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Diplegic Cerebral Palsy in Swedish Term and Preterm Children

Differences in Reduced Optimality, Relations to Neurology and Pathogenetic Factors

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Abstract

An unselected series of 93 Swedish diplegic children born in 1969–1976 and subgrouped into 49 term (TDC) and 44 preterm (PDC) cases were analyzed for differences in reduced optimality in pre- and perinatal conditions, these also being related to degree of handicap, associated neurology and conventional pathogenetic grouping. Comparisons of the reduced optimality with those of a dyskinetic and a control series were also made. TDC were shown to have more severe handicaps and more additional neurologic abnormalities than PDC. The profile of reduced optimality was weighted in TDC to items pointing to fetal maladjustment/deprivation and birth asphyxia and in PDC to items accompanying preterm birth and to postpartal items. The optimality of diplegics was in general more reduced than in controls and less than in dyskinetics. This was especially true for TDC.

Differences in the background mechanisms of the diplegia between TDC and PDC were indicated from dissimilarities in the combined patterns of reduced optimality and conventional pathogenetic grouping. Postpartal complications predominated among PDC. A prepartal factor as the only cause of the diplegia was likely in 41% of TDC, and as a contributory cause in another 24%. Birth asphyxia, present in 31% of the TDC, was never the only risk factor among infants born at term.

Introduction

Since *Little* described diplegic cerebral palsy (CP) (*Little* 1862), much has been written about this condition. In recent years, interest has mainly been focused on low birth weight (LBW) children, who are known to run a particular risk of developing diplegic CP. Nevertheless, 40–60% of diplegic children are of normal birth weight (*Churchill* 1958, *McDonald* 1964, *Ingram* 1964, *Hagberg* et al 1975) and these cases are in general known to be more complex as regards handicaps (*Churchill* 1958), pathogenetic factors and presumed background mechanisms (*McDonald* 1964, *Ingram* 1964).

Preterm birth with its consequences certainly still constitutes the main single risk factor correlated to spastic diplegia. The neuropathologic correlates in LBW diplegia are today generally accepted to be periventricular infarctions and/or hemorrhages in the preterm brain (*Banker* and *Larroche* 1962, *Pape* and *Wigglesworth* 1979), and the pathophysiologic ones neonatal negative events secondary to immaturity. For diplegia in term babies of normal birth weights there is no indication of a corresponding uniformity in neuropathologic correlates. The causes seem to be much more heterogeneous and little is known about the pathogenetic background factors. It was therefore considered of interest to compare term (TDC) and preterm (PDC) diplegic children born in recent years, and included in the continuously ongoing southwest-Swedish CP panorama study (*Hagberg* 1979). This series certainly has the drawback of being retrospective, but has the advantage of being unselected and of containing data sufficiently detailed to permit analyses of optimality.

The aim of this study was to apply the optimality concept proposed by *Prechtl* (1968) on an unselected series of diplegic CP children, subgrouped into TDC and PDC, in order 1) to try to establish correlations between the reduced optimality in pre- and perinatal conditions, on the one hand, and subsequent clinical features and their complexity and probable pathogenesis on the other, and 2) to compare the patterns of reduced optimality in TDC and PDC with those of a series of dyskinetic CP (*Kyllerman* 1983) and of a control series to the latter (*Kyllerman* and *Hagberg* 1983).

Definitions

CP was defined as a non-progressive "disorder of movement and posture due to a defect or lesion of the immature brain" (*Bax* 1964). *Diplegic CP* was subgrouped into spastic and ataxic diplegia, as described by *Hagberg* et al (1975). *Spastic diplegia* meant spastic pareses of the lower extremities with a variable but lesser involvement of the upper limbs. This entity included varieties from very slight forms classified as paraplegia in many other studies to severe forms probably often classified elsewhere as tetraplegia. *Ataxic diplegics* had

in addition to their spasticity ataxic traits, especially dyssynergia and intention tremor in their upper limbs. *Preterm birth* was that occurring before and *term birth* after the completion of the 37th week of gestation (< 259 days and ⩾ 259 days respectively). *LBW* was a birth weight (BW) ⩽ 2500 g. *Small for gestational age* (SGA) was BW ⩽ −2.0 standard deviations (SD) and *appropriate for gestational age* (AGA) BW > −2.0 SD from the mean for gestational age (GA) of a Swedish growth chart (*Karlberg* et al 1977). *Prepartal period* was the time from the first day of the last menstruation to the onset of labor resulting in delivery, *partal period* the time from the onset of labor until establishment of respiration and *postpartal period* the time after establishment of respiration until the 7th day of life.

Intrauterine asphyxia was considered to be present when there were records of miscoloured amniotic fluid and/or a fetal heart rate < 100 or > 160 and *extrauterine asphyxia* when respiration was not established after one minute and/or active resuscitation was needed.

Hypoxia was defined as all kinds of respiratory disturbances during the 1st week of life after respiration had been established.

Hyperbilirubinemia was considered to be present when the total serum bilirubin level was > 255 μmol/l (15 mg/100 ml) when BW was ⩽ 2500 g, or > 340 μmol/l (20 mg/100 ml) when BW > 2500 g, or in the case of exchange transfusion.

Definitions related to *optimality* are all given in the paper of *Kyllerman* and *Hagberg* in this issue of the journal (*Kyllerman* and *Hagberg* 1983).

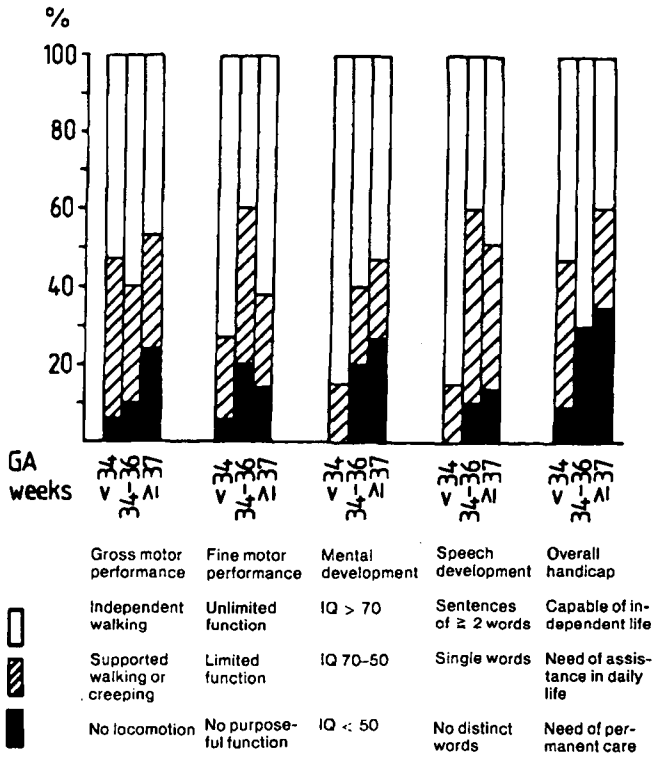

Fig. 1 Degree of handicap in 49 term and 44 preterm diplegic children

Clinical material and methods

An inventory was made of children with CP born in 1969–76 in the southwest region of Sweden. During this period 98 cases of diplegia had been registered. Four cases with undoubtedly postnatal causes (two with postnatal acquired infections at 3 weeks and 5 months of age respectively, one with respiratory arrest at 3 weeks of age and one who had an accident at two months of age) were excluded. One term case with as much spastic diplegic as dystonic signs was considered not representative for this study and excluded. Among the 93 remaining cases, 78 were classified as spastic and 15 as ataxic diplegia. All cases were at least four years old at the neurological subgrouping and controversial cases were re-evaluated at follow-up. From habilitation unit records the development of gross and fine motor performance, intellectual capacity and speech ability and any additional handicaps and neurologic abnormalities at the age of four years were noted. The severity of the overall handicap was assessed. When scrutinizing the pre- and perinatal histories the optimality concept proposed by *Prechtl* (1968) was applied. In all cases the obstetric, delivery and neonatal records were thus analyzed in detail and checked against a list of 34 items structured by *Kyllerman* and *Hagberg* (1983) and described in detail in this issue of the journal. In parallel, ordinary risk factors were recorded in the conventional way. Familial forms with simple inheritance, cerebral malformations, obvious prenatal syndromes and unequivocal infections were classified as causes independent of the presence or absence of other complications. Bleeding in pregnancy in PDC was not considered to be a risk factor but a precursor of the preterm birth. Otherwise no attempt was made to grade the risk factors when more than one was present.

For statistical purposes, the X^2 test for general contingency

Table I Additional neurologic abnormalities in 49 term and 44 preterm diplegic children. GA = gestational age

	Preterm GA < 34w n = 34	Preterm GA 34–36w n = 10	Term GA ⩾ 37w n = 49	p
Hydrocephalus	3	0	7	n. s.
Major malformations of CNS	0	1	7	< 0.05
Optic atrophy	0	0	2	n. s.
Congenital cataract	0	0	1	n. s.
Squint	18	5	15	< 0.10
Epilepsy	3	2	10	n. s.

tables, the X^2 test for fourfold tables with *Yates*'s correction, the exact test for fourfold tables, the *Mann Whitney*'s U-test and linear regression analysis were used.

Results

Among the 93 diplegic children there were 49 TDC and 44 PDC. The rate of preterm birth, 47% (44/93), differed highly significant from that in the general population of about 6%. The risk of developing diplegia among preterm children was 14 times that among children born at term (44/6: 49/94). Ataxic diplegia was found more often in the TDC group (12/49) than in the PDC (3/44), $p < 0.05$. The proportion of SGA infants was highly increased in the TDC group, being 14% (7/49) compared with the expected 2.3%, ($p < 0.001$). In the PDC group the proportion of SGA was 2.3% (1/44). There were four term and seven preterm twins, and two of these term infants were SGA.

Handicaps and additional neurologic abnormalities

As seen in Figure 1, the degree of handicap increased with GA. When PDC was subgrouped into those born before and after the 34th completed week (< 238 and $\geqslant 238$ days respectively), the very preterm group was better off throughout. The most striking differences referred to *mental and speech development*, where none in the very preterm group was severely mentally retarded or unable to speak distinct words. These differences were statistically significant ($p < 0.01$ and < 0.05 respectively). The tendency to an increasing degree of handicap with GA was also obvious in the *gross motor performance* and *overall handicap*, but did not quite reach significance ($p < 0.10$). Fifty-seven percent (25/44) of PDC and 39% (19/49) of TDC were estimated to be able to live an independent life, that is to manage without assistance in activities of daily living. The proportion of *hydrocephalus* and *malformations* of the central nervous system (CNS) was higher among TDC (Table I). Primary hydrocephalus (CNS malformations) was present in seven cases, all term, and secondary hydrocephalus (cisternal block/resorptive failure) in three cases, all preterm. The CNS malformations associated with hydrocephalus were: aqueduct stenosis (4 cases), corpus callosum agenesia (1 case), complex spina bifida syndrome (1 case) and subarachnoid cyst (1 case). CNS malformation without concomitant hydrocephalus was found in one preterm case with septum pellucidum agenesia, a girl born after 36 weeks of gestation. In TDC, hydrocephalus was more often correlated with ataxic than spastic diplegia (33% [4/12] and 8% [3/37] respectively, $p < 0.05$). *Squint* was found less often among TDC (31%; 15/49) than among PDC (52%; 23/44).

Reduced optimality in pre- and perinatal conditions

The percentile distributions of the *reduced optimality* scores are shown in Table II. The median total score was 4 in TDC and 7 in PDC. The total *rate of reduced optimality, as shown in Table III*, was 14.6% in TDC and 21.9% in PDC. The higher median reduced optimality score and also the increase of the reduced optimality rate in PDC were mainly due to contribution of reduced optimality in the prepartal items 12 (BW) and 13 (GA) and in postpartal items. The reduced optimality rates per item showed obvious differences between TDC and PDC (Table III). The history of TDC significantly more often included a lack of optimality in items 8 (toxemia) and 14 (leanness). In the PDC group, a reduced optimality in typical predictors of prematurity, e.g. in items 7 (threatened abortion) and 16 (rupture of membranes) and in neonatal clinical conditions and treatment of them, e.g. in items 25 (respiratory disturbance), 30 (hyperbilirubinemia) and 31 (acidosis), were found in significantly higher rates.

Table II Percentile distribution of reduced optimality scores in term (TDC) and preterm (PDC) diplegic children

Score	Percentile								
	3	5	10	25	50	75	90	95	97
TDC	0	1	1	2	4	7	11	12	12
PDC	3	3	5	5	7	9	11	12	13
All	1	1	2	4	6	9	11	12	12

Conventional pathogenetic grouping

The pathogenesis of the diplegia assessed from traditional risk factors showed highly significant different patterns between TDC and PDC ($p < 0.001$) (Table IV). In 41% (20/49) of TDC, compared with 2% (1/44) of PDC, a pure *prepartal* origin was probable. A genetic cause was present in a boy born at term with hereditary hydrocephalus due to aqueduct stenosis. A prenatal syndrome of unknown type was diagnosed in a girl born at term as the 9th child. Five term infants had CNS malformations, all combined with hydrocephalus. In five term infants an intrauterine infection was the probable cause of the diplegia (1 toxoplasmosis, 2 rubella, 1 cytomegalovirosis and 1 severe virosis of unknown type). Eight term infants had had signs of late fetal deprivation of supply as listed in group A II, Table IV. The only preterm child classified as prepartal had a septum pellucidum agenesia, and was born after 36 weeks of gestation with a BW of 2470 g. A pure *partal* origin was probable in one single preterm boy with severe extrauterine asphyxia but rapid normalization at resuscitation. In 2% (1/49) of TDC, compared with 39% (17/44) of PDC, a pure *postpartal* origin was probable. The only term case had a streptococcal meningitis when five days old. All the 17 preterm cases had had hypoxia, in six cases combined with hyperbilirubinemia. Thirty-seven percent (18/49) of TDC and 45% (20/44) of PDC had patterns of *combined risk factors* from two or more periods. Among TDC, prepartal risk factors were present in a higher proportion than in PDC (67% [12/18] and 30% [6/20] respectively). Hyperbilirubinemia had not occurred in any of the 18 TDC but had been present in four of the 20 PDC. In 20% (10/49) of TDC and 11% (5/44) of PDC none of the above-mentioned risk factors were present.

Association between reduced optimality, conventional pathogenetic groups and degrees of handicaps

The median reduced optimality score increased progressively through the pathogenetic groups listed in Table IV, being 3 in group A I, 4 in A II, 6 in C and 9 in D respectively. In group E the median was 2. There was no or very little difference between TDC and PDC. The degree of overall handicap was highest in group A I, followed by group D, term, where 62% (8/13) and 44% (8/18) respectively were dependent on permanent care. The lowest degree of overall handicap was found in groups C and D among PDC born before 34 weeks of

Table III Distribution of reduced optimality per item in 49 term and 44 preterm diplegic children

Item		Term		Preterm		
		n	%	n	%	p
1. Maternal age		16	32.7	9	20.5	
2. Previous pregnancies		4	8.2	5	11.4	
3. Pregnancy number		3	6.1	1	2.3	
4. Pregnancy interval		8	16.3	4	9.1	
5. Antenatal care		2	4.1	2	4.5	
6. Maternal disorder		8	16.3	6	13.6	
7. Threatened abortion		4	8.2	16	36.4	< 0.01
8. Toxemic signs		9	18.4	1	2.3	< 0.05
9. Hemolytic disease		0	0	1	2.3	
10. Placental infarction		8	16.3	2	4.5	
11. Single pregnancy		4	8.2	7	15.9	
12. Birthweight	⩽ 2500 g	7	14.3	39	88.6	< 0.001
	> 4500 g	0	0	–	–	
13. Gestational age	< 259 days	–	–	44	100	
	> 293 days	9	18.4	–	–	
14. Birth weight for birth length	⩽ −1.0 SD	15	30.6	5	11.4	< 0.05
	< 1.0 SD	7	14.3	6	13.6	
		104	**15.2**	**148**	**24.0**	
15. Labor		3	6.1	1	2.3	
16. Rupture of membranes		3	6.1	13	29.5	< 0.001
17. Fetal heart rate		13	26.5	7	15.9	
18. Presentation		3	6.1	4	9.1	
19. Amniotic fluid		14	28.6	6	13.6	
20. Cord		1	2.0	1	2.3	
21. Instrumental delivery		10	20.4	9	20.5	
22. Placental ablation		3	6.1	4	9.1	
23. Respiratory establishment		8	16.3	8	18.2	
24. Resuscitation		15	30.6	19	43.2	
		73	**14.9**	**72**	**16.4**	
25. Respiratory disturbance		19	38.8	34	77.3	< 0.001
26. Apnea		5	10.2	12	27.3	
27. Respiratory treatment		5	10.2	11	25.0	
28. Cardic arrest		0	0	2	4.5	
29. Temperature		2	4.1	5	11.4	
30. Hyperbilirubinemia		0	0	13	29.5	<0.001
31. Acidosis		6	12.2	15	34.1	< 0.05
32. Hypoglycemia		7	14.3	2	4.5	
33. Cerebral irritation		16	32.7	7	15.9	
34. Cerebral depression		7	14.3	6	13.6	
		67	**13.7**	**107**	**24.3**	
Total		244	14.6	327	21.9	

gestation, where 53% (17/32) could manage daily life without assistance and only 6% (2/32) were in need of permanent care.

No significant correlation was found between reduced optimality score and degree of overall handicap. However, when group A I with low reduced optimality scores and high degrees of overall handicap was excluded, there was a positive correlation in TDC ($y = 1.37 + 0.08\,x$; $t = 2.31$; $p < 0.05$). Despite significance, the predictive value of the reduced optimality score on the degree of handicap was low (13.2%; $r = 0.36$). No corresponding correlation was demonstrated in PDC ($r = -0.03$).

Prolonged asphyxia/hypoxia was significantly correlated to a more severe overall handicap, severe gross motor disturbances and severe mental retardation (Table V). This tendency was particularly obvious for TDC.

In TDC reduced optimality items 33 and 34 (cerebral irritation and depression) were associated with a more severe outcome. Forty-three percent (9/21) with reduced optimality in either of these items had a severe overall handicap, while 29% (6/21) were able to live an independent life, compared with 29% (8/28) and 46% (13/28) respectively for those fulfilling the criteria for optimality in the same items ($p < 0.10$).

Comparison of reduced optimality between diplegic, control and dyskinetic series

The cumulative frequency distribution of *reduced optimality scores* in the prepartal, partal and postpartal periods com-

Table IV Conventional pathogenetic grouping in 49 term and 44 preterm diplegic children

	Preterm n = 44		Term n = 49	
A Pure prepartal		1		12
I Genetic		1		
Syndromes/CNS malformations	1		6	
Infection			5	
		0		8
II Maternal disease (diabetes etc.)				
Bleeding in pregnancy when term				
Toxicosis, placental infarction				
Small for gestional age				
B Pure partal		1		0
Ablatio placenta				
Extrauterine asphyxia	1			
C Pure postpartal		17		1
Neonatal hypoxia	11			
Hypoxia + hyperbilirubinemia	6			
Infection			1	
D Combined		20		18
A II + B ± C	4		9	
A II + C	2		3	
B + C	14		6	
E None of the above		5		10
Total		44		49

Table VI Reduced optimality rates in diplegic cases compared with controls and dyskinetic cases

Period	Reduced optimality rates (percent)		
	Term controls	TDC	Term dyskinetics
Prepartal	8.3^{xxx}	15.2	15.2
Partal	5.3^{xxx}	14.9	27.1^{xxx}
Postpartal	0.9^{xxx}	13.7	24.3^{xxx}
Total	5.3^{xxx}	14.6	21.4^{xxx}
Period	Reduced optimality rates (percent)		
	Preterm controls	PDC	Preterm dyskinetics
Prepartal	20.4	24.0	25.1
Partal	17.1	16.4	17.4
Postpartal	7.9^{xxx}	24.3	30.8^{x}
Total	15.8^{xx}	21.9	24.5

^{x} $p < 0.05$; ^{xx} $p < 0.01$; ^{xxx} $p < 0.001$ (compared to diplegic cases).

pared with the controls (Fig. 2 a and b) showed that the diplegic cases had significantly more reduced optimality scores, which, however, never reached the high figures of the dyskinetic series. The differences were most striking in the term group.

Also in the comparison of *reduced optimality* subscores the diplegics fell between controls and dyskinetics. Eighty-five percent of TDC, compared with 64% of term controls and 91% of term dyskinetics, had reduced optimality in the prepartal period and of these 61, 34, and 79% respectively simul-

Table V Association between prolonged asphyxia/hypoxia and degree of handicap in term (TDC) and preterm (PDC) diplegic children

	TDC			PDC 34–36 w			PDC < 34 w			Total			
	I[a] n	II[a] n	III[a] n	I[a] n	II[a] n	III[a] n	I[a] n	II[a] n	III[a] n	I[a] n	II[a] n	III[a] n	
Overall handicap													x
Capable of independent life	10	0	2	3	2	1	9	5	2	22	7	5	
Need of assistance in daily life	2	1	2	0	0	0	6	6	1	8	7	3	
Need of permanent care	1	2	5	0	1	1	1	1	0	2	4	6	
Gross motor performance													x
Independent walking	12	0	2	2	2	1	9	5	2	23	7	5	
Supported walking or creeping	1	2	2	1	1	1	6	6	1	8	9	4	
No locomotion	0	1	5	0	0	0	1	1	0	1	2	5	
Mental development													xxx
IQ > 70	10	1	3	3	1	1	13	11	3	26	13	7	
IQ 70–50	2	1	2	0	2	0	3	1	0	5	4	2	
IQ < 50	1	1	4	0	0	1	0	0	0	1	1	5	
Total	13	3	9	3	3	2	16	12	3	32	18	14	

[a] I = one; II = two; III = three records of intrauterine asphyxia (items 17/19), extrauterine asphyxia (items 23/24) or hypoxia (items 25/26/27/28/31)
^{x} $p < 0.05$, ^{xxx} $p < 0.001$

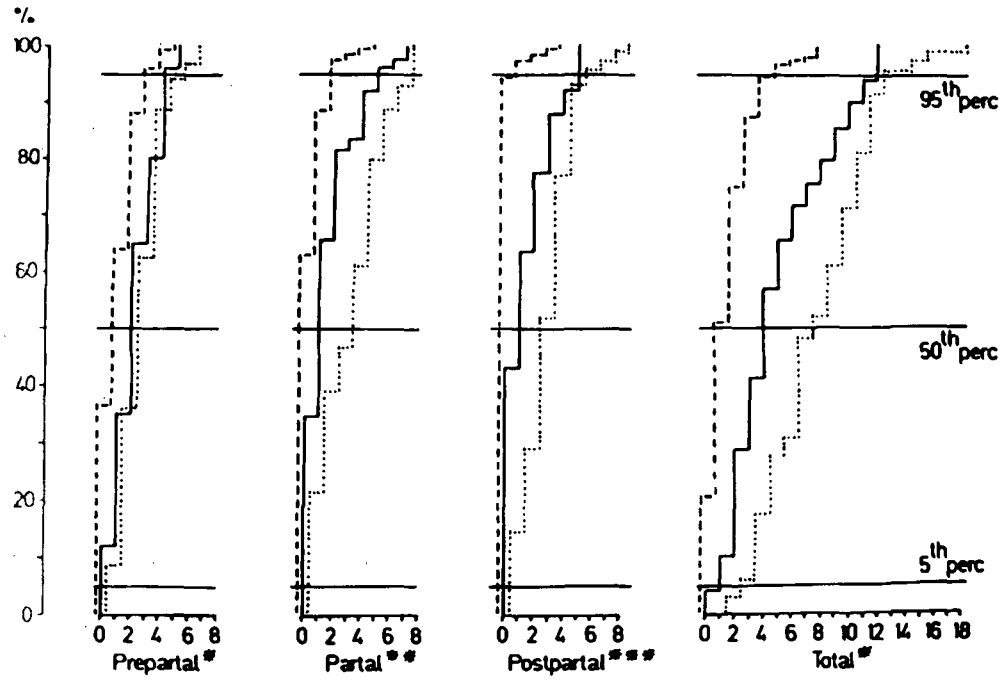

Fig. 2a

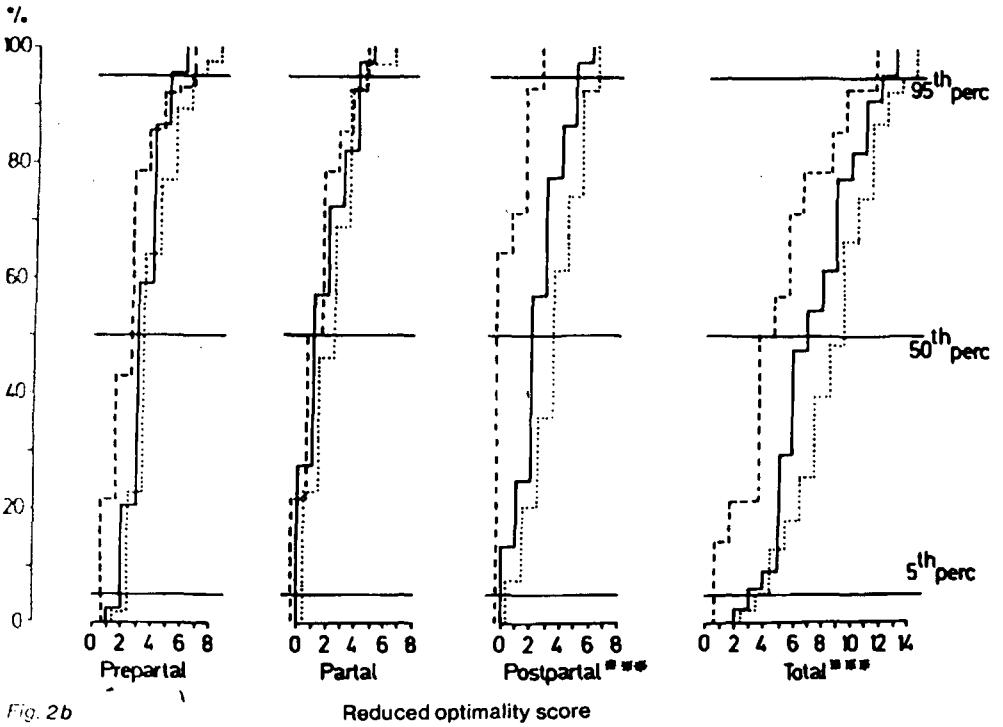

Fig. 2b

Fig. 2 Cumulative frequency distributions of reduced optimality scores in *a)* term and *b)* preterm diplegic cases compared with control and dyskinetic series. (--- Control series; — Diplegic cases; ... Dyskinetic cases)
* $p < 0.05$,
** $p < 0.01$,
*** $p < 0.001$

taneously had reduced optimality in the partal period. Of those who had reduced optimality in both the prepartal and partal periods, 80% of TDC, as against 11% of term controls and 88% of term dyskinetics, also had reduced optimality in the postpartal period. In PDC the differences were obvious only postpartally. Eighty-seven percent of PDC, compared with 36% of preterm controls and 93% of preterm dyskinetics, who showed reduced optimality in both the prepartal and partal periods, also had reduced optimality in the postpartal period.

Comparisons of *the reduced optimality rates* showed that TDC had significantly higher rates than term controls in all three periods and significantly lower rates than term dyskinetics in the partal and postpartal periods. In PDC the differences from the preterm controls as well as from the preterm dyskinetics were referable to the postpartal period (Table VI). Comparison of the reduced optimality rates per item (Table VII) showed that the differences between diplegic children and controls were distributed among the same items where differences were present between dyskinetics and controls. Excep-

tions among TDC were items 9 (hemolytic disease), 16 (rupture of membranes), 29 (body temperature) and 30 (hyperbilirubinemia), and among PDC items 29 (body temperature), 30 (hyperbilirubinemia) and 34 (cerebral depression), where diplegics did not differ from controls. In items 23, 24, 33 and 34, which have been shown to be associated with the severity of the handicap, TDC fell significantly between term controls and term dyskinetics. The high proportions of reduced optimality in items 21 (instrumental delivery) and 27 (respirator treatment) were supposed to be time trends, as the diplegic children had later birth years than controls and dyskinetics.

Discussion

It has previously been established that compared with PDC, TDC more often are mentally retarded, suffer from epilepsy and have additional neurological defects (*Childs* and *Evans* 1954, *Churchill* 1958, *Russell* 1960, *Ingram* 1964, *McDonald* 1964). This was confirmed from our series, which also revealed that gross motor, fine motor, speech and overall handicaps were all, on the average, more severe in the TDC group (Fig. 1). No fewer than 27% of our TDC children were severely mentally retarded (IQ < 50), in contrast to 5% among PDC. Severe mental retardation was not at all represented among very preterm diplegic babies. This is well in accordance with recent findings in Swedish studies of mental retardation epidemiology (*Gustavson* et al 1977). Such differences underline that TDC and PDC – with a modest number of intermediate transitional cases – still on the whole represent separable populations which can be distinguished as to type of neurology and extent of brain involvement. Differences in background mechanisms between TDC and PDC are indicated from observed dissimilarities in the patterns of reduced optimality. Those associated with fetal deprivation of supply (e.g. toxemia, infarction of placenta, leanness at birth) and with intrauterine asphyxia (abnormal fetal heart rate, discoloured amniotic fluid) were relatively more often found in TDC than PDC, whereas those associated with preterm birth (e.g. threatening abortion, premature rupture of membranes) and with postpartal outcome occurred relatively more often in PDC than in TDC.

In a comparison of the profiles of reduced optimality of TDC and PDC with those of term and preterm dyskinetic CP (*Kyllerman* 1983), the patterns on the whole showed obvious similarities in corresponding groups, but with variations in degree. However, two particular outstanding differences were noted. Firstly, a reduced optimality in items connected with hyperbilirubinemia were of no relevance either for TDC or for PDC, but were of major significance for dyskinetic CP, particularly preterm cases. Secondly, when asphyxia had been present, the severity and acuteness was in general greater among dyskinetic term cases than among TDC. It is concluded that these differences in the patterns of reduced optimality might be of relevance for the neurological type of CP syndrome which can be expected to develop, and for the structural location of the underlying brain damage. This would be in good agreement with the variability in resulting neurology in primates following experimentally induced asphyxia of different types and severity (*Myers* 1975) and with autopsy findings on brains exposed to birth asphyxia (*Pape* and *Wigglesworth* 1979).

Table VII Items with significantly different reduced optimality rates (percent) in diplegic cases compared with controls and dyskinetic cases

	Term control n = 215	diplegic cases n = 49	dyskinetic cases n = 69	Preterm control n = 14	diplegic cases n = 44	dyskinetic cases n = 39
9 Hemolytic disease	0.9	0	11.6^{xx}	0	2.3	10.3
10 Placental infarction	4.2^{xx}	16.3	7.2	0	4.5	7.7
11 Multiple pregnancy	0.5^{xx}	14.3	4.3	0	15.9	7.7
12 BW ≤ 2500 g	1.4^{xxx}	14.3	7.2	42.9^{xx}	88.6	76.9
14 BW/BL ≤ −1.0 SD	14.9^{x}	30.6	40.6	42.9^{x}	11.4	17.9
15 Pathological labor	12.6	6.1	26.1^{x}	14.3	2.3	12.8
16 Rupture of membranes	10.2	6.1	21.7^{x}	35.7	29.5	46.2
17 Fetal heart rate	3.7^{xxx}	26.5	29.0	14.3	15.9	5.1
18 Presentation	5.6	6.1	24.6^{x}	35.7^{x}	9.1	18.0
19 Amniotic fluid	11.6^{xx}	28.6	39.1	14.3	13.6	7.7
21 Instrumental delivery	3.3^{xx}	20.4	21.7	14.3	20.4	7.7
23 Respiratory establishment	0^{xxx}	16.3	44.9^{xxx}	14.3	18.2	25.6
24 Resuscitation	1.4^{xxx}	30.6	52.2^{xxx}	14.3^{x}	43.2	30.8
25 Respiratory disturbance	0.9^{xxx}	38.8	49.3	21.4^{xxx}	77.3	74.4
26 Apnea	0^{xxx}	10.2	7.2	0^{x}	27.3	28.2
27 Respiratory treatment	0	10.2	4.3	0^{x}	25.0	2.6
29 Temperature	2.8	4.0	43.5^{xxx}	14.3	11.4	41.0^{xx}
30 Hyperbilirubinemia	1.4	0	14.5^{xx}	14.3	29.5	64.1^{xx}
31 Acidosis	0.5^{xxx}	12.2	11.6	14.3	34.1	30.8
32 Hypoglycemia	0^{xxx}	14.3	4.3	0	4.5	2.6
33 Cerebral irritation	1.9^{xxx}	32.7	62.3^{xx}	0	15.9	25.6
34 Cerebral depression	1.9^{xx}	14.3	44.9^{xxx}	14.3	13.6	33.3

$^{x}p < 0.05$; $^{xx}p < 0.01$; $^{xxx}p < 0.001$ (compared to diplegic cases)

Table VIII Schematic tabulation of different causes/pathogenetic factors in diplegia in term babies

Prenatal
Simple genetic forms (*Ingram* 1964, *Gustavson* et al 1969)
Familial spastic diplegias – different genetic types
Familial ataxic diplegias – different genetic types
Cerebral malformation syndromes (*Malamud* et al 1964; *Ingram* 1964; *Christensen* and *Melchior* 1967; *Glenting* 1970)
Certain microcephaly syndromes
Cortical dysplasias
Corpus callosum agenesia
Teratogenic conditions (some?)
Maternal deficiencies (*Drillien et al 1962; Ingram* 1964; *Glenting* 1970)
Subfertility, previous abortions or still births
Chronic maternal disorders
Abnormalities of pregnancy (*Ingram* 1964; *Lyon* 1970; *Hagberg* et al 1976)
Intrauterine infections – ToRCH complex
Intrauterine ischemia
Other fetal deprivation syndromes
Perinatal[a]
Birth asphyxia (*Norman* 1963; *Ingram* 1964)
Predisposed prenatal risk cases?
Neonatal hypoxia/ischemia (*De Reuck* et al 1972)
Predisposed prenatal risk cases?
Hyperosmolarity leading to periventricular hemorrhages (*Pape* and *Wigglesworth* 1979)
Predisposed prenatal risk cases?
CNS infections
Postnatal[b]
Progressive infantile hydrocephalus (*Hagberg* 1966)
Predominantly non-shunted cases
Cerebral venous thrombosis (*Ingram* 1964)
Predominantly postinfectious
Postencephalitic states, encephalomyelites (*Glenting* 1970; *Lademan* 1978)
Virus encephalopathies
Purulent meningitis

a) Delivery and first week of life
b) From 8th day of postnatal life to two years of age

Compared with term controls (*Kyllerman* and *Hagberg* 1983), the overrepresentation of reduced optimality in our TDC group was – as could be expected from the known complexity of different background mechanisms – broadly scattered over prepartal, partal and postpartal items. A high rate of abnormalities in the fertility history, previous pregnancies and earlier stages of the pregnancy in question in mothers of TDC were reported in the early sixties from Edinburgh (*Drillien* et al 1962, *Drillien* et al 1964, *Ingram* 1964). According to *Ingram* (*Ingram* 1955, 1964) disorders of the last trimester of pregnancy among TDC mothers included preeclamptic toxemia and antepartum hemorrhage. The common combination in our TDC group of reduced optimality in various prepartal items with reduced optimality in partal items, particularly asphyxia, indicates the pathogenetic importance of unfavourable interactions between prepartal and partal complications.

Compared with preterm controls, reduced optimality in PDC connected with preterm birth per se and with postpartal complications were found in higher rates. This is compatible with postpartal development of leukomalacias which are known to occur as a result of insufficient blood perfusion and/or matrix hemorrhages to the apparently extremely vulnerable periventricular structures of the premature brain (*Pape* and *Wigglesworth* 1979). Such patterns of reduced optimality were found to be particularly valid for the very preterm group (GA < 34 w) comprising the very LBW cases, usually AGA. The PDC group of 34–36 weeks' gestation was, in consequence of its definition, found to be more mixed with a number of patterns transitional to the TDC group.

A broad panorama of different causes of or pathogenetic factors in diplegia in children born at term has been proven or postulated in various studies through the years, which are summarized in Table VIII. However, the quantitative distribution among different pathogenetic groups has been little analyzed. Our study indicates that a prepartal cause or cluster of causes is probable as the only etiology in 41 % of the TDC cases and as a contributory factor in another 24 %. Birth asphyxia, present in 31 %, never appeared as the only risk factor, but in combination with preceding prepartal or succeeding postpartal complications. No doubt, isolated periventricular leukomalacias due to asphyxia and leading secondarily to local defective oxygen perfusion can occur also in term children late in pregnancy, during delivery or in early postnatal life (*De Reuck* et al 1972, *Armstrong* and *Norman* 1974). It is reasonable to believe that such periventricular infarctions and bleedings predominantly occur when predisposing complications have paved the way. More than half of our TDC with birth asphyxia were mentally retarded. It may be suspected that these children had suffered from cortical hypoxic/ischemic damage corresponding to the higher vulnerability of the cortex in their more mature brains as compared with the situation in PDC.

To summarize, the results of our study have confirmed clear differences between TDC and PDC in the severity of the handicap and in patterns of causes and background factors. The application of the optimality concept revealed that reduced optimality scores in diplegics were higher than in controls and lower than in dyskinetics and confirmed previously reported general differences in reduced optimality between term and preterm infants. For scientific purposes, optimality analyses were found to give a far better modulated and more accurate synthesis of multifactorial and complex background factor clusterings than conventional pathogenetic grouping alone. However, for prognostic information of the degree and type of expected handicap this design of optimal conditions cannot be expected to give any substantial guidance in clinical practice.

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References

(1) Armstrong, D., Norman, M. G.: Periventricular leucomalacia in neonates. Arch. Dis. Child. 49: 367–375 (1974).
(2) Banker, B. Q., Larroche, J. C.: Periventricular leukomalacia of infancy: A form of neonatal anoxic encephalopathy. Arch. Neurol. 7: 386–410 (1962).
(3) Bax, M.: Terminology and classification of cerebral palsy. Dev. Med. Child. Neurol. 6: 295–297 (1964).
(4) Childs, B., Evans, P. R.: Birthweight of children with cerebral palsy. Lancet I: 642–645 (1954).
(5) Christensen, E., Melchior, J.: Cerebral palsy. A clinical and neuropathological study. Clinics in Dev. Med. 25, Heinemann Medical Books Ltd. London (1967).
(6) Churchill, J. A.: The relationship of Little's disease to premature birth. Am. J. Dis. Child. 96: 32–38 (1958).
(7) De Reuck, J., Chattha, A. S., Richardson, E. P.: Pathogenesis and evolution of periventricular leucomalacia in infancy. Arch. Neurol. 27: 229–236 (1972).
(8) Drillien, C. M., Ingram, T. T. S., Russell, E. M.: Comparative aetiological studies of congenital diplegia in Scotland. Arch. Dis. Child. 37: 282–288 (1962).
(9) Drillien, C. M., Ingram, T. T. S., Russell, E. M.: Further studies of the causes of diplegia in children. Develop. Med. Child. Neurol. 6: 241–249 (1964).
(10) Gleerup, P.: Etiology of congenital spastic cerebral palsy E.A.D. Forlag København (1970).
(11) Gustavson, K.-H., Hagberg, B., Sanner, G.: Identical syndromes of cerebral palsy in the same family. Acta Paediatr. Scand. 58: 330–340 (1969).
(12) Gustavson, K.-H., Hagberg, B. Hagberg, G., Sars, K.: Severe mental retardation in a Swedish county. I. Epidemiology, gestational age, birth weight and associated CNS handicap in children born 1959–70. Acta Paediatr. Scand. 66: 373–379 (1977).
(13) Hagberg, B.: Epidemiological and preventive aspects of cerebral palsy and severe mental retardation in Sweden. Eur. J. Pediatr. 130: 71–78 (1979).
(14) Hagberg, B., Hagberg, G., Olow, I.: The changing panorama of cerebral palsy in Sweden 1954–70. I. Analysis of the general changes. Acta Paediatr. Scand. 64: 187–192 (1975).
(15) Hagberg, G., Hagberg B., Olow, I.: The changing panorama of cerebral palsy in Sweden 1954–70. III. The importance of fetal deprivation of supply. Acta Paediatr. Scand. 65: 403–408 (1976).
(16) Hagberg, B., Sjögren, I.: The chronic brain syndrome of infantile hydrocephalus. Amer. J. Dis. Child. 112: 189–196 (1966).
(17) Ingram, T. T. S.: The early manifestations and course of diplegia in childhood. Arch. Dis. Child. 30: 244–250 (1955).
(18) Ingram, T. T. S.: Paediatric aspects of cerebral palsy. E & S Livingstone Ltd., Edinburgh and London (1964).
(19) Karlberg, P., Priolisi, A., Landström, T., Selstam. U.: Clinical analysis of causes of death with emphasis on perinatal mortality. In: F. Falker, ed. Fundamentals of mortality risks during the perinatal period and infancy. Monographs in Paediatrics 9: 106 (1977).
(20) Kyllerman, M.: Reduced optimality in pre- and perinatal conditions in dyskinetic cerebral palsy. Distribution and comparison to controls. Neuropediatrics 14: 29–36 (1983).
(21) Kyllerman, M., Hagberg, G.: Reduced optimality in pre- and perinatal conditions in a Swedish newborn population. Neuropediatrics 14: 37–42 (1983).
(22) Lademann, A.: Postneonatally acquired cerebral palsy. A study of the aetiology, clinical findings and prognosis in 170 cases. Acta Neurol. Scand. 57 (Suppl. 65, 1978).
(23) Little, W. J.: On the influence of abnormal parturition, difficult labour, premature birth and asphyxia neonatorum on the mental and physical condition of the child, especially in relation to deformities. Transactions of the obstetrical society of London 111: 293 (1862).
(24) Lyon, G.: Les encéphalopathies congénitales non évolutives. Louvain Méd. 89: 341–353 (1970).
(25) Malamud, N., Itabashi, H. H., Castor, J., Messinger, H. B.: An etiologic and diagnostic study of cerebral palsy. J. Pediatr. 65: 270–293 (1964).
(26) McDonald, A. D.: The aetiology of spastic diplegia. Dev. Med. Child. Neurol. 6: 277–285 (1964).
(27) Myers, R. E.: Four patterns of perinatal brain damage and their conditions of occurrence in primates. Adv. Neurol. 10: 223–234 (1975).
(28) Norman, R. M.: Patterns of symmetrical brain damage. In: Selective vulnerability of the brain to hypoxia, pp 243–249. Oxford: Blackwells (1963).
(29) Pape, K. E., Wigglesworth, J. S.: Haemorrhage, ischaemia and the perinatal brain. Clinics in Developmental Medicine 69/70. Heinemann Medical Books Ltd. London (1979).
(30) Prechtl, H. F. R.: Neurological findings in newborn infants after pre-, and paranatal complications. In: Jonxis, J. H. P. et al ed.: Aspects of prematurity and dysmaturity. Nutricia Symposium 1967: 303–321. Leiden, Holland: HE Stenfert Kroese N.V. (1968).
(31) Russell, E. M.: Correlation between birth-weight and clinical findings in diplegia. Arch. Dis. Child. 35: 548–551 (1960).

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