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A Longitudinal Study of Developmental Outcome of Infants With Bronchopulmonary Dysplasia and Very Low Birth Weight

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Abstract

Objective—Bronchopulmonary dysplasia (BPD) is now the leading cause of lung disease in US infants. In a large regional cohort, we tested the hypothesis that despite innovations in neonatal care, very low birth weight (VLBW) infants (<1500 g) with BPD had poorer developmental outcomes than nonaffected infants during the first 3 years of life, and that BPD predicted poorer outcome beyond the effects of other risk factors.

Methods—Three groups of infants (122 with BPD, 84 VLBW without BPD, and 123 full-term) were followed longitudinally to 3 years of age with the Bayley Scales of Mental and Motor Development. Comparison groups of VLBW infants without BPD and full-term infants did not differ in sex, race, or socioeconomic status. Statistical analyses included hierarchical and stepwise multiple regression.

Results—Infants with BPD performed more poorly at all ages. By 3 years, cognitive and/or motor development was in the range of retardation (<70 standard score) for 21% to 22% of infants with BPD. In multiple regression analyses controlling for socioeconomic and neonatal risk conditions, BPD had an independent negative effect on motor outcome at 3 years. Neurologic risk, a summary measure of neurologic problems other than intraventricular hemorrhage, and the presence of BPD independently predicted motor delay. By 3 years, social class, race, and neurologic risk predicted mental outcome, suggesting that the specific effects of BPD are primarily on the motor domain.

Conclusions—In VLBW infants, BPD predicts poorer motor outcome at 3 years, after control for other risks. Cohorts of infants with BPD also had higher rates of mental retardation, associated

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with greater neurologic and social risk. These findings underscore the need for intensive prevention and habilitation efforts for this growing group of VLBW survivors, as well as investigation into the potential role of BPD in the higher rates of learning disabilities in VLBW cohorts at school age.

Improved survival rates for smaller, sicker, very low birth weight (VLBW) infants related to advances in neonatal intensive care have resulted in a corollary increase in incidence of bronchopulmonary dysplasia (BPD).[1] BPD, virtually unknown a generation ago, is now the third leading cause of chronic lung disease in children, and the leading cause of lung disease in infants in the United States,[2,3] with >7000 infants diagnosed yearly.

BPD is the term used to describe the clinical, radiographic, and pathologic sequelae of prolonged mechanical ventilation occurring in the lungs of some newborn infants.[1] BPD most often occurs in ventilated preterm infants and is inversely related to gestational age.[4] Pulmonary immaturity, oxygen toxicity, and barotrauma are paramount in the etiology of BPD.[4,5]

Previous studies addressing developmental outcome for infants with BPD have been inconsistent in their findings, with many reporting poorer growth and developmental outcomes and greater evidence of neurologic problems, particularly cerebral palsy.[5–10] Sample sizes of most studies are small, (generally <30), and BPD has been variously defined and confounded with other medical conditions known to relate to poor outcome, ie, intraventricular hemorrhage, periventricular leukomalacia, and lower gestational age.[9,12,13] Impact of social class and racial parameters on outcome has also been rarely assessed,[12] leading to debate about whether the negative sequelae of BPD are secondary to associated deleterious medical or social conditions or independent effects. Most studies were completed before routine use of cranial ultrasound evaluations in neonatal nurseries. Information was not available regarding the contribution of intraventricular hemorrhage and periventricular leukomalacia to developmental delays.[6,12] Some studies averaged mental and motor outcome scores[7] or used scores uncorrected for prematurity,[9] making interpretation of findings problematic. In addition, there is little information describing the development of infants with BPD after the introduction of exogenous surfactant therapy, which was expected to improve pulmonary and developmental outcomes in premature infants with respiratory complications.[14,15] This study evaluated outcomes of infants born during a period after surfactant and postnatal steroid use had become standard practice. Despite these innovations, BPD infants were hypothesized to perform more poorly on developmental assessments to 3 years of age compared with VLBW infants without BPD and with full-term infants of similar age, race, gender, and socioeconomic status (SES).

SUBJECTS

All infants with VLBW and BPD admitted to the neonatal intensive care units (NICU) of hospitals in the Cleveland region were eligible for the study, and were prospectively, consecutively recruited. For the approximately four-county region, all infants with BPD were cared for in the NICU of the three participating hospitals, which had the only level 3 NICU facilities in the region, providing an exhaustive regional sample. Infants with BPD

were preterm, <1500 g at birth, requiring supplementary oxygen for >28 days, with radiographic evidence of chronic lung disease.[4] A partial stratification sampling strategy was adopted to enroll adequate numbers of subjects without socioeconomic disadvantage or severe neurologic risk so that these factors could be investigated in data analyses. Infants diagnosed with BPD who were free of neurologic problems other than grades I and II intraventricular hemorrhage and who were not socially disadvantaged (ie, Hollingshead classification IV and V)[16] were exhaustively recruited. The remainder was recruited randomly by approaching the family of the next available BPD diagnosed-infant who could be accommodated in the follow-up schedule. Parents of infants with BPD were approached by a research assistant in the NICU as soon as possible after the diagnosis of BPD was made by the attending physician.

For each infant with BPD, the next-born VLBW comparison infant without BPD of the same race and SES born during the same period was recruited. Term infants were recruited from the newborn nurseries. Information about the study and return addressed postcards were provided to all mothers in the nurseries. For each infant with BPD enrolled, the next term infant equivalent in race and SES with a returned postcard indicating parental willingness to participate was recruited, if eligibility criteria were met. Infants with major congenital malformations or drug exposure or whose mothers had major psychiatric or physical illness, human immunodeficiency virus, or mental retardation, or who lived >2 hours driving distance were excluded. VLBW infants without BPD were preterm, of <1500 g birth weight, and required oxygen supplementation for <14 days. Term infants had no diagnosed medical illnesses or abnormalities at birth and were >36 weeks' gestational age and >2500 g birth weight for singleton infants.

During the recruitment period (1989 to 1991), 250 infants with BPD were identified, of whom 89 were excluded (35 for drug/alcohol exposure, 21 for all other exclusions, and 33 who could not be accommodated into the testing schedule, all of whom were by definition of lower SES, being on public assistance), leaving 161 eligible VLBW infants with BPD. Twenty (12%) refused the study, 14 (9%) died, and 5 (3%) were unable to be contacted. Of 122 infants enrolled, 7 died, 1 withdrew before 8 months of age, and 4 were lost to follow-up, leaving 110 (96% of survivors) infants with at least one follow-up visit. Of these, 97 (88%) were seen at 8 months, 91 (83%) at 12 months, 94 (86%) at 2 years, and 98 (89%) at 3 years.

Of 214 VLBW infants without BPD, 24 were excluded for drug/alcohol exposure, 34 for oxygen supplementation for 21 to 28 days, and 46 for all other exclusions, leaving 110 eligible VLBW infants without BPD, of whom 8 (7%) were unable to be contacted and 18 (16%) refused the study. Of 84 recruited, 2 withdrew, and 1 was lost. One infant died at 2 years of age. Of 81 (96%) with a follow-up visit, 52 (64%) were seen at 8 months, 59 (73%) at 12 months, 70 (88%) at 2 years, and 70 (80%) at 3 years. Of 123 term infants, 6 withdrew and 5 were lost. Of 112 (91%) seen for follow-up, 97 (87%) were seen at 8 months, 101 (90%) at 12 months, 99 (88%) at 2 years, and 95 (85%) at 3 years.

METHODS

Neonatal medical information and demographic data taken from the hospital chart or maternal interview included the following: infant gestational age based on a combination of Ballard[17] examination and dates from the last menstrual period, birth weight (in grams), length and head circumference (in centimeters), Apgar scores at 1 and 5 minutes, and the presence/absence of respiratory distress syndrome and BPD. Noted were the presence/absence of patent ductus arteriosus, necrotizing enterocolitis (proven with or without surgery), retinopathy of prematurity (ROP), abnormal hearing test results, number of days that ventilator support was required, number of days that supplemental oxygen was used, peak bilirubin levels, and septicemia. Presence/absence of the following neurologic abnormalities was noted: minor neurologic malformations, seizures, echodense lesions, porencephaly, hydrocephalus, ventriculoperitoneal shunt, meningitis, and periventricular leukomalacia. A summary variable (the neurologic risk score) using 0 for absence and 1 for presence of any of the above neurologic risk factors was calculated. The neurologic risk score ranged from 0 to 8.

Cranial ultrasound studies were obtained prospectively for all VLBW infants during their hospital stay. Protocols for ultrasound studies were similar across the three NICU facilities from which infants were recruited. For two sites, protocols were identical, with all infants screened at 3, 10, and 30 days after birth. At the third site, all infants were screened at 7 days, with follow-up clinically determined. Thus, all infants were screened prospectively within the first week of life. For intraventricular hemorrhage, a rating of severity based on extent of lesion was devised; no hemorrhage on ultrasonography was scored as 0, and lesions were graded from 1 to 4 based on the criteria of Papile.[18] Ratings were based on the most severe lesion diagnosed. For the present study, intraventricular hemorrhage was evaluated separately from the summary neurologic risk score.

Procedures

Assessments included administration of the Mental and Motor Scales of the Bayley Scales of Infant Development[19] at 8, 12, 24, and 36 months (corrected ages). At 3 years, the revised version of the scales was used.[20] The scales yield two separate standard score indices, the Mental Development Index (MDI), reflecting overall cognitive development, and the Psychomotor Index (PDI), reflecting fine and gross motor development, with 100 ± 15 indicating the mean ± 1 SD for each index. Because normative data on the Bayley Scales yield a standard score range restricted from 50 to 150 (± 2 SD), lower scores were extrapolated based on tables developed by Naglieri.[21] The Bayley Scales are widely used for research and clinical purposes with premature infants, and their use allowed for the assessment of both term and preterm infants who varied extensively in their capabilities at 3 years of age. The Bayley Mental Scale administered between 30 and 42 months of age correlates highly (>.70) with other standardized intelligence tests given at the same age.[20]

This study was approved by the institutional review boards of the hospitals that participated, and maternal informed consent was obtained for all subjects.

Analyses

We compared MDI values and PDI values at each age of infants with BPD to VLBW infants without BPD and term infants. For group comparisons of VLBW infants with and without BPD and term infants, within each period, analysis of variance was used with standard scores as the dependent measures, followed by Duncan's multiple range test, which corrects for the number of comparisons. To compare the medical complications of VLBW infants, with and without BPD, *t* tests for continuous data, χ^2 for categoric variables, or *z* tests with correction for continuity for proportions were used.[22] For nonparametric data comparison, the Wilcoxon test was used.

To test the hypothesis that BPD predicted poorer developmental outcome after control for demographic and perinatal risk factors, hierarchical multiple regression analysis was used. To assess the total predictive power of BPD versus other medical risk factors, stepwise multiple regression was used.[23] Hierarchical regression analyses allowed control for the effects of other covariates before assessing the effect of BPD, indicating the variance in outcome predicted independently by BPD. In stepwise regression analyses, factors that differed between BPD and non-BPD VLBW groups were entered into the equation, allowing for statistical computation of the predictors that best accounted for outcomes.

RESULTS

Subject Demographic and Neurologic Risk Factors

Infants with BPD were of lower birth weight and gestational age than VLBW and term infants. Race, social class, gender, and maternal marital and educational status did not differ among groups (see Table 1). The BPD group had a higher overall neurologic risk score and more intraventricular hemorrhage (see Table 2).

The sampling strategy yielded adequate numbers of subjects across SES groups so that this variable could be investigated relative to BPD outcomes, ie, for the BPD group at 3 years, 47% were of social class I to III (middle and up) and 53% of IV and V (lower), based on the Hollingshead[16] classification.

In terms of other perinatal complications, BPD infants had increased incidence of ROP (43% vs 4%; $\chi^2 = 39.2$; $P < .001$). The three VLBW infants had grade I ROP. Of the 51 BPD infants with ROP, 19 (37%) had grade I, 12 (24%) grade II, 15 (29%) grade in, 1 (2%) grade IV, and 4 (7%) unknown, using the most severe grade diagnosed eye. Infants with BPD had more patent ductus arteriosus (56% vs 18%; $\chi^2 = 29.7$; $P < .001$), septicemia (47% vs 24%; $\chi^2 = 11.2$; $P < .001$), and lower peak bilirubin (8.3 ± 3 vs 9.1 ± 3, $t = 1.9$; $P < .05$). Consistent with their diagnosis, BPD infants also had higher incidence of apnea (84% vs 65%; $P < .01$), respiratory distress syndrome (94% vs 69%; $P < .001$), and lower Apgar scores at 1 (4.0 vs 5.5; $P < .001$), and 5 minutes (6.3 vs 7.2; $P < .01$). A total of 72% of VLBW infants without BPD had also been on some mechanical ventilation versus 98% of BPD infants ($P < .01$). The majority of infants were inborn (87% of BPD and 91% of VLBW). There were no differences in incidence of necrotizing enterocolitis (4% vs 6%) or in abnormal neonatal hearing results (16% vs 11%). Surfactant was used in treatment of 51

(42%) of infants with BPD and 9 (11%) without BPD. Postnatal steroids were used in treatment of 35 (29%) of infants with BPD and none without.

Developmental Outcome

Infants with BPD achieved standard scores significantly lower than VLBW and term infants on both Bayley Mental and Motor scales at all ages (Tables 3 and 4). MDI scores were in the mentally retarded range (<70) for 18% to 21% of the BPD group at each age, 6% to 11% of the VLBW group without BPD, and <5% of the term group. Motor outcomes were similarly delayed, with 20% to 27% of BPD infants scoring >2 SD units below the mean (PDI <70) at each age tested. Less than 10% of the VLBW group scored in this range, and <3% of the term group. Neurosensory abnormalities were increased in the BPD group, which had more visual impairments (5% vs 0%; $P < .05$) and higher incidence of tracheostomy (3% vs 0; $P < .05$). Groups were not different in occurrence of cerebral palsy (8% vs 2%) or in hearing impairments requiring auditory aids (3% vs 1%). Of the three BPD children with bilateral hearing impairment, one had mild–moderate hearing loss and two had moderately severe loss. The one VLBW child had mild loss.

Adjusted Effects of BPD on Developmental Outcome

We performed hierarchical multiple regression analyses[23] to test the hypothesis that the effects of BPD on developmental outcome remain significant after control for demographic and perinatal risk factors. Hierarchical analyses allowed control for the effects of other covariates before assessing effects of BPD. Control variables included race (white = 0; nonwhite = 1), SES (Hollingshead two-factor index ranging from 1 (high) to 5 (low), multiple birth status (singleton = 0; multiple = 1), gestational age, birth weight, neurologic risk summary score, 0–8 severity of intraventricular hemorrhage, 0–4 patent ductus arteriosus, proven sepsis, ROP (all 0 = absent; 1 = present), and peak bilirubin levels. Race, social class, and multiple birth were entered sequentially and evaluated first, followed by perinatal medical risk variables in the order noted above, followed by presence/absence of BPD (0 = absent, 1 = present) on the final step.

After controlling for other social and medical risk variables, BPD had significant independent effects, predicting poorer motor outcome, and a 10-point decrement in standard score, after all other significant risks were controlled (Table 5). Neurologic risk score and BPD accounted for 21% ($F = 13.4$; $P < .001$) of the variance in motor outcome at 3 years. Once BPD and neurologic risk were accounted for, effects of birth weight and gestational age on motor development were not significant.

Poorer mental developmental outcome at 3 years, in contrast, was predicted by minority race, lower social class, lower birth weight, and neurologic risk score. After control for these risks, BPD did not predict MDI. Only neurologic risk score was a significant medical predictor of mental outcome, however, accounting for 11% of the variance ($F = 20.7$; $P < .000$). Social class and race also significantly increased prediction of cognitive outcome, but birth weight did not increase prediction of outcome once neurologic risk was accounted for.

Table 6 presents results from the stepwise regression model ranking risk factors in order of magnitude of effect and the number of standard score (PDI or MDI) points changed by the risk factor. BPD independently accounted for a 12-point decrement in motor score at 3 years, indicating a total effect size of .80, ie, a medium to large effect, whereas neurologic risk yielded an additional 14-point decrement and a large effect size of .93. In terms of mental outcomes, neurologic risk accounted for a decrement of 10 MDI points, exerting a medium effect size of .66, whereas race and social class factors accounted together for a large effect size of .87.

There were differential effects of social class, BPD, and VLBW on mental and motor outcomes. Cognitive outcomes were significantly associated with social class within all risk groups, with a 12- to 22-point difference in cognitive outcome scores between the highest (social class I) and lowest (V) groups, irrespective of infant risk status. Additive effects of low social class, VLBW, and the presence of BPD are illustrated in the occurrence of mental retardation (MDI <70) within social class and preterm groups at 3 years of age. Among children with BPD, 26% of children in SES classes IV and V had MDI scores <70, in contrast to 14% in classes I–III. Among VLBW children without BPD, 19% of children in the lowest social classes were so classified, compared with <2% in classes I–III. For term children, <3% of middle class or higher SES children versus 7% in the lowest social classes were thus classified. There was no impact of social class on motor outcome, however, with standard scores ranging from 83 to 87 across all SES groups for the BPD infants and from 93 to 105 for VLBW and term infants, irrespective of SES.

Some studies have suggested that a definition of BPD reflecting oxygen dependence at 36 weeks' gestational age might better identify infants at risk than the 28-day cutoff used in this study. Therefore, within the BPD group, we compared MDI and PDI scores of infants based on the 36-week definition with those obtained from the current sample. There were no differences in mean MDI or PDI scores at any age tested.

DISCUSSION

The present study investigated the impact of BPD on infant developmental outcome in a prospective, longitudinal study of VLBW and term infants to 3 years of age. BPD was a significant, independent predictor of poorer motor outcome at 3 years of age, confirming previous findings in smaller, less well-controlled samples with shorter follow-up periods.[6–12] These results remained statistically significant after control for confounding demographic and medical variables, with BPD associated with a 10- to 12-point decrement in PDI scores at 3 years, compared with VLBW infants without BPD. Incidence of mental and/or motor retardation[24] reached 21% in the BPD cohort by 3 years, even though sample recruitment was designed to exhaustively recruit the healthiest BPD infants. Our findings indicated that mental retardation was associated primarily with neurologic risk, low social class, and minority race, whereas motor retardation was associated with neurologic risk and BPD. Our sample represents regional outcomes, avoiding the bias of hospital-based studies, and sampling procedures allowed recruitment of a cohort large enough to assess multiple medical and social-demographic risk factors.

Our findings are consistent with Northway's 23-year follow-up of BPD survivors, which found they had an increased history of school delay; used more special education classes; and displayed more abnormalities of coordination, gait, and muscle tone than did cohort controls.[2] Vohr et al, in a 10- to 12-year follow-up study, found that BPD survivors had smaller head circumferences, were smaller in size, and had increased neurologic problems compared with VLBW controls.[6] Robertson et al, in an 8-year follow-up study, found a lower intelligence quotient for those receiving supplemental oxygen for the longest time.[25] Recent school-age follow-up of extremely low birth weight infants also found mental retardation associated with prolonged oxygen dependence, even after birth weight and other neonatal complications were considered.[26] The pathophysiology that leads to infants with BPD having greater developmental delay is probably multifactorial and may include chronic intermittent hypoxia, growth deficiencies, and altered environmental stimulation.[27–29]

Central nervous system pathology in infants with BPD shows brain atrophy and gliosis compatible with chronic hypoxia.[30] Prolonged ventilator and oxygen dependence may result in repeated episodes of hypoxia and acidosis leading to hypoxic–ischemic cerebral injury and increased mortality and morbidity.[31–33] Laboratory confirmation of such chronic hypoxia is seen in the frequent finding of polycythemia. BPD spells secondary to reactive airways or esophageal reflux can be expected to result in chronic episodic hypoxia.

Northway[1] originally perceived that BPD might have significant neurologic ramifications. More recently, Volpe[30] proposed that the spectrum of long-term neurologic correlates in infants with BPD includes selective neuronal injury. Nonprogressive cognitive defects are more commonly seen and presumed to correlate with cerebral cortical neuronal loss and diffuse white matter injury. Progressive and nonprogressive neurologic disease are less commonly seen, but represent the more severe sequelae of neuronal injury.[34,35]

Observations that deficiencies in home oxygen therapy have been associated with poor weight gain may give credence to the possibility of poor central nervous system growth as well. Clinically unsuspected hypoxia during sleep, sleep apnea, and hypoxic airway constriction have been reported in infants with moderate to severe BPD.[36–38] Recurrent oxygen desaturations have been observed during and immediately after oral feedings in infants with BPD who had been discharged previously from the hospital after weaning from supplemental oxygen.[39]

Finally, environmental factors such as those associated with hospitalization and feeding problems may affect ultimate mental development. Dyspnea and lower respiratory tract infection were more frequent and severe among infants with BPD resulting in more infants with BPD requiring rehospitalization during the first year of life.[40] However, the pronounced effect of BPD on 3-year motor outcome suggests a more direct neurologic insult, in contrast to sociodemographic factors, which affected cognitive function, but was unrelated to motor development in this cohort.

In contrast to motor outcome, 3-year mental outcome was significantly negatively affected by minority race and lower social class, demonstrating the importance of postnatal environmental factors to mental developmental outcome. Consistent with another study,[41,42]

the additive effects of BPD, VLBW, low social class, and minority race resulted in higher rates of mental retardation at 3 years in lower SES, African-American children than in children who were not socially disadvantaged. Because 3-year mental outcomes predict school-age academic functioning,[43] our results suggest the need for close follow-up and early intensive interventions for infants with VLBW and BPD, especially among low SES groups. It is encouraging that postnatal environmental factors can have a significant positive impact on BPD and VLBW survivors in mental developmental outcome. Our findings indicate that in terms of mental outcome only, children with history of VLBW and BPD who do not have neurologic sequelae are indistinguishable from VLBW children without BPD at 3 years. Whether the motor deficits associated with BPD at 3 years persist and have implications for the higher rates of learning disabilities in VLBW cohorts at school age needs to be evaluated through longitudinal studies.

New modalities of treatment will not only increase survival of extremely low birth weight infants, but hopefully decrease the incidence of BPD as well. However, currently, increased survival has resulted in growing numbers of infants with BPD.[44] Efforts to prevent prematurity,[45] the increasing use of prenatal steroids,[47] and improvement in treatment modalities for respiratory distress syndrome will all prevent significant respiratory mortality and morbidity. In infants with BPD, improved care stressing nutrition,[48] careful monitoring of oxygen saturations,[39] and developmental habilitation efforts[49] may help maximize ultimate developmental outcome.

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ABBREVIATIONS

BPD	bronchopulmonary dysplasia
VLBW	very low birth weight
SES	socioeconomic status
NICU	neonatal intensive care unit
ROP	retinopathy of prematurity
MDI	Mental Development Index
PDI	Psychomotor Development Index

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TABLE 1

Demographic and Medical Characteristics

	BPD (n = 122) Mean ± SD	VLBW (n = 84) Mean ± SD	Term (n = 123) Mean ± SD	*F*	*P*
Birthweight (g)	956 ± 248	1252 ± 178	3451 ± 526	1633	<.001*
Gestational age (weeks)	27 ± 2	30 ± 2	40 ± 1	1416	.001*
Social class	3.5 ± 1	3.6 ± 1	3.6 ± 1	0.7	.71
Total oxygen (days)†	67 ± 6	4 ± 1	0 ± 0		.001‡§
Race (% white)	55	48	51	1.1	.58
Gender (% male)	52	43	50	1.9	.39
Multiple birth (%)	21	43	10	31.5	.001 ‖

*BPD < VLBW < *T*, *P* < .05.

†Median ± SE.

‡BPD and VLBW > *T*, *P* < .05.

§Wilcoxon Test.

‖VLBW > BPD and *T*, *P* < .05.

TABLE 2

Neurologic Complications by Group

	BPD (n = 122) n (%)	VLBW (n = 84) n (%)	χ^2	*P*
Minor neurologic malformations	1 (1)	1 (1)	0.1*	<1.0
Seizures	8 (7)	0 (0)	5.7*	.02
Echodense lesions	21 (17)	10 (12)	1.1	.30
Porencephaly	4 (3)	3 (4)	0.0*	1.00
Hydrocephalus	11 (9)	4 (5)	1.3	.28
Ventriculoperitoneal shunt	3 (3)	1 (1)	0.4	.64
Meningitis	2 (2)	0 (0)	1.4*	.51
Periventricular leukomalacia	10 (8)	5 (6)	0.4	.54
Neurologic risk scored‡	0 ± .09	0 ± .01	—	.001‡
Intraventricular hemorrhage	53 (43)	15 (18)	13.9	.01
Grades I–II	35 (28)	12 (14)	5.3	.02
Grades III–IV	18 (15)	3 (4)	6.8	.01

*Fisher's exact test.

†Median ± SE. The neurologic risk score is the sum of all neurologic complications except for intraventricular hemorrhage. Scores ranged from 0–7 for the BPD cohort and 0–6 for the VLBW cohort.

‡Wilcoxon Test.

TABLE 3

Bayley Mental Scale Scores (MDI) by Corrected Ages Group

Age	BPD		VLBW		Term		*F*	*P*
	Mean ± SD	R*	Mean ± SD	R	Mean ± SD	R		
8 Months	92 ± 28	10–145	104 ± 22	38–150	112 ± 19	76–150	17.5	<.001†
% < 70	18%		6%		0		21.5	.004†
12 Months	91 ± 29	10–142	104 ± 20	54–134	113 ± 15	74–150	24.1	.001†
% < 70	22%		7%		0		28.8	.001†
2 Years	86 ± 27	16–137	99 ± 24	50–150	107 ± 21	54–150	17.9	.001†
% < 70	26%		10%		1%		29.0	.001†
3 Years	84 ± 24	10–116	90 ± 16	38–126	96 ± 12	57–127	11.2	.001†
% < 70	21%		11%		4%		13.1	.001†

*R, range.

†BPD < VLBW and *T*, *P* < .05.

‡BPD < VLBW < *T*, *P* < .05.

TABLE 4

Bayley Motor Scale Scores (PDI) by Corrected Ages Group

Age	BPD		VLBW		Term		*F*	*P*
	Mean ± SD	R*	Mean ± SD	R	Mean ± SD	R		
8 Months	90 ± 27	10–133	104 ± 22	38–138	112 ± 16	80–150	24.4	<.001†
% < 70	21%		9%		0		23.7	.001†
12 Months	83 ± 25	10–124	100 ± 16	55–132	104 ± 15	62–136	29.6	.001†
% < 70	27%		5%		1%		38.1	.001†
2 Years	84 ± 30	8–141	102 ± 20	33–145	109 ± 14	77–150	31.5	.001†
% < 70	23%		1%		0		38.4	.001†
3 Years	84 ± 29	8–127	98 ± 20	33–122	103 ± 15	58–128	17.6	.001†
% < 70	20%		9%		1%		19.9	.001†

*R, range.

†BPD < VLBW and *T*, *P* < .05.

TABLE 5

Hierarchical Multiple Regression Analyses of the Effects of Bronchopulmonary Dysplasia on Mental and Motor Outcome at 3 Years

Step	Measure	PDI			MDI		
		*b**	SE	*P*	*b*	SE	*P*
1	Race	5.6	4.0	<.17	−11.6	3.2	<.001
2	Social class	−.3	2.0	.89	−2.8	1.6	.08
3	Multiple birth	−1.4	4.5	.75	1.4	3.6	.70
4	Gestational age	1.5	0.8	.06	.9	0.6	.17
5	Birthweight	.01	.008	.05	.01	.01	.05
6	Neurologic Risk Score	−13.7	2.4	.001	−9.8	2.0	.001
7	Intraventricular hemorrhage	.8	2.3	.73	.5	1.8	.80
8	Patent ductus arteriosus	−6.0	4.1	.15	−5.1	3.3	.12
9	Septicemia	−3.4	3.9	.39	−.6	3.2	.86
10	Retinopathy of prematurity	10.6	5.7	.06	5.1	4.6	.27
11	Bilirubin	.2	.8	.85	−.5	.6	.48
	R^2		.20			.23	
12	Bronchopulmonary dysplasia	−10.0	4.3	.02	−3.7	3.7	.32
	R^2		.22			.23	

* *b* Indicates unstandardized regression coefficient.

TABLE 6

Effects of Risk Factors on 3-Year MDI and PDI

Risk Factor	Outcome		
	MDI		PDI
	Change in Standard Score	Risk Factor	Change in Standard Score
Neurologic risk score	−10	Neurologic risk	−14
Minority race	−8	BPD	−12
Social class	−4		

All other risk factors were nonsignificant; includes above risk factors, as well as multiple birth, gestational age, birth weight, ROP, intraventricular hemorrhage, patent ductus arteriosus, septicemia, and bilirubin level.