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CHILD STUDY UNIT

September 22, 1981

George A. Evanoff
Vice Chancellor
Personnel and Student Services

Dear Chancellor Evanoff,

I would like to recommend Donya Harvin for the Chancellor's Award for University Employees. Donya has faithfully served the Department of Pediatrics and the University of California Medical Center since 1946 when she began developmental assessments of children in the Cerebral Palsy program with Dr. Peter Cohen. As former Director of the Child Study Unit, I have worked almost daily with Donya since she joined our staff in 1949.

Donya is, and has been one of the essential members of this unit. Over the years, her developmental and psychological assessments of infants and children have been a model of excellence which has greatly influenced the other psychologists in the Child Study Unit and the Bay Area Community. Her professional expertise and creative ideas have been vital in developing the multidisciplinary teaching program for medical students, pediatric housestaff and fellows, for which the Child Study Unit has a national reputation. Donya has always given and continues to give of her superb professional and teaching skills far beyond that required for her position. She has participated in numerous symposia, workshops and post-graduate courses at UCSF and the Bay Area in educating physicians, health and school professionals about childrens' learning and developmental disorders.

Donya's extra effort has been vital in achieving the Child Study Unit's grant support over the years for our multidisciplinary teaching program. During her service to the University, Donya has also collaborated in research efforts of the Unit, resulting in eight publications. The data for long term evaluation of infants at risk in the Nursery Follow-Up Program has been achieved largely through Donya's careful and conscientious follow-up of these children over the past 16 years. Such long term dedication to a research study is an invaluable contribution to the Pediatric Department's scholarly endeavors, and one which Dr. Tooley has documented. Donya is a professional who gives extra time to her patient evaluations and to teaching; she always takes work home. Over the years, she has given many, many hours of extra service to the University.

In summary, because of Donya Harvin's professional excellence, creative work, extra effort far beyond that required by her position, and dedication to the Child Study Unit and UCSF for the past 35 years, she is most deserving of this award.

Sincerely,

Helen Gofman, M.D.
Associate Professor, Pediatrics
Program Director, Child Study Unit

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The University and Bay Area communities lost a loyal and gifted member with the recent death of Mrs. Donya Harvin, who had provided professional services to UCSF from 1946 to the present.

As Assistant Clinical Professor of Pediatrics and senior psychologist, she was an integral part of the Child Study Unit (now the Division of Behavioral and Developmental Pediatrics). Donya Harvin taught many generations of medical students, pediatric housestaff and fellows, nursing students and psychology trainees about psychological development and assessment, especially in children with chronic illness, handicaps and developmental problems. During these years she provided psychological evaluations for the child patients of many medical faculty at UCSF and for pediatricians in the Bay Area. She was an outstanding teacher and clinician and highly regarded by her colleagues and patients.

She participated in many of the research studies of the Child Study Unit, and is a co-author of over 15 publications. These include: protocols for developmental screening of children as part of their medical examinations, studies of children with specific learning disorders, follow-up studies with the Department of Otolaryngology of children with delayed language development. Since the institution of the Nursery Follow-up Program with Dr. William Tooley, Donya Harvin had carried out periodic developmental evaluations on nearly 1000 infants and children from 1965 to the present.

Over the years, Donya Harvin made major contributions to public and private schools in the Bay Area and Northern California through consultations regarding students (who number in the thousands), and by participating in in-service and continuing education programs for school personnel.

From 1976 to her death, she was a founding board member of Sterne School, a private school for students with specific learning disabilities, grades 5 through 12. Her family (she leaves her husband Spence Harvin, two sons and two grand children) prefers donations to the Donya Harvin Memorial Scholarship Fund which has been established in her memory at Sterne School, 2490 Jackson Street, San Francisco, CA 94115.

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DEVELOPMENT OF CHILDREN WHO HAD RECEIVED INTRA-UTERINE TRANSFUSIONS

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ABSTRACT. Sixty-six nonhydropic fetuses received intra-uterine transfusions for severe erythroblastosis fetalis; 24 survived the neonatal period—the youngest is now more than 1 year and the oldest 5 years of age. Serial evaluations of growth and development of the survivors were compared with their course in the perinatal period. Twenty-one were normal; one suffered severe central nervous system damage associated with severe cardiorespiratory failure, prolonged acidosis, and hypoxia during the neonatal period; one has a handicap due to hearing loss and one has a speech handicap. The results support the use of intra-uterine transfusion in appropriately selected fetuses when combined with aggressive treatment of cardiorespiratory distress and hyperbilirubinemia during the neonatal period.

Pediatrics, 47:689, 1971, ERYTHROBLASTOSIS FETALIS, INTRA-UTERINE TRANSFUSION, GROWTH AND DEVELOPMENT, INTELLIGENCE.

INTRA-UTERINE intraperitoneal transfusion (IUT) for the treatment of fetuses severely affected with erythroblastosis fetalis has been used in many medical centers since its first description by Liley in 1963.[1] When used on fetuses not yet hydropic, this procedure has significantly reduced perinatal mortality.[2-4] However, there has been only one report[3] of the subsequent development of a group of survivors of IUT and the ultimate outcome of these infants is still in doubt. This is a report of results of a study of the growth and development of 24 such children.

PATIENT MATERIAL

The recent report of Fong, *et al.*[4] details the prenatal aspects of our IUT program, including its indications during the time when the first 14 survivors in this study were transfused and born. Our indications and technics for IUT have not changed.

During a 58-month period ending 2 years ago, 66 fetuses affected with erythroblastosis fetalis but not hydropic (assessed by radiography and absence of significant ascites) received one or more IUTs for isoimmune hemolytic disease and were subsequently delivered at this medical center, or were stillborn. Twenty-four of these 66 survived the neonatal period and are now at least 1-year-old.

Cardiopulmonary Status in the Perinatal Period

In asphyxiated infants there were usually at least three measurements of pH and blood gas tensions during the first hour of life. In disease which persisted after this, a measurement was made whenever there was any clinically detectable change in condition.

Cardiorespiratory distress was classified as follows: (1) intrapartum: asphyxia at birth (low Apgar score or acidosis) or signs of distress in the first 5 to 10 minutes of life; (2) transient: retractions, tachypnea, and grunting limited to the first 1 to 2 days of

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life; (3) idiopathic respiratory distress syndrome (IRDS): retractions, tachypnea, grunting lasting more than 48 hours, and diffuse atelectasis on x-ray.

Clinical Management in the Neonatal Period

Initial resuscitation included: assisted ventilation when appropriate; catheterization of umbilical artery and vein for determination of arterial blood oxygen (P_aO_2) and carbon dioxide (P_aCO_2) tensions, pH (pH_a), hematocrit, measurement of arterial and central venous pressures, and administration of alkali, albumin, and transfusions. Small exchange transfusions of packed red cells were used to correct severe anemia and to increase or decrease blood volume for maintenance of normal intravascular pressures. Albumin infusions were also used for blood volume expansion and to maintain the albumin concentration at 3 gm/100 ml. Exchange transfusions were performed as often as necessary to keep the concentration of serum indirect bilirubin below 18 mg/100 ml. Blood glucose concentration was frequently measured and intravascular infusions of glucose were given as necessary to keep the glucose level at 40 mg% or higher.

LONG-TERM FOLLOW-UP

We evaluated each survivor at ages 4, 8, 12, 18, and 24 months, and yearly thereafter. The evaluation included a complete physical and neurological examination; hearing testing; parent interviews by a social worker; developmental evaluation by the same examiner twice in the first year and each visit thereafter, by the Catell Scale of Infant Intelligence (DQ) up to 3 years of age, and thereafter by Stanford Binet (L-M) Scale (IQ). Speech and language skills were tested after 18 months by (1) informal testing of articulation in response to presentation of toys; (2) Peabody Picture Vocabulary Test, (3) Mecham Verbal Language Inventory Test; and (4) Illinois Test of Psycholinguistic Ability (ITPA). The results of the last two tests were scored in terms of Language Quotient (LQ).

RESULTS

The results are presented in Table I and the Appendices.

Prenatal Course and Condition at Birth

The number of IUTs varied from 1 to 4 and gestational age (GA) at the first IUT from 24 to 33 weeks. All infants were born prematurely (GA 30-37 weeks); infant 12 was underweight for GA. The severity of hemolytic disease varied widely. Cord blood bilirubin and albumin values are shown in Appendix A. Some degree of hydrops was present in seven infants, mild or "pre-hydrops" in six, and severe hydrops in one. Some degree of intrapartum cardiorespiratory distress was found present in 16 infants.

Neonatal Course (Table I and Appendix A)

In six infants, intrapartum cardiorespiratory distress responded rapidly to resuscitative measures. In nine others, it was followed by transient cardiorespiratory distress, and in one (1) by severe IRDS. One infant who had no signs of intrapartum distress developed moderately severe IRDS.

Indirect bilirubin concentrations greater than 18 mg/100 ml were due to transient peaks which occurred just before exchange transfusions. In none was the level more than 20 mg/100 ml for more than 2 hours. With the exception of infant 1, the maximum levels of bilirubin did not occur during sustained severe acidosis or hypoxia. Serum albumin concentration was greater than 3 gm/100 ml in all by 6 hours of age.

Generally, the lowest levels of pH_a and P_aO_2 were observed during the first hour of life, when indirect bilirubin concentration was low. A pH_a of 7.20 or less or a P_aO_2 of 40 mm Hg or less, or both, were measured after 1 hour of age in only four infants (1,3,20,21). This degree of hypoxia and/or acidosis was known to be transient in three infants and did not occur at a time when bilirubin concentrations were greatest.

TABLE I

Patient Number	GA at first IUT	Number IUT	At birth		Apgar		Cord blood PCV	Maximum Indirect Bilirubin mg/100 ml /age hr	Latest		Comments
			Wt (kg)	GA (wk)	1′	5′			DQ or IQ/age	LQ/age	
1	32	1	2.3	35	7	5	32	18/84	died		ICD, severe IRDS; onset 1st 15′ life,* (signs of kernicterus during first week)
2	28	2	2.3	37	9	9	33	14/5 da	112/5	113/5	
3	27	2	2.2	36	6	9	47	20.7/57	95/4	92/4	Moderately severe IRDS, onset at 30′ life
4	31	1	2.2	36	4	8	18	20.5/92	114/5	93/5	ICD, transient RD
5	33	1	2.4	36	7	9	28	16.5/29	93/5	102/5	
6	29	3	2.2	35	9	9	31	22.4/24	97/4	77/4	
7	28	2	1.8	30	8	9	35	21.5/9	115/4	111/3	ICD, transient RD
8	31	2	1.8	33	4	9	27	19.4/44	137/4	114/4	ICD, transient RD
9	30	3	2.3	34	8	9	43	14.5/68	123/4	97/3	
10	24	4	3.2	37	4	7	28	1.4/27	109/4	92/3	anti-Kell disease
11	27	3	3.2	37	5	8	20	14.8/5 da	96/4	89/3	ICD
12	24	4	1.4	34	2	4	47	21.3/30	93/2	—	ICD, underwt for GA
13	29	3	2.0	34	7	9	34	20/30	111/3	94/3	ICD, transient RD
14	30	3	2.5	36	1	9	41	10.1/44	84/3	83/3	ICD, severe thrombocytopenia
15	30	2	2.8	35	5	8	46	26.7/55	101/3	111/3	ICD, all other indirect bilirubin <20 mg/100 ml
16	32	2	2.7	37	1	8	28	15.2/45	80/2	79/2	ICD, transient RD, severe thrombocytopenia
17	29	4	3.2	36	1	5	26	13.7/33	no follow-up		ICD
18	30	3	2.5	37	8	9	29	8/60	118/2	111/2	
19	29	2	2.0	35	6	9	26	23.4/48	incomplete follow-up*		ICD, transient RD
20	27.5	2	2.0	32	5	7	23	20.5/31	97/1-1/2	67/1-1/2	ICD, transient RD
21	30	2	2.5	35	3	7	33	18.3/42	no direct evaluation*		ICD
22	31	1	1.9	34	8	9	29	18.7/51	105/1-1/2	100/1-1/2	
23	27	2	1.9	34	2	6	20	9/23	87/1		ICD, transient RD
24	31	1	2.7	35	4	9	28	19.5/4 da	95/1		ICD transient RD, mild

* See text.
GA = Gestational age.
IUT = Intra-uterine transfusion.
ICD = Intrapartum cardiorespiratory distress.
Transient RD = Transient cardiorespiratory distress.
IRDS = Idiopathic respiratory distress syndrome.

In one (1) it was prolonged and occurred when the indirect bilirubin concentration was highest. This infant was quite different from the rest of the group in that resuscitation and therapy to correct acidosis and hypoxia were used much less vigorously and he had the most severe IRDS. During the second half of the first week of life he had signs typical of clinical kernicterus.

All infants received kanamycin during the neonatal period, and infant 20 received a very large total dose. No clinical or chemical hypoglycemia was detected in any infant during the neonatal period.

Infancy and Childhood

Of the 24 survivors, five were not followed in the prescribed fashion: infant 17 was lost to follow-up; infant 19 was followed sporadically until age 15 months; infant 21 was followed until age 5 months when her family moved to Norway and since then we have received detailed written descriptions of her development; infant 3 was initially lost to follow-up but returned for evaluation at 4 years of age; infant 1 died before reaching 1 year of age—signs of severe central nervous system damage had been evident when last seen by us.

Physical Growth

By 6 months of age, height, weight, and head circumference were normal in all infants and normal growth patterns were maintained thereafter.

General Health

All appeared well nourished throughout the period of evaluation. The only common medical problem after discharge from the nursery was anemia during the first 2 months of life; five infants required transfusions of packed red blood cells. Three were hospitalized with acute infections in the first year but responded rapidly to treatment.

Neurological Findings

Infant 1 had spastic paraplegia and died at age 7 months in another hospital; his brain was reportedly "normal" on necropsy. Infant 20 had some hearing loss. All other infants were free of specific abnormal neurological signs.

Developmental Assessment (Table I and Appendix C)

There was a tendency for the relative level of achievement to improve with increasing age (Appendix B). Fourteen infants were tested at some time before 1 year of age and only three scored in the average range at that time; the rest scored "appreciably below average" or even lower. Twelve of the 14 infants have been followed up to or beyond 18 months, and on most recent testing, achieved composite scores in a range from "dull normal" (84) to "very superior" (137).

Four infants have not been evaluated beyond 1 to 1½ years—three are performing at an average level, the other appreciably below average (DQ 87).

Infant 21 seems to be performing at an appropriate level for age on the basis of a written report from the mother. Infant 19 never had psychometric testing but when last examined at age 15 months he had reached developmental milestones which were appropriate for age.

Of three infants who have currently been tested only up to 2 years, infant 16 was "appreciably below average" with a quotient of 80, and has not shown any improvement over his earlier performance. The other two infants have achieved quotients of 93 (low average) and 118 (appreciably above average); in both there was evidence of increasing relative achievement after 1 year of age.

Of 13 followed to or beyond 3 years of age, the range of IQ was 84 (dull average) to 137 (very superior); however, infant 6 still shows marked inconsistencies in his ability pattern. The pattern of improved performance with increasing age was evident in most (Appendix B). In eight infants there was continued improvement after 2 years of age; in several, this was quite striking, with increases in score of greater than 20 points between age 2 and 5 years. Only infant 14 had improving performance on earlier testing but had a notable decline during the third year of life.

Speech and Hearing Studies

One 2-year-old infant (20) had a consistent hearing loss which may be partly sensorineural. She received the largest dose of kanamycin of any of the infants. To date, the rest of the infants appear to have normal hearing.

The LQ from the Mecham or ITPA tended to be delayed (Table I and Appendix C). The LQ was usually lower than the IQ.

On evaluating the profiles of achievement in the various areas tested, a consistent pattern was evident. Development of expressive language skills tended to lag behind the overall level of achievement. This was true even of some whose composite scores placed them in the "above average" or "superior" categories at 3 or 4 years of age. At the last testing this pattern was still present in all but three cases.

Many of the infants had poor speech articulation at 2 years of age; however, this skill improved in several children on retesting at 3 to 5 years of age, although it remained poor in infants 3 and 6.

Sociologic Evaluation

Most of the families were middle class—12 lower-middle (clerical or blue collar workers), five middle (teacher, foreman), five upper-middle (executive, physician), and two lower class.

Six mothers had a mildly positive maternal attitude toward their children. A strongly positive attitude was present from birth onward in 13 mothers, 12 of whom had given birth previously to an infant who had died during the neonatal period and/or had a stillborn due to erythroblastosis. In contrast, four mothers had an ambivalent attitude toward their infants initially, only one of whom had given birth previously to a critically ill or a stillborn infant. The attitude of one mother changed to a distinctly positive one during her infant's first year of life, while the other three have maintained a somewhat detached attitude. No mother in this group had a truly negative maternal attitude, although one was not evaluated. Compared with other groups being followed in our Clinic (premature, small-for-gestational-age, and severe IRDS), there appears to be a far greater proportion of mothers of IUT infants with a positive maternal response.

Interpretation

Because of the tendency of developmental testing for relative achievement to improve during the first, second, and sometimes the third year of life, we have considered patient 16 to be only suspect of having a mild handicap; patient 23, having been followed only to age 1 year, is not yet considered "suspect" because her quotient at 1 year is similar to that of several older subjects who had this same level at 1 year of age but who are now performing at normal or above-normal levels.

Combining the results of all forms of evaluation, some degree of handicap was diagnosed in three infants (1, 6, 20), and seriously suspected in a fourth (16). This was severe in infant 1 and appeared to be related to the combination of severe cardiorespiratory distress (which was not treated aggressively) and hyperbilirubinemia. The handicaps were milder in the other two infants. The moderate speech handicap of infant 6 was not obviously related to the degree of prematurity, severity of bilirubinemia, acidosis, or hypoxia when his course was compared with the rest of the group. The moderate sensorineural hearing loss of infant 20 could equally well be blamed upon kanamycin (she received a total dose in excess of that reported to be nonototoxic in infants),[5] bilirubin,[6] or other unknown factors.[5] Patient 16 is, as yet, only suspected of having a handicap. He was asphyxiated at birth but improved rapidly, had only transient respiratory distress, and hyperbilirubinemia was well controlled.

DISCUSSION

Most of the children in this group were at great risk of suffering central nervous system injury during the neonatal period because of their prematurity, high incidence of birth asphyxia, cardiorespiratory distress, and hyperbilirubinemia. The greatest risk was probably due to the interaction of all these factors.

Premature infants with jaundice, and concomitant hypoxia and acidosis are known to be particularly susceptible to bilirubin toxicity.[7] Animal experimentation suggests that these other variables, or hypoalbuminemia, will enhance the toxicity of

indirect bilirubin.[8,9] Theoretically, therapy directed at correction of such abnormalities in blood chemistry should reverse this effect. The outcome of the infants in this group with cardiorespiratory distress who received vigorous early therapy (directed at correction of acidosis and hypoxia and enhancement of plasma bilirubin binding capacity) is encouraging. The only patient who appeared to suffer severe central nervous system injury did not receive vigorous therapy for cardiorespiratory distress but, since this was a single case, its significance is open to question. However, the outcome of the entire group tends to support the rationale for the therapy used in most infants. This does not necessarily mean that the level of control generally achieved should be accepted as a satisfactory endpoint. Perhaps better control would give better results.

As a group, mothers whose fetuses received IUT were preselected in terms of socioeconomic and personal factors. They received good early prenatal care, which allowed detection of severe erythroblastosis, and must have been strongly motivated to have children before they would submit to IUT. Hence, it is not surprising that they tended to be highly maternalistic mothers of middle-class families. It would also appear that maternal attitude is influenced by experiences with past pregnancies, in that occurrence of previous fetal or neonatal death correlates with strongly positive maternal attitudes. No doubt differences in background will have an increasing effect upon developmental and intellectual performance in these children as they grow older. At present, we have not attempted to take this into account in evaluating their performance on testing.

The considerable variation in performance on developmental testing, plus the tendency for relative performance to continue to improve with age throughout the first 2 and 3 years of life is of particular interest, and creates some major complications for our evaluation. There is keen interest in the ultimate outcome of survivors of IUT in order to decide upon the wisdom of continuing such programs. Unless one waits until they reach late childhood or adulthood, one must attempt to predict ultimate outcome on the basis of performance in early childhood. Our data suggest that single evaluations of performance, particularly under 2 years of age, may be misleading and inadequate to assess the long-term results of IUT. At present four patients in our group have some form of handicap, or are seriously suspected of it. The lags in language skill development in some of the others suggest the possibility that mild handicaps may appear when they are older or could be evaluated with more refined technics. However, at present one can at least say they are grossly intact neurologically.

Gregg and Hutchinson[3] have pointed out that there is no true control group against which to compare survivors of IUT. It would be very difficult to find a group matched for severity of hemolytic disease at birth, prematurity, severity of cardiorespiratory distress, quality of neonatal care, and type of home environment who had not received IUT. At this stage in the history of IUT, the main purpose of evaluating survivors is to determine the wisdom of continuing such a procedure. This must be determined on the basis of whether or not most of the survivors are neurologically intact. For this purpose, comparison with the normal population (the basis of developmental and intelligence quotients) seems appropriate. At present, the outcome in this group can be characterized generally as satisfactory. It appears, therefore, that IUT does not seem to salvage a significant number of fetuses who have suffered severe brain damage *in utero*.

CONCLUSION

We tentatively conclude that, when IUT is used in appropriately selected fetuses and combined with aggressive therapy during the neonatal period, most survivors will be neurologically intact. The results of our study and those of Gregg and Hutchinson[3] support the continuation of IUT.

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APPENDIX A

NEONATAL COURSE

Patient Number	*Cord blood*			*Hydrops**	*Lowest*		*Exchange transfusions*	*Albumin infusion*	*Kanamycin total dose (mg)*	*Comments*
	Bilirubin		*Albumin*		*pH/age (min)*	P_aO_2/*age (min)*				
	Indirect	*Direct*								
1	7.8	2.0	—	+1	7.16/12 hr (venous blood)	No arterial catheter	4	+	244	No alkali for acidosis until 12 hours of age (see text)
2	3.9	0.4	—	0	7.40/15	107/4 hr	1		380	
3	8.9	0.5	—	0	7.22/30	38/49 hr	2	+	165	All other pH > 7.29, P_{O_2} > 49
4	3.7	0.9	2.3	+1	7.22/41	71/41	2	+	110	
5	2.9	0.6	2.9	0	7.36/33 (venous)	No arterial catheter	0	+	170	
6	9.5	0.8	3.4	0	7.23/8	79/90	4	+	110	
7	6.9	0.8	2.5	+1	7.10/15	42/27 hr	4	+	135	All other pH > 7.25
8	5.8	1.4	—	0	7.34/60	49/5–1/2 hr	3	+	70	No blood gas measurements during resuscitation
9	3.5	0.5	2.6	0	7.23/18	33/26	0		100	All other pH ≥ 7.31, P_{O_2} ≥ 66 mm Hg
10	0.5	0.6	3.4	0	7.32/17	50/36	1		126	anti-Kell disease
11	7.5	10.5†	2.4	+3	7.20/7	41/7	1	+	380	Peak direct bilirubin 39 at 70 hours
12	7.2	0.7	2.3	+1	7.19/9	18/9	5	+	154	All other pH > 7.33; P_{O_2} ≥ 47

APPENDIX A (*Continued*)

Patient Number	Cord blood: Bilirubin: Indirect	Cord blood: Bilirubin: Direct	Cord blood: Albumin	Hydrops*	Lowest: pH/age (min)	Lowest: P_{aO_2}/age (min)	Exchange transfusions	Albumin infusion	Kanamycin total dose (mg)	Comments
13	6.1	1.8	3.4	+1	7.22/12	28/12	2		140	
14	2.2	0.8	3.4	0	7.21/8	55/6	0		190	
15	4.2	0.3	3.0	0	7.16/4	37/4	1	+	225	Peak bilirubin due to transient abrupt rise after albumin infusion (all others <20 mg/100 ml)
16	5.5	0.7	2.3	0	7.19/4	36/13	1		180	
17	4.7	1.3	3.0	0	7.22/5 (venous)	No arterial catheter	1	+	322	
18	3.3	1.1	3.3	0	7.31/5-1/2	47/21	1		170	
19	4.4	0.8	3.2	0	7.15/4	40/19	4	+	225	
20	6.8	0.5	2.9	0	7.12/21	37/72 hr	4	+	400	See text
21	3.9	0.5	3.3	0	7.15/43 hr	26/43 hr	1	+	144	See text
22	5.7	0.8	3.5	0	7.16/6	43/29	2		120	
23	4.0	0.8	2.7	+1	7.26/25 hr	40/6 hr	1/2	+	154	
24	3.7	0.3	3.1	0	7.25/47	34/15	3	+	225	

* Hydrops = +1 hepatosplenomegaly + minimal peripheral edema.
+2 same as +1 but with pronounced edema but no ascites.
+3 detectable ascites or pleural effusion.
+4 massive feature-deforming anasarca.

† Liver function studies normal at 6 months of age.

APPENDIX B

DEVELOPMENTAL (CATTELL) AND INTELLIGENCE QUOTIENTS (STANFORD-BINET L-M)

Patient Number	Months at time of study (±2): 5	8	12	18	24	30	36	48	60
1	Died								
2	103		98	114		100	99	109	112
3								95	
4		89	89	103	89		89	99	114
5					87			100	93
6	59		83	89		88	84	97	
7			78	92	104		111	115	
8			92	85	93		123	137	
9	75		96	98	81	81	106	123	
10	70		90		88		99	109	
11	63		89	100	96		84	96	
12		64	80	93	93				
13	53		87	96	106		111		
14	50		71		91		84		
15	80			102	101		101		
16			80		80				
17*									
18	95		104	107	118				

* No follow-up.

APPENDIX B (*Continued*)

Patient Number	*Months at time of study (±2)*								
	5	*8*	*12*	*18*	*24*	*30*	*36*	*48*	*60*
19									
20		80		97					
21*									
22			85	105					
23		80	87						
24	62		95						

* No follow-up.

APPENDIX C

RESULTS OF AUDIOLOGIC, SPEECH, AND LANGUAGE EVALUATION

Patient Number	*H-response*		*9–18 months*		*19–30 months*				*31–42 months*				*43–60 months*			
	0–4 (months)	*5–8*	*H*	*M*	*H*	*P (%)*	*A*	*M (LQ)*	*H*	*P (%)*	*A*	*M (LQ)*	*H*	*P %*	*A*	*Meor ITPA (LQ)*
1	nd															
2	+	+	+						+	61	Fair	93	+		Fair	113
3													+	21	Poor	92
4	+	+	+		+		Poor	79	+	28	Fair	84	+	24	Fair	93
5	+				+	4	Poor	83					+		Good	102
6	+		+		+		Poor	65	+	52	Poor	69	+	56	Poor	77
7	+	−	+		+	92	Poor	312	+	94	Fair	111				
8	+	+	+				Good	92	+		Good	92	+	54	Fair	114
9	+	−	+		+	86	Good	110	+	47		97				
10	+	+	+						+	56	Fair	92				
11	+	−	+	95					+	28	Fair	89				
12	+		+													
13	+	+	+	88	+		Fair	100	+		Poor	94				
14	+	+	+	80	+		Fair	92	+	21	Poor	83				
15	+		+	95	+		Fair	100	+		Good	111				
16	+	−	+	84	+		Poor	79								
17	nd															
18	+		+	111	+											
19	+		+													
20	−	−	−	67	Moderate											
21	+	+		100												
22	+	+	+													
23	+	+	+													
24	0	+	+													

\+ = Present or normal response.
− = Absent or abnormal response.
A = articulation.
H = hearing.
ITPA = Illinois Test of Psycholinguistic Ability.
LQ = Language Quotient.
M = Mecham Test.
nd = not done.
P = Peabody Test.

Learning Disabilities in Children with Birth Weights ≤1500 Grams

By Jane V. Hunt, William H. Tooley, and Donya Harvin

THE intellectual outcome of very small preterm infants whose survival has required neonatal intensive care is of great concern. Developmental problems occur with greater than normal frequency in this population, the reported incidence being linked to the age of assessment, the level of neonatal care available at birth, the kinds of complications that occur, and the subsequent socioeconomic environment of the infant. Despite the known high risk status of the group, it is not yet possible to predict the long-term outcome of most infants with any confidence.

Only the most severe of the enduring handicaps are clearly detectable during the first year of life. They include frank cerebral palsy, severe mental retardation, and blindness. In most centers providing modern neonatal care the reported incidence of such handicaps has declined even as survival rates have improved,[1,2] attesting to the general success of treatment. The incidence of severe handicaps reported in recent years has ranged from 5% to 15% for infants with birth weights below 1500 grams, differences depending upon such factors as the defining criteria used and the way in which the low birth weight population was recruited. This is in contrast to the much higher proportion of crippling problems reported in infants of this birth weight born in the 1940s and 1950s.[3,4]

Milder problems noted in infancy are not necessarily predictive of enduring disabilities. Even when the neonate or infant shows evidence of mild clinical neurological dysfunction, some of these symptoms may be transient and not significantly associated with future mental development.[5,6] Conversely, normal development in infancy does not guarantee normal intellectual abilities in childhood. In a comparison of development from infancy to early childhood[7] we noted normal infant development for most children with subsequent childhood disabilities. Even mental retardation could not be predicted in all cases. Only a third of the group with IQs below 68 in childhood had developmental scores in the retarded range during the first year of life.

Some problems, such as language lags may be noted by 2 to 3 years of age, although the long-term significance of such delays is not always predictable. Other intellectual handicaps may be identified as the child approaches school age but some may not be determined with certainty until school progress can be evaluated. The correlation of IQ with the social and educational status of children's families usually begins to reach significance at 2 to 3 years and IQ stability across age within a group of children (expressed by significant cross-age correlations) is generally established by age 4. These general trends do not, of course, hold true for all individuals. Also, some specific disabilities are not reflected in the IQ level and children with average or higher IQs may have learning disabilities that interfere with normal school placement or progress.

All of the above considerations emphasize the importance of longitudinal studies in determining the true risk status of very low birth weight infants. The determination of intellectual outcome obviously depends upon the ages used to define outcome as well as the socioeconomic status of the population and the kinds of handicaps included in the determination. These considerations blur some comparisons among follow-up studies. More important, they make comparisons across years of intensive care experience difficult within the same center, for today's infants and yesterday's eight-year-olds obviously are not readily equated beyond the determination of the most severe handicaps.

A major variation among studies is the way in which the infants are recruited. Differences in both survival rates and outcome are to be expected for centers treating infants born in that hospital (inborn) or infants born elsewhere and transferred for intensive care (outborn). The two kinds of popula-

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tions are not strictly comparable because outborn infants must survive long enough to be transported to the special care center, must be considered ill enough for transfer, and usually do not have the same level of specialized care available in the first hours of life. It is generally believed that inborn infants are at a decided advantage[8,9] and there has been an increasing emphasis on prenatal transport of infants whose mothers threaten very premature delivery. This practice has increased the numbers of small preterm infants born in special care centers.

An appreciation of the difficulties inherent in long-term studies is evident in recent reports. In a review of the history of neonatal care practices and evaluations of outcome, Desmond and co-authors[10] concluded that the outcome for very low birth weight infants born in the 1970s and treated with modern neonatal intensive care appeared to be generally good but they cautioned that complete determination of intellectual outcome could not be made until all reached school age. Optimism also was expressed for low birth weight infants (inborn and outborn) who received neonatal care at University College Hospital, London from 1966–1976.[11] General improvement in childhood status was noted over time and, of 50 children assessed at 8 years, 76% were attending normal schools and had no detectable handicaps. Less optimism was evident in a report from Hammersmith Hospital, London that evaluated a 15 year experience (1961–1975) with inborn infants of the same low birth weight.[12] No significant change over time was noted in the incidence of major or minor handicaps and the incidence of normal outcome in childhood was 28% for 138 children. It was noted that these children were predominantly from disadvantaged homes and that relatively low IQs might be expected. This report generated a lively correspondence to the Lancet which ended with an editorial stating it is too early to assess the results of modern perinatal care.[13] Discrepancies among studies emphasize the importance of demographic considerations when long-term outcome is evaluated. Each center conducting longitudinal studies adds to the total picture of the risk status of very low birth weight infants. Our study provides a comparison for inborn infants born in approximately the same years as the Hammersmith study, but into largely middle-class families.

THE STUDY

We began a longitudinal follow-up study of the survivors of neonatal intensive care at the University of California in San Francisco in 1965. For one of our study groups we attempted to enroll all inborn infants with birth weights at or below 1500 grams born from 1965 through 1978 and all with weights below 1350 grams thereafter. The only deliberate exclusions were infants with chromosomal abnormalities known to be associated with mental retardation. In fact, only one such infant survived.

Survival 1965–1981

Survival over three time periods is shown in Table 1. The increase in numbers of survivors over time reflects both improving survival rates and also a dramatic gain in the numbers born in our hospital after 1975. The gain is primarily the result of the current emphasis on the transport of high risk mothers for treatment and delivery at a special care center.

Seventeen infants died after they were discharged from the hospital. Four had severe congenital anomalies, two had marked chronic lung disease, two had recurrent infections with immunodeficiency and one died at 9 years of age with a malignancy. The other eight deaths occurred during the first year of life and were unexpected and unexplained. This high incidence of Sudden Infant Death Syndrome has been noted before in infants of very low birth weight.

Table 1. Infants Born at the University of California in San Francisco, 1965–1981, with Birth Weights ≤ 1500 g

	1965–69	1970–75	1976–81	Total
Born	100	128	289	517
Died, neonatal	52	46	62	188
Died, post-discharge	3	6	8	17
Survived	45	76	219	340
(Percent survived)	(45.0)	(59.4)	(75.8)	(65.8)

Table 2. Survival By Birth Weight (BW) Categories for Three Time Periods

	Born	Survived	% Survived
BW < 750 g			
1965–69	8	0	0
1970–75	12	1	8.3
1976–81	27	6	22.2
BW 750–1000 g			
1965–69	26	7	26.9
1970–75	24	6	25.0
1976–81	77	46	59.7
BW 1001–1250 g			
1965–69	31	17	54.8
1970–75	41	29	70.7
1976–81	81	70	86.4
BW 1251–1500 g			
1965–69	35	21	60.0
1970–75	51	41	80.4
1976–81	104	97	93.3

The association between birth weight and survival across time are shown in Table 2. There were only 14 survivors with birth weights at or below 1000 grams in the first two time periods, but there were 52 survivors in the most recent period. The increase in numbers of very small survivors is illustrative of the problems encountered when different treatment epochs are compared.

Outcome 1965–1975

Children born in the first two epochs, 1965 1975, have now reached school age. Demographic characteristics of this group have been described elsewhere.[7] The families are predominantly middle-class and Caucasian. The modal parent education level (averaged for both parents where appropriate) is high school graduate, but approximately 18% had some college education and another 21% averaged college graduate or higher. The high risk status of the population is clearly indicated by the survival statistics in Table 1; there were 228 live births and 121 survivors (53%) during those years. Of the survivors, 11 (9.1%) were never seen in follow-up, another 6 children were evaluated only during the first year of life (1 was considered abnormal), 3 children were last seen at 2 or 3 years of age (1 was abnormal), and 102 (84.3%) have been evaluated at age 4 or older. Of the latter group, 60 have been evaluated most recently at 8 or 11 years.

At 4 through 6 years the test battery includes the Stanford-Binet, L-M. At 8 and 11 years the standard IQ test given is the Wechsler Intelligence Scale for Children (WISC). Also, children are given a global rating following each evaluation, which we have compressed for this discussion into three categories: normal, suspect and abnormal. The rating is a clinical judgment, based on the child's performance on a battery of tests. In addition, the children are rated on a broad spectrum of specific intellectual factors. These specific ratings have been developed to augment written reports, assuring that the clinical status of each child will be considered across a consistent range of functional abilities.

Neurological Sequelae

Very few of the survivors had serious neurological abnormalities. Four developed hydrocephalus in the neonatal period probably secondary to intracranial hemorrhages. Three of these had ventriculo-peritoneal shunts and one had a lumbo-peritoneal shunt which were subsequently removed. These 4 children are slightly clumsy but have no gross neuromotor dysfunction. One girl is normal at age 8 (IQ 120). Two boys and one girl are abnormal (IQs 81, 77 and 74). Five children have mild spastic diplegia. They have not required braces and ambulate without difficulty. One of them is suspect (IQ 97), two have definite intellectual disabilities (IQs 75, 81) and two are retarded. One of the latter is blind and the other has marked visual impairment. One child without spastic diplegia is retarded and blind. Three blind children had birth weights of 1000 grams or less. Three children have moderate conductive hearing loss. They had recurrent middle ear infections in infancy.

IQ Categories

Outcome by IQ categories for the 102 children (44 males and 58 females) is presented in Table 3. While available, data are from assessments at age 6 (76 cases). Outcome was determined for the remainder at age 5 (10 cases), 4 (10 cases) or 8 years (6 cases). Overall, the outcome data in Table 3 represent intellectual status determined primarily at the age of school entry.

There was little difference in outcome between the two time periods, except that the incidence of retarded children was sharply reduced during the second epoch. The total with IQs in the retarded

Table 3. Outcome by IQ Categories for 102 Children, 4 Years or Older, Born 1965–75

IQ	Category	1965–69	(%)	1970–75	(%)	Total	(%)
< 68	Retarded	6	(15.8)	2	(3.1)	8	(7.8)
68–83	Borderline	6	(15.8)	11	(17.2)	17	(16.7)
≥ 84	Handicaps	8	(21.1)	13	(20.3)	21	(20.6)
Total Handicap		20	(52.6)	26	(40.6)	46	(45.1)
≥ 84	Suspect	7	(18.4)	16	(25.0)	23	(22.5)
≥ 84	Normal	11	(28.9)	22	(34.4)	33	(32.4)
Total No Handicap		18	(47.4)	38	(59.4)	56	(54.9)
	Total	38		64		102	

range was approximately 8% and comparable to data from other studies of very low birth weight populations. Another 17% of the children had definite intellectual problems, with scores in the borderline range of intelligence (IQ 68 to 83). In our middle-class sample such scores were invariably judged to be abnormal, with further evidence for specific intellectual deficits.

A substantial subgroup of children (20.6%) had scores in the normal range, but had intellectual disabilities that were expected to interfere with normal school progress and achievement (e.g. language comprehension and/or visual motor integration problems). Most, but not all of these children had scores below 100, and there was only a general correspondence between measured IQ and intellectual status for all children with scores in the normal range. Another subgroup (22.5%) was rated "suspect" by the examiners on the basis of intellectual performance, i.e., prediction of school success was considered somewhat problematic although no definite handicaps were identified. The numbers presented in Table 3 indicate that, contrary to fears that had been expressed by some investigators, increasing survival rates across the two epochs did not result in a corresponding increase in the numbers of handicapped children. There were no significant differences between time periods in average birth weight or gestational age.

Sex differences in outcome, either in general or between the two time periods, cannot be determined with any confidence in this population. There was a disproportionate number of females born in the second time period (65.6%) compared with the first (42.1%). Moreover, the incidence of hyaline membrane disease varied between the sexes over the two time periods, with only two females (of 14 children) with that condition in the first period, but with 20 (of 27) in the second period having this important neonatal complication. Therefore, year of birth, hyaline membrane disease and sex are confounded in our data.

Hyaline Membrane Disease

One of the major neonatal problems of very low birth weight infants is hyaline membrane disease (HMD). Until the last decade, HMD was the cause of most of the deaths in infants of very low birth weight. Great changes were being made in therapy for this condition between 1965 and the present.[14] Treatment from 1965–1969 consisted mainly of the administration of oxygen. The use of continuous positive airway pressure was begun in 1970 and during the second epoch, 1970–1975, it was the principal form of therapy. In that era intermittent mandatory ventilation was begun only when infants with HMD had apnea. Data for the 102 children tested at age 4 years or older were considered according to the presence or absence of HMD. The incidence of HMD was comparable in each epoch, being 36.8% for those born in 1965–1969 and 40.6% for those born in 1970–1975. The reduction in total handicaps between epochs noted in Table 3 was greater for those with HMD; the incidence changed from 71.4% (1965–1969) to 53.8% (1970–1975). Data for all 102 children are presented in Table 4. The percentage of handicaps was significantly higher for children who had HMD (60% vs. 35.5%). However, the relatively large number of children in the "suspect" category who did not have HMD suggests that this distinction must be reviewed as the children proceed further in school. Nevertheless, the evidence indicates that some of the conditions or complications or HMD were adding to the risk status of very low birth weight infants, even into childhood.

Table 4. Hyaline Membrane Disease (HMD) and Intellectual Status for 102 Children with BW ≤ 1500 g

IQ	Category	HMD	(%)	No HMD	(%)
< 68	Retarded	4	(10.0)	4	(6.5)
68–83	Borderline	10	(25.0)	7	(11.3)
≥ 84	Handicaps	10	(25.0)	11	(17.7)
Total Handicaps		24	(60.0)	22	(35.5)
≥ 84	Suspect	6	(15.0)	17	(27.4)
≥ 84	Normal	10	(25.0)	23	(37.1)
Total Not Handicaps		16	(40.0)	40	(64.5)
	Total	40		62	

Intrauterine Growth Retardation

Infants who are very small for gestational age (SGA) often are considered separately in studies of very low birth weight infants. They are relatively more mature at birth than are those of comparable birth weight who are appropriate for gestational age, a possible advantage. On the other hand, problems associated with fetal malnutrition might influence long-term intellectual development. There were 23 SGA survivors, 20 of whom were tested at 4 years or older. These infants had birth weights below the third percentile for gestational age by California standards,[15] representing the extreme of SGA infants.

There was one retarded child in the SGA group. Four children had IQs in the borderline range of intelligence and six others had intellectual deficits but normal IQs, a total of 55% with handicaps. The incidence of handicaps was comparable to that found for the whole group of 102 children. A slight increase in handicaps across time periods was noted, unlike the overall decrease found for the larger group. Of the 10 SGA children born from 1965–1969, only one had HMD whereas six of 10 born in the second time period had HMD. Outcome was more influenced by HMD than by SGA status during the second period. It appears from our data that neonatal status, and probably survival, was enhanced for SGA infants compared with others born during the first epoch of intensive care. However, the long-term outcome for the SGA group was not different from all born in the same period.

Birth Weight ≤1000 Grams

The outcome of children with birth weights at or below 1000 grams is of special interest because the number of such survivors in our population has increased rapidly since 1975 (see Table 2). There were 14 survivors in the first two time periods and all were followed into childhood. Three were also SGA. Differences in outcome were evident across time. Of the eight children born in 1965–1969, seven were handicapped and three had scores in the retarded range; one child was considered suspect. For those born in 1970–1975, two had handicaps, one scoring in the retarded range (birth weight of 570 grams). Three of the six children from the second epoch were considered entirely normal. This group of smallest infants clearly was at special risk for severe handicap. Although it comprised only a fraction of the total population studied (13.7%), it included 50% of the retarded children. The shift across time periods is very encouraging, particularly the finding that 50% of those in the second period were normal.

LEARNING DISABILITIES

Children who are functioning in the borderline range of intelligence, or who have scores in the normal range but with evidence for significant learning disabilities, constitute the majority of intellectual problems identified in the very low birth weight group. The validity of ascribing such disabilities to low birth weight depends, in part, upon the incidence of such problems expected in the general population. There is no good agreement on this point, and the reported incidence of learning disabilities at school age ranges from 5 to 20%. In our population the incidence appears likely to be 37% (excluding children with peers in the retarded range), or almost twice that of the highest normal estimate.

Sibling Controls

We are testing siblings of the low birth weight children to provide a more direct comparison with a normal group. Where available, one sibling who was not low birth weight is being evaluated once, on the same tests as the study child, at age 4 years or older. Where there is a choice, preference is given to a sibling of the same sex. Sibling pairs can be compared at the same age. To date we have tested only 19 pairs, including three sets of twins where one had a birth weight above 1500 grams. The average IQ difference was 14.6 points, with the control group testing higher. When twins were excluded, the average difference was 16.7 IQ

points, equivalent to one standard deviation. This small group represents a cross-section of the categories defined in Table 3: none retarded, 5 borderline, 4 with IQ above 84 but with disabilities, 4 suspect, and 6 normal. Excluding twins, there were only 4 instances where the study child was within 10 IQ points of the control sibling. The average IQ difference between pairs in the normal category was 10.8 points. Although these findings are only preliminary they suggest that most of the low birth weight children were disadvantaged in childhood when compared with their siblings, regardless of designated outcome.

Clinical Ratings

As noted, the IQ, while broadly predictive of school success, does not identify all children with significant learning and language disabilities. For this reason, children are given both a global rating and specific functional ratings at each evaluation. We have reported the frequency of specific abnormal ratings at 6 years of age for 64 very high risk children who were assessed repeatedly in infancy.[16] The most common disabilities were in language comprehension (abnormal ratings for "language as a cognitive tool," "language tracking and processing" and "language comprehension") and in visual-motor integration skills (as measured by two separate clinical instruments). A smaller subgroup of children had problems with attention, concentration and impulse control. Other problems such as poor fine motor control and speech articulation were also noted. Approximately one-third of the children in this earlier study were from the very low birth weight population.

As noted, 67 of the 102 low birth weight children were evaluated at 6 years, the remainder being assessed at 4, 5, or 8 years. The intercorrelations between scores and also between ratings at 4 through 6 years are high and therefore interchangeable for general purposes. However, for a more specific description of intellectual status those tested at age 6 can be considered separately to describe the major intellectual problems noted as the children entered school. The ratings for language comprehension and visual-motor integration skills (VMI) were examined. In all, 33 children (49%) had one or both of these disabilities. There were 25 children with language comprehension problems and 20 with abnormal VMI ratings, 12 children having both problems. Twenty-four children (36%) had neither disability, although 5 of these had other problems, such as distractibility and poor impulse control that gave them a general rating of no better than "suspect." Many children were suspect for VMI problems at this age. Only a few had a discrete handicap, that is either normal language but abnormal VMI (7 cases) or abnormal language but normal VMI (6 cases). Although approximately half the group seemed to be at definite risk at the age of school entry, the problems were not well defined at this age.

The group with normal IQ but with abnormal global ratings is of special interest. VMI problems might be anticipated because the Binet IQ is heavily weighted for verbal abilities. Of the 21 children in this category (see Table 3), 17 were tested at age 6. An inspection of their specific disabilities does not confirm the hypothesis of VMI problems, for 10 were rated abnormal on VMI and 9 were abnormal on language ratings (5 with both problems). The remaining 3 children were considered abnormal on the basis of other intellectual handicaps. For these "normal but not normal" children, as for the low birth weight group as a whole, educational problems appeared to be emerging at 6 years of age but were not well defined.

Comparisons Between Early and Middle Childhood

A longer view down the developmental road is provided by those children who have reached at least 8 years of age. The WISC scores and the general and specific ratings described for younger ages were available for comparisons. Fifty-three children (born in 1965–1973) were tested at both ages. The results are presented in Table 5.

Those who were identified as being in the retarded and borderline categories of intellectual functioning in early childhood continue to be so identified in middle childhood. Although the numbers are too small to be conclusive, it appears that those who had IQs in the normal range are not so predictable. Nearly one-third of such children who were identified as abnormal had improved status by global ratings, although the average IQ was not improved. (The Verbal IQ of the WISC is also presented in Table 5 for comparison with the more verbally based Binet IQ.) Those who were considered suspect at the earlier age showed shifts to better or poorer status in equal numbers.

Table 5. IQ Comparisons at 4 to 6 Years and 8 Years for 53 Children

IQ	Category	N	Binet IQ 4–6 Yrs.	WISC IQ 8 Yrs.	WISC Verbal IQ	Ratings at 8 Years Normal	Suspect	Abnormal
< 68	Retarded	2	57.5	46.0	52. (n = 1)			2
68–83	Borderline	10	75.9	77.0	78.2			10
≥ 84	Handicaps	10	99.1	93.4	96.3		3	7
≥ 84	Suspect	11	100.5	105.5	102.4	4	3	4
≥ 84	Normal	20	112.4	105.1	106.8	9	7	4
					Total	13	13	27

Most disconcerting in this array of score comparisons is the shift to a less satisfactory status for 16 of the 20 children who were considered normal at school entry. In this group the shift in status was accompanied by a decrease in average IQ. The four children now rated abnormal are strikingly similar. All are girls who are judged to be adequate in rote skills but definitely lacking in abstract abilities, both verbal and non-verbal. They are now struggling in school as the educational tasks have become more complex, despite a good initial adjustment. Even though IQs remain in the normal range at 8 years, the closer look reveals that learning disabilities continue to be identified at middle childhood and considerable shifting of status toward both better and poorer functioning can be anticipated for those children with IQs in the normal range.

DISCUSSION

We have presented our data in broad strokes, with the hope and expectation that others with similar studies will find these results useful. The strengths and limitations of the longitudinal method are evident in all such studies, our own included.

Conclusions about outcome are not exactly conclusions, even at 8 years of age. Many factors in the children's environments, as well as their own innate capacities, doubtless influence the kinds of problems we find and the extent of those problems. For children from reasonably advantaged backgrounds, as was the case for the majority of our population, compensations can occur that belie earliest predictions. Normal infancy and early childhood may follow even after severe neonatal illness and complications. However, it appears that, for some children such compensations are not enough. Learning disabilities sometimes emerge at older ages when the intellectual demands of school require more complex and fluid intellectual capacities.

Although the total incidence of childhood intellectual disabilities may be high in a very low birth weight population, the evidence indicates that severe handicaps are few in our own and other recent studies.[17,18] The quality of life for most children appears to be reasonably good. A major goal of longitudinal studies is to identify the less severe problems at younger ages. Early remediation of identifiable problems is receiving increasing attention and we no longer anticipate a one-to-one association between early insults to the central nervous system and outcome. Nevertheless, the high risk status of low birth weight children continues to suggest that neonatal factors contribute to intellectual problems. A retrospective look at neonatal intensive care from the perspective of childhood status is of major importance in assessing the total effects of such care.

Perhaps the most compelling conclusion from our study is the importance of monitoring high risk infants well into childhood. At present, the true incidence of handicap cannot be determined in any other way. Also, parents and children may need professional support and intervention for the first time at much older ages than we have previously supposed.

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The University and Bay Area communities lost a loyal and gifted member with the recent death of Mrs. Donya Harvin, who had provided professional services to UCSF from 1946 to the present.

As Assistant Clinical Professor of Pediatrics and senior psychologist, she was an integral part of the Child Study Unit (now the Division of Behavioral and Developmental Pediatrics), Donya Harvin taught many generations of medical students, pediatric housestaff and fellows, nursing students and psychology trainees about psychological development and assessment, especially in children with chronic illness, handicaps and developmental problems. During these years she provided psychological evaluations for the child patients of many medical faculty at UCSF and for pediatricians in the Bay Area. She was an outstanding teacher and clinician and highly regarded by her colleagues and patients.

She participated in many of the research studies of the Child Study Unit, and is a co-author of over 15 publications. These include: protocols for developmental screening of children as part of their medical examinations, studies of children with specific learning disorders, follow-up studies with the Department of Otolaryngology of children with delayed language development. Since the institution of the Nursery Follow-up Program with Dr. William Tooley, Donya Harvin had carried out periodic developmental evaluations on nearly 1000 infants and children from 1965 to the present.

Over the years, Donya Harvin made major contributions to public and private schools in the Bay Area and Northern California through consultations regarding students (who number in the thousands), and by participating in in-service and continuing education programs for school personnel.

From 1976 to her death, she was a founding board member of Sterne School, a private school for students with specific learning disabilities, grades 5 through 12. Her family (she leaves her husband Spence Harvin, two sons and two grand children) prefers donations to the Donya Harvin Memorial Scholarship Fund which has been established in her memory at Sterne School, 2490 Jackson Street, San Francisco, CA 94115.