births in successive pregnancy outcomes: results from a longitudinal study of births in Norway. *Early Hum. Dev.* **14**, 187–200
6. Bayley, N. (1969). *Bayley Scales of Infant Development.* Psychological Corporation, New York
7. Berg, A. T. (1988). Childhood neurological morbidity and its association with gestational age, intrauterine growth retardation and perinatal stress. *Pediatr. and Peri. Epidemiol.* **2**, 229–239
8. Bhat, R., Raju, T. N. K. and Vidyasagar, D. (1978). Immediate and longterm outcome of infants less than 1000 grams. *Crit. Care Med.* **6**, 147–150
9. Bjerre, B. and Bjerre I. (1976). Significance of obstetric factors in prognosis of low birth weight children. *Acta Pediatr. Scan.* **5**, 577–583
10. Bruiniks, R. H. (1978). *Bruiniks-Oseretsky Test of Motor Proficiency.* Minnesota, American Guidance Service
11. Carr-Hill, R. and Samphier, M. (1983). Birth weight and reproductive careers. *J. Biosoc. Sci.* **15**, 453–464
12. Charlton, M., Carse, E. A, Gore, J. R. and Yu, V. Y. H. (1989). Significance of preschool behaviour for 8 year outcome in infants < 1000 grams. *Proceedings of the Seventh Congress of the Australian Perinatal Society*
13. Chase, H. P., Welch, N. N. and Dabiere, C. S. (1972). Alterations in human brain biochemistry following intrauterine growth retardation. *Pediatrics* **50**, 403–411
14. Chiswick, M. L. (1985). Intrauterine growth retardation. *Brit. Med. J.* **291**, 403–411
15. Commey J. O. O. and Fitzhardinge, P. M. (1979). Handicap in the preterm small for gestational age infant. *J. Pediatr.* **94**, 779–786
16. Denckla, M. B. (1979). Childhood learning disabilities. In: Heilman, K. M. and Valensteing, E. (eds.) *Clinical Neuropsychology*, pp. 535–573. Oxford University Press, New York

17. Dobbing, J. and Sands, J. (1971). Vulnerability of the developing brain. *Biol. Neonate* **19**, 354–362
18. Forse, R. A., Ackman, C. F. D. and Fraser, F. C. (1985). Possible teratogenic effects of artificial insemination by donor. *Clin. Genet.* **28**, 23–26
19. Gilles, F. H., Leviton, A. and Dooling, E. C. (1983). The epidemiology of delayed myelination. In: Gilles, F. H., Leviton, A. and Dooling, E. C. (eds.) *The Developing Human Brain: Growth and Epidemiologic Neuropathology*, pp. 150–171. John Wright, Littleton
20. Hack, M., Breslau, N. and Fanaroff, A. A. (1989). Differential effects of intrauterine and postnatal brain growth failure in infants of very low birth weight. *Am. J. Dis. Child.* **143**, 63–68
21. Hoskins, E. M., Elliot, E., Shennan, A. T., Skidmore, M. B. and Keith, E. (1983). Outcome of low birthweight infants born at a perinatal center. *Am. J. Obstets. Gynecol.* **145**, 135–140
22. Jones, D. L. and Hemphill, W. (1974). *Height, weight and other physical characteristics of New South Wales children. Part 11. Children under 5 years of age.* Government Printer, New South Wales
23. Kitchen, W., Ford, G. W., Orgill, A. A., Rickards, A., Astbury, J., Lissenden, J., Bajuk, B., Yu, V. Y. H., Drew, J. and Campbell N. (1984). Outcome of infants of birthweight 500–999 g: a regional study of 1979–1980 births. *J. Pediatr.* **104**, 921–927
24. Kitchen, W. H. (1968a). The relationship between birthweight and gestational age in an Australian hospital population. *Aust. Paediatr. J.* **4**, 29–37
25. Kitchen, W. H. (1968b). Head circumference, length and placental weight of infants in an Australian hospital population. *Austr. Paediatr. J.* **4**, 105–109
26. Nellhaus, G. (1968). Head circumference from birth to 18 years. *Pediatrics* **41**, 106–114
27. Kitchen, W. H., Ryan, M. M. and Rickards, A. L. (1987). Longitudinal study of very low birthweight infants: Impairments, health and distance growth to 14 years of age. *Aust. Peadiatr. J.* **23**, 335–338
28. Kraybill, E. N., Kennedy, C. A., Teplin, S. W. and Campbell, S. K. (1984). Infants with birth weights less than 1001 g: survival, growth and development. *Am. J. Dis. Child.* **138**, 837–842
29. Orgill, A. A., Astbury, J., Bajuk, B. and Yu, V. Y. H. (1982). Early development of infants 1000 g or less at birth. *Arch. Dis. Child.* **57**, 823–827
30. Ounsted, M. (1985). Intrauterine growth retardation. *Brit. Med. J.* **291**, 1200–1201
31. Ounsted, M. (1988). Small for dates babies: a developmental update. *Peadiatr. Perinat. Epidemiol.* **2**, 203–207
32. Smart, J. L., Adlard, B. P. F. and Dobbing, J. (1974). Further studies of body growth and brain development in 'small for dates' rats. *Biol. Neonate.* **25**, 135–150
33. Tanner, J. M., Whitehouse, R. H. and Takaishi, M. (1966). Standards from birth to maturity for height, weight, height velocity and weight velocity. *Arch. Dis. Child.* **41**, 454–457
34. Teberg, A. J., Pena, I. and Hoppenbrouwers, T. (1987). Factors involved in the decline of the developmental quotient in the very low birth weight infant during the first two years. *J. Perinatol.* **7**, 199–203
35. Teberg, A. J., Walther, F. J. and Pena, I. C. (1988). Mortality, morbidity, and outcome of the small for gestational age infant. *Semin. Perinatol.* **12**, 84–94
36. Tejani, N. A. (1982). Recurrence of intrauterine growth retardation. *Obstet. and Gynecol.* **59**, 329–331
37. Touwen, B. C. L. (1979). *The examination of the child with minor neurological dysfunction.* 2nd edition. Clinics in Developmental Medicine, No 71. S.I.M.P. with Heinemann Medical, London

38. Tudehope, D. I., Burns, Y., Callaghan, M., Mohay, H. and Silcock, A. (1983). The relationship between intrauterine and postnatal growth on the subsequent psychomotor development of very low birthweight (VLBW) infants. *Aust. Paediatr. J.* **19**, 3–8
39. Vohr, B. R., Oh, W., Rosenfield, A. G. and Cowett, R. M. (1979). The preterm, small for gestational age infant: a two year follow up study. *Am. J. Obstet. Gynecol.* **133**, 425–431
40. Vohr, B. R. and Oh, W. (1983). Growth and development in preterm infants small for gestational age. *J. Pediatr.* **103**, 941–945
41. Wechsler, D. (1967). *Wechsler Preschool and Primary Scale of Intelligence*. Psychological Corporation, New York
42. Yu, V. Y. H., Orgill, A. A., Bajuk, B. and Astbury, J. (1984). Survival and 2 year outcome of extremely preterm infants. *Brit. J. Obstet. Gynaecol.* **9**, 640–646
43. Yu, V. Y. H., Wong, P. Y., Bajuk, B., Orgill, A. A. and Astbury, J. (1986). Outcome of extremely low birthweight infants. *Brit. J. Obstet. Gynaecol.* **93**, 162–170
44. Yu, V. Y. H. (1987). Survival and neurodevelopment outcome of preterm infants. In: Yu, V. Y. H. and Wood, E. C. (eds.) *Prematurity*, pp. 223–245. Churchill Livingstone, London