

Prognosis for infants weighing 1000 g or less at birth

ANN L. STEWART, DIANE M. TURCAN, GRACE RAWLINGS, AND E. O. R. REYNOLDS

From the Departments of Paediatrics and Obstetrics, University College Hospital Medical School, London

SUMMARY During the 10 years 1966-1975, 148 infants weighing ≤ 1000 g were admitted to the Neonatal Unit of University College Hospital. 48 (32%) survived the neonatal period. The neonatal survival rate for infants weighing ≤ 750 g was 8% and for infants weighing 751-1000 g, 41%. 9 infants died later, leaving 39 (26%) long-term survivors, all of whom are being followed-up. The progress of the 27 older children, born in 1966-74 (median birthweight 899 g, range 648-998 g; median gestational age 28 weeks, range 24-35 weeks) was assessed at ages between 15 months and 8 years (median, 3 years). No abnormalities were detected in 21 infants (78%); 2 (7%) had major handicaps and 4 (15%) minor handicaps. We conclude that provided intensive care methods are available, the prognosis for infants weighing ≤ 1000 g is now better than in the past.

In the past the chances of survival for infants of very low birthweight (≤ 1500 g) were poor, and a high proportion of the survivors subsequently proved to be mentally or physically handicapped (Knobloch *et al.*, 1956; Drillien, 1958, 1966/67; Lubchenco *et al.*, 1963b; McDonald, 1967). More recently, with improvements in obstetric and neonatal care, the survival rate of these infants has increased, and follow-up studies from neonatal intensive care units show a much lower incidence of major handicap (Rawlings *et al.*, 1971; Calâme and Prod'hom, 1972; Stewart and Reynolds, 1974; Francis-Williams and Davies, 1974; Davies and Tizard, 1975). Virtually no information is available about the late prognosis of the very smallest infants, those weighing 1000 g or less at birth, because so few of them have survived to be followed up (Lubchenco *et al.*, 1963b; Alden *et al.*, 1972; Fitzhardinge and Ramsay, 1973; Fitzhardinge, 1975).

We report here survival rates for infants weighing 1000 g or less who were treated at University College Hospital (UCH) during the 10-year period 1966-1975, and the outcome for those infants who were born in the 9 years 1966-1974.

Patients and methods

During 1966-1975, 148 infants weighing 1000 g or less were admitted; 69 were born in UCH, 5 came from home, where they had been unexpectedly born, and 74 were transferred from 34 hospitals within a radius of 70 miles.

Obstetric and neonatal management. Methods used in the care of the infants who were born during 1966-70 have been described by Stewart and Reynolds (1974). Particular attention was paid to the prevention and treatment, whenever possible, of any abnormality that might be lethal or damage the brain, such as birth trauma, hypoxia before or after birth, hypothermia, acidaemia, dehydration, hypoglycaemia, hyperbilirubinaemia, abnormalities of haemostasis, and inadequate calorie intake.

Since 1970, additional methods have been introduced. For example, the lecithin-sphingomyelin ratio in amniotic fluid was measured in order to help decide whether an infant at high risk *in utero* should be delivered (Gluck *et al.*, 1971). There was an increase in the number of mothers referred by obstetricians in outlying hospitals for delivery at UCH and in the number of times medical or nursing staff from UCH were asked to be present at delivery in the referring hospitals when transfer of the mother was not practicable. A new transport incubator (Blake *et al.*, 1975a) which was equipped with facilities for monitoring heart rate, body temperature, and inspired oxygen concentration as well as for applying continuous positive airway pressure (CPAP) and mechanical ventilation, made the transfer of sick infants simpler.

Infants were sometimes nursed under radiant heaters, instead of in incubators, if frequent access was required. CPAP was introduced for the treatment of hyaline membrane disease in 1971 and from then until 1974, it was usually applied through an endotracheal tube. More recently a face-mask has been substituted whenever possible (Allen *et al.*,

Received 13 May 1976

1975), both for CPAP and mechanical ventilation, so as to avoid the difficulties associated with prolonged intubation. Since 1974 apnoea due to immature control of breathing ('preterm apnoea') has also been treated by mask-CPAP and mask-ventilation. Continuously recording umbilical artery catheter-tip oxygen electrodes (Conway *et al.*, 1976) and sometimes transcutaneous oxygen electrodes (Huch *et al.*, 1974; Jolly, *et al.*, 1976) were used to monitor the arterial oxygen tension (P_{aO_2}) of infants with respiratory illnesses. Total or partial parenteral nutrition given via a percutaneously inserted silicon rubber catheter with its tip sited in or near the right atrium (Shaw, 1973), was provided for infants who could not be adequately fed through a nasogastric tube. This was found to be particularly helpful during the weaning of infants from ventilatory aids. The routine measurement of coagulation factors allowed haemostatic defects to be detected and treated, usually by a one-blood-volume exchange transfusion with fresh blood. Sibs, as well as parents, have been encouraged to visit the neonatal unit (Blake *et al.*, 1975b) so that good inter-family relationships could be maintained and developed.

Throughout the whole period of the study, our general approach to the management of infants weighing 1000 g or less was to give optimal care both before and after birth, provided the period of gestation was above about 23 weeks. If, however, it became clear that irreversible and crippling damage to the brain or other organs had occurred, then treatment was withdrawn.

Follow-up

Infancy (<3 years of age). The children were seen (by A.L.S.) 2 weeks after discharge and then at intervals which increased from a few weeks to 6 months. Their progress was discussed with the parents, they were examined clinically and, for the first 18 months, their development was assessed according to the Developmental Screening Inventory (Knobloch *et al.*, 1966).

Preschool period (3 and 4 years). Clinical examinations continued and at 3½ years of age the first psychological assessment was made by a clinical psychologist. Evaluation was usually with the Stanford-Binet (From LM) Intelligence Scale (Terman and Merrill, 1961) but the Merrill-Palmer Scale (Stutsman, 1931) was also used for children who spoke little English or were very shy. Further details of the methods used during infancy and the preschool period have been given by Stewart and Reynolds (1974).

The children's age was regarded as their chronological age less the number of weeks that they had been born before term. After the age of 5 years this adjustment was no longer considered necessary.

Children at school (5–8 years). At 5 years, an audiogram, refraction, and an ophthalmoscopic examination were done, and since 1975 the children have been tested with the McCarthy Scale of Children's Abilities (McCarthy, 1970) and the Frankfurter Test of Concentration (Raatz and Möhling, 1971). At 8 years, a detailed clinical, neurological, and psychological assessment was carried out, including the Wechsler Intelligence Scale for Children (Wechsler, 1949). The children were also asked to do a selection of attainment, motor, perceptual, and learning tasks, including the Bender Gestalt Copying Test (Koppitz, 1964). Part of the assessment at 8 years was done in the child's school, where the teachers were interviewed and requested to give a report and to complete the Bristol Social Adjustment Guide (Stott and Marston, 1971).

Results

Population and survival. 60 of the 148 infants were born to primagravidae, 68 to mothers who had previously had live or stillborn infants, and 20 to mothers who had had abortions only. 55 pregnancies had been complicated by bleeding, 28 by hypertension or pre-eclampsia, and in 13 Shirodkar sutures had been inserted.

One hundred (68%) of the total of 148 infants died during the neonatal period (28 days). 9 infants (6%) died later, aged 29 days to 14 weeks, leaving 39 survivors (26%) all of whom are being followed up. Means and medians for birthweight and period of gestation are given in Table 1. Table 2 shows the neonatal survival rate during each of the study years. A higher proportion of infants survived during the latter 5 years ($\chi^2=4.5$, $P < 0.05$). Tables 3 and 4 give survival rates by birthweight and gestational age. Details of the population of infants admitted and of the effect of various perinatal events on survival are in Table 5. The survival rate was greater in girls than boys ($\chi^2=4.3$, $P < 0.05$), and in small-for-gestational-age infants, with birthweights below the 10th centile (Lubchenco *et al.*, 1963a) than in infants whose weight was appropriate-for-gestational age ($\chi^2=16.7$, $P < 0.001$). More infants delivered by caesarean section (64%) survived than those delivered vaginally (27%; $\chi^2=9.9$, $P < 0.01$). A higher proportion of infants delivered by caesarean section were, however, small for gestational age (64% vs. 19%). The mean time taken by the survivors to regain their birthweight was 14

Table 1 Birthweight and gestational age of infants weighing ≤ 1000 g admitted during 1966–1975

	All infants (n=148)	Neonatal survivors (n=48)	Neonatal deaths (n=100)	Long-term survivors (n=39)
Birthweight (g)				
Mean	826	881	808	878
Median	878	892	830	883
Range	500–1000	648–1000	500–1000	648–1000
Gestation (w)				
Mean	27	29	26	29
Median	27	28	26	29
Range	22–39	24–35	22–39	24–35

Table 2 Neonatal (28-day) survival rates of infants weighing ≤ 1000 g admitted during 1966–1975

Year	UCH		Referred to UCH		Total survived (%)
	Survived (n)	Died (n)	Survived (n)	Died (n)	
1966	2	6	2	5	27
1967	0	2	2	3	28
1968	2	7	3	3	33
1969	2	10	0	1	15
1970	1	4	0	5	10
1971	1	6	2	2	27
1972	0	2	1	5	13
1973	4	5	5	6	45
1974	2	8	6	10	31
1975	0	5	13	5	57
Total	14 (20%)	55	34 (42%)	45	32

9 infants died after the neonatal period, 4 in 1968, 2 in 1973, and one each in 1972, 1974, and 1975.

Table 3 Neonatal survival rates by birthweight of infants weighing ≤ 1000 g admitted during 1966–1975

Birthweight (g)	UCH		Referred to UCH		Total survived (%)
	Survived (n)	Died (n)	Survived (n)	Died (n)	
500–750	0	20	3	14	8
751–1000	14	35	31	31	41
Total	14 (20%)	55	34 (42%)	45	32

One of the infants dying after the neonatal period weighed 750 g and the other 8, 751–1000 g.

Table 4 Neonatal survival rates by gestation of infants weighing ≤ 1000 g admitted during 1966–1975

Gestation (w)	UCH		Referred		Total survived (%)
	Survived (no. of infants)	Died (no. of infants)	Survived (no. of infants)	Died (no. of infants)	
22–23	0	4	0	0	0
24–25	0	20	4	12	11
26–27	5	17	11	21	30
28–29	3	11	11	10	40
30–31	4	2	3	1	70
32–40	2	1	5	1	78
Total	14 (20%)	55	34 (42%)	45	32

6 of the infants dying after the neonatal period were born at gestational ages ≤ 27 weeks, and the other 3, > 27 weeks.

Table 5 *Details of the obstetric and neonatal histories of the 148 infants weighing ≤ 1000 g admitted during 1966-75*

	Total	Survived neonatal period (> 28 d) (and %)	Postneonatal deaths
Population			
Boys	66	15 (23)	5
Girls	82	33 (40)	4
Singletons	114	41 (36)	7
From multiple pregnancies	34	7 (21)	2
Social class* I-II	-	13	-
III	-	8	-
IV-V	-	12	-
Unclassified†	-	7	-
Congenital defects‡	10	3 (30)	-
Mode of delivery			
Vertex	93	25 (27)	6
Breech	33	9 (27)	2
Caesarean section	22	14 (64)	1
Small for gestational age	38	22 (58)	2
Respiratory problems			
Intubated at birth	68	19 (28)	1
Delay before onset of spontaneous breathing > 5 min	65	12 (18)	1
> 15 min	33	1 (3)	0
Base excess within 2h of birth -15 to -20 mmol/l	9	1 (11)	1
< -20 mmol/l	11	0	0
Hyaline membrane disease	62	12 (19)	5
Preterm apnoea—onset <24h	74	12 (16)	4
onset >24h	29	20 (69)	3
Mechanical ventilation and/or CPAP used	113	35 (31)	8
Convulsions	18	9 (50)	4
Total parenteral nutrition used	37	16 (43)	3
Jaundice (indirect plasma bilirubin >10 mg/100 ml; 171 μ mol/l)	32	15 (53)	3
Exchange transfusion for			
Hyperbilirubinaemia and/or rhesus haemolytic disease	10	5 (50)	0
Defective haemostasis, anaemia, or sepsis	9	4 (44)	1

*General Register Office (1966).

†Unmarried or student father.

‡3 multiple, 2 Potter's syndrome, 2 hypoplastic lungs, 2 congenital cataracts, and 1 Duane's syndrome.

days (range 0.38 days); 10 of them were hypoglycaemic (blood glucose <25 mg/100 ml; <1.39 mmol/l) at some time during the neonatal period.

Seventeen infants born at UCH (birthweight 500-965 g, mean 713 g; gestation 22-39 weeks, median 24 weeks) were in very poor condition at birth and not resuscitated. A further 10 infants (birthweight 610-980 g, mean 735 g; gestation 23-26 weeks, mean 24 weeks) were intubated at birth but because adequate gas exchange could not be achieved, resuscitation was abandoned. In 29 infants (birthweight 510-1000 g, mean 843 g; gestation 22-31 weeks, mean 27 weeks) of the remaining 81 who died, life-support systems including mechanical ventilation were withdrawn because of severe and persistent neurological abnormalities, including unresponsiveness, fits, and abnormal movements (25 infants); massive lung fibrosis (3), or multiple congenital defects (1).

The majority (68%) of deaths occurred in the first 48 hours, the median age being 26 hours (15 min-14 weeks). Necropsies were performed on 79 of the 100 infants who died in the neonatal period, and on 7 of the 9 who died later. The principal findings and the presumed cause of death in

the infants who did not have a necropsy are in Table 6. Coexisting intraventricular or subarachnoid haemorrhage and hyaline membrane disease were found in 34 (43%) of the infants. 17 of the 24 infants who had a necropsy, in whom treatment was stopped because irreversible damage was thought to have occurred, were found to have intracranial bleeding, and the remainder, sepsis, multiple congenital malformations, or infarcted bowel.

Follow-up. The 12 infants born in 1975 were too young for meaningful assessment. The 14 children aged 15 months to 3 years (mean 2 years 2 months) were also too young for accurate estimates of intellectual function, but the developmental quotients (DQ) of the 13 of these 14 who attend UCH were normal (>80). One of the 13 was, however, partially deaf. The 14th child lives in Ghana, and reports from his parents and local medical practitioner suggest that he is developing normally. He was found to have bilateral polar cataracts before discharge from hospital aged 4 months, but these were not expected to interfere with vision.

Follow-up data from the 27 children aged 15 months or more are summarized in Table 7.

Table 6 Principal necropsy findings and cause of death in 86 infants and in 23 infants having no necropsy. (Many infants appear under more than one heading)

	Neonatal deaths		Postneonatal deaths	
	Necropsy	No necropsy	Necropsy	No necropsy
Intraventricular haemorrhage (IVH)	37	2	0	0
Subarachnoid haemorrhage (without IVH)	6	0	0	0
Hyaline membrane disease	29	6	0	0
Sepsis	10	2	2	0
Lung fibrosis	5	0	5	1
Congenital malformations	5	0	2	1
'Immaturity'	12	11	0	0

Table 7 Incidence of handicap at follow-up among the 27 infants weighing ≤ 1000 g born during 1966–1974 at ages between 15 months and 8 years (median, 3 years)

Normal	21 (78%)
Major handicap	2 (7%)
Cerebral palsy and severely mentally retarded	1
Partial sight (cataracts)	1
Minor handicap	4 (15%)
Minimal cerebral damage (IQ 72)	1
Minimal cerebral damage and partially deaf (IQ 80)	1
High-tone deafness	2

Major handicap is defined as a disability that prevents, or is likely to prevent, the child from going to a normal school, or causes serious interference with normal function in society. Minor handicap is defined as a disability that does not, or is unlikely to, prevent the child from going to a normal school, or to interfere seriously with normal life.

Eight children included in Table 7 were aged 3 to 7 years when last assessed. The mental development of 6 of them was normal, and their mean IQ was 94 (range 79–124). One of these 6 children was partially sighted as a result of congenital cataracts. The seventh child had a high-tone hearing loss of moderate degree but was considered to have normal mental development, and the remaining child had cerebral palsy and was severely mentally retarded.

The 5 oldest children in Table 7 had detailed assessments when aged 8 years. Their mean IQ was 87 (range 72–104) and none had behavioural or visual abnormalities. The IQs of 3 of the 8-year-olds were 81, 100, and 104, and their educational attainments were appropriate for their underlying functional levels. The fourth child, with an IQ of 72, was retarded in educational performance but he was well integrated in a normal primary school, where he received special help. The fifth child had an IQ of 80, and difficulty in learning language. She had a 40 decibel hearing loss in both ears, due to secretory otitis media, but was thought also to have sustained minimal cerebral damage. After spending

3 years in the communications unit of a special school she was transferred to a normal school.

Discussion

Survival. The survival rates from earlier studies of infants weighing 1000 g or less are given in Table 8. Because the data are so scanty, the available information about infants who weighed ≤ 1250 g has also been included. The survival rate of these extremely low birthweight infants hardly appears to have changed during the past 20 years. The data must, however, be interpreted cautiously, because the numbers are so small, and in the past some of the infants were almost certainly regarded as abortions, or registered as stillbirths. At UCH the increase in survival rate since 1966 (Table 2) was due mainly to an improvement in the survival of infants referred from other hospitals. Although 17 (22%) needed mechanical ventilation in transit, they were probably selected for referral because they were in relatively good condition and it is most unlikely that they were representative of the whole population of infants weighing ≤ 1000 g born in the referring hospitals.

The main factors that influenced the probability of survival for the infants in this study were the same as those previously reported for infants weighing ≤ 1500 g (Stewart and Reynolds, 1974). Adverse factors included decreasing gestation (Table 2), asphyxia around the time of birth (Table 5), and the presence of the two main illnesses found at necropsy (Table 6), hyaline membrane disease and intraventricular haemorrhage. By using improved methods for prevention of perinatal asphyxia and for the management of hyaline membrane disease, survival rates for infants weighing ≤ 1000 g may be expected to increase. Little, so far, is known about the pathogenesis of the other important cause of death, intraventricular haemorrhage. Nevertheless there is a strong association with asphyxia, and it has been suggested that asphyxia causes increased intravascular pressures which rupture vessels in the germinal matrix (Cole *et al.*, 1974; Wigglesworth and Hambleton,

Table 8 Survival rate and incidence of major handicap in published series of infants weighing ≤ 1000 g or ≤ 1250 g

Author	Years children were born	Neonatal survival (%)	No. studied	Age (yr)	Major handicap (no. of children and %)
≤ 1000 g					
Lubchenco <i>et al.</i> (1963b)	1947-50	—	7	10	7 (100)
Fitzhardinge and Ramsay (1973)*	1960-66	—	5‡	5	2 (40)
Francis-Williams and Davies (1974)	1961-68	—	12‡	> 4	2 (17)
Alden <i>et al.</i> (1972)	1965-70	13	20	> 10 m	6 (30)
Present study	1966-75	32	27	1-8	2 (7)
≤ 1250 g					
Lubchenco <i>et al.</i> (1963b)	1947-50	—	27	10	22 (81)
Drillien (1969)	1953-60	—	36	> 7	23 (64)
Fitzhardinge and Ramsay (1973)*	1960-66	33	32	5	9 (28)
Vapaavuori and Riih� (1970)†	1966-67	45	22	2	?3 (14)
Fitzhardinge (1975)*	1970-72	30	19	1	5 (26)

*Appropriate-for-gestational-age infants only.

†Infants weighing 850-1250 g.

‡Personal communication, 1976.

1975). If so, this condition should eventually become preventable as asphyxia becomes easier to avoid.

Two very favourable, and probably related, factors that influenced survival were smallness for gestational age and delivery by caesarean section (Table 5). There is evidence that fetuses who are 'stressed' *in utero* have more mature enzyme systems than expected, particularly in the lung (Avery, 1973), thus lessening the risk of death from hyaline membrane disease. These infants are, as in the present study, often delivered by caesarean section, because of uncontrollable maternal hypertension.

Whatever the reason, the finding that the survival rate of infants delivered by caesarean section was so very much higher than for those born vaginally (Table 5) poses a difficult obstetric problem. If a very low birthweight fetus is at high risk of death *in utero* or if evidence of impending asphyxia is detected during labour, is delivery by caesarean section justified? The neonatal survival rate for infants weighing 1001-1500 g born in this hospital in 1974 and 1975 was 83% (40 out of 48 infants survived), and the long-term prognosis for infants of this weight now appears to be good (Stewart and Reynolds, 1974; Francis-Williams and Davies, 1974). We suggest that for infants who are expected to weigh more than 1000 g, with gestational ages greater than about 27 weeks, and particularly if they are small for gestational age, caesarean section is entirely justifiable. For smaller fetuses, with gestational ages less than this, it becomes progressively less reasonable to advise caesarean section, but the penalty to the infant of not doing so may be severe asphyxia and a bad long-term prognosis.

Handicap. 20 or more years ago very little was known about the potentially lethal or brain-damag-

ing biochemical hazards which very low birthweight infants have to withstand to survive; and the incidence of handicap in the smallest survivors was very high, 64-100% (Table 8). Since then, methods have been developed for the prevention of many of these hazards. It is not surprising, therefore, to find that the incidence of major handicap among the survivors has fallen (Table 8). In the present study it was 7% (Table 7). Also, 15% have so far been found to have minor handicap. The number of handicapped children was too small for meaningful conclusions to be drawn about the cause of the handicap. Nevertheless, it is noteworthy that the 3 children with cerebral problems (Table 7) all had apnoeic spells which required endotracheal intubation and mechanical ventilation for relief, and 2 of them had very high plasma levels of indirect bilirubin, 16.3 and 21.2 mg/100 ml (279 and 363 $\mu\text{mol/l}$). Furthermore, one of the 2 children with high-tone deafness was a breech delivery, the other was born by caesarean section after a prolapsed cord, and both were jaundiced, with plasma indirect bilirubin levels of 17.4 and 8.0 mg/100 ml (298 and 137 $\mu\text{mol/l}$). A history suggestive of hypoxia, together with jaundice, has been found to be significantly related to the subsequent presence of major handicap in our previous study of infants weighing ≤ 1500 g (Stewart and Reynolds, 1974). We suspect, therefore, that asphyxial episodes and jaundice were the main causes of handicap in the infants in the present report.

Organization of care. Because so few infants weigh ≤ 1000 g at birth and because they all require sophisticated methods of management it is important to try to ensure that they are delivered in hospitals with neonatal intensive care units. When this is not

possible, we believe that they should be transferred to an intensive care unit immediately after birth, before irreversible damage has occurred, by the staff of the unit who should attend the delivery whenever this can be arranged. If these extremely vulnerable infants are looked after in hospitals that are not properly staffed and equipped to do so, their prognosis is likely to be bad, similar to that found in the earlier studies (Table 8) of infants born before intensive care methods were available.

Ethics. Although the outlook for infants weighing ≤ 1000 g is improving, survival rates remain low and there is still an appreciable, though falling, risk of handicap in the survivors. At gestations below 24 weeks, survival becomes extremely improbable. Decisions have therefore to be made about how far to pursue intensive care, particularly in the smallest infants. In our view, optimal care both before and after birth should be given to any infant who is at a gestation of 24 weeks or more, so that whenever possible potentially brain-damaging hazards can be prevented. If, however, it becomes clear that the infant has an abnormality such as a large intraventricular haemorrhage that is virtually certain to lead to major handicap, then we believe that intensive care methods for sustaining life should, after full consultation among all those involved, be withdrawn.

We thank the staff of the Neonatal Unit for their devoted care of the infants, and the staff of the Children's Outpatient Department, Mr. D. P. Greaves, Miss E. Slembeck, Dr. A. Taghizadeh, and the Research and Statistics Department of the Inner London Education Authority for their help. This study was supported by grants from the Dept. of Health and Birthright.

References

- Alden, E. R., Mandelkorn, T., Woodrum, D. E., Wennberg, R. P., Parks, C. P., and Hodson, A. (1972). Morbidity and mortality of infants weighing less than 1000 g in an intensive care nursery. *Pediatrics*, **50**, 40-49.
- Allen, L. P., Blake, A. M., Durbin, G. M., Ingram, D., Reynolds, E. O. R., and Wimberley, P. D. (1975). Continuous positive airway pressure and mechanical ventilation by face-mask in newborn infants. *British Medical Journal*, **4**, 137-139.
- Avery, M. E. (1973). What is new in our understanding of perinatal pulmonary problems? *Pediatric Research*, **7**, 842-845.
- Blake, A. M., McIntosh, N., Reynolds, E. O. R., and St. Andrew, D. (1975a). Transport of newborn infants for intensive care. *British Medical Journal*, **4**, 13-19.
- Blake, A., Stewart, A. L., and Turcan, D. (1975b). Parents of babies of very low birthweight: long term follow up. *Parent-Infant Interaction*, p. 271. Ciba Foundation Symposium No. 33 (New Series). Associated Scientific Publishers, Amsterdam.
- Calàme, A., and Prod'hom, L. S. (1972). Prognostic vital et qualité de survie prématurés pesant 1500 g et moins à la naissance soignés en 1966-1968. *Schweizerische Medizinische Wochenschrift*, **102**, 65-70.
- Cole, V. A., Durbin, G. M., Olafsson, A., Reynolds, E. O. R., Rivers, R. P. A., and Smith, J. F. (1974). Pathogenesis of intraventricular haemorrhage in newborn infants. *Archives of Disease in Childhood*, **49**, 722-728.
- Conway, M., Durbin, G. M., Ingram, D., McIntosh, N., Parker, D., Reynolds, E. O. R., and Soutter, L. P. (1976). Continuous monitoring of arterial oxygen tension using a catheter-tip polarographic electrode in infants. *Pediatrics*, **57**, 244-250.
- Davies, P. A., and Tizard, J. P. M. (1975). Very low birthweight and subsequent neurological defect. *Developmental Medicine and Child Neurology*, **17**, 3-17.
- Drillien, C. M. (1958). Growth and development in a group of children of very low birth weight. *Archives of Disease in Childhood*, **33**, 10-18.
- Drillien, C. M. (1966/67). The long-term prospects for babies of low birth weight. *Hospital Medicine*, **1**, 937-944.
- Fitzhardinge, P. M. (1975). Early growth and development in low-birthweight infants following treatment in an intensive care nursery. *Pediatrics*, **56**, 162-172.
- Fitzhardinge, P. M., and Ramsay, M. (1973). The improving outlook for the small prematurely born infant. *Developmental Medicine and Child Neurology*, **15**, 447-459.
- Francis-Williams, J., and Davies, P. A. (1974). Very low birthweight and later intelligence. *Developmental Medicine and Child Neurology*, **16**, 709-728.
- General Register Office (1966). *Classifications of Occupations*. HMSO, London.
- Gluck, L., Kulovich, M. V., Borer, R. C., Brenner, P. H., Anderson, G. G., and Spellacy, W. N. (1971). Diagnosis of the respiratory distress syndrome by amniocentesis. *American Journal of Obstetrics and Gynecology*, **109**, 440-445.
- Huch, R., Lübbers, D. W., and Huch, A. (1974). Reliability of transcutaneous monitoring of arterial P_{O_2} in newborn infants. *Archives of Disease in Childhood*, **49**, 213-218.
- Jolly, P., Reynolds, E. O. R., and Soutter, L. P. (1976). Comparison of transcutaneous oxygen tension ($t_{c}P_{O_2}$) and arterial oxygen tension ($P_{a}O_2$) in newborn infants. (Abst.) *Pediatric Research*, **10**, 890.
- Knobloch, H., Rider, R., Harper, P., and Pasamanick, B. (1956). Neuropsychiatric sequelae of prematurity (1956). *Journal of the American Medical Association*, **161**, 581-585.
- Knobloch, H., Pasamanick, B., and Sherard, E. S. (1966). A developmental screening inventory for infants. *Pediatrics*, **38**, 1095-1108.
- Koppitz, E. M. (1964). *The Bender-Gestalt Test for Young Children*. Grune and Stratton, New York.
- Lubchenco, L. O., Hansman, C., Dressler, M., and Boyd, E. (1963a). Intrauterine growth as estimated from live-born birthweight data to 24 to 32 weeks of gestation. *Pediatrics*, **32**, 793-800.
- Lubchenco, L. O., Horner, F. A., Reed, L. H., Hix, I. E., Metcalf, D., Cohig, R., Elliott, H. C., and Bourg, M. (1963b). Sequelae of premature birth. *American Journal of Diseases of Children*, **106**, 101-115.
- McCarthy, D. (1970). *McCarthy Scales of Children's Ability*. Psychological Corporation, New York.
- McDonald, A. D. (1967). *Children of Very Low Birthweight*. Heinemann, London.
- Raatz, V., and Möhling, R. (1971). *Frankfurter Tests für Fünfjährige-Konzentration, FTF-K. Deutsche Schultests*. Deutscher Institut für Internationale Pädagogische Forschung, Frankfurt.

- Rawlings, G., Reynolds, E. O. R., Stewart, A., and Strang, L. B. (1971). Changing prognosis for infants of very low birth weight. *Lancet*, *1*, 516-519.
- Shaw, J. C. L. (1973). Parenteral nutrition in the management of sick low birthweight infants. *Pediatric Clinics of North America*, *20*, 333-358.
- Stewart, A. L., and Reynolds, E. O. R. (1974). Improved prognosis for infants of very low birthweight. *Pediatrics*, *54*, 724-735.
- Stott, D. H., and Marston, N. C. (1971). *The Child in School. Bristol Social Adjustment Guide Nos. 1 and 2*, 4th ed. University of London Press, London.
- Stutsman, R. (1931). *Mental Measurement of Pre-school Children*. Harcourt, Brace, and World, New York.
- Terman, L. M., and Merrill, M. A. (1961). *Stanford-Binet Intelligence Scale*. Harrup, London.
- Vapaavuori, E. K., and Riih , N. C. R. (1970). Intensive care of small premature infants. *Acta Paediatrica Scandinavica*, *59*, 353-362.
- Wechsler, D. (1949). *Manual of Wechsler Intelligence Scale for Children*. Psychological Corporation, New York.
- Wigglesworth, J. S., and Hambleton, G. (1975). Origin of intra-ventricular haemorrhage in the premature newborn infant. *Neuropathology and Applied Neurobiology*, *1*, 316.

Correspondence to Dr. A. L. Stewart, Department of Paediatrics, University College Hospital Medical School, Huntley Street, London WC1.